Exocrine Pancreatic Insufficiency

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"To eat is human, to digest divine."
Charles Copeland

CLINICAL IMPORTANCE

Malassimilation is failure of nutrients to pass across the intestinal wall in quantities sufficient to maintain body weight and condition (Jacobs et al, 1989). Malassimilation can be caused by either maldigestive or malabsorptive diseases. Malabsorption occurs with diseases that alter the structure and function of the small intestinal mucosa including the lymphatics. Maldigestion occurs with defects in intraluminal digestion and may result from gastric, pancreatic or biliary dysfunction. Exocrine pancreatic insufficiency (EPI) refers to a partial or complete deficiency of pancreatic enzymes and is the most common cause of maldigestion in dogs (Williams, 1994). Occurring most commonly in young dogs as a congenital disorder, pancreatic acinar atrophy, EPI may also develop as a sequela to acute and chronic pancreatitis (Williams, 1994) or pancreatic neoplasia (Westermarck and Wiberg, 2003). EPI is rare in cats but has been reported to occur in juvenile and acquired forms (Williams, 1994a; Steiner and Williams, 2000).

PATIENT ASSESSMENT

History and Physical Examination

Dogs and cats with EPI have a history of chronic small bowel diarrhea, weight loss and failure to thrive (Raiha and Westermarck, 1989). Pets with EPI defecate frequently (six to 10 bowel movements per day) and stools are typically voluminous, greasy, foul smelling and pale in color. When stained with Sudan III and examined microscopically, fat droplets are readily identified in such feces (**Figure 66-1**). Polyphagia, borborygmus, flatulence, pica and coprophagia are often reported. Vomiting and polydipsia occur less commonly (Raiha and Westermarck, 1989; Westermarck and Wiberg, 2003).

Affected dogs and cats generally have a normal appearance except for poor body condition (body condition score [BCS] 1/5 to 2/5) and poor coat quality. Cats with EPI may soil the coat in the perineal region (Steiner and Williams, 2000). Animals with pancreatic atrophy will be stunted in comparison to unaffected littermates or breed standards. Severely affected
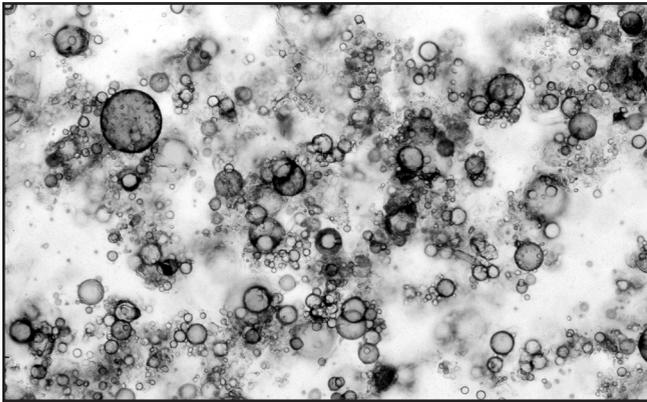
Figure 66-1. Feces stained with Sudan stain demonstrating increased amounts of fat (note globules) typical of exocrine pancreatic insufficiency. (Courtesy Dr. Robert Sherding, College of Veterinary Medicine, The Ohio State University, Columbus.)

patients may have hemorrhages due to a vitamin K-deficient coagulopathy (Perry et al, 1991).

Laboratory and Other Clinical Information

A presumptive diagnosis of EPI is often based on the signalment and patient history. Definitive diagnosis is achieved by radioimmunoassay of serum trypsin-like immunoreactivity (TLI). Low fasting TLI values (<2.5 μg/l) indicate EPI in dogs and cats (Williams and Batt, 1983, 1988; Steiner and Williams, 1996, 2000; Williams, 2006). This sensitive, specific, easy to perform serologic assay has replaced older tests including the bentiromide-PABA challenge, assay of fecal proteolytic activity, x-ray film digestion test and oral fat challenges. TLI measures serum levels of pancreatic trypsin and trypsinogen. Trypsinogen leaks out of pancreatic acini in trace amounts in healthy animals (normal canine serum TLI values = 5.0 to 35.0 μg/l, normal feline serum TLI values = 17.0 to 50.0 μg/l). In EPI, pancreatic acinar atrophy and fibrosis result in reduced serum TLI values. Serum amylase, isoamylase and lipase concentrations are of little value in diagnosing EPI due to pancreatic atrophy (Steiner et al, 2006). These tests may be of benefit when EPI occurs in conjunction with pancreatitis (Meyer and Williams, 1992).

Risk Factors

EPI due to pancreatic acinar atrophy is most common in young, large-breed dogs. German shepherd dogs, Eurasians and rough-coated collies appear to have a genetic predisposition to pancreatic acinar atrophy; however, any breed can be affected (Williams, 1994; Westermarck and Wiberg, 2003; Proschowsky and Fredholm, 2007). In the German shepherd dog and rough-coated collie, the pancreatic acinar atrophy appears to be an autosomal recessive disorder (Moeller et al, 2002) with an estimated disease prevalence of 1% (Westermarck and Wiberg, 2003). In the Eurasian dog breed, the inheritance pattern also appears to be autosomal recessive, but no candidate genes could be identified (Proschowsky and Fredholm, 2007). It is likely that the condition is multifactorial.

Acquired EPI may occur as a consequence of severe or recurrent pancreatic inflammation and resultant fibrosis. Thus, risk factors for acquired EPI are the same as for pancreatitis (Chapter 67).

Etiopathogenesis

Juvenile EPI results from atrophy of pancreatic acinar tissue rather than from congenital hypoplasia (Westermarck and Wiberg, 2003; Steiner, 2008). The disease has been subdivided into subclinical and clinical phases (Wiberg et al, 1999). Reports suggest that histopathologic evidence of atrophy is present before the onset of clinical signs (Westermarck et al, 1993; Wiberg et al, 1999). In the subclinical phase, atrophied and normal acinar cells are present in the pancreatic parenchyma along with a lymphocytic inflammatory infiltrate. The lymphocytic infiltrate suggests an autoimmune reaction. A prospective, placebo-controlled trial of an immunosuppressive drug (azathioprine) in dogs with subclinical EPI demonstrated the natural course of the pancreatic acinar atrophy to be extremely variable with some dogs remaining in the subclinical phase for many years without immunosuppressive therapy (Wiberg and Westermarck, 2002). Unfortunately, the authors were unable to identify markers predictive of disease progression.

Clinical signs do not develop until 85 to 90% of functional exocrine tissue is lost (Jacobs et al, 1989), usually when patients are six to 18 months old (Westermarck et al, 1993). Subnormal serum TLI levels may be present in the subclinical phase even when clinical signs are not present (Wiberg et al, 1999a).

In the juvenile form of EPI, endocrine function is usually normal and diabetes mellitus does not develop. In rare cases, EPI and diabetes mellitus may occur concurrently in young dogs and cats (Sherding, 1979; Boari et al, 1994).

The acquired form of EPI arises as a consequence of the inflammation and fibrosis of endstage chronic pancreatitis (Watson, 1995). Diabetes mellitus may develop concurrently because pancreatic islet cells are similarly affected. EPI may occur as a consequence of pancreatic adenocarcinoma or cholecystoduodenostomy (Williams, 1994).

Several mechanisms are responsible for the severe nutrient malassimilation that occurs in EPI. Most important, the deficiency of pancreatic enzymes results in a failure of intraluminal digestion and inability of the patient to effectively use nutrients. In addition, the lack of other pancreatic secretory products, including bicarbonate, gastrointestinal (GI) trophic factors, antimicrobial factors and intrinsic factor contribute to impaired GI function and nutrient malassimilation. Intestinal mucosal enzyme activity is impaired in experimental and naturally occurring EPI (Williams, 1996). Impaired mucosal enzyme function results in abnormal sugar, amino acid and fatty acid transport. The cause for the intestinal mucosal abnormality is unknown but is suspected to result from the absence of trophic pancreatic secretions and concurrent small intestinal bacterial overgrowth (SIBO).

Dogs with EPI commonly have SIBO because they lack the antibacterial factors present in pancreatic secretions and have

changes in immunity secondary to malnutrition (Williams et al, 1987; Westermarck et al, 1993a; Simpson et al, 1990). In addition, many German shepherd dogs with EPI also have IgA deficiency (Batt et al, 1991; Whitbread et al, 1984). Bacterial overgrowth contributes to malnutrition in EPI by destroying exposed brush border enzymes and consuming unabsorbed intraluminal nutrients. In addition, bacterial hydroxylation of fatty acids may exacerbate fat malabsorption and contribute to osmotic and secretory diarrhea.

Diarrhea in EPI is usually characterized as osmotic. Distal ileal and colonic microflora ferment undigested sugars and fats, releasing osmotically active particles. These particles drive fluid into the gut lumen, which overwhelms the colonic capacity for water reabsorption. Additionally, hydroxy fatty acids formed from bacterial metabolism of undigested fats can trigger secretory diarrhea.

Key Nutritional Factors

Key nutritional factors for patients with EPI are listed in **Table 66-1** and are discussed in more detail below.

Digestibility

The primary nutritional factor in the management of EPI is food digestibility. The use of highly digestible foods (fat and digestible [soluble] carbohydrate ≥90% and protein ≥87%) should be coupled with the addition of pancreatic enzyme preparations to the food. In one study, the combination of a highly digestible commercial veterinary therapeutic food plus pancreatic enzymes provided more metabolizable energy to dogs with EPI than a grocery brand food with pancreatic enzyme supplementation (Pidgeon, 1982). Further studies using naturally occurring EPI cases also demonstrated the benefits of feeding highly digestible foods (Westermarck et al, 1990, 1995).

Highly digestible veterinary therapeutic foods contain meat and carbohydrate sources that have been highly refined to increase digestibility. Typical ingredients in such commercial foods include egg, cottage cheese and muscle and organ meats. Carbohydrates in highly digestible foods are primarily starches of corn, rice, barley and wheat, which are readily digested if properly cooked.

Fat

Steatorrhea is the most prominent clinical sign in patients with EPI. As discussed above, feeding a highly digestible food in conjunction with pancreatic enzyme supplementation is more effective than simply decreasing the fat content of the current food (Pidgeon, 1982; Westermarck et al, 1995). Dry matter (DM) dietary fat levels for patients with EPI should be in the range of 10 to 15% for dogs and 15 to 25% for cats. Overall fat digestion of a highly digestible food with added pancreatic enzymes can exceed 70% in dogs with EPI (Pidgeon, 1982). The addition of medium-chain triglycerides (MCT) to the food can result in increased total fat assimilation because they are more water soluble and are digested and absorbed by mechanisms independent of those used for long-chain triglycerides. However, supplemen-

Table 66-1. Key nutritional factors for foods for patients with exocrine pancreatic insufficiency.*

Factors	Recommended levels
Digestibility	≥87% for protein and ≥90% for fat and digestible carbohydrate
Fat	10 to 15% for dogs
	15 to 25% for cats
Fiber	≤5%**

*Nutrients expressed on a dry matter basis.
**Lower is better.

tation of foods with MCT generally decreases the food's palatability, which may decrease total food intake and thus be counterproductive. This is not necessarily true for commercial foods that contain MCT. Addition of MCT is unnecessary in most cases (Rutz et al, 2004) (Box 58-1).

Feeding high-fat growth-type foods (>27% DM fat) in conjunction with pancreatic enzymes has been associated with increased frequency of defecation, poor fecal consistency and higher fecal fat content in canine EPI as compared to results obtained from feeding lower fat diets (Westermarck et al, 2006).

Fiber

Foods for patients with EPI should contain very little fiber (≤5% DM, lower is better) to maximize food digestibility. Dietary fiber impairs pancreatic enzyme activity in vitro. Decreasing the fiber content from 4% to less than 1% in a study of people with EPI decreased fecal weight and fat excretion by one-third and reduced bloating and flatus (Dutta and Hlasko, 1985). In a three-week dietary trial in dogs with EPI, feeding a low-fat (7% DM), high-fiber (25% DM) food in conjunction with pancreatic enzymes resulted in mild weight loss, increased consumption of food and increased fecal mass and defecation frequency (Westermarck and Wiberg, 2006). These findings are likely attributable to the low fat and caloric content of the food and the effect of high fiber levels on food digestibility. Interestingly, stool quality in these patients was considered good (firmer) as compared to feces produced when the dogs were fed higher fat foods.

Other Nutritional Factors
Vitamins

Micronutrients should be considered in the dietary management of patients with malassimilation. In EPI, the lack of pancreatic lipase results in failed solubilization and absorption of the fat-soluble vitamins A, D, E and K. Vitamins A and D may be initially administered intramuscularly (0.5 to 1 ml divided into two intramuscular sites every three months), if fat absorption remains impaired. Supplementation of vitamins A and D should be reserved for patients with demonstrably low levels of these vitamins or ongoing fat malabsorption because oversupplementation may be harmful.

Vitamin E supplementation (400 to 500 IU, per os, q24h) may be beneficial when serum concentrations are very low. Clinically, vitamin K deficiency has been described (Perry et al,

Table 66-2. Key nutritional factors in selected commercial veterinary therapeutic foods for dogs with exocrine pancreatic insufficiency compared to recommended levels.*

Dry foods	Protein digestibility (%)	Fat digestibility (%)	Carbohydrate digestibility (%)	Fat (%)	Crude fiber (%)
Recommended levels	≥87	≥90	≥90	10-15	≤5**
Hill's Prescription Diet i/d Canine	92	93	94	14.1	2.7
Iams Veterinary Formula Intestinal Low-Residue	na	na	na	10.7	2.1
Medi-Cal Gastro Formula	na	na	na	13.9	1.9
Purina Veterinary Diets EN GastroENteric Formula***	84.5	91.4	94.4	12.6	1.5
Purina Veterinary Diets HA Hypoallergenic Formula***	90.7	93.1	95.7	10.54	1.58
Royal Canin Veterinary Diet Low Fat LF 20	na	na	na	6.6	2.3
Royal Canin Veterinary Diet Hypoallergenic HP 19	na	na	na	20.9	2.3

Moist foods	Protein digestibility (%)	Fat digestibility (%)	Carbohydrate digestibility (%)	Fat (%)	Crude fiber (%)
Recommended levels	≥87	≥90	≥90	10-15	≤5**
Hill's Prescription Diet i/d Canine	88	94	93	14.9	1.0
Iams Veterinary Formula Intestinal Low-Residue	na	na	na	13.2	3.9
Medi-Cal Gastro Formula	na	na	na	11.7	1.0
Purina Veterinary Diets EN GastroENteric Formula***	85.1	95.6	92.2	13.8	0.9
Royal Canin Veterinary Diet Low Fat LF	na	na	na	6.9	3.0

Key: na = information not available from manufacturer.
*All values are on a dry matter basis; values obtained from manufacturer.
**Lower is better.
***Contains medium-chain triglycerides; see text.

1991). Severe hemorrhage may occur when vitamin K stores are depleted because of the vitamin's pivotal role in the post-translational carboxylation of coagulation factors. Parenteral supplementation of vitamin K_1 is recommended (5 to 20 mg, q12h) if coagulopathies are detected in dogs and cats with EPI.

Folate and cobalamin are also of concern. Dogs and cats with EPI often have low serum cobalamin concentrations (Williams, 1996). Reports have identified cobalamin deficiency in 82% of dogs (Batchelor et al, 2007) and 60% of cats (Steiner and Williams, 2000) with EPI. Cobalamin deficiency has been associated with poor outcomes in canine EPI (Batchelor et al, 2007). Several mechanisms may play a role in the development of cobalamin deficiency in EPI. The absence of pancreatic bicarbonate secretion may reduce the intestinal luminal pH and the affinity of cobalamin for intrinsic factor (Simpson et al, 1989). Additionally, the pancreas appears to be the primary source of intrinsic factor in dogs and cats rather than the gastric mucosa (Simpson et al, 1989; Fyfe, 1993). Finally, when SIBO is present, the proximal gut microflora may consume dietary cobalamin before it can be absorbed (Batt and Morgan, 1982; Williams, 1991). If serum levels of cobalamin are low, weekly supplementation by subcutaneous or intramuscular routes is recommended (100 to 250 µg for cats; 250 to 1,200 µg for dogs) for six weeks or until serum cobalamin concentration normalizes (Williams, 1996; Steiner, 2008). Long-term monitoring of serum cobalamin levels is recommended in dogs and cats with EPI to avoid a recurrence (Williams, 2006).

Serum folate levels are elevated in most dogs with EPI probably due to SIBO and bacterial elaboration of folate (Williams, 1996). Serum folate concentration may be decreased, however, in dogs with EPI and concurrent enteropathies involving the ileum (Williams, 1996). In such cases, parenteral supplementa-

tion of folate (0.5 to 1 mg, per os q24h) is recommended until the ileal pathology is resolved. Folate deficiency inhibits pancreatic exocrine function in rats (Balaghi and Wagner, 1995).

Minerals
Dogs with experimentally induced EPI had reduced serum and tissue levels of zinc and copper (Adamama-Moraitour et al, 2001). Similar findings have been recognized in some human patients with EPI (Watson et al, 1988) and are speculated to be due to a deficiency in a pancreatic zinc-binding factor, which facilitates zinc transport and absorption within the intestinal epithelium. However, zinc and copper levels have been investigated in spontaneous cases of EPI and were not found to be low (Williams, 1992). Thus, routine supplementation of these minerals does not seem to be warranted in EPI.

FEEDING PLAN

Dietary management is an essential component in the medical management of patients with maldigestive diseases. Dietary intake should meet the patient's nutrient needs in a form that promotes nutrient absorption. The organs of the GI tract have very large reserve capacities and the small intestine has a very large and efficient absorptive area. About 90% of the pancreas must be dysfunctional before clinical signs of maldigestion are seen (Jacobs et al, 1989). Consequently, patients with clinical signs of maldigestion have very little digestive capacity remaining.

Assess and Select the Food
Levels of key nutritional factors should be evaluated in foods currently fed to patients with EPI and compared with recom-

Table 66-3. Key nutritional factors in selected commercial veterinary therapeutic foods for cats with exocrine pancreatic insufficiency compared to recommended levels.*

Dry foods	Protein digestibility (%)	Fat digestibility (%)	Carbohydrate digestibility (%)	Fat (%)	Crude fiber (%)
Recommended levels	≥87	≥90	≥90	15-25	≤5**
Hill's Prescription Diet i/d Feline	88	92	90	20.2	2.8
Iams Veterinary Formula Intestinal Low-Residue	na	na	na	13.7	1.8
Medi-Cal Hypoallergenic/Gastro	na	na	na	11.5	3.1
Purina Veterinary Diets EN GastroENteric Formula	94.0	93.1	79.7	18.4	1.3
Royal Canin Veterinary Diets Hypoallergenic HP 23	na	na	na	21.5	4.8

Moist foods	Protein digestibility (%)	Fat digestibility (%)	Carbohydrate digestibility (%)	Fat (%)	Crude fiber (%)
Recommended levels	≥87	≥90	≥90	15-25	≤5**
Hill's Prescription Diet i/d Feline	91	89	91	24.1	2.4
Iams Veterinary Formula Intestinal Low-Residue	na	na	na	11.7	3.7
Medi-Cal Hypoallergenic/Gastro	na	na	na	35.9	1.2

Key: na = information not available from manufacturer.
*All values are on a dry matter basis; values obtained from manufacturer.
**Lower is better.

mended levels. Information from this aspect of assessment is essential for making any changes to foods currently provided. Changing to a more appropriate food is indicated if key nutritional factors in the food currently provided do not match recommended levels.

Selected commercial veterinary therapeutic foods that are highly digestible and designed for canine and feline patients with GI disease are listed in **Tables 66-2** and **66-3**, respectively. These foods are marketed for patients with EPI. For comparative purposes, these tables include recommended levels of key nutritional factors. Feeding these foods to patients with EPI often allows smaller amounts of pancreatic enzyme preparations to be used, which results in significant cost savings for pet owners, especially those with large-breed dogs. Foods for young, growing dogs and cats with EPI should also meet the optimal levels of key nutritional factors for growth (Chapters 17 [puppies] and 24 [kittens]).

Assess and Determine the Feeding Method

Because the feeding method is often altered in patients with EPI, a thorough assessment should include verification of the feeding method currently being used. Items to consider include feeding frequency, amount fed, how the food is offered, access to other food and who feeds the pet. All of this information should have been gathered when the dietary history was obtained.

Patients presenting with signs of malnutrition due to chronic maldigestion should be given parenteral nutritional support during the diagnostic workup. Parenteral nutrition in the management of these patients is primarily supportive, may be essential in the initial stages of case management and improves the patient's disposition. Parenteral nutrition also improves caloric, protein and micronutrient balances in veterinary patients, thereby decreasing risks associated with diagnostic procedures including exploratory surgery. Continued administration of

parenteral nutrition (more than three days) is necessary in debilitated patients as a supportive procedure until nutrients can be adequately absorbed. Parenteral nutrition can be performed at most practices in a manner similar to other fluid therapies (Chapter 26).

Patients with EPI usually should be fed multiple small meals per day with pancreatic enzyme supplementation to improve digestibility. At home, feeding at least two to three times daily helps prevent dietary overload and osmotic diarrhea. The daily energy requirement of underweight patients should be increased above that for healthy patients (2 x resting energy requirement for their estimated ideal weight) until ideal body weight and condition (BCS 2.5/5 to 3.5/5) are reached. Even after patients reach ideal body weight, it may be necessary to offer an above average amount of food to offset the persistent degree of malabsorption. Pancreatic enzymes should be added immediately before feeding. (See below.)

ADJUNCTIVE MEDICAL MANAGEMENT

Supplemental Pancreatic Enzymes

In addition to dietary management, effective treatment of EPI requires oral administration of pancreatic enzymes. Most often, pancreatic enzymes are supplied as dried, powdered extracts of bovine or porcine pancreas (**Table 66-4**). Such powder extracts are typically more effective than tablets or capsules (Westermarck, 1987; Steiner, 2008). Tablets, capsules and enteric-coated preparations are not recommended. Lipase activity of pancreatic enzyme preparations varies markedly. Generally, the more expensive preparations have better lipase activity.

If available, raw bovine, porcine or ovine pancreas can be effective (Westermarck et al, 1990). Raw pancreas can be frozen in individual doses for several months without losing enzyme activity. Dogs should receive 30 to 90 g (1 to 3 oz.) of freshly thawed, chopped pancreas, whereas cats should

Table 66-4. Enzyme preparations used in patients with exocrine pancreatic insufficiency.*

Products (manufacturers)	Lipase	Protease	Amylase	Formulation
Viokase-V Powder (Fort Dodge)	71,400	388,000	460,000	Powder
Viokase-V Tablets (Fort Dodge)	9,000	57,000	64,000	Tablets
Viokase Powder (Axcan Scandipharm)	16,800	70,000	70,000	Powder
Pancrezyme Powder (Daniels Pharmaceuticals)	71,400	388,000	460,000	Powder
Pancrezyme Tablets (Daniels Pharmaceuticals)	9,000	57,000	64,000	Tablets
Pancrease MT16 Capsules (McNeil)	18,000	18,000	48,000	Enteric-coated microtablets
Pancrease MT20 Capsules (McNeil)	20,000	44,000	56,000	Enteric-coated microtablets
Pancreatic Plus Powder (Butler)	71,400	388,000	460,000	Powder
Pancreatic Plus Tablets (Butler)	9,000	57,000	64,000	Tablets
Pancrelipase Capsules (Mutual)	18,000	18,000	48,000	Enteric-coated pellets
Lypex Pancreatic Enzyme Capsules (Vio-Vet)	30,000	18,750	1,200	Capsules

*Enzymatic contents (IU) per capsule, tablet or tsp of powder (2.8 g).

receive 30 g (1 oz.) of chopped pancreas per meal (Steiner, 2008).

Pancreatic enzyme supplementation for dogs should be initiated at a dose of 1 tsp of powdered pancreatic extract per 10 kg body weight at each meal. For cats, a starting dose of 1 tsp should be administered with each meal (Suzuki et al, 1997). Enzymes should be mixed with food immediately before the meal is fed. Owners may be able to decrease the dose of pancreatic enzymes based on their pet's response. Most dogs require at least 1 tsp of enzymes per meal (Williams, 1996).

Despite the administration of pancreatic enzyme preparations, fat digestion does not return to normal in dogs with EPI. Inactivation of pancreatic lipase by the acidic pH of the stomach is likely responsible for failure to normalize fat digestion (Williams, 1994).

Antacids and H$_2$-Receptor Blockers

Antacids and H$_2$-receptor blockers have been recommended in the therapeutic regimen to reduce gastric acid-induced destruction of orally administered enzymes. This practice, however, is costly and does not increase efficacy of pancreatic enzyme supplementation (Williams, 1994). Concurrent oral administration of sodium bicarbonate or bile salts and pre-incubation of the meal with pancreatic enzymes are also unnecessary (Williams, 1994, 1996). In one study, adding digestive enzymes to food 20 to 30 minutes before feeding did not improve the response to dietary management (Pidgeon, 1980).

Antibiotics

Oral antibiotics may be necessary to resolve clinical signs in dogs and cats with concurrent SIBO. Tetracycline (20 mg/kg body weight, per os, t.i.d. for 21 days) or tylosin (25 mg/kg body weight, per os, b.i.d. for six weeks) is most often recommended for this purpose; however, metronidazole (10 to 20 mg/kg body weight, per os, every 24 hours for seven to 14 days) may be more effective if SIBO with anaerobic organisms is suspected.

Insulin

Concurrent diabetes mellitus in EPI cases must be managed with insulin. Unfortunately, the fiber-enhanced foods often recommended for diabetic pets are contraindicated for those with EPI (Remillard and Thatcher, 1989). Dietary management of patients with concurrent diabetes mellitus and EPI often requires a modified profile of key nutritional factors. In many cases, foods containing 10 to 15% DM fat, 50 to 55% DM complex, digestible (soluble) carbohydrate and 5 to 10% total dietary fiber can be used.

REASSESSMENT

The prognosis for long-term response to treatment is good in dogs with EPI. In one study, 19% of affected dogs were euthanized within one year of diagnosis due to cost of treatment and/or persistence of clinical signs; however, the median survival time was more than 60 months (Batchelor et al, 2007).

Clinical signs usually resolve within three to five days with proper dietary and enzyme therapy, and weight gain is evident by five to 10 days. Successfully managed canine cases of EPI are recognized by weight gain (0.5 to 1 kg per week) and improved body condition and stool consistency. The food and enzyme dose should be reevaluated if less satisfactory results are obtained. In a retrospective study of dogs with EPI, approximately 10% of patients still had soft to diarrheic stools and 20% were considered underweight (owners' assessment) after 12 months of treatment (Batchelor et al, 2007). Often, the initial dose of pancreatic enzymes is inadequate and must be increased. Every effort should be made to rule out concurrent small bowel disease (e.g., eosinophilic gastroenteritis, lymphoplasmacytic enteritis, SIBO) or diabetes mellitus when clinical response is unsatisfactory. In addition, serum cobalamin levels should be assessed to ensure that cobalamin nutriture is adequate. If not, parenteral cobalamin supplementation should be initiated as described above.

Pancreatic enzyme extract may cause oral mucosal irritation resulting in hemorrhage and reluctance to eat (Rutz et al, 2002; Snead, 2006). If this occurs, decreasing the dose and mixing the pancreatic enzyme powder well in the food may resolve the issue. If not, feeding raw pancreas should be considered.

Well-compensated patients should be evaluated immediately if a change or decline in condition is noted. Feeding more food than expected may be necessary to compensate for

decreased digestibility and to maintain optimal body weight and condition. Regaining or maintaining optimal body weight and condition, normal activity level, improved disposition and absence of clinical signs are measures of successful dietary management.

CASE 66-1

Chronic Diarrhea in a German Shepherd Crossbred Dog

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Patient Assessment

A two-and-one-half-year-old neutered male German shepherd crossbred dog was examined for chronic diarrhea, polyphagia and weight loss of six months' duration. The feces were characteristic of small bowel disorders: watery to semi-formed consistency, clay-colored, large volumes passed two to three times per day, no melena or hematochezia and only small amounts of mucus. Body weight had decreased over the past six months from 34 kg to 22 kg and body condition was now poor (body condition score [BCS] 1/5). The dog's coat was dull and brittle.

Diagnostic evaluation included a complete blood count (normal), serum biochemistry profile (normal except for mild elevations in liver enzyme activity), urinalysis (normal), direct fecal smear and fecal flotation for parasites (negative), fecal stain for fat (positive) and testing for serum concentrations of canine trypsin-like immunoreactivity (TLI), cobalamin and folate. Serum canine TLI concentration was decreased (0.6 mg/l, normal 5 to 35), serum cobalamin concentration was decreased (150 ng/l, normal 225 to 1,680) and serum folate concentration was increased (23.4 mg/l, normal 6.7 to 17.4).

Assess and the Food and Feeding Method

The dog had been fed several commercial dry foods free choice during the past six months. A veterinary therapeutic food (Limited Ingredient Diet: Canine Whitefish and Potato[a]) had been fed for the last two months as an elimination trial for suspected food allergy. The dog was fed five cups per day (1,645 kcal [6.88 MJ]).

Questions

1. What is the tentative diagnosis?
2. What are the key nutritional factors for this dog?
3. Outline a feeding plan (foods and feeding method) for this patient.
4. What ancillary therapy is indicated to complement the feeding plan?

Answers and Discussion

1. A history of chronic diarrhea, steatorrhea and weight loss in a young German shepherd dog suggests exocrine pancreatic insufficiency (EPI) or some other cause of malassimilation (i.e., maldigestion or malabsorption). The decreased serum TLI concentration confirms that EPI is present. Mild increases in hepatic enzyme activity are often seen in patients with EPI. Liver disease does not need to be evaluated further unless hepatic enzyme activity continues to increase or if response to therapy is suboptimal. The decreased serum cobalamin concentration and increased serum folate concentration are consistent with small intestinal bacterial overgrowth (SIBO). Increased numbers of many species of bacteria generate large quantities of folate, which is available for absorption via specific carriers in the proximal small intestine. In contrast, most bacteria compete for available intraluminal cobalamin and thereby reduce its uptake in the distal small intestine. SIBO commonly occurs as a secondary problem associated with EPI. The poor coat probably reflects protein-calorie malnutrition and essential fatty acid deficiency.

2. Key nutritional factors to consider in patients with EPI include food digestibility and fat and fiber content. Selected vitamins are sometimes important. The use of highly digestible foods (fat and digestible carbohydrate ≥90% and protein ≥87%) in conjunction with pancreatic enzyme supplements provides more metabolizable nutrients to dogs with EPI than use of foods with average digestibility and comparable supplementation. Although steatorrhea due to fat malassimilation is a prominent sign in patients with EPI, fat restriction is unnecessary. Moderate dietary fat levels in conjunction with pancreatic enzyme supplementation are more effective than simply decreasing the fat content of the food. Some forms of dietary fiber impair pancreatic enzyme activi-

ty in vitro and may have similar effects in animals. Therefore, excess dietary fiber should be avoided (≤5% fiber, dry matter basis) in these patients. Fat-soluble vitamins, cobalamin and folate are sometimes nutrients of concern in patients with EPI complicated by SIBO. Such patients may develop deficiencies in one or more fat-soluble vitamins. Clinical signs of vitamin K deficiency (vitamin K-responsive coagulopathy) have been described in patients with EPI. Several mechanisms may play a role in cobalamin deficiency including alterations in intestinal luminal pH, decreased levels of intrinsic factor and SIBO. Serum folate concentrations are often elevated in EPI patients with SIBO but may be decreased in patients with concurrent enteropathies.

3. Dogs with EPI should be fed commercial or homemade foods that are highly digestible, moderate in fat and low in fiber (**Table 66-2**). The initial daily energy requirement (DER) should be estimated as 2 x resting energy requirement using an ideal body weight of 34 kg (DER = 2,180 kcal [9.12 MJ]). The DER should be adjusted based on weekly assessments of fecal quantity/quality and body weight and condition. Parenteral administration of fat-soluble and B-complex vitamins is also appropriate.

4. Pancreatic enzyme supplementation is necessary using either dried pancreatic extracts (1 tsp/10 kg body weight with meal) or raw bovine, porcine or ovine pancreas (30 g/10 kg body weight with meal). Powdered extracts are usually preferred to tablets and capsules. The amount can be gradually decreased to find the minimum effective dose after clinical improvement occurs. Broad-spectrum antimicrobial therapy is appropriate for most cases of SIBO; oral oxytetracycline or tylosin is often recommended. However, SIBO is often self-limiting in patients with EPI if dietary alterations and pancreatic enzyme supplementation are successful in controlling clinical signs. SIBO is clinically significant in some patients with EPI, so recovery will not be complete unless antimicrobial therapy is given.

Progress Notes

The food was changed to a commercial dry veterinary therapeutic food that was highly digestible, moderate in fat and low in fiber (Prescription Diet i/d Canine[b]). Two tsp of dried pancreatic extract (Pancrezyme[c]) were mixed thoroughly with two cups of slightly moistened food just before feeding. This mixture was fed three times daily.

The dog ate this mixture well and the diarrhea gradually decreased over the next six to eight weeks. As the dog's stool improved, body weight increased, body condition improved and the dog's coat became shinier and less brittle. A body weight of 31 kg and BCS of 3/5 were reached approximately 12 weeks after initiating therapy. At that time the dosage of dried pancreatic extract was reduced to 1.5 tsp with each meal and plans were made to further reduce the dosage if clinical signs did not return.

Endnotes

a. Innovative Veterinary Diets, Newport, KY, USA.
b. Hill's Pet Nutrition, Inc., Topeka, KS, USA.
c. Daniels Pharmaceuticals Inc., St Petersburg, FL, USA.

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