Malabsorption Syndromes in Small Animals

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Malabsorption is the defective uptake of a dietary constituent resulting from interference with its digestion or absorption, due to either exocrine pancreatic insufficiency (EPI) or small-intestinal disease. Malabsorption typically results in diarrhea, altered appetite, and weight loss, but a number of animals (especially cats) will not have overt diarrhea because of the ability of the colon to conserve water.

The primary function of the small intestine is digestion and absorption of nutrients, and it occurs in sequential phases: intraluminal digestion, mucosal digestion and absorption, and delivery of nutrients to the body. Many chronic, small-intestinal diseases cause malabsorption by interfering with one or several of these processes. Malabsorptive syndromes have been studied in most detail in dogs, but basic diagnostic and therapeutic principles are relevant to other species.

Physiology:

The normal digestive processes convert polymeric dietary nutrients into forms (mainly monomers) that can cross the luminal surface (brush border) of intestinal absorptive epithelial cells (ie, enterocytes). Most digestive enzymes are secreted by the pancreas; EPI is thus a major cause of malabsorption. Terminal digestion before absorption is performed by brush border enzymes, either at the brush border surface of the enterocyte in association with transport proteins for the specific products, or when released into the intestinal lumen through cleavage by pancreatic peptidases or through loss of senescent enterocytes.

The main dietary carbohydrates are starch, glycogen, sucrose, and lactose. Starch and glycogen are first hydrolyzed by pancreatic amylase to the oligosaccharides maltose, maltotriose, and α-limit dextrins. These oligosaccharides and ingested disaccharides (sucrose, lactose) are further hydrolyzed to monosaccharides by enzymes located on the brush border of the enterocytes. Brush border lactase activity declines after weaning, especially in cats, and animals may become lactose intolerant, especially if the brush border has been damaged by another disease. The final products of mucosal hydrolysis (glucose, galactose, and fructose) are actively transported into the enterocyte by sodium-linked carrier-mediated processes, driven by a sodium-potassium ATPase. Once in the cell, glucose is not used by the glycolytic pathway but is passed by facilitated diffusion via a transport protein on the basolateral enterocyte membrane down a concentration gradient into the extracellular space, and then by diffusion into the portal venous circulation.

Protein digestion and absorption follow a similar pattern. Proteolytic enzymes from the stomach and pancreas degrade protein into a mixture of short-chain oligopeptides, dipeptides, and amino acids. Oligopeptides are further hydrolyzed by brush-border peptidases to dipeptides and amino acids that cross the brush-border membrane on specific carrier proteins.

Fat-soluble molecules do not need specific carriers to cross the phospholipid barrier of the brush border. However, intraluminal degradation of large lipids is essential. Fat in the duodenum stimulates release of cholecystokinin, which, in turn, stimulates secretion of pancreatic lipase. After solubilization by bile salt micelles, triglycerides are digested by pancreatic lipase to monoglycerides and free fatty acids. At the enterocyte membrane, the monoglycerides and free fatty acids disaggregate from the micelle and are passively absorbed into the cell. Released bile acids remain within the lumen and are ultimately reabsorbed by the ileum and undergo enterohepatic recycling. Once inside the cell, the monoglycerides and free fatty acids are reesterified to triglycerides and incorporated into chylomicrons, which subsequently enter the central lacteal of the villus, being delivered to the venous circulation via the thoracic duct. Medium-chain triglycerides (C_8–C_{10}) may be absorbed directly into the portal blood, providing an alternative route for fat uptake in case of lymphatic obstruction, but some do normally enter the circulation via the thoracic duct. Consequently, they are no longer recommended in management of lymphangiectasia.

Etiology and Pathophysiology:

Malabsorption is a consequence of interference with mechanisms responsible for either the degradation or absorption of dietary constituents (see Table: Mechanisms of Malabsorption).

Mechanisms of Malabsorption

Location	Disease	Mechanism
Luminal	Exocrine pancreatic insufficiency	Lack of pancreatic enzymes (maldigestion)
Luminal	Antibiotic-responsive diarrhea, secondary small-intestinal bacterial overgrowth	Bacterial activity: bile salt deconjugation, fatty acid hydroxylation, competition for cobalamin and nutrients
Mucosal	Inflammatory bowel disease, infectious enteropathies, dietary sensitivities, neoplastic infiltration	Mucosal damage: inflammation, brush border defects, disturbed enterocyte function, reduction of surface area
Mucosal	Villous atrophy	Reduction in surface area, immature enterocytes due to increased cell turnover
Mucosal	Brush border enzyme deficiencies	Lactase deficiency, diffuse small-intestinal disease
Postmucosal	Lymphangiectasia	Lymphatic obstruction impairs delivery of chylomicrons
Postmucosal	Vasculitis, portal hypertension	Impaired delivery

Diseases that disrupt the synthesis or secretion of digestive pancreatic enzymes cause maldigestion with subsequent malabsorption, so that the end result is the same. An important syndrome is EPI (see Exocrine Pancreatic Insufficiency in Small Animals), which occurs if there is a loss of ~85%–90% of exocrine pancreatic mass. EPI is characterized by severe maldigestion-malabsorption of starch, protein, and most notably, fat. In dogs, EPI is most commonly due to acinar atrophy; chronic pancreatitis is less common and is seen in older animals, and pancreatic hypoplasia is a rare congenital cause. EPI in dogs is often complicated by secondary antibiotic-responsive diarrhea, which further disrupts nutrient digestion and absorption. EPI is relatively uncommon in cats and is most frequently due to chronic pancreatitis.

Intraluminal effects of bacteria can also have important consequences. Bacterial deconjugation of bile salts interferes with micelle formation, which results in malabsorption of lipid. Deconjugated bile salts and hydroxy fatty acids exacerbate diarrhea by stimulating colonic secretion. True small-intestinal bacterial overgrowth (SIBO) can be secondary to defective gastric acid secretion, interference with normal motility or mechanical obstruction of the intestine, interference with the function of the ileocecal valve, and local immunodeficiency. In other cases, there is no evidence of overgrowth and no defined cause but a lack of overt mucosal damage. However, a positive response to antibiotic therapy indicates that the malabsorption is related to bacteria, perhaps in how the innate immune system (toll-like receptors) respond to bacterial components. Originally called idiopathic SIBO, this syndrome is better termed antibiotic-responsive diarrhea (ARD).

Fat malabsorption may also be seen with a deficiency of intraluminal bile salts due to cholestatic liver disease, biliary obstruction, or ileal disease resulting in defective absorption of conjugated bile salts.

Small-intestinal disease can cause malabsorption by reduction of the number or function of individual enterocytes. Diffuse diseases of the mucosa can result in reduced activities of brush border enzymes, decreased carrier-protein function, decreased mucosal absorptive surface area, and interference with final transport of nutrients into the circulation. Weight loss may be compounded by reduced nutrient intake due to inappetence. In addition, malabsorbed nutrients exert strong intraluminal osmotic effects that diminish intestinal and colonic absorption of water and electrolytes, resulting in diarrhea. This may be exacerbated if mucosal damage is accompanied by intestinal inflammation, which can cause secretory and permeability diarrhea.

Potential causes of mucosal damage include idiopathic inflammatory bowel disease (IBD), enteric pathogens (eg, enteric viruses, pathogenic bacteria, *Giardia*, *Histoplasma*, *Pythium*), dietary sensitivity, ARD, and intestinal neoplasia (eg, lymphosarcoma). Histologic changes such as villous atrophy and infiltration with inflammatory cells indicate intestinal disease but do not identify the underlying cause. For example, lymphocytic-plasmacytic enteritis may be a common response pattern of the intestinal mucosa to more than one provocative agent, particularly microbial and dietary antigens. Definite associations with parasites, pathogenic bacteria, and dietary sensitivity have been demonstrated in dogs, but often the underlying cause cannot be identified.

Mucosal damage may also occur without obvious changes under light microscopy. This is typified by infection with enteropathogenic *Escherichia coli* (which specifically cause ultrastructural damage to microvilli in an attaching-effacing lesion) and by ARD in dogs, which can cause biochemical damage to the intestinal brush border, interfering with enterocyte function.

The main brush border enzyme deficiency reported is a relative lactase deficiency, leading to milk intolerance in adult dogs and cats. Acquired brush border defects also may be seen in the course of generalized small-intestinal disease.

Postmucosal obstruction may be seen with lymphatic obstruction (especially lymphangiectasia) and vascular compromise (portal hypertension, vasculitis). Intestinal lymphangiectasia causes intestinal protein loss as well as severe fat malabsorption.

Usually, in malabsorption a number of nutrients are affected and consequently diarrhea occurs; malabsorption of a single ingredient without any GI signs is rare (eg, selective cobalamin malabsorption in Giant Schnauzers, Australian Shepherds, and Border Collies). Again, it should be noted that the large absorptive capacity of the colon may prevent overt diarrhea in some animals (especially cats) despite significant malabsorption and weight loss.

Clinical Findings:

Clinical signs of malabsorption are mainly the result of lack of nutrient uptake and losses in the feces. The duration, severity, and primary cause determine the severity of signs, which typically include chronic diarrhea, weight loss, and altered appetite (anorexia or polyphagia). The absence of diarrhea does not exclude the possibility of severe GI disease. Weight loss may be substantial despite a ravenous appetite, sometimes characterized by coprophagia and pica. Typically, animals with malabsorption are systemically well unless there is severe inflammation or neoplasia. Nonspecific signs may include dehydration, anemia, and ascites or edema in cases of hypoproteinemia. Thickened bowel loops or enlarged mesenteric lymph nodes may be palpable, especially in cats.

Diagnosis:

Chronic diarrhea and weight loss are nonspecific signs common to a variety of systemic and metabolic diseases, as well as malabsorption, although, typically, systemic diseases cause anorexia. A thorough diagnostic approach in dogs and cats with signs suggestive of malabsorption is therefore needed to help exclude association with possible underlying systemic or metabolic disease. A precise diagnosis is also important to determine treatment and prognosis.

The history is particularly important, because it may suggest specific dietary intolerance, indiscretion, or sensitivity. Weight loss may indicate malabsorption or protein-losing enteropathy (PLE) but may also be due to anorexia, vomiting, or extraintestinal disease. Small- and large-intestinal diarrhea may be distinguished by a number of features (see Table: Differentiation of Small-Intestinal from Large-Intestinal Diarrhea). This distinction is more helpful in dogs than in cats, which rarely have exclusively large-intestinal disease. Suspected large-intestinal disease in dogs may be further evaluated by colonoscopic biopsy of the large intestine. However, if signs of large-intestinal disease are accompanied by weight loss or large volumes of feces, then there is probably also concurrent small-intestinal disease.

A thorough physical examination should be performed. Abdominal palpation is essential to identify abnormalities, and rectal examination is required even when no large-intestinal disease is suspected, both to provide a fecal sample and possibly to identify previously unreported melena. In older cats, the thyroid should be palpated carefully and serum T_4 assayed, because signs of hyperthyroidism can closely mimic those of malabsorption.

Initial evaluation should include a CBC, biochemical profile, urinalysis, fecal examination, abdominal ultrasonography and, when indicated by clinical signs or abnormal abdominal palpation, plain radiography. Hematologic correlates in small-intestinal diseases sometimes include anemia of chronic blood loss (microcytic, hypochromic) or chronic inflammation (normocytic, normochromic); neutrophilia and/or monocytosis associated with intestinal inflammation, infectious enteropathies, or neoplasia; eosinophilia associated with parasitism and eosinophilic enteritis; and lymphopenia that

may be associated with intestinal lymphangiectasia in dogs. Lymphocytosis in a dog with diarrhea raises the suspicion of hypoadrenocorticism.

Biochemical tests and urinalysis help to exclude systemic diseases that cause chronic diarrhea, most notably hypoadrenocorticism, protein-losing nephropathies, renal failure, and liver disease. Hypoproteinemia frequently is secondary to PLE and is seen more commonly in dogs than cats. In most cases of PLE, serum albumin and globulin are both low, but a low albumin alone does not exclude it; inflammatory bowel disease (IBD) and neoplasia are rarely associated with hyperglobulinemia as well as hypoalbuminemia. Liver enzymes (ALT, AST) may be increased as a consequence of increased intestinal permeability, allowing more antigens to reach the liver; in such cases, a bile acid stimulation test as well as ultrasonography should be performed to exclude primary liver disease. However, in cats there may be concurrent IBD and cholangitis. Hypocholesterolemia may develop with fat malabsorption and is most notable in lymphangiectasia. Urinalysis is important to exclude renal causes of hypoalbuminemia and/or renal disease. However, sometimes both may be seen together (eg, the familial PLE and nephropathy of Soft-coated Wheaten Terriers). Hyperthyroidism in cats should be excluded by measuring serum T_4 concentrations. Serologic tests for feline leukemia and feline immunodeficiency viruses should also be performed, not only because both may be associated with secondary, chronic diarrhea but also because they are important prognostic factors. Feline infectious peritonitis and toxoplasmosis have also been described as occasional causes of chronic diarrhea in cats.

The presence of fat, undigested muscle fibers, or starch in feces may provide indirect evidence for malabsorption, but these are unreliable. Feces should be examined for parasites (especially hookworms and *Giardia* in dogs and *Tritrichomonas* and *Giardia* in cats) and potentially pathogenic bacteria (including *Salmonella* and *Campylobacter*). Speciation of *Campylobacter* isolates by PCR allows distinction of the pathogenic *C jejuni* from the more common and probable commensal *C upsaliensis*. Pathogenic *Escherichia coli* are emerging as a potentially important problem in dogs, but molecular techniques to identify genes encoding pathogenicity determinants are required for diagnosis. *Giardia* can be detected using serial zinc sulfate fecal flotations or a commercially available ELISA; the latter is easier to perform, and its sensitivity is better than fecal flotation performed by inexperienced personnel. *Tritrichomonas* typically causes colitis in cats rather than malabsorption and is best diagnosed by pouch culture or PCR. Detection of excessive leukocytes on fecal cytology may indicate chronic intestinal inflammation or the presence of enteric pathogens. Cytology of rectal scrapings may reveal *Histoplasma* organisms.

Abdominal radiography is more useful when vomiting is present or palpable abnormalities are detected, but ultrasonography is an important part of the investigation of most small-intestinal diseases. It can be used to measure intestinal wall thickness, layering, and luminal diameter and to detect other intestinal lesions (eg, masses, intussusception), mesenteric lymphadenopathy (in neoplasia and inflammatory bowel disease), and abnormalities in other organs. Mucosal striations have been associated with lymphatic dilatation.

Once obvious dietary, systemic, parasitic, and infectious causes of chronic small-intestinal diarrhea have been eliminated, the next step is differentiation of EPI from intestinal malabsorption; the diagnosis of EPI is relatively straightforward, whereas that of small-intestinal disease is more complex. Numerous tests have been used for dogs and cats with suspected EPI, but they are too inaccurate or impractical to be recommended. Assay of serum trypsin-like immunoreactivity (TLI) is a highly sensitive and specific test and should be used for diagnosis of EPI. This assay measures trypsinogen, some of which normally leaks from the pancreas into the blood, thereby providing an indirect assessment of functional pancreatic tissue. In EPI, functional exocrine tissue is severely depleted and serum TLI concentrations are extremely low, clearly distinguishing EPI from other causes of

malabsorption. This test requires a fasted serum sample. Species-specific canine and feline TLI tests are available.

The diagnosis of small-intestinal disease is difficult because of limitations of routine screening procedures, the need for biopsy, and frequently the absence of diagnostic histologic changes. Bacteriologic culture of duodenal fluid obtained endoscopically or at laparotomy has been used to confirm a diagnosis of ARD. However, the exact cut-off point at which small-intestinal bacterial numbers are considered excessive is a matter of debate, because numbers $>10^5$ total or $>10^4$ obligate anaerobic colony-forming units (CFU)/mL may be found in apparently clinically healthy dogs, depending on circumstances, including environment, diet, scavenging, and coprophagia.

The assay of serum folate and cobalamin (vitamin B_{12}) concentrations can be a helpful initial test in assessment of small-intestinal disease. Folate is absorbed primarily by the proximal small intestine (jejunum), whereas cobalamin is absorbed by the distal small intestine (ileum). As a result, serum folate concentrations can be decreased in proximal small-intestinal diseases, serum cobalamin concentrations can be decreased in distal diseases, and both can be decreased in diffuse enteropathies. Other factors such as the severity, extent, and duration of a mucosal abnormality; dietary intake; and vitamin supplementation also influence these concentrations. In addition, EPI can affect serum folate and cobalamin concentrations, and changes in serum folate and cobalamin concentrations are unreliable for the diagnosis of ARD and secondary antibiotic-responsive diarrhea. The validity of serum folate and cobalamin concentrations as markers of small-intestinal disease in cats is less clear, but low serum cobalamin concentrations may be found with both small-intestinal disease and EPI. Hypocobalaminemia is particularly associated with IBD and alimentary lymphoma and results in metabolic changes, including methylmalonic acidemia, that can lead to anorexia; low cobalamin concentrations are an indication for parenteral supplementation.

A further indirect approach to detect small-intestinal disease is assessment of intestinal function and permeability by oral administration of test substances that are subsequently measured in blood or urine samples. Historically, the xylose absorption test was used to assess intestinal function, but it was insensitive, especially in cats, and is no longer used. Measurements of the differential absorption of d-xylose/3-o-methyl-d-glucose and of intestinal permeability have not been shown to be clinically useful. Hydrogen breath testing after oral administration of individual sugars was considered a simple test to detect malabsorption and to assess transit time, but it has also fallen out of favor. Attempts to diagnose ARD by breath hydrogen or measurement of serum unconjugated bile acids were unreliable, because bacterial numbers may not actually be increased in ARD.

IV administration of ^{51}Cr-labeled albumin (or $^{51}CrCl_3$ to label endogenous albumin) has been used historically to document PLE in dogs. Measurement of 3-day fecal excretion of this radioactive marker provides an estimation of labeled albumin and hence protein loss into the intestinal lumen. However, its use is very limited because of the use of radioactive markers. An alternative approach is the measurement of α-1 protease inhibitor in the feces. This plasma protein is lost into the intestinal lumen together with albumin, but unlike albumin it is an antiprotease and is excreted in the feces essentially intact. Species-specific assays have been developed. Three fresh fecal samples passed by spontaneous evacuation are required; any GI bleeding invalidates the result.

Definitive diagnosis of chronic small-intestinal disease typically includes histologic examination of intestinal biopsies taken by endoscopy or at laparotomy. Endoscopy is minimally invasive and allows visualization of the mucosa and targeted biopsy sampling. However, endoscopic mucosal biopsies may not always give an adequate representation of deeper disease and are limited to the parts of the small intestine (duodenum and sometimes proximal jejunum and ileum) that can be visualized via colonoscopy. Endoscopic biopsy is preferred initially because the risk of intestinal surgical wound

dehiscence can exceed 10% in debilitated, malnourished, or hypoproteinemic animals. However, surgery is the preferred option when there is a concern about deeper or extraintestinal disease or a focal lesion. If a laparotomy is performed, multiple elliptical, longitudinal biopsy samples should be collected from the duodenum, jejunum, and ileum; mesenteric lymph nodes should be biopsied and other organs examined.

Histologic examination of intestinal biopsy specimens can identify morphologic changes in intestinal inflammation (including lymphocytic-plasmacytic enteritis and eosinophilic enteritis), intestinal lymphangiectasia, villous atrophy, and intestinal neoplasia. The description of morphologic abnormalities can provide a baseline to evaluate response to treatment if sequential small-intestinal biopsies are possible. Morphologic abnormalities may also provide prognostic information, because more severe enteropathies tend to be more difficult to manage. However, there may be minimal or no obvious abnormalities in certain disorders (eg, ARD) despite considerable interference with intestinal function. Histologic descriptions alone provide little information on possible etiology or underlying mechanisms of damage, which would clearly assist effective management. Furthermore, inconsistencies in histologic descriptions between pathologists is a recognized problem. However, the World Small Animal Veterinary Association GI Standardization Group has published a descriptive template as a basis for concordance.

Treatment:

Treatment of malabsorption involves treatment of the primary cause (if identified), dietary therapy, and management of complications. Management of EPI in dogs is relatively straightforward (see Exocrine Pancreatic Insufficiency in Small Animals) and includes feeding a low-fiber diet that contains moderate levels of fat or highly digestible fat, very digestible carbohydrate, and high-quality protein. Specific treatment involves lifelong supplementation of each meal with pancreatic extract. Powdered extracts (1 tsp/10 kg body wt) are preferable to tablets, capsules, and most enteric-coated preparations. Fresh or frozen pancreas can be used as an alternative (100 g/meal for an adult German Shepherd). If the response to pancreatic replacement therapy is poor, secondary antibiotic-responsive diarrhea may be suspected, and the animal should be treated concurrently with oral antibiotics for ≥1 mo (see below). Acid suppressants (eg, H_2-receptor blockers, such as cimetidine or ranitidine; proton pump inhibitors, such as omeprazole) may be given 20 min before a meal to inhibit acid secretion and to minimize acid degradation of enzymes in the pancreatic extract, but they are expensive and their value is questionable. Oral multivitamin supplementation should be considered as supportive therapy, but cobalamin (500–1,000 mcg/wk until normalized) should be given parenterally. Dietary requirements of cats with EPI can generally be met by conventional commercial diets, but pancreatic replacement therapy is still needed, as well as parenteral cobalamin supplementation in cats with low serum cobalamin concentrations.

Effective treatment of **small-intestinal disease** depends on the nature of the disorder, but therapy may be empirical when a specific diagnosis cannot be made. In dogs with ARD, a low-fat diet may help by minimizing secretory diarrhea due to bacterial metabolism of fatty acids and bile salts. Oral broad-spectrum antibiotic therapy with oxytetracycline (10–20 mg/kg, tid for 28 days) has been successful. Metronidazole (10–20 mg/kg, bid) and tylosin (20 mg/kg, tid) are effective alternatives; there is rarely a need to use other antibiotics, and the nontargeted use of fluoroquinolones should be avoided. Repeated or longterm treatment may be necessary in dogs with **idiopathic ARD**. Vitamin supplementation may be helpful, particularly for animals with cobalamin deficiency. Secondary antibiotic-responsive diarrhea usually resolves with appropriate management of the underlying disease, but idiopathic ARD can be difficult to control, especially in young German Shepherds, which are predisposed to developing the condition.

Dietary modification is an important aspect of the management of small-intestinal disease in both dogs and cats. Diets generally contain moderate levels of limited protein sources and highly digestible carbohydrates (to reduce protein antigenicity, reduce osmolar effects, and improve nutrient availability) and low to moderate levels of fat. In addition, they are lactose and gluten free; may be fiber-restricted; and may contain increased levels of antioxidants, prebiotics (eg, fructo-oligosaccharides), or omega-3 fatty acids. These additives are thought to modulate the inflammatory response and increase the health of the bacterial gut flora and enterocytes. Treatment with an exclusion diet consisting of a single novel protein source or a hydrolyzed protein should be used as trial therapy when dietary sensitivity is suspected. Intestinal inflammation is sometimes a manifestation of dietary sensitivity, and an initial exclusion food trial is indicated in mild cases of IBD before other treatments. Boiled white rice and potato are suitable carbohydrate sources, while fish, lamb, or chicken are often used as a protein source, depending on the dietary history. Cottage cheese, horsemeat, rabbit, or venison may be acceptable alternatives. Commercial exclusion diets are not necessary to diagnose food hypersensitivity; however, they are preferred for maintenance to reduce potential dietary imbalances. Protein hydrolysates may be the most effective diets to detect dietary sensitivity. The response to an exclusion diet is often rapid, but the diet must be fed for at least 3 and, in a few cases, up to 10 wk before being considered a failure. Oral prednisolone (1 mg/kg, bid for 2–4 wk, followed by a reducing dose) in combination with an exclusion diet may be useful in animals in which idiopathic IBD is suspected but dietary sensitivity has not yet been excluded.

Treatment of **idiopathic inflammatory bowel disease** should initially attempt to eliminate or control an underlying antigenic stimulus that may be playing a primary or secondary role in the damage. Treatment should first involve the use of a protein hydrolysate diet. The diet should comprise digestible carbohydrate (preferably rice, which is most digestible) and high-quality protein. Restriction of fat content may also be valuable and can minimize the secretory diarrhea that is a consequence of bacterial metabolism of fatty acids and bile salts. Oral prednisolone (1 mg/kg, bid for 1 mo, followed by a reducing dose) is indicated in cases of intestinal disease with an obvious inflammatory component, such as lymphocytic-plasmacytic enteritis and eosinophilic enteritis. In more severe cases, it may be necessary to add chlorambucil (2–6 mg/m^2/day, PO, until remission, followed by drug tapering) in cats or azathioprine (2–2.5 mg/kg/day) in dogs.

Cats are often given adjunctive metronidazole (10 mg/kg, bid); the beneficial effect of metronidazole may be a result of an inhibition of cell-mediated immune responses as well as anaerobic antibacterial activity. However, the value of metronidazole in combination with prednisolone in the treatment of IBD in dogs has been questioned.

In **lymphangiectasia**, a severely fat-restricted, calorie-dense, highly digestible diet reduces diarrhea but tends to exacerbate weight loss. Supplementation with fat-soluble vitamins is advised, and additional medium-chain triglycerides have been recommended as an easily absorbable fat source that bypasses the lymphatics, although this mechanism is now doubted. Prednisone/prednisolone therapy may be beneficial for its anti-inflammatory and immunosuppressive effects, especially if there is associated lipogranulomatous lymphangitis. The response to treatment is variable; clinical signs may sometimes abate for months or even years, but the longterm prognosis is grave.

Giardiasis can be treated with metronidazole or fenbendazole, and **histoplasmosis** with itraconazole (cats) or ketoconazole (dogs), with or without amphotericin B. In cases of **lymphosarcoma**, treatment involves an appropriate chemotherapy regimen, but response is poor in dogs and in cats with lymphoblastic forms. In cats, treatment of **small-cell villous lymphoma** with oral prednisone and chlorambucil is associated with prolonged remission.

Prognosis:

The prognosis in cases of malabsorption is good if there is a simple solution, eg, 85% of cases of EPI respond well to enzyme replacement therapy. The prognosis is worse the more severe the small-intestinal pathology. A poorer prognosis has been associated with severe intestinal inflammation, neoplastic disease, severe weight loss, hypoalbuminemia and ascites (PLE), anorexia, and hypocobalaminemia.