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PROTEIN-LOSING ENTEROPATHIES
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Excessive loss of plasma or enteric protein into the gastrointestinal tract is referred to as a state of protein-losing enteropathy (PLE). The loss of protein into the gastrointestinal tract in a PLE is different from the protein maldigestion of exocrine pancreatic insufficiency (see Pancreatic Pathophysiology) or protein malabsorption of gluten enteropathy. PLE occurs in association with several gastrointestinal disorders, including intestinal lymphangitis and lymphangiectasia, gastrointestinal neoplasia, foreign bodies, intussusception, non-neoplastic ulcer, small intestinal bacterial overgrowth, granulomatous enteritis, and severe inflammatory bowel disease.

There are three pathophysiologic mechanisms for protein loss from the gut: (1) inflammation or erosion affecting the normal barrier properties of the gut, e.g., inflammatory bowel disease, foreign bodies, intussusception; (2) lymphatic transport disorders, e.g., lymphangitis and lymphangiectasia; and, (3) vascular disturbances, e.g., ulcer and malignancy. The panhypoproteinemia (hypoalbuminemia and hypoglobulinemia) of PLE usually distinguishes the hypoalbuminemia of protein-losing nephropathy and liver disease. Concurrent hypocholesterolemia and lymphocytopenia may further suggest a lymphatic transport disorder as the underlying cause of a PLE.

Intestinal Neoplasia
Lymphosarcoma, adenocarcinoma, and mast cell tumors are the most common tumors of the gastrointestinal tract in cats. Lymphosarcoma quite often involves diffuse segments of the bowel, whereas adenocarcinomas and mast cell tumors are usually more focal. Weight loss, anorexia, and diarrhea are the most important clinical signs.

Intestinal lymphoma may develop over many months, and affected animals usually present with clinical signs of weight loss and diarrhea. Histologically, lymphosarcoma is usually characterized by diffuse mucosal and submucosal infiltration of neoplastic lymphocytes. Malabsorption results from progressively reduced absorptive area in intestinal villi. Diffuse thickening of the small intestine and mesenteric lymphadenopathy are frequent physical examination findings, although these same findings can be observed in cats with moderate to severe inflammatory bowel disease. Ultrasonography is useful in evaluating intestinal thickness and mesenteric lymph nodes, but definitive diagnosis requires endoscopic or full thickness biopsies.

Food Sensitivity
Adverse reactions to food (food sensitivities) include those mediated by the immune system (food allergies) and those without an immunological basis (food intolerances). Until recent times, objective evidence for food sensitivity has been somewhat lacking in the cat. Adverse reactions to food are usually suspected when an association is made between the ingestion of a certain food and the appearance of a clinical sign. The diagnosis is then confirmed by dietary elimination-challenge studies. Alternative methods of diagnosis have been proposed in other species, including assay of serum antigen-specific IgE and gastroscopic food sensitivity testing. A commercial assay of cat antigen-specific IgE in serum is now available, but the sensitivity and specificity of the assay have not yet been determined. Gastroscopic food sensitivity testing has been applied to G.I. diagnosis in the dog, but has the distinct disadvantage of diagnosing just one type of food sensitivity – immediate type I hypersensitivity.

In a recent study of 55 cats with chronic idiopathic gastrointestinal problems (diarrhea and/or vomiting for > 2 weeks), 29% of cats were diagnosed with food sensitivity based on dietary
elimination/challenge studies. Another 20% of cats had resolution of clinical signs on the elimination diet but did not recur after challenge with their original diet. The foods or food ingredients responsible for the clinical signs were dietary staples (e.g., beef, wheat, and corn gluten). Fifty % of affected cats were sensitive to more than one food ingredient. Assays of serum antigen-specific IgE had limited value as screening tests, and gastroscopic food sensitivity testing was not helpful. The authors concluded that adverse reactions to dietary staples were common in their population of cats, and that affected cats responded well to selected-protein (e.g., chicken or venison-based) diets.

**Exocrine Pancreatic Insufficiency**

Exocrine pancreatic insufficiency (EPI) is an uncommon cause of chronic diarrhea in cats. Insufficiency results from failure of synthesis and secretion of pancreatic digestive enzymes. The natural history of feline exocrine pancreatic insufficiency is poorly understood, but many cases are thought to result from chronic pancreatitis. As with dogs, clinical signs reported in cats with EPI include weight loss, soft voluminous feces, and greasy soiling of the haircoat. Affected cats may also have an antecedent history of recurring bouts of acute pancreatitis (e.g., anorexia, lethargy, vomiting) culminating in chronic pancreatitis and EPI.

The diagnosis of EPI in cats has been technically difficult. Clinical signs in affected cats are not pathognomonic for EPI, clinicopathologic data are fairly non-specific, imaging findings are inconsistent, and the severity of pancreatic histologic changes are not always directly related to the severity of clinical signs. A feline-specific radioimmunoassay for trypsin-like immunoreactivity (TLI) has been developed, and a recent paper suggests that it may prove useful in the diagnosis of this disease. In that study, TLI concentrations less than 8 μg/L (reference range = 17-49 μg/L) were reported in 17/20 cats with clinical signs compatible with EPI (e.g., weight loss, loose voluminous feces, greasy soiling of the hair coat) and at least one other finding, e.g., decreased fecal proteolytic activity, exploratory laparotomy or necropsy findings compatible with EPI, or favorable response to pancreatic enzyme replacement therapy.

**Gastrointestinal Infection**

Any of the acute infectious diseases of the gastrointestinal tract can develop into chronic disease and/or carrier states. The most important of these are Campylobacter sp., Salmonella sp., Trichomonas sp., Toxocara sp., Toxoplasma sp., Cryptosporidium sp., Giardia sp., and feline corona (FIP), leukemia (FeLV), and immunodeficiency (FIV) viruses. Therefore, the routine medical investigation of any cat affected with chronic diarrhea should include direct and indirect fecal examinations for helminths (Toxocara) and protozoa (Toxoplasma, Giardia, Trichomonas, Cryptosporidium), bacterial culture of feces (Salmonella, Campylobacter), and serologies (FeLV, FIV, Toxoplasma, Cryptosporidium). It should be pointed, however, that cats with chronic diarrhea do not necessarily have a greater incidence of any of these infectious agents when compared to healthy cats without diarrhea or other G.I. clinical signs. In other words, a positive result does not necessarily imply that the infectious agent is the underlying cause of the clinical signs.

**Small Intestinal Bacterial Overgrowth**

Small intestinal bacterial overgrowth (SIBO) is a syndrome of dogs and humans associated with the proliferation of aerobic and/or anaerobic bacteria of the small intestine, and the subsequent development of related clinical signs, e.g., diarrhea, weight loss, and vomiting. Clinical signs result from bacterial metabolism of exogenous and endogenous intraluminal constituents, and from the production of metabolites (e.g., deconjugated bile acids and hydroxylated fatty acids) with adverse effects on the intestinal or colonic mucosa. Diagnosis is usually achieved by direct duodenal fluid or mucosal biopsy and culture, determinations of serum folate and cobalamin (B12), measurements of serum total unconjugated bile acids, or response to therapy with antibiotics. Dogs with this syndrome appear to respond to appropriate short courses of antibiotics, e.g., metronidazole, tylosin, or oxytetracycline.
**Inflammatory Bowel Disease**

Inflammatory bowel disease (IBD) is a term that is applied to a group of gastrointestinal disorders characterized by histologic inflammation (neutrophilic, lymphocytic, eosinophilic, granulomatous) and gastrointestinal clinical signs (vomiting, diarrhea, anorexia, and weight loss). Canine IBD appears to be a generalized immune response, and is probably different from forms of IBD (Crohn’s Disease and ulcerative colitis) in humans. See other notes (Canine I.B.D.) at this same meeting for more detail.

**Intestinal Lymphangiectasia**

Intestinal lymphangiectasia is one of the most important protein-losing enteropathies in dogs. Affected animals suffer from severe weight loss and deterioration in body condition, hypoproteinemia, hypocholesterolemia, and lymphocytopenia. Excessive loss of plasma or enteric protein into the gastrointestinal tract is referred to as a state of protein-losing enteropathy (PLE). The loss of protein into the gastrointestinal tract in a PLE is different from the protein maldigestion of exocrine pancreatic insufficiency or protein malabsorption of gluten enteropathy. PLE occurs in association with several gastrointestinal disorders, including intestinal lymphangitis and lymphangiectasia, gastrointestinal neoplasia, foreign bodies, intussusception, non-neoplastic ulcer, small intestinal bacterial overgrowth, granulomatous enteritis, and severe inflammatory bowel disease.