Protein-losing enteropathies (PLE) are a spectrum of diseases occurring primarily in dogs that manifest in non-specific protein loss through the gastrointestinal tract. Although commonly called an enteropathy, the protein loss can also occur through the stomach, small or large intestine. Protein losing enteropathies can be primary (e.g., genetic or heritable disorders such as occurs in Soft Coated Wheaton Terriers or Basenji’s) or secondary to another problem. Table 1 lists of common diseases associated with protein-losing enteropathies, particularly of note are any of the gastroenterides, lymphangiectasia and inflammatory bowel disease. Therapy of these diseases must be aimed at treatment of the primary problem, but nutritional therapy is an essential aspect of success. This paper will review the important aspects of nutritional therapy of IBD and PLE in dogs.

**Inflammatory Bowel Disease (IBD)**

The first key point is to remember that there are many causes of GI inflammation, so just because you find lymphocytes and plasma cells or eosinophils on an intestinal biopsy, it does NOT confirm IBD. IBD is a chronic, idiopathic disease of the intestinal tract that has no identifiable cause. Thus in addition to finding inflammatory infiltrates in the GI mucosa, you must carefully and thoroughly eliminate the other causes of intestinal inflammation (e.g., dietary intolerance/allergy, bacterial enteritis, etc.). Because a diagnosis of IBD is a concession that only symptomatic therapy remains, the long term prognosis is more guarded (than if we have a diagnosis and specific therapy). Finally, if a specific treatment can be employed, we may be able to avoid using high doses of anti-inflammatory or immunosuppressive drugs (with substantial short and long term side effects), or at least be able to use smaller doses for a shorter time.

Lymphocytic plasmacytic enteritis (LPE) is primarily a disease of middle aged to older dogs, and is rarely seen in young dogs. It is well known that the gut is a massive immune organ – responding to a very large number and variety of food, bacterial, parasitic, and other antigens on a daily basis. Thus, it is not surprising that the response to exposure to some of these antigens is increased numbers of lymphocytes and plasma cells or even other cell types such as eosinophils. In particular, it is impossible at this time to distinguish the primary cause of these inflammatory infiltrates in the gut wall. Thus, appropriately performed food trials to eliminate adverse reactions to foods as the cause of the infiltrate are essential. Remember, an appropriate food trial may require at least 6-8 weeks to achieve reversal of signs (it takes 2-3 weeks for the old antigens to be removed from the body and then more time for the body to resolve the inflammatory lesions). It is reasonable to use anti-inflammatory doses of prednisone during this time, but the dose should be tapered over several
weeks, and use the response to diet to gauge the real effect of the therapy.

Possibly the most difficult (and important) aspect of conducting a food trial to rule out food allergy as the cause of gut inflammation is the dietary history. Many over the counter pet foods contain a wide variety of protein sources, so it can be quite difficult to identify a commercial diet that is truly novel. For this reason, many clinicians have utilized hydrolyzed protein diets as their trial diet in the hopes that the hydrosylates will have low immunogenicity. Unfortunately, making the proteins smaller does not prevent the epitopes which are responsible for activating the immune reaction from being exposed. In fact, in humans, hydrosylates can be even more antigenic in some children, resulting in anaphylaxis and other hypersensitivity reactions. Further refinement of proteins (into elemental amino acid forms) will be required to completely eliminate this problem. In addition to the problems with persistent antigenicity, hydrolyzed protein diets also may have changes in taste and digestibility, and as the proteins are hydrolyzed into smaller and smaller forms, the osmolarity of the diets increases – this has been blamed in humans and pets for diarrhea that results in animals fed these diets. Finally, it is important to recognize that difference commercial products contain different sources of protein hydrosylate – and it has been shown that while not all animals known to be allergic to a protein will react to the hydrolyzed version of that protein, at least 20% will – thus illustrating the limitations of using these diets as the definitive means of ruling out an adverse reaction to food. Nevertheless, because novel protein diets have been proven effective in dogs with IBD, and because hydrolyzed diets have the advantage of not sensitizing the patient to a new protein during the initial treatment phase, they are a very reasonable choice for a dog with IBD.

Cobalamin is vitamin B12, and is an essential cofactor in many body energy reactions, cellular growth and repair processes, and in liver glutathione (anti-oxidant) metabolism. Many dogs with severe intestinal disease, and especially IBD have cobalamin deficiency – which can be associated with persistent diarrhea and lack of response to therapy. Deficiency is corrected by replacement with injectable cyanocobalamin at a dose of 25 ug/kg once/week for 4-6 weeks, then once monthly thereafter, as needed to maintain normal serum levels. In dogs with true IBD that require life long therapy to control their signs, it is possible they will require life long B12 injections as well. Remember, it may take as long as 3-4 weeks, once starting appropriate therapy for the IBD to see any response, so it is important to be patient and not expect an immediate response.

**Protein Losing Enteropathies (PLE)**

Protein losing enteropathies (PLE) comprise a complex group of gastrointestinal (GI) diseases causing severe loss of proteins (especially
albumin and similar sized proteins) from the GI tract. The clinical signs of PLE commonly include anorexia, weight loss and small bowel diarrhea. PLE can be a primary disease entity, such as the disorders that occur in Yorkies, Basenji’s, Lundehunds, and soft coated Wheaten terriers, but is most often secondary to a wide variety of diseases and disorders of the small bowel (e.g. lymphangiectasia, infiltrative diseases of the bowel, IBD, etc). One of the most challenging aspects of therapy of PLE is selection of an appropriate diet. This will be the focus of the following section.

Treatment

The initial treatment of dogs with severe PLE may require aggressive intravenous therapy for correction of the hypoalbuminemia, electrolyte, and mineral abnormalities. Plasma or hetastarch (or other colloid) therapy (10-20 ml/kg) is often administered to provide both plasma proteins and coagulation factors in dogs that are severely edematous or who are hypercoagulable (e.g. have significant risk of developing pulmonary/venous thromboembolism) from low antithrombin levels. Alternatively, total parenteral nutrition (TPN) may be initiated to provide a source of protein and energy, as well as to improve oncotic pressure. Nutritional support in the form of elemental diets may be required in dogs with severe PLE – no matter what the cause, as the gut may not be able to appropriately digest or absorb the nutrients in polymeric (intact) diets. There are a variety of human enteral nutrition supplements that can be used, but a low fat, lactose free diet is preferred (e.g. Vivonex TEN). Most other human elementals are not low fat and thus are not good choices for PLE patients. Vivonex alone should only be used as a short term diet, as it is too low in protein to support the nitrogen and amino acid requirements of dogs (and especially cats). For long term nutritional support using elemental diets, amino acid supplements and vitamins must be added to provide a more balanced diet or they must be used in combination with another diet. In these dogs, a combination of the elemental diet, with a hydrolyzed diet, or a homemade ultra-low fat highly digestible diet may be effective. The hydrolyzed diets are often reasonable choices because they are low fat and highly digestible, but not all animals do well on them. Homemade diets are frequently chosen for severe PLE patients because they can serve several important focuses: 1) the protein source can be novel and highly digestible (e.g. turkey, venison, egg), 2) the amount of fat can be easily controlled (no fat to ultra-low fat) – which is extremely important for PLE management, and 3) they are typically highly palatable.

Dogs with less severe hypoalbuminemia (e.g. albumin > 1.5 < 2.0 g/dl) can often be started on a commercial diet designed for GI disease. The key to dietary management of PLE is finding a diet that is low fat, highly digestible and well tolerated (e.g. does not cause diarrhea), but that allows the gut to absorb the proteins presented to it. Many of the ultra low fat commercial diets also contain increased dietary fiber, which is potentially detrimental to PLE patients, as the fiber will reduce the availability and digestion of proteins and
carbohydrates in the small bowel. One ultra low fat diet (< 3 g/100 kcal) that
does not contain high dietary fiber is Royal Canin/Waltham Low Fat. This diet is
a good choice in many patients with mild to moderate PLE. Alternatively, two
other highly digestible diets are reasonable choices because of their low fat
content (e.g. Purina EN, and Iam’s Low Residue); however, these diets may not
be low enough in fat to be as effective. The commercially available
hypoallergenic diets designed for treatment of dietary intolerance or allergy may
seem like reasonable options for drugs with PLE, however, the primary
drawback with these diets is that they are not ultra low fat diets. In fact, most
have only modest reductions in fat content compared to normal diets – to
maintain their palatability. Thus, if a you believe that a novel protein diet is
needed for management of the disease (based on the histopathology), a
homemade diet (using lean meat sources) or hydrolyzed diet is recommended
are the current choices, and they are highly digestible, low fat, and contain
proteins in their peptide forms which are more easily absorbed, even in the
presence of significant GI disease.

In addition to dietary therapy, which is the main stay of therapy for PLE,
specific therapy is required to treat the primary cause (e.g. steroids for IBD,
chemotherapy for lymphoma, etc). In many cases of lymphangiectasia or
idiopathic PLE, steroid therapy is still initiated to reduce the immunologic
component suspected to contribute to the ongoing clinical deterioration. Most
dogs also have some component of antibiotic responsive diarrhea and require
metronidazole, tetracycline, tylosin, or other long term antibiotic therapy to
control signs and prevent bacterial overgrowth. Supplementation with calcium,
magnesium and fat-soluble vitamins is often required, and should be used in
cases where dietary therapy alone does not correct the imbalances. Serum
cobalamin levels should also be measured, as cobalamin levels often decrease
in animals with severe GI disease, and cobalamin is essential for growth and
repair of the gut epithelium. However, in most cases, the most important aspect
of therapy is finding an appropriate diet and providing the necessary additional
supplementation. For dogs with PLE that can be controlled with specific dietary
and pharmacologic therapy, the long term prognosis is fair to good.
Nevertheless, the most severely affected dogs may not respond to therapy or
relapse soon after the initial treatment, and succumb to either complications or
worsening PLE.

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