

Chronic Diarrhea - Protein Losing Enteropathies

“Enteropathy” is the medical term for “condition of the intestine.” A protein losing enteropathy is a condition of the intestine that results in protein loss from the blood, through diarrhea.

Causes of PLE

There are many potential causes of PLE, and the condition if severe can be potentially life threatening if left undiagnosed and untreated. Some of the possible causes of PLE are listed below:

- genetic or inherited disorders such as occurs in Soft Coated Wheaten Terriers, Basenji's and Norwegian Lundehunds.
- lymphangiectasia – dilation of the lymph vessels in the intestines so that proteins and fats can not be absorbed.
- inflammatory bowel disease – invasions of the intestines by white blood cells, so the tissues fail to absorb nutrients and fluids as they should. Sometimes this happens in response to a food allergy, and other times it seems to be autoimmune disease of no apparent cause.
- Diffuse cancer of the intestinal tract.
- Fungal infection of the intestinal tract.
- Parvovirus can cause PLE in infected puppies, as can the panleukopenia virus in cats.

Treatment of PLE must be aimed at treatment of the primary problem, but nutritional therapy is an essential aspect of success.

Signs of PLE

The most common symptoms of PLE are weight loss and diarrhea, but vomiting, loss of appetite or other signs such as eating strange things (called Pica) can occur, depending on the primary cause. If the blood protein albumin gets dangerously low, swelling of the feet can occur, as can distension of the belly with fluid, and accumulation of fluid around the lungs, in the chest cavity. If this gets severe enough, the lungs can fill with fluid and difficulty breathing can result.

Anything that causes chronic diarrhea, including PLE, can result in the intestine telescoping on itself and possibly becoming obstructed (called “intussusception”). If severe, this can cause profus vomiting and abdominal pain. This often requires surgical correction, and can be diagnosed by ultrasound of abdomen.

Dogs are more frequently afflicted with PLE than are cats, and some dog breeds are genetically predisposed (Soft Coated Wheaten Terriers, Basenjis, Norwegian Lundehunds). PLE is rarely seen in puppies, but if it is, parasites and intussusception are the most common causes.

Diagnosing the Cause of PLE

As stated previously, it is difficult to treat PLE if the cause is unknown. The following tests may be recommended to diagnose the cause of PLE.

- *CBC* – complete blood count – assesses numbers of red and white blood cells. Can give clues as to presence of infection, inflammation or anemia which need to be treated.
- *General Health Profile* – can show signs of other tissues which might be affected by auto-immune disease, such as liver, kidneys, etc. With PLE, the blood proteins albumin and globulin will both be low. Albumin less than 1.5 is dangerous, and potentially life threatening. Cholesterol is often low with PLE.

- *Urinalysis* – loss of protein in the urine can be another sign of auto-immune disease. Pets with PLE can have secondary infection from bacteria that moves across the inflamed intestines into the blood stream. This can sometimes result in urinary tract infection which might be seen in a urinalysis. If the urinalysis shows significant protein in the urine without urinary tract infection, a *urine protein creatinine ratio* may be recommended, so assess for kidney disease that causes loss of protein.
- *Electrolytes* – Addison's disease, a condition of poorly functioning adrenal glands can cause electrolyte abnormalities as well as PLE. If Addison's disease is suspected based on electrolyte abnormalities or history, a timed blood test such as *ACTH Stimulation Test* or *Low Dose Dexamethasone Test* may be recommended.
- *Heartworm Test (dog) or Feline Leukemia/FIV Test* – Both of these conditions can cause PLE in rare cases. If your pet has not been tested for these diseases in the past year, the appropriate test might be recommended.
- *Gastrointestinal (GI) Panel* – this consists of 4 tests.
 1. *TLI – Trypsin Like Immunoreactivity* – this tests for failure of the body to produce digestive enzymes. This condition is called "exocrine pancreatic insufficiency" or EPI.
 2. *PLI – Pancreatic Lipase Immunoreactivity* – tests for inflammation in the pancreas (pancreatitis) that will need to be treated if present.
 3. *B12 (cobalamin, cyanocobalamin)* – If this value is low, your pet will need to take weekly B12 injections until B12 is normalized. Low B12 can be caused by any severe small intestinal disease, EPI, or abnormal bacteria in the small intestines. The last condition is called small intestinal bacterial overgrowth, or SIBO.
 4. *Folate* – another B vitamin that can be increased by severe small intestinal disease or SIBO.
- *Bile acids* – The protein albumin is made by the liver, so liver dysfunction can also cause low albumin. The bile acids test is test of liver function, and may be indicated if liver disease needs to be ruled out. Liver disease usually causes albumin but not globulin to be low. PLE causes both proteins to be low. But some pets can have both PLE and liver disease.
- *Fecal tests (flotation, direct wet mount, cytology, rectal scraping)* – to look for parasites and fungal organisms, which if present need to be treated.
- *fecal alpha 1 protease inhibitor (fecal A1PI)* - In dogs where GI protein loss is also suspected, but also have concurrent loss of protein from the kidneys or liver disease, this test should be performed. The alpha 1 PI assay requires collection of 3 separate, freshly passed fecal samples into a special tube. The test is the only available assay to accurately determine the presence of PLE. However, it does not provide a cause.
- *Ultrasound of the Abdomen* – using an ultrasound allows us to look inside the abdomen at the organs to look for problems which might indicated the cause of the PLE, without causing harm or pain to the patient. Pets with PLE might have thickened intestines, fluid in the belly or chest, of enlarged lymph nodes in the abdomen.
- *Intestinal biopsies* – this is necessary to know for sure the cause of PLE. There are two options.
 1. *Flexible endoscopy* – similar to colonoscopy that people over 50 are often familiar with, biopsies of the stomach, small intestine and colon can be taken with the use of a flexible endoscope. No sutures or surgery are required, and pets are usually ready to go home the next day. At this time, we refer animals to Houston, Dallas, or College Station for biopsies taken by endoscope. Our clinic does not have a flexible endoscope.

2. *Exploratory surgery of the abdomen* – this is more invasive and harder on the patient, but more information can be collected with this kind of biopsy than endoscopic biopsies. Full thickness biopsies of the intestines can be taken with surgery, while only the inner 2 layers can be sampled with biopsies taken with a scope. IF the problem is in the outer layers, endoscopic biopsies will not be diagnostic. Another advantage of surgical biopsies is that any other abnormal tissues can also be sampled for biopsy – pancreas, liver, lymph nodes, kidneys, spleen, etc. Dogs with dangerously low protein can have trouble healing after surgery, as their intestines do not absorb nutrition properly.

Dogs with mild PLE may have no abnormalities on bloodwork early in the disease process. But as things go on over weeks to months, bloodwork abnormalities will begin to show up.

Treatment of PLE

The following are some of the treatments for PLE that might be recommended, depending on the cause.

- *Antibiotics* – almost all dogs and cats with PLE require antibiotic therapy, as unhealthy intestinal tissue allows harmful bacterial overgrowth in the gut. Metronidazole, Tylan, or tetracycline are most commonly used. Some pets can be weaned off antibiotics, and some need low dose antibiotic treatment long term.
- *Probiotics* – Probiotics are the “good bacteria” that normally live in the gut, and that can fade away during chronic diarrhea. You have to be careful which brands you use. We recommend Culturelle. Any dog with chronic diarrhea or PLE could benefit from Culturelle. Some pets with PLE can be weaned off probiotics, and some need to take them long term.
- *Dewormers* – even if no parasites are found on fecal examination, all dogs with chronic diarrhea should be treated with a broad spectrum dewormer such as fenbendazole (Panacur) early on in the treatment process.
- *Vitamin B12* – Cobalamin (or cyanocobalamin) is vitamin B12, and is an essential cofactor in many body energy reactions, cellular growth and repair processes, and liver metabolism. Many dogs with severe intestinal disease, and especially IBD have B12 deficiency--which can be associated with persistent diarrhea and lack of response to therapy. Deficiency is corrected by replacement with weekly injections of B12. Oral B12 supplementation does not work as well for PLE, but may be OK if the problem can be brought into remission. B12 injections are usually given once weekly for 6 weeks, then once monthly thereafter, as needed to maintain normal serum levels. In dogs with true IBD or PLE that require lifelong therapy to control their signs, it is possible they will require lifelong 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.
- *Low fat, low fiber diet* – Pets with PLE do not process fat or fiber well, so they need to be fed low fat, high digestible, low fiber diets.
 - Low fat diets such as Hill's R/D, Hill's W/D, Purina OM and Purina DC are low in fat, but too high in fiber for pets with PLE/
 - Intestinal diets such as Hill's I/D, Purina EN and Iam's Low Residue are OK chronic diarrhea caused by mild disease, but too high in fat for most dogs with PLE to digest.
 - Hydrolyzed diets such as Hill's Z/D and Purina HA are highly digestible and low in fat, but some dogs do not digest them well, and they continue to have diarrhea.
 - Royal Canin/Waltham Low fat is an excellent choice, but can be hard to find. It is highly digestible, very low in fat, and low in fiber.
 - Home made diets are a great deal of work, but can be tailored to be both highly digestible and hypoallergenic, can be very low in fat, can be guaranteed to contain no chemical or preservatives, and pets tend to eat them very well.

- *Hypoallergenic food trial for IBD* – A 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 inflammation. For a food trial to be effective at all, ONLY the hypoallergenic can be fed – no cheating, unless they are the protein and carbohydrate source in the hypoallergenic diet chosen. Feeding things off the diet will render ineffective all your hard work for many weeks. Hill's D/D and IVD Limited Antigen Diets are examples of hypoallergenic diets. Hydrolyzed diets are also hypoallergenic in about 80% of pets with IBD. Home made diet is a great deal of work, but really is the best truly hypoallergenic diet.
- *Prednisone for IBD* – corticosteroids such as prednisone are the mainstay of treatment of IBD. If prednisone is not tolerated, other drugs to suppress the immune system can be used. If they get on the proper diet, some dogs and cats with IBD can be weaned off of prednisone, and some can not.
- *Pancreatic enzymes* – these are added to the food in cases of EPI, and often eventually become the only treatment necessary to keep the pet in good health. Tablets don't tend to work as well as powders. Some brands are much more effective than others.
- *Chemotherapy* – if a particular kind of cancer (lymphoma) is diagnosed.
- *Adrenal hormone replacement* – if Addison's disease is diagnosed. Percorten or Flurinef are most commonly used. Very low dose prednisone is also indicated in some cases.
- *Emergency treatment* for dangerously low protein and electrolyte abnormalities – this is necessary only in severe cases of PLE, and involved intravenous therapy with fluids, electrolytes, and protein replacements. In the most cases, referral to a specialty hospital for intravenous feeding may be necessary in order to preserve life while treatments have time to work.

Prognosis for PLE

Prognosis for PLE is variable, and depends at least somewhat on the cause of PLE. If caused by a problem that is generally easily and completely treated (EPI, Addison's Disease), prognosis is excellent.