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GASTROINTESTINAL FUNCTION TESTING - WHY IT IS IMPORTANT

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Laboratory evaluation of intestinal function

Serum folate concentration

Folate is a water-soluble B-vitamin that is plentiful in most commercial pet foods. However, folate in the diet is mostly supplied as folate polyglutamate, which can not be readily absorbed. In the proximal small intestine folate polyglutamate is deconjugated by folate deconjugase and the resulting folate monoglutamate is absorbed by specific folate carriers in the proximal small intestine. During severe proximal small intestinal disease, either folate polyglutamate is no longer deconjugated or folate monoglutamate is no longer absorbed, leading to folate malabsorption; if the condition continues for a significant period of time, folate body stores are depleted and serum folate concentration decreases. The same is true if the patient has diffuse small intestinal disease. Many bacterial species synthesize folate and it is believed that an increased number of bacterial species (i.e., small intestinal bacterial overgrowth) can lead to significant increases in serum folate concentrations.

Serum cobalamin concentration

Cobalamin (vitamin B12) is also a water-soluble vitamin that is plentiful in most commercial pet foods. Dietary cobalamin is bound to dietary protein and cannot be absorbed in this form. In the stomach dietary protein is digested, cobalamin is released, and the free cobalamin is immediately bound by R-protein. In the small intestine R-protein is digested by pancreatic proteases and the released cobalamin is bound by intrinsic factor. In dogs 90% and in cats 99% of intrinsic factor is secreted by the exocrine pancreas. This is different from human beings where a larger portion of intrinsic factor is secreted by the stomach. Intrinsic factor cobalamin complexes are absorbed by specific receptors in the ileum. Distal small intestinal disease, if severe, will lead to destruction of cobalamin receptors in the ileum leading to cobalamin malabsorption. Cobalamin malabsorption will ultimately lead to depletion of cobalamin body stores and cobalamin deficiency. In a recent study, 61% of 80 cats with clinical signs of chronic gastrointestinal disease had decreased serum cobalamin concentrations. (1) Diffuse small intestinal disease can also lead to cobalamin malabsorption as long as the ileum is involved in the disease process. Exocrine pancreatic insufficiency also commonly leads to cobalamin deficiency, since most intrinsic factor is synthesized by the exocrine pancreas. Finally, an increased number of bacterial species in the small intestine will lead to competition for the available cobalamin and may also lead to cobalamin deficiency. Cobalamin is essential for many biochemical reactions in the body and virtually all tissues need cobalamin for proper function. (2) Clinical signs of cobalamin deficiency can vary. Some patients may just show lethargy, anorexia, and weight loss, while others may show diarrhea, intermittent septic episodes, or even neurological signs. Thus, cobalamin deficiency can lead to further clinical signs and thus needs to be addressed therapeutically.

Fecal α1-proteinase inhibitor concentration

Many gastrointestinal disorders, if severe, can be associated with gastrointestinal protein loss. The gold standard for the diagnosis of gastrointestinal protein loss is 51Cr-albumin excretion but this diagnostic test is labor- and time intensive and is also associated with exposure of patient and personnel to radioactivity. Assays for the measurement of canine and feline α1-proteinase inhibitor in feces have been developed. Alpha1-proteinase inhibitor (α1-PI) is synthesized in the liver and inhibits a variety of different proteins, most importantly elastase, but also trypsin, and others. Alpha1-proteinase inhibitor has a molecular mass of approximately 60,000 Da, which is similar to that of albumin. Thus, when gastrointestinal disease is severe enough to be associated with gastrointestinal albumin loss, α1-PI is lost as well. In contrast to albumin, α1-PI is not hydrolyzed by digestive and bacterial proteinases in the gastrointestinal tract. This is due to the fact that α1-PI is a proteinase inhibitor. Therefore, α1-PI can be measured by use of a species-specific immunoassay in feces. Currently, assays for both canine and feline α1-PI are only available through the Gastrointestinal Laboratory at Texas A&M University (www.cvm.tamu.edu/gilab).

Laboratory evaluation of hepatobiliary function

Serum bile acids concentrations

Pre- and postprandial serum bile acid concentrations are used for the diagnosis of hepatic impairment and portosystemic shunting. Food is withheld from the patient for 12 hours and a serum sample is collected. A small amount of food, rich in fat, is fed to stimulate gall bladder contraction and another serum sample is collected 2 hours later. When hepatic function is significantly impaired, extraction of bile acids from the portal blood becomes less efficient and both pre- and postprandial serum bile acids concentrations increase.
In patients with portosystemic vascular anomalies pre-prandial bile acids concentrations maybe only slightly increased, while post-prandial serum bile acids concentrations are often severely increased. In some normal patients paradoxical results are observed in that pre-prandial serum bile acids concentrations are higher than post-prandial concentrations. It has been speculated that this finding is due to gall bladder contraction without food intake. Recently, the use of sulfated and non-sulfated urinary bile acid concentrations in dogs and cats with suspected hepatic disease has been described. However, further studies are necessary before replacement of serum bile acid concentrations can be recommended.1,3,4

**Laboratory evaluation of exocrine pancreatic function**

**Serum lipase and amylase activities**

Serum lipase and amylase activities have been used for the diagnosis of human and canine pancreatitis for several decades. However, in both species it has been well recognized that serum lipase and amylase activities are neither very sensitive nor very specific for pancreatitis.

**Serum trypsin-like immunoreactivity concentration (TLI)**

Pancreatic acinar cells synthesize and secrete trypsinogen, an inactive pre-form (zymogen) of trypsin. Almost all trypsinogen is secreted into the duct system and is released into the duodenum. However, a small amount of trypsinogen is also released into the vascular space and can be measured by species-specific immunoassays for measurement of trypsin-like immunoreactivity (TLI). Dogs and cats with exocrine pancreatic insufficiency have a lack of pancreatic acinar cells and thus a severely decreased serum TLI concentration. A serum canine TLI ≤ 2.5 μg/L or a serum feline TLI concentration ≤ 8 μg/L have been shown to be highly specific for EPI.

Pancreatic inflammation can lead to an increased release of trypsinogen and trypsin into the vascular space. However, serum TLI concentration has a limited sensitivity for pancreatitis in both dogs and cats.

**Serum pancreatic lipase immunoreactivity concentration (PLI)**

Many different cell types in the body synthesize and secrete lipases. In contrast to catalytic assays for the measurement of lipase activity, use of immunoassays does allow for the specific measurement of lipase originating from the exocrine pancreas. Immunoassay for the measurement of serum concentrations of pancreatic lipase (Spec cPLTM in dogs and fPLI in cats) have recently been developed and validated.

Serum PLI has been shown to be highly specific for exocrine pancreatic function. Also, the sensitivity of different minimally-invasive diagnostic tests was compared in dogs with biopsy-proven pancreatitis. The sensitivity of serum TLI concentration was below 35%, that of serum lipase activity less than 55%, and ultrasonography 68%. In contrast, the sensitivity of serum cPLI concentration for pancreatitis was above 80%.5

Clinical studies in cats have shown similar results. In a study of cats with spontaneous pancreatitis serum fPLI concentration was more sensitive and more specific than serum fTLI concentration or abdominal ultrasonography.6

Thus, in both dogs and cats serum PLI concentration (in dogs measured as Spec cPL) is the most sensitive and specific diagnostic test for pancreatitis currently available. Currently, the fPLI assay is only available through the Gastrointestinal Laboratory at Texas A&M University (www.cvm.tamu.edu/gilab). Also, recently, a bedside test for a semiquantitative assessment of cPLI concentration, SNAP cPL, has been introduced. A negative SNAP test virtually rules out pancreatitis. A positive test result needs to be followed up by measurement of a Spec cPL in the laboratory.

**References**