

Serum Trypsin-like Immunoreactivity (TLI) in Cats and Dogs

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Introduction

Diseases of the pancreas are increasingly recognized in cats and dogs. The most common include inflammation of the pancreas (pancreatitis) and exocrine pancreatic insufficiency (EPI), a condition of reduced pancreatic function that results in digestive malabsorption. Conventional diagnostic approaches for both EPI (assay of digestive enzyme activity in feces) and pancreatitis (assay of serum amylase and lipase activities, abdominal radiography, and ultrasonography) offer limited sensitivity and specificity. Studies indicate, however, that trypsin-like immunoreactivity (TLI), a pancreas-specific enzyme, demonstrates high clinical sensitivity and specificity for the detection of EPI in both cats and dogs. In addition, although no single specific test currently exists for pancreatitis in these animals, TLI may assist in its evaluation when used in conjunction with other diagnostic tests.

TLI assays

Species-specific TLI assays detect both trypsinogen and trypsin in serum. Trypsinogen, the inactive enzyme precursor (zymogen) of the digestive enzyme trypsin, is synthesized and stored exclusively within the acinar cells of the pancreas. A small amount of this stored zymogen is continually released into the circulation, where it is a normal trace constituent of blood. Trypsin, on the other hand, enters the bloodstream only in the presence of pancreatic inflammation.

EPI

EPI occurs as a result of insufficient synthesis and secretion (less than 10 to 15 percent of normal) of digestive enzymes by the pancreatic acinar tissue, leading to inadequate nutrient absorption. Without enzyme therapy, the animal will suffer from severe malnutrition and eventually die. Clinical signs in both species are variable and nonspecific but commonly include chronic diarrhea, poor hair coat and weight loss, despite normal or increased appetite. Less commonly, affected animals may be intermittently anorexic and show other signs secondary to malabsorption of micronutrients, most notably of cobalamin (vitamin B12) in cats.

Loss of functional exocrine pancreatic tissue leading to clinical signs of EPI is accompanied by markedly decreased concentrations of serum TLI. Radioimmunoassay of TLI in canine serum (cTLI) has proved to be a remarkably specific and sensitive test for EPI since its

introduction approximately two decades ago (Figure 1). The relatively recent development of an assay for TLI in feline serum (fTLI) has allowed increased recognition of EPI in cats (Figure 2), a diagnosis that was formerly difficult to make. TLI is now considered the test of choice for EPI in both dogs and cats.

It is recommended that serum cobalamin and folate also be assayed in any patient with signs suggestive of EPI, since results of these tests may reveal concurrent or alternative intestinal disease, and correction of vitamin deficiencies may be required for an optimal response to digestive enzyme replacement therapy.

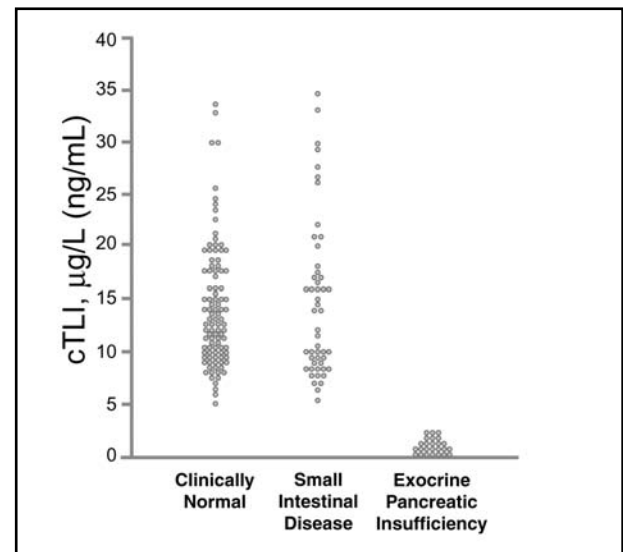


Figure 1. Serum cTLI in 100 clinically normal dogs, 50 dogs with small intestinal disease and 25 dogs with EPI. Redrawn from Williams et al. *J Am Vet Med Assoc* 1988;192:195-201.

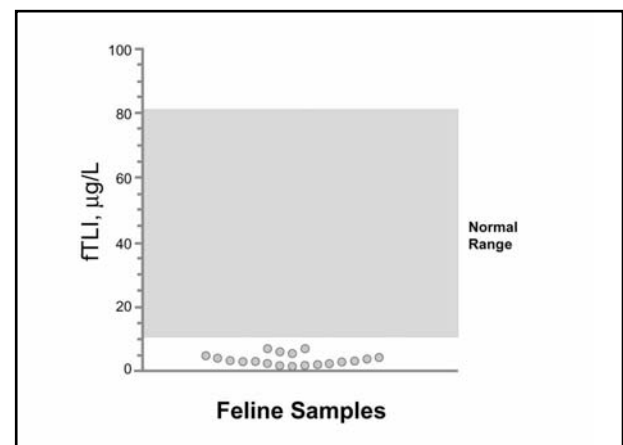


Figure 2. Reduced fTLI values in cats with EPI compared to the normal range (12–82 $\mu\text{g/L}$) for cats, indicated by shaded area.

Pancreatitis

Clinical signs of pancreatic inflammation range from subtle subclinical disease to severe acute pancreatitis. Acute pancreatitis is characterized by sudden onset of depression, lethargy and anorexia in both dogs and cats. Vomiting and abdominal discomfort are also common in dogs, but less so in cats. Many nonspecific clinical laboratory abnormalities may be seen, including changes in blood glucose, calcium, magnesium, serum lipids, liver enzymes and bilirubin. Ultrasonographic examination of the abdomen may reveal evidence of pancreatitis in about 30 to 40 percent of cases when performed by experienced operators, but such expertise is often not available.

Serum TLI concentrations may be increased in association with pancreatitis for various reasons. Experimental studies have shown that serum TLI concentrations increase rapidly after induction of acute pancreatitis in dogs and cats, sometimes reaching values far greater than 20 times the upper limit seen in healthy animals. The half-lives of trypsinogen and trypsin in plasma are short, however (less than 20 minutes), and values return to those of healthy controls relatively quickly, sometimes within 3 to 4 days (Figure 3). In some patients, transient subnormal values are seen during recovery from acute disease. Diagnostically, elevated values are most commonly noted shortly after onset of clinical signs, after which diagnostic sensitivity may not be as great.

Trypsinogen is cleared from the blood fairly rapidly by glomerular filtration. Consequently, if renal function is compromised, serum TLI may increase. It is interesting to note in such cases that cats display a much lower threshold for TLI fluctuations than dogs. Whereas serum canine TLI remains essentially static unless severe renal impairment exists, elevations in serum feline TLI occur with only moderately compromised renal function. Available data,

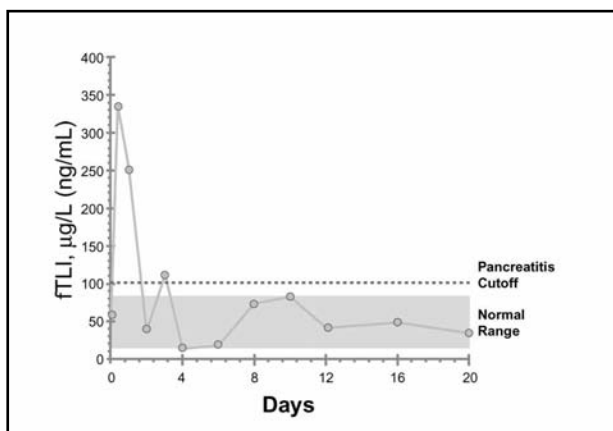


Figure 3. Serum fTLI values in a cat during acute transient experimental pancreatitis. The dotted line represents the laboratory's cutoff for chronic and acute pancreatitis. Courtesy of David Williams, Joerg Steiner and Craig Ruaux, GI Laboratory, Texas A&M University.

however, indicate that serum creatinine values must be highly elevated (greater than 5 mg/L in dogs and 4 mg/L in cats) for significant increases in serum TLI to occur (2- to 3-fold above the upper limit of the reference range).

Interpreting TLI test results and sample handling

Food is usually withheld from the patient for 12 hours prior to drawing blood for a serum TLI assay. Studies have confirmed that serum TLI rises after feeding, but such increases are minimal, and values are not elevated beyond the upper limit of the reference range in dogs and cats. In patients with less than a total loss of pancreatic tissue, however, such transient increases may lead to subnormal but equivocal test results. Therefore, repeat testing of samples collected after fasting is recommended whenever equivocal results are obtained. Repeatedly equivocal results usually reflect chronic pancreatitis with a partial loss of pancreatic acinar cell mass. Continued destruction of acinar cells may eventually lead to EPI in such patients, but the timing of any such progression is unpredictable.

While the half-life of TLI in the blood circulation is rather short (less than 20 minutes), it is very stable in serum and plasma for up to 7 days of unrefrigerated storage. Serum TLI is unaffected by prolonged freezing at -20°C , or by repeated freezing and thawing.

Conclusion

The TLI assay reliably differentiates EPI from other causes of malabsorption such as small intestinal disease, preventing unnecessary and expensive treatment for an illness an animal may not have. Once diagnosed, EPI can be effectively controlled in most dogs and cats through dietary supplementation of pancreatic enzymes. Pancreatitis, on the other hand, is a more complicated disorder, and obtaining the earliest possible diagnosis is critical to the animal's prognosis. Using the TLI assay in conjunction with other appropriate diagnostic tests can aid in a faster, more accurate diagnosis.



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