Numerous advances have been made in tests and technology to allow for less-invasive diagnosis of GI disease. Serum concentrations of the B vitamins cobalamin and folate can be used as markers of GI (and pancreatic) disease, and are also helpful in localizing disease to the proximal small intestine (SI, folate) or ileum (cobalamin). Both of these water-soluble vitamins are abundant in commercial canine diets, and therefore deficiency due to inadequate intake is unlikely.

Cobalamin is primarily found in animal proteins, and is released in the stomach during initial digestion. It is bound to R-protein, which carries cobalamin into the duodenum. Pancreatic enzymes digest R-protein, and the liberated cobalamin is then bound by intrinsic factor, which is secreted by the exocrine pancreas. This complex prevents bacterial utilization of cobalamin during its transit in the GI tract, until it is absorbed via cobalamin receptors in the ileum. Transcobalmin binds cobalamin for transport through the bloodstream. Cobalamin deficiency is indicative of diffuse or distal SI disease/malabsorption, or pancreatic insufficiency (due to decreased intrinsic factor secretion). Dysbiosis can cause hypocobalaminemia as well, through increased utilization of cobalamin by GI bacteria. Rarely vegetarian diets may result in cobalamin deficiency. Additionally, congenital cobalamin deficiencies are seen occasionally. Cobalamin supplementation can be either parenteral or oral (usually given as cyanocobalamin). Cobalamin excess is of no known clinical significance.

Ingested folate complexes are broken down by folate deconjugase present in the proximal SI. Folate carriers, also present in the proximal SI transport folate monoglutamate into the blood, where it is distributed to the tissues for utilization. Large amounts of folate are generated by bacteria in the distal SI and large intestine, however there are no folate carriers in those regions to absorb it. Folate deficiency is indicative of proximal SI disease; supplementation is of unknown benefit, but is unlikely to have deleterious effects. Folate excess is typically a marker of dysbiosis (previously called small intestinal bacterial overgrowth [SIBO]). It occurs when the folate-producing bacteria, which are normally limited to the distal SI and colon, become excessive or move to more proximal regions of the GI tract. In these locations the folate can be absorbed.

Gastrointestinal hemorrhage is a common clinical finding in dogs, and may manifest as hematemesis (vomiting of blood), melena (passage of digested blood) or hematochezia (passage of frank blood). Hemorrhage may occur due to disruption of the mucosa, coagulation disorders (particularly platelets), or ingestion of blood (nasal cavity, lower respiratory tract, etc.). Occult bleeding is very common; a large amount of blood must be lost in a short period of time before melena can be appreciated grossly. Anemia (regenerative or iron-deficiency), hypoproteinemia and increased BUN:creatinine ratio (>30) can all be indirect indicators of GI blood loss. Many drugs can cause GI ulcers, as can primary disease of the GI tract, neopasia, many metabolic diseases, and direct trauma to the GI tract by foreign material or caustic substances.
Evaluation for causes for GI bleeding include a complete blood count, chemistry panel, and other routine lab tests. Imaging can be useful for identifying ulcers, however radiographs and ultrasound are not very sensitive for detection. Endoscopy and direct visualization of the GI mucosa is the gold standard for diagnosis. This requires general anesthesia, specialized equipment and endoscopic training. It is also limited to the stomach and proximal duodenum. Capsule endoscopy has been used for nearly 20 years in humans for the diagnosis of GI bleeding, and has recently become available for use in dogs. It allows non-invasive visualization of the GI mucosa along the entire length of the SI. Fecal occult blood testing is readily available, simple to perform and inexpensive. It lacks sensitivity and specificity, however, and false-positive results are common due to ingested hemoglobin from meat-based diets. 72 hours of a vegetarian diet is recommended prior to testing.

Clostridial diarrhea is a major cause of morbidity and mortality in humans. This genus of bacteria is often implicated as a cause of diarrhea in dogs as well, but is confounded by the fact that the organism can be found in many dogs with normal stool. Clostridia can elaborate numerous toxins, and a newly identified toxin, CPnetF, appears to be consistently found in cases of acute hemorrhagic diarrhea syndrome (previously known as HGE). Testing for this toxin is no widely available through a commercial laboratory. Treatment consists of antibiotics (metronidazole, tylosin or clindamycin are common choices). In humans with chronic C. difficile diarrhea, fecal transplant has been repeatedly shown superior to antibiotic therapy in most cases. Anecdotal evidence suggests this may be a good treatment for dogs as well. Multi-strain probiotics could also be considered for additional treatment.

Protein-losing enteropathy (PLE) can cause severe and even life threatening signs in dogs. Underlying causes of PLE include primary GI disease (lymphangiectasia, severe IBD, GI lymphoma, histoplasmosis, pythiosis, etc), may be breed-related, or the result of non-GI disase (EPI, hypoadrenocorticism). Clinical signs of weight loss, muscle atrophy, diarrhea, inappetance and fluid accumulation are common, though not all dogs with severe PLE will manifest diarrhea. Panhypoproteinemia (low albumin and globulin) is the hallmark of PLE; hypocholesterolemia, hypocalcemia, hypomagnesemia and lymphopenia are also commonly identified. Further complicating diagnosis is over-production of globulins due to chronic inflammatory/infectious disease counteracting the increased loss of globulins through the GI tract. This can result in a normal serum globulin concentration. Measurement of fecal α1-proteinase inhibitor is a non-invasive way to confirm protein loss through the GI tract. It is similar in size to albumin, therefore is lost at a similar rate. Unlike albumin, which is rapidly degraded by digestive enzymes in the gut, α1-proteinase inhibitor resists degradation, and can be measured in feces. Three consecutive, fresh fecal samples are collected, and must be frozen immediately in special tubes for submission to the lab.

Pancreatitis, the most common disorder of the exocrine pancreas, remains a diagnostic challenge despite intense research. Serum amylase and lipase lack sensitivity and specificity, and are of little utility in establishing a diagnosis. TLI is typically elevated in canine pancreatitis, but this has usually abated by the time a
sample is collected for measurement. Results also have a several day turn around
time, further limiting utility. Abdominal ultrasound has variable sensitivity
depending on skill level of the ultrasonographer and quality of equipment, but is a
critical component for diagnosis. Pancreas-specific lipase facilitated diagnosis
greatly, because it is very sensitive for pancreatic inflammation. However, it should
never be used as the sole diagnostic, as many diseases that mimic pancreatitis can
cause an increase in cPL yet pancreatitis is NOT the cause of clinical signs.
Measurement of cPL in the effusion of dogs with pancreatitis may be of utility.
Definitive diagnosis of pancreatitis requires exclusion of other causes, and a
combination of clinical picture, imaging findings and cPL measurement.