Diagnosing Acute Pancreatitis in Dogs

Kirstin Mix, DVM
Christopher Jones, DVM, DACVIM
Gulf Coast Veterinary Specialists
Houston, Texas

ABSTRACT: Canine acute pancreatitis is challenging to diagnose and treat. Because this disease has the potential for severe morbidity and mortality, accurate and timely diagnosis is important. The ideal diagnostic test would be highly sensitive and specific, practical, affordable, and readily available. Because no one diagnostic test fits these criteria, the diagnosis of acute pancreatitis must be made based on evidence from a variety of diagnostic tests and clinical judgment. This article reviews some of the tests available to diagnose pancreatitis.

Pancreatitis is the most common disease of the canine exocrine pancreas, but accurate diagnosis and reliable treatment of this disease remain challenging. Based on a necropsy study\textsuperscript{1} evaluating the prevalence of inflammatory lesions within the pancreas, 64.4% of dogs have histologic evidence of pancreatic inflammation, although the clinical significance of these lesions is not clear. In humans, it is suspected that up to 90% of cases of pancreatitis remain unrecognized and undiagnosed.\textsuperscript{2} This may also be the case in veterinary patients. Timely and accurate diagnosis of pancreatitis is essential because pancreatitis can be associated with significant morbidity and mortality. This article reviews the sensitivity, specificity, and practicality of the different diagnostic modalities available to diagnose pancreatitis.

PANCREAS PHYSIOLOGY

The major function of the exocrine pancreas is production, storage, and secretion of digestive enzymes important for degradation of ingested proteins, fats, and polysaccharides. These digestive enzymes are produced by the pancreatic acinar cells, where they are stored until the pancreas is stimulated to secrete them into the duodenum. Most dogs have two pancreatic ducts: the pancreatic duct and the accessory pancreatic duct (Figure 1). Most pancreatic cells are pancreatic acinar cells. Approximately 1% to 2% of pancreatic cells are endocrine cells.

Because pancreatic digestive enzymes can damage normal tissues within the body (including the pancreas), the pancreas has several defense mechanisms to protect itself from autodigestion or damage from these digestive enzymes.\textsuperscript{3} The first defense mechanism of the pancreas against autodigestion or damage from pancreatic enzymes is production, storage, and secretion of pancreatic digestive enzymes in their inactive forms, called zymogens. Within the pancreatic acinar cells, the zymogens are segregated into zymogen granules, thus protecting other cellular contents from contact with the zymogens. In healthy animals, zymogens are activated after they are secreted into the...
diabetes with exposure to the duodenal enzyme enteropeptidase. The zymogen trypsinogen is initially activated to its active form, trypsin, releasing the protein trypsin activation peptide. Trypsin then activates the other pancreatic zymogens to their active forms. Another defense mechanism of the pancreas against autodigestion is trypsin inhibitor, which inhibits trypsin activity in the event that this enzyme is inappropriately activated within the pancreatic acinar cells. Trypsin inhibitor is produced and stored along with the pancreatic zymogens.

Both acute and chronic forms of pancreatitis occur in dogs, with the acute form being more clinically recognized. Acute pancreatitis is thought to occur primarily because of inappropriate activation of zymogens to their active forms within the pancreas, thereby resulting in autodigestion of pancreatic tissue. Following activation of pancreatic enzymes, pancreatic inflammation and necrosis may occur, resulting in activation of inflammatory mediators and free radicals. Depending on the severity of inflammation, pancreatic edema may occur, resulting in leakage of pancreatic digestive enzymes into the peritoneal space or the intravascular space. The body is initially able to protect itself from damage due to the presence of pancreatic enzymes in the intravascular and peritoneal spaces. α-Macroglobulins and other protease inhibitors exist in systemic circulation and can bind to the pancreatic digestive enzymes, thereby inactivating them and expediting their removal from the body. There is a finite supply of α-macroglobulins and protease inhibitors in circulation. Once this supply is exhausted, the circulating digestive enzymes result in widespread inflammation and activation of the coagulation, fibrinolytic, and complement cascades. Affected individuals may develop disseminated intravascular coagulation, shock, and multiorgan failure.

The clinical course of pancreatitis is highly variable, ranging from subclinical to life-threatening disease. Because of the potential for life-threatening complications, timely and accurate diagnosis of pancreatitis is essential. The ideal diagnostic test for pancreatitis would be highly sensitive and specific, practical, noninvasive, and readily available.
Diagnosing Acute Pancreatitis in Dogs

and readily available. It is also important that diagnostic test results be available quickly, especially in critically ill patients. This article reviews the clinical history and physical examination findings, imaging techniques, hematologic and biochemical findings, serologic testing, and biopsy techniques involved in diagnosing acute pancreatitis in dogs.

HISTORY AND PHYSICAL EXAMINATION

The clinical presentation of acute pancreatitis is highly variable. Many affected dogs have a mild, self-limited course of disease, and some of these patients remain subclinical. It is suspected that most dogs with pancreatitis remain undiagnosed. Middle-aged, female dogs are more likely to develop acute pancreatitis than are other patient populations. There is a clinical impression that this disease is more common in miniature schnauzers and anecdotal evidence that pancreatitis is more likely to occur after consumption of a fatty meal. Other historical factors, such as abdominal trauma or exposure to certain drugs (e.g., azathioprine, L-asparaginase, corticosteroids), may also raise clinical suspicion of pancreatitis.

In a study of dogs with fatal, acute pancreatitis, the most common clinical signs were dehydration, anorexia, vomiting, weakness, abdominal pain, diarrhea, and icterus (Table 1). Fever, renal failure, respiratory compromise, cardiovascular shock, and multiorgan failure have also been recognized in patients with severe forms of acute pancreatitis. It is important to recognize that the history and clinical signs associated with pancreatitis have poor specificity because they may be associated with numerous other diseases.

RADIOGRAPHY, ULTRASONOGRAPHY, AND COMPUTED TOMOGRAPHY

The most commonly used imaging techniques for assessing the pancreas in veterinary patients are abdominal radiography and ultrasonography. In human medicine, computed tomography (CT) is routinely used to assess patients suspected of having pancreatitis. The value of this imaging modality has not been widely evaluated in diagnosing pancreatitis in veterinary patients.

Abdominal radiography should be performed in every patient suspected of having pancreatitis. Radiographic changes and specificity associated with pancreatitis are variable but may include loss of detail in the cranial abdomen, displacement of the stomach to the left, and displacement of the duodenum to the right or ventrally. The colon may be displaced caudally in some patients. In a retrospective study of fatal cases of canine pancreatitis, only 24% of dogs had radiographic abnormalities attributable to pancreatitis. Therefore, abdominal radiography has a low sensitivity in diagnosing pancreatitis. The primary benefit of abdominal radiography in patients suspected of having pancreatitis is that it allows assessment of other organs in the abdominal cavity. As previously discussed, clinical signs of pancreatitis are nonspecific and could be related to many other diseases of the abdomen, such as gastroin-
Diagnosing Acute Pancreatitis in Dogs

Abdominal radiography is widely available, safe, noninvasive, and relatively inexpensive. Images may be evaluated immediately, which is important in critically ill patients.

Abdominal ultrasonography is useful in assessing patients suspected of having pancreatitis. Ultrasonographic findings consistent with acute pancreatitis include an enlarged pancreas, a hypoechoic mass in the region of the pancreas, a hyperechoic region within the pancreas, generalized or localized free abdominal fluid, and thickening of the stomach or duodenal walls. Complications of pancreatitis, such as pancreatic abscesses or pseudocysts, may also be identified via ultrasonography. Ultrasonographic evaluation of the pancreas is more sensitive in diagnosing pancreatitis than is radiographic evaluation. One study identified ultrasonographic changes consistent with pancreatitis in 68% of cases. Ultrasonographic evaluation of the pancreas is technically challenging, and the diagnostic value of this imaging modality depends on the expertise of the ultrasonographer. Because pancreatic lesions may be detected but not clinically significant, the significance of pancreatic abnormalities identified via ultrasonography must be interpreted in light of a patient’s clinical signs. Major advantages of abdominal ultrasonography are that it is noninvasive, it is relatively inexpensive, information can be obtained immediately, and other abdominal organs can be evaluated simultaneously. Abdominal ultrasonography may be performed without sedation in most patients.

CT is the most widely used diagnostic test in assessing pancreatitis in humans and is considered the most effective method of detecting inflammatory disease of the pancreas. However, limited information is available regarding the value of CT in veterinary patients. Almost all humans with pancreatitis have some abnormalities that can be identified via CT, such as local or diffuse pancreatic enlargement, edema, pancreatic pseudocysts, or necrosis. Peripancreatic changes, including the presence of peripancreatic fluid and thickening of tissue in the pancreatic regions, may also be noted (Figure 3). Intravenous and oral contrast enhancement improve the accuracy of CT in humans. There also appears to be a correlation between the severity of changes identified via CT and the severity of the patient’s disease. In one veterinary study, the use of helical CT was compared with serologic testing and abdominal ultrasonography in diagnosing pancreatitis in cats. In this study, CT was found to be less sensitive and less specific than abdominal ultrasonography in diagnosing pancreatitis. To our knowledge, a similar study has not been conducted in dogs. A major concern with the use of CT in diagnosing pancreatitis in dogs is the requirement of anesthesia to obtain images. Even in sedated or moribund patients, motion artifact interferes with accurate CT of the pancreas. The suitability of an individual patient for anesthesia must be assessed before pursuing abdominal CT. The availability of CT is limited and may be financially prohibitive for some owners.

HEMATOLOGY AND BIOCHEMISTRY

A complete blood cell count should be conducted on all patients clinically suspected of having pancreatitis.
Neutrophilia with a left shift is commonly recognized and was identified in 55% of cases in one study.\(^7\) Anemia and thrombocytopenia may be recognized and may be early indications of disseminated intravascular coagulation.\(^7\) Conversely, an elevated packed cell volume may be observed secondary to hemoconcentration resulting from dehydration.\(^2,7\)

Evaluation of a serum biochemistry panel is indicated in patients suspected of having pancreatitis (see box on page 229). Elevated amylase and lipase levels have long been associated with a diagnosis of pancreatitis.\(^1\) However, studies\(^2\) have failed to demonstrate a reliable predictive value for these enzymes. Hyperamylasemia and hyperlipasemia have poor specificity for pancreatitis. Approximately 50% of dogs with elevated amylase and lipase levels have pancreatitis. Reported sensitivities of these enzymes for a diagnosis of pancreatitis are 50% to 70%.\(^2\) Neither amylase nor lipase are pancreas-specific because both enzymes are produced in sites other than the pancreas, such as the gastrointestinal tract and the liver. Furthermore, both enzymes are excreted via the kidneys, and decreased kidney function has been shown to result in hyperamylasemia and hyperlipasemia.\(^19\) Hypolipasemia or low-normal serum levels of lipase should decrease clinical suspicion of pancreatitis in dogs, although this finding does not exclude the possibility of pancreatitis.\(^11\) It is important to remember that the presence of normal serum amylase and lipase values does not exclude the possibility of a diagnosis of pancreatitis. Furthermore, elevations in these enzymes are not, by themselves, diagnostic of pancreatitis.

Several biochemical abnormalities are commonly identified in patients with pancreatitis. Many patients with pancreatitis have elevated total protein levels, likely secondary to dehydration. Elevated liver enzyme levels are common and may reflect hepatocellular injury due to local inflammatory mediators originating from the pancreas. Multiorgan dysfunction may also result in liver damage. Hyperbilirubinemia may occur secondary to bile duct obstruction. Azotemia is common in this patient population and may be prerenal or renal in origin. Prerenal azotemia develops as a result of dehydration. Renal azotemia may occur secondary to hypovolemia or shock or may be associated with multiorgan dysfunction.\(^3\) Azotemic patients must be monitored carefully. If azotemia does not resolve with fluid therapy, the possibility of renal failure must be considered.

Hyperglycemia is commonly identified in dogs with pancreatitis. Possible causes of hyperglycemia include stress hyperglycemia or diabetes mellitus. Stress hyperglycemia is less common and less severe in dogs than in cats.\(^3\) In a retrospective study,\(^7\) 29.7% of dogs with fatal pancreatitis were hyperglycemic at initial presentation. Of these dogs, 63% were persistently hyperglycemic and were diagnosed as diabetic.\(^7\)

Hypoglycemia may be recognized in dogs with severe pancreatitis and may occur as a result of septic complications of pancreatitis or concurrent liver disease.\(^7\) Hypercholesterolemia and hyperlipidemia are commonly identified in dogs with pancreatitis. These findings may be evident via gross examination, even if the patient has not recently eaten.\(^3\) Mild to moderate hypocalcemia has also been reported in dogs with pancreatitis. Hypocalcemia is thought to occur as a result of deposition of calcium salts within the pancreas, which occurs secondary to pancreatic inflammation. Hypocalcemia is rarely severe enough to result in clinical signs related to low serum calcium.\(^4\) However, a study\(^20\) in cats with pancreatitis revealed that patients with low ionized calcium had a worse prognosis compared with patients with normal ionized calcium. To our knowledge, no such study has been reported in dogs.

**MARKERS OF PANCREATIC ENZYME ACTIVATION**

Trypsin activation peptide (TAP) may be measured in the serum or urine of patients clinically suspected of having pancreatitis. Inappropriate activation of trypsinogen to its active form, trypsin, within the pancreas is important in the pathogenesis of acute pancreatitis. During activation of trypsinogen to trypsin, TAP is released into the pancreas, where it may diffuse into the intravascular or peritoneal space. Studies\(^3\) in rodents have demonstrated a rise in TAP shortly after induction of pancreati-
Diagnosing Acute Pancreatitis in Dogs

MARKERS OF PANCREATIC INFLAMMATION

C-reactive protein (CRP) is an acute-phase reactant produced by the liver in response to inflammation, infection, or trauma. CRP has been used in humans as a predictor of the severity of inflammation in patients with acute pancreatitis. In humans, measurement of CRP has shown value in assessing the severity of acute pancreatitis, with more severe cases demonstrating higher levels of CRP. A study in dogs with pancreatitis has shown elevated levels of CRP in dogs with pancreatic necrosis compared with dogs with edematous pancreatitis. Therefore, CRP may have value as a prognostic indicator in dogs with pancreatitis. Another study demonstrated higher CRP levels in dogs with acute pancreatitis compared with levels in healthy dogs. Because CRP may be elevated with any inflammatory disease or subsequent to trauma, the specificity of CRP is questionable. A more practical application of this test, rather than the diagnosis of pancreatitis, may be as a tool to monitor the progression or resolution of pancreatitis or as a prognostic indicator.

SEROLOGIC MARKERS OF PANCREATITIS

Two major serologic markers have been used to diagnose pancreatitis: trypsin-like immunoreactivity (TLI) and pancreatic lipase immunoreactivity (PLI). Both of these are used as pancreas-specific tests. TLI testing, which is serologic, detects serum trypsinogen, trypsin, and trypsin molecules bound to protease inhibitors. TLI testing is well known to be highly sensitive and specific for the diagnosis of exocrine pancreatic insufficiency. In experimentally induced pancreatitis, serum levels of TLI have been shown to increase. Experimental models of pancreatitis seem to produce a rapid rise of TLI following induction of pancreatitis. One study showed a sensitivity of 33% and a specificity of 65% for dogs with naturally occurring pancreatitis. Results of TLI testing are not immediately available, and the sensitivity of this test for the diagnosis of pancreatitis is poor. Therefore, measurement of TLI is not considered useful in diag-

Figure 4. Laparoscopy of the pancreas.

Laparoscopic image of a healthy canine pancreas and healthy surrounding tissue. Note the light pink appearance of the pancreas. The organ does not appear hemorrhagic or edematous.

Laparoscopic image of an inflamed pancreas showing an edematous and erythematous pancreas. The surrounding mesentery is hemorrhagic. Biopsy of the pancreas proved that the patient had pancreatitis.
nosing pancreatitis.

Development of a PLI assay has occurred fairly recently, and this test shows promise as a sensitive and specific method of diagnosing pancreatitis in dogs. PLI measures pancreas-specific lipase in serum; therefore, lipase originating from other sources in the body, such as the stomach and salivary glands, cannot be measured with this test. Pancreatic lipase is antigenically unique compared with lipase produced in other parts of the body. Reported sensitivity of PLI testing to diagnose pancreatitis is greater than 80%. Serum PLI levels appear to be highly sensitive in diagnosing pancreatitis. The presence of renal failure does not appear to result in elevated PLI levels. To date, serum PLI is considered the single best blood test for diagnosing pancreatitis in dogs. The major drawback of this test is that results are generally not available for several days because of the limited availability of the test. This delay in results is problematic, particularly in critically ill patients.

**PANCREATIC BIOPSY AND FINE-NEEDLE ASPIRATION**

Biopsy of the pancreas remains the gold standard in diagnosing canine acute pancreatitis. Pancreatic biopsy may be performed via laparoscopy or laparotomy. Visual inspection of the pancreas may confirm suspected pancreatitis. However, a normal gross appearance of the pancreas does not exclude the possibility of microscopic pancreatic inflammation and clinically significant pancreatitis. Laparoscopic evaluation of the pancreas is less invasive than laparotomy. The right limb and central body of the pancreas can be visually inspected via laparoscopy. The surrounding mesentery can also be assessed. The left limb of the pancreas is challenging to visualize laparoscopically (Figure 4). The benefit of pancreatic visualization and biopsy must be weighed against the potential risks of anesthesia to the individual patient. If the decision to pursue laparotomy or laparoscopy is made, the abdomen should be thoroughly explored, if possible. Biopsy of the pancreas is highly specific, but the sensitivity of pancreatic biopsy is poor because pancreatitis may be localized to small regions within the pancreas.

Ultrasound-guided fine-needle aspiration of the pancreas may be performed to obtain a diagnosis of pancreatitis. This procedure can generally be performed without anesthesia and may reveal inflammation, necrosis, or sepsis of the pancreas. Pancreatic fine-needle aspiration is best performed by an experienced ultrasonographer because the pancreas can be difficult to identify and assess via ultrasonography, as previously discussed. Because of the regional nature of pancreatitis, normal results of fine-needle aspiration cannot exclude a diagnosis of pancreatitis. Therefore, fine-needle aspiration of the pancreas is a relatively specific, but not sensitive, diagnostic test for pancreatitis.

**CONCLUSION**

Definitive diagnosis of acute pancreatitis in dogs remains challenging. The clinical diagnosis of acute pancreatitis can be made based on the collective interpretation of history, clinical signs, biochemical abnormalities, serologic testing, imaging studies, and cytology or histopathology. The ideal diagnostic test for pancreatitis would be highly sensitive and specific, readily available, affordable, and noninvasive. Unfortunately, the ideal diagnostic test for pancreatitis does not exist. The clinical presentation of patients with pancreatitis is highly variable, and this disease can result in severe morbidity or death in some patients. Pancreatitis remains a uniquely challenging disease to diagnose and manage. The possibility of this disease must be considered in critically ill patients or patients with appropriate clinical signs.

**REFERENCES**

b. Normal serum amylase and lipase levels eliminate the possibility of a diagnosis of pancreatitis.
c. Low or low-normal serum lipase decreases the clinical suggestion of pancreatitis.
d. Both amylase and lipase are produced in extrapancreatic sites within the body.

7. Which hematologic or biochemical abnormality is diagnostic of acute pancreatitis?
   a. hyperbilirubinemia
   b. neutrophilia with a left shift
   c. hypercholesterolemia
   d. none of the above

8. Which statement regarding CRP is correct?
   a. An elevated CRP level is diagnostic of pancreatitis.
   b. CRP appears to have high specificity but poor sensitivity in diagnosing pancreatitis.
   c. CRP appears to have high sensitivity but poor specificity in diagnosing pancreatitis.
   d. CRP is produced within the pancreas and leaks from edematous pancreatic tissue during pancreatitis.

9. Which statement regarding PLI and serum lipase is correct?
   a. PLI measures pancreas-specific lipase, which is antigenically unique from lipase produced in other sites of the body.
   b. Extrapancreatic disease such as renal failure can result in elevated serum lipase levels but does not appear to affect PLI levels.
   c. A drawback of PLI measurement is that test results are not readily available.
   d. all of the above

10. Which test is the gold standard in diagnosing canine pancreatitis?
    a. pancreatic biopsy  
    b. TLI  
    c. abdominal ultrasonography  
    d. abdominal CT