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**CANINE PANCREATITIS - FROM CLINICAL SUSPICION TO DIAGNOSIS**

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**Introduction**

Inflammatory disorders of the canine pancreas can be acute or chronic. Acute pancreatitis is defined as a rapid onset of inflammation that can either be mild edematous or severe necrotic with lethal outcome. The clinical prevalence is 0.32-2.0% and the prevalence at necropsies 0.42-0.71%. Chronic pancreatitis is defined as a continuous inflammation resulting in fibrosis and functional (endocrine, exocrine) insufficiency. The histological classification differentiates between chronic fibrosing and chronic recurrent pancreatitis. Complications of chronic pancreatitis are acute necrosis, pseudocysts, and abscesses. The clinical prevalence has not been reported so far. Retrospective studies reported a prevalence of 0.21-0.38% at necropsies. They probably underestimated the true prevalence of chronic pancreatitis. A recent report of necropsies performed in 200 first opinion cases revealed a prevalence of 34% for chronic pancreatitis with 57% of the cases showing moderate or marked inflammation. Dachshounds and cocker spaniels have been reported to be predisposed to acute pancreatitis. Breeds with reported increased risk for chronic pancreatitis are cavalier King Charles and cocker spaniels, collies, and boxers. Canine pancreatitis remains diagnostically challenging despite major improvements in diagnostic methods, because of non-pathognomonic clinical signs that largely depend on the type and duration of pancreatic inflammation and its systemic consequences.

**Clinical signs**

Canine pancreatitis shows a wide spectrum of possible clinical signs with different severity. The differential diagnostic list includes primary diseases of the gastrointestinal, hepatobiliary and urogenital tract, intraabdominal tumors, splenic torsion and hypoadrenocorticism. Clinical signs of canine pancreatitis can be acute in onset as in acute or acute-on-chronic pancreatitis. Acute pancreatitis causes mainly gastrointestinal signs such as vomiting, diarrhea and cranial abdominal pain paired with apathy and anorexia. In case of an acute necrotizing pancreatitis, signs of systemic effects can occur such as weakness, dehydration, hypovolemia, fever, tachycardia, arrhythmia, jaundice, abnormal bleeding tendency, hypovolemic shock, acute respiratory distress syndrome (ARDS), and death. Very rarely, abdominal palpation can reveal a mass in the cranial abdomen. Since acute necrotizing pancreatitis is commonly lethal without proper treatment it is advisable to suppose an acute pancreatitis when a patient with abdominal discomfort shows signs of systemic illness. The patient should be treated accordingly until pancreatitis is proven or ruled out by objective diagnostic procedures. In case of severe clinical signs, repeated blood pressure measurement is suggested to monitor hypovolemic shock. Chronic fibrosing pancreatitis remains often subclinical throughout the whole life. In some cases it leads eventually to endocrine and exocrine pancreatic insufficiency. In contrast, chronic recurrent pancreatitis causes repeatedly more or less severe episodes of gastrointestinal signs with or without abdominal discomfort. It is known from humans and dogs that 'burned out chronic pancreatitis' is associated with a decreased amount of pain episodes but diabetes mellitus and EPI. Occasionally chronic pancreatitis can develop into acute-on-chronic pancreatitis and show a more aggressive clinical picture with pancreatic necrosis and sometimes lethal outcome. When pancreatitis is suspected, the combination of clinical signs, laboratory tests results, and findings of imaging techniques are required to reveal or rule out pancreatitis. The combination of all diagnostic methods is also needed to assess the severity and the prognosis. Some of the clinical, laboratory and imaging procedures need to be performed repeatedly to monitor the treatment success especially in acute pancreatitis.

**Laboratory tests for diagnosis and severity assessment**

Laboratory tests have to be divided into tests for the diagnosis of pancreatitis and tests that help to assess the severity of the disease and its systemic consequences. Parameters that have been favored to diagnose canine pancreatitis are the serum activities of amylase and lipase, and the serum concentration of canine pancreatic lipase. Serum parameters with reported low diagnostic value are canine trypsin-like immunoreactivity, canine α2-macroglobulin, canine α1-protease inhibitor-trypsin-complex and plasma or urine trypsinogen activation peptide. Amylase and lipase Serum amylase and lipase activity originates not only from the pancreas. Amylases are produced in intestine, liver, salivary glands and muscles. Lipases originate also from other sources e.g. gastric mucosa. Therefore,
other diseases such as gastritis, hepatopathies, diabetic ketoacidosis, renal failure, and neoplasia or medications (dexamethasone, Glucantime (meglumine antimonate)) can lead to an increase in serum activity of both enzymes without evidence of pancreatitis. It is also known that the values of both enzymes can be in the reference range although a patient suffers from acute pancreatitis. Studies revealed a sensitivity and specificity for amylase activity of 62.1% and 57.1%, respectively. They were for lipase activity 73.3% and 55.2%, respectively. The advantage of both parameters is their immediate availability using in-house tests. Their disadvantage is the high probability of false positive and false negative results with regard to an acute pancreatitis. There are no studies about their diagnostic value in chronic pancreatitis but it is supposed that there is even a higher amount of false negative results.

Canine pancreatic lipase (cPL) is of pancreatic origin only. Therefore increases in cPL reflect its release from the pancreas. The sensitivity for an acute pancreatitis was in one study 81.8%. It was reported, that serum cPL is not elevated in dogs that suffered from gastritis or received glucocorticoids. However, dogs with experimentally induced chronic renal failure had increased cPL values that were still lower than an empirically chosen cut off value for pancreatitis of 250 μg/L. There has been only one study, reporting a lower sensitivity of cPL compared to serum amylase and lipase activity. In this study, ultrasound of the pancreas was used as the gold standard to differentiate dogs with normal pancreas from patients with pancreatic changes. The authors discuss a bias on the results due to the possible inclusion of dogs with acute and chronic pancreatitis. Nearly all abstracts published so far support the conclusion that cPL seems to be the most reliable diagnostic parameter for acute pancreatitis.

Recently, a snap test for cPL (Snap® cPL™, Idexx) has passed the laboratory validation. It has been marketed as a screening test for elevated cPL values in dogs suspect for pancreatitis. When clinical studies prove the expected high value of cPL to diagnose or exclude pancreatitis in dogs, it will be a major break through to diagnose diseases of the 'hidden organ'.

Other tests
Canine pancreatic elastase can also be determined in serum. The parameter shows some promise to diagnose acute pancreatitis.

Laboratory parameters that are important to rule out other organ diseases than pancreatitis and to assess disease severity are hematology and clinical chemistry (liver, kidney, metabolism and coagulation profiles, electrolytes, and blood gas analysis). Extended laboratory profiles are necessary since especially necrotic pancreatitis can lead to multi-organ disease/failure and finally death.

Possible systemic complications of acute pancreatitis are renal failure, diabetes mellitus, disseminated intravascular coagulation, and ARDS. Hyperbilirubinemia occurs with extrahepatic biliary obstruction due to mass forming pancreatic diseases (necrosis, pseudocyst, abscess, neoplasia). Urinalysis is indicated to assess renal function, rule out pyelonephritis, and reveal diabetes mellitus / diabetic ketoacidosis in association with pancreatitis.

Determination of serum canine C-reactive protein concentrations as a non-specific marker of inflammation seems to be of prognostic value since it is markedly increased in necrotizing pancreatitis. Regular laboratory control examinations help to decide about treatment intensity and to check treatment success. In patients with severe clinical illness the frequency of laboratory tests depends on the degree of laboratory abnormalities. In case of increased serum amylase and lipase values, repeated in-house measurements may help to assess the treatment success. Whether the snap cPL test can be of some use to monitor patients with acute pancreatitis needs to be assessed. Repeated laboratory tests should be combined with repeated abdominal ultrasound exams, especially when the patient shows a mass forming pancreatitis with extrahepatic icterus. Repeated clinical, laboratory and ultrasound examinations help to decide whether a surgical approach is indicated. In dogs with mild or repeated clinical signs and laboratory evidence of pancreatitis, patient monitoring helps to decide in favor of more advanced imaging techniques (CT, ERCP) or pancreatic biopsy to diagnose chronic pancreatitis.

Determination of lipase activity in abdominal fluid has been repeatedly suggested. In a recent study lipase activity was significantly higher in dogs with ascites due to acute pancreatitis than in patients with ascites of other causes. However, few patients with acute pancreatitis develop enough intra-abdominal fluid for sampling and further analysis.

Imaging techniques
Abdominal radiography is rarely diagnostic for pancreatic diseases but necessary for severity assessment and for differential diagnostic purposes. Thoracic radiographs can reveal ARDS and thoracic effusion as signs of severe necrotizing pancreatitis.

Abdominal ultrasound is currently the imaging technique of choice to reveal especially mass forming pancreatic disease, due to its easy accessibility and relatively high sensitivity and specificity. The first sign of pancreatitis is an increased echogenicity of the pancreatic tissue. In cases of severe inflammation with mass forming pancreatic necrosis or abscess, the pancreas shows a decreased echogenicity surrounded by an echodense margin of irregular shape. It can be difficult to
differentiate pancreatic necrosis from pancreatic carcinoma with ultrasound, especially when the tumor has not metastasized into the liver yet. Pancreatic cysts or pseudocysts are echo free areas of different size within the pancreatic region. However, gas accumulation in the stomach and duodenum or severe abdominal pain can cause difficulties in assessing the pancreatic area with ultrasound. Fine needle aspiration for cytology and aspiration of fluid out of pseudocysts can be performed successfully.15-16

Contrast enhanced computed tomography has been shown to be of benefit in humans to decide for and plan surgical interventions. Reports of using CT scans in dogs are sparse but assess the technique as a diagnostic improvement.17,18

Pancreatic biopsy
The main indication for pancreatic biopsy is the differentiation between necrosis and tumor and to diagnose chronic pancreatitis. Multiple biopsies should be taken via laparoscopy or laparotomy because of the patchy distribution of morphologic abnormalities in pancreatic diseases.19-20

References