Acute pancreatitis in the dog

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It is generally believed that pancreatitis develops when there is activation of digestive enzymes within the gland and subsequent autodigestion. The location of the initiation of enzyme activation is thought to begin at the intercellular level, but the exact mechanism is unclear at this time. Experimental studies have shown that excessive acinar stimulation may be involved. Other observations suggest that the depletion of acinar glutathione in the pancreas may stimulate oxidative stress and that contributes to tissue injury. Certain drugs are also associated with development of pancreatitis. Pancreatitis and subsequent autodigestion may be mild associated with an edematous pancreatitis or may become more severe associated with pancreatic acinar necrosis. It is the more severe pancreatic necrosis that tends to have the severe clinical signs and a poorer prognosis associated with systemic disease, such as systemic inflammatory response syndrome (SIRS) or multiple organ dysfunction (MODS).

Clinical conditions
In most cases the etiology of pancreatitis is never determined. In many cases overnutrition is a common factor likely causing excessive acinar enzyme secretion. The ingestion of high-fat diets especially in the obese patient is a well-accepted risk factor. Animals getting into the trash also have a higher risk of developing pancreatitis. Hyperlipoproteinemia is common with pancreatitis and whether this is a result of fat necrosis secondary to the pancreatitis or possibly the hyperlipidemia resulting in pancreatic ischemia is unknown. It is postulated that high concentrations of triglycerides may become activated by pancreatic lipase and produce pancreatitis. Pancreatitis is common in Schnauzers and other dogs that have a primary hyperlipidemia. A number of drugs are also shown to cause pancreatitis including thiazides, furosemide, tetracycline, L-asparaginase, and azathioprine. I personally believe azathioprine is by far the most common drug causing pancreatitis. The role of corticosteroids as a cause of pancreatitis has been suggested but as yet is unproved and is still controversial. In a study of 70 dogs with confirmed pancreatitis certain risk factors were identified (note that the animals included in this study were all necropsy cases and thus likely had severe disease). It was concluded that the breed, overweight body condition, small breed size, prior gastrointestinal diseases, diabetes mellitus, hyperadrenocorticism, and hypothyroidism were risk factors for developing acute pancreatitis. It is thought that around one fourth of the dogs presented with acute diabetes mellitus also have concurrent pancreatitis. No concurrent medications, glucocorticoid therapy, anesthesia, or trauma were associated with increased risk.

Dogs having surgery (within 2 weeks before onset of signs) is also a risk factor. The breeds most commonly involved include Yorkshire terriers, toy poodles, and miniature Schnauzers.

Acute or chronic vomiting is a major clinical sign associated with pancreatitis. The clinical spectrum can vary dramatically from case to case. In the above study of 70 dogs with severe pancreatitis, vomiting (90%), weakness (79%), abdominal pain (58%),
dehydration (46%), and diarrhea (33%) were reported. In experimental pancreatitis, colitis signs (often a bloody mucoid stool) were common presumably due to the extension of inflammation from the inflamed pancreas to the transverse colon that lies in close proximity to the pancreas. Severe cases also have systemic clinical signs such as fever or even cardiovascular shock.

**Diagnosis**

Laboratory findings are quite variable and to some extent parallel the severity of the clinical disease. Leukocytosis is usually present and the biochemistry profile will show variable changes. Azotemia, elevated liver enzymes, increases in total bilirubin, hyperglycemia and hypokalemia may also be present. When disseminated intravascular coagulopathy (DIC) and coagulopathies occur, it generally reflects a poor prognosis.

Amylase and lipase have been used for years to diagnose pancreatitis in the dog but unfortunately they are not consistently reliable. The specificity of amylase and lipase approximates 50% likely due to factors such as azotemia increasing serum amylase and lipase due to decreased renal removal and dexamethasone sometimes increasing serum lipase levels. More recently cPLI or Spec cPL was found to be more diagnostic. A prospective study of cases with clinical evidence of pancreatitis found the test had a 93% sensitivity and a 78% specificity using the IDEXX cutoff value of <200 µg/L as normal. The conclusion was if the Spec cPL was < 200 µg/L (normal) that it was likely that the patient did not have pancreatitis. If the value was above the normal reference range pancreatitis should be included in the differential diagnosis and other tests are required to support the diagnosis.

Traditional lipase is measured using a catalytic assay. More recently newer lipase assays including a DGGR lipase and a Fuji dry chemistry assay appear to have better correlation with PLI activity. Antech now offers a Precision Pancreatic Specific Lipase (Precision PSL) on their profiles. Further studies are required to support these initial observations. At this point interpretation should be similar to Spec cPL; if normal unlikely pancreatitis and if abnormal could be pancreatitis as the primary disease.

Abdominal radiographs may reveal increased density, diminished contrast and granularity in the right cranial abdomen with displacement of the stomach to the left, and widening of the angle between the stomach and the duodenum. A non-homogenous mass and loss of echodensity in the area of the pancreas is often noted on ultrasonographic examination. Occasionally dogs having pancreatitis may also have thoracic effusion, probably due to extension of inflammation through the diaphragm. One study found the sensitivity of ultrasound to be 68% but this varies based on operator skill. We will frequently perform a fine needle aspiration of suspected areas of pancreatitis; cytology showing suppurative inflammation also supports the diagnosis. We consider cytology to be safe as a diagnostic tool. Abdominocentesis and cytology is also very helpful if effusion is present. Suppurative nonseptic inflammation is the typical finding and is rarely septic.

**Treatment**

For humans suffering from acute pancreatitis there is an important short therapeutic window for successful management. It is considered to be the first 36-48 hours after hospital admission. Survival rates decrease and complication rates increase if treatment is delayed. The importance of rapid fluid therapy to
maintaining adequate microcirculation within the pancreas and to prevent inflammatory cytokine release improves survival. These principles can also be extrapolated to the management of canine acute pancreatitis, rapid recognition and appropriate therapy. A Comparative GI Society group in 2006 felt the 4 most important therapies in acute pancreatitis include fluid therapy, analgesia, antiemetics and nutrition (figure).

**Fluid and electrolyte** therapy is given in virtually every case of pancreatitis for improving pancreatic perfusion and correcting the effects of fluid loss into the peritoneal cavity, and vomiting losses coupled with the vasoactive factors released from the pancreas producing a hypovolemic or possibly endotoxic shock. Fluid losses through vomiting may also result in a hypochloremic metabolic alkalosis. Most cases, however, usually have a metabolic acidosis with depletion of total potassium stores. A balanced crystalloid electrolyte solution often supplemented with additional potassium is indicated in almost all cases. Careful monitoring of electrolyte concentrations and patient hydration and renal output is essential in the severe pancreatitis case. Colloids such as Hetastarch have been recommended in the past but recent information suggests it is associated with acute kidney injury and consequently we do not use this product. Experimental studies of pancreatitis found aggressive fluid replacement prevented progression of edematous pancreatitis to the more severe necrotizing pancreatitis.

When protein levels decline plasma therapy has been suggested for improving oncotic pressure, pancreatic perfusion, and replacing protease inhibitors. More recently there have been questions on the benefit of fresh frozen plasma for protease replacement and one study failed to demonstrate the benefit in patients given plasma compared with those only given crystalloids. Probably the most important use of plasma is for factor replacement associated with coagulopathies or DIC.

**Analgesics** should be considered in all patients with pancreatitis, even if there is no outward evidence of abdominal pain. For mild pain buprenorphine (0.1-0.2 mg/kg intravenously [IV], intramuscularly [IM] q 4-6 has needed) is suggested. Moderate to more severe pain morphine (0.1-0.5 mg/kg IV, subcutaneously [SC], or IM as needed) or fentanyl is given as a continuous rate infusion (CRI, 2-5 µg/kg/hour) or 4-10 µg/kg SC, IM not to exceed 500 µg/dog. With severe pain we increase the dose of fentanyl (5-10 µg/kg/hour) and may add either ketamine (0.2-0.4 mg/kg/hour CRI) or lidocaine (5-30 µg/kg/min CRI). The animals should be monitored for side effects, particularly respiratory depression. Narcotics do decrease gastrointestinal motility that is in theory a potential downside for their use. In some cases there is severe wind-up pain and alternative measures may be required to block the pain before traditional analgesics are effective. Spinal blocks and local analgesia should be considered in this case. We have treated some patients having severe abdominal pain with some success using intrathoracic or intra-abdominal placement of local anesthesia. Either bupivacaine (1-2 mg/kg) or Ropivacaine (1-2 mg/kg) can be used. Ropivacaine has less side effects (CAN and cardiovascular) is my preference. We generally use a butterfly catheter or over-the-needle-catheter placed in the 8th mid-intercostal space or peritoneal cavity near the pancreas. Following injections the dog is rolled around and placed on its back so the anesthesia will drain into the area of the vagal nerves.

**Antiemetics** usually are given routinely if the patient has nausea and vomiting to help prevent fluid loss and make the patient more comfortable and possibly enhance return to early nutrition. The ideal antiemetic for pancreatitis should work both centrally and peripherally. Metoclopramide is suggested by some for their antiemetic effects and to improve gastrointestinal tone (0.2-0.4 mg/kg four times daily [QID] PO or SC, or 0.01–0.02 mg/kg/hr CRI). Metoclopramide, a dopamine antagonist, has poor prokinetic effects and is limited as an antiemetic in that it only works centrally. The dopamine
antagonists may also decrease pancreatic perfusion. Anticholinergic agents are contraindicated because of profound effects on decreasing GI motility and little if any effects in decreasing pancreatic secretion. The serotonin antagonists such as ondansetron is a broad spectrum antiemetic but may have some effects in decreasing GI motility as well. My antiemetic of choice is maropitant (Cerenia, 1 mg/kg every 24 hours given SC or IV slowly or 2 mg/kg every 24 hours given PO). It is a broad-spectrum antiemetic that works both centrally and peripherally. Recent evidence by us has shown that maropitant also blocks visceral pain – at least in a visceral pain model given at the dose 1 mg/kg. There is also evidence that maropitant helps with nausea as well although this is a subjective concept. Maropitant is a neurokinin-1 antagonist that blocks receptors found in the emetic center, CRTZ, and in peripheral afferent nerves. At higher doses it is effective blocking vestibular input from motion sickness.

**Antibiotics** should be considered for prophylactic therapy in the severe case or whenever there is evidence of sepsis or pancreatic infection. Infectious etiology of pancreatitis is rare in dogs but an experimental pancreatitis study in dogs suggests antibiotic therapy improves survival. Broad-spectrum antibiotics effective against aerobes and anaerobes should be given. I generally place my severe pancreatitis cases on a second-generation cephalosporin or a combination of amoxicillin and enrofloxacin for this purpose.

**Nutritional supplementation** in severe pancreatitis cases very important. Enteral nutrition is favored over parenteral nutrition. Pancreatic rest in the form of fasting has been the traditional recommendation for any patient with pancreatitis by giving nothing per OS (NPO) for several days. The belief is that feeding results in the release of pancreatic secretory stimuli that will stimulate pancreatic secretions and exacerbate the pancreatitis. Studies have now shown, however, that adequate nutrition improves survival in experimental and human pancreatitis. We now believe that severe vomiting and/or pain associated with eating would be the only reasons to fast patients. If the patient is not expected to be eating on its own within 3 days nutritional support is indicated. Nutrition not only improves patient survival but improves gut integrity. Parenteral nutrition is expensive and fraught with complications. It appears that enteral feeding does not significantly increase pancreatic secretions and actually improves gut integrity, with clinical improvement in the patients being fed. Free choice feeding or tube feeding (nasoesophageal, esophageal, gastrostomy or jejunostomy tube feeding) should be considered in moderate to severe cases. Some prefer low fat liquid nutrition that requires use of human products (Vivonex TEN™ (powder) 3% fat 1 Kcal/ml). Others feed CliniCare™ Canine/Feline Liquid Diet (45% fat, Abbott Animal Health) through a small-diameter feeding tube. During recovery I generally feed a low-fat diet given in small frequent meals.

**Surgery** for pancreatitis is controversial and indications would include septic peritonitis, to lavage the abdomen, treatment of pancreatic abscesses, feeding tube placement, or possibly for treatment of a biliary obstruction. Surgery for pancreatitis or obstructive biliary tract disease generally has a guarded prognosis. However we have a small series of cases that underwent laparoscopic exploration, lavage and jejunostomy tube placement that did well. Most obstructive biliary complications will resolve as the pancreatic inflammation obstructing the common bile duct resolves. In some cases we will place a temporary biliary stent if there is significant cholestasis.

**Other therapy** should be considered only after careful evaluation of the individual case. Because oxidative damage is thought to be the result of cellular membrane death antioxidants may be of benefit in the acute management of cases. Studies show that perfusion of the pancreas with free radical scavengers ameliorates the severity of pancreatitis in experimental canine models. Vitamin E is a potent membrane...
antioxidant and S-adenosyl L-methionine (SAMe) replaces glutathione stores that may have some benefit in pancreatitis. Pancreatic enzyme supplementation has been reported to decrease the pain that accompanies chronic pancreatitis in humans by the feedback inhibition by endogenous pancreatic enzyme secretion. It is not known if enzymes are helpful in acute cases. NSAID therapy is contraindicated and there is yet no evidence that corticosteroids are indicated or beneficial for acute pancreatitis. Hypertriglyceridemia is common in the Schnauzer and contributes to secondary pancreatitis. Triglycerides >500 mg/dL present after a 12- to 18-hour fasted sample should be treated first with a low fat diet (RC Low Fat or Hills I/D Low fat). If they persist omega-3 dose (70–100 mg/kg body weight) should be added and increased as needed up to the National Research Council safe upper limit (200 mg/kg body weight). Lastly I would consider gemfibrozil (dogs, 7.5 mg/kg body weight PO q12h; cats, 10 mg/kg body weight PO q12h). Gemfibrozil does have side effects and should only be considered only when diet cannot maintain serum triglyceride <500 mg/dL.

Complications of pancreatitis include diabetes mellitus, septic peritonitis and pancreatic abscess formation. Diabetes is treated with insulin therapy. Septic peritonitis or pancreatic abscess formation requires surgery. In both conditions the prognosis is guarded to poor.

Selected references


Drugs commonly used in pancreatitis therapy

<table>
<thead>
<tr>
<th>Action</th>
<th>Drug</th>
<th>Dose</th>
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<th>Frequency</th>
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