ACUTE PANCREATITIS IN DOGS AND CATS: AN UPDATE

P. Jane Armstrong, DVM, MS, MBA, Diplomate ACVIM
University of Minnesota

Nomenclature

Confusion surrounds the nomenclature of pancreatitis in veterinary medicine because pathological classification is dependent on histological descriptions, and pancreatic biopsy is rarely undertaken ante-mortem. Clinically, the histological differentiation between acute pancreatitis (AP), acute pancreatic necrosis (APN), and recurrent acute pancreatitis is seldom determined. Therefore, clinical nomenclature usually relates to the severity and longevity of clinical signs. Mild AP does not cause multi-system failure and has an uncomplicated recovery, whilst severe AP or APN can cause multi-system failure. Acute pancreatitis is not associated with fibrosis or exocrine atrophy. Chronic pancreatitis is not well characterized clinically in either species, but is thought to be more common in cats than in dogs. Evidence of lymphocytic-plasmacytic infiltrations are present in the pancreas of many ill and/or older pets, confounding the correlation with clinical disease.

Pathophysiology

Our current understanding of the pathophysiology of AP in dogs and cats is extrapolated from human and experimental models. Acute pancreatitis is characterized by inflammation of the exocrine pancreatic tissue and disturbance of pancreatic microcirculation. Most investigators believe that AP is caused by the unregulated activation of trypsin within pancreatic acinar cells. Enzyme activation within the pancreas leads to autodigestion of the gland and local inflammation. The process starts when intracellular protective mechanisms to prevent trypsinogen activation or to reduce trypsin activity (such as the physical separation of zymogen granules and lysosomal granules, specific trypsin inhibitors and low intracellular ionized calcium concentrations) are overwhelmed. Initial activation of trypsin may occur with oxidative stress or hypotension. After intracellular activation of trypsinogen, several enzymes, including elastase and phospholipase A_2, and the complement and kinin pathways are activated. Activated pancreatic enzymes are then released into pancreatic tissue, and local inflammation ensues. Trypsin and chymotrypsin are directly capable of initiating neutrophil migration into the pancreas, with subsequent production of reactive oxygen species and nitric oxide (NO) causing ongoing inflammation. A complex and interdependent ‘cytokine storm’ ensues, with multiple cytokines stimulating inflammation. Activation of endothothelial cells enables transendothelial migration of leukocytes. Neutrophils are implicated in causing a shift from apoptosis (a feature of AP) to necrosis (a feature of APN). There is concurrent alteration in pancreatic circulation that exacerbates inflammation. One aspect that may provide an opportunity to intervene pharmacologically is the role of Substance P, which is expressed at high levels in a mouse AP model. Expression of Substance P appeared to be particularly related to lung injury, and it appears that that NO and Substance P synergistically amplify pain and inflammation. AP can result in

local complications (such as acinar cell necrosis or pseudocyst formation) and injury in remote locations (i.e., lungs) following release of mediators from the pancreas or extrapancreatic organs, such as the liver.

Risk Factors: Dogs

Potential etiologies that can cause, or are associated with, AP in dogs include dietary factors, hyperlipoproteinemia, certain drugs and toxins, hypercalcemia, duct obstruction, duodenal/biliary reflux, pancreatic trauma, and ischemia/reperfusion. Despite this relatively long list, many cases remain idiopathic. Dogs >5 years old that are overweight or obese appear to be at higher risk for developing AP. There is no clear sex predisposition. Miniature Schnauzers, Yorkshire and Silky Terriers, non-sporting breeds and perhaps miniature poodles are at increased risk. Hereditary pancreatiitis occurs in people but has not been shown in any dog breeds. An initial study suggesting that a variation of the SPINK gene is associated with panreatitis in Minature Schnauzers was refuted by a subsequent larger study. Hypertriglyceridemia is a risk factor and may be why Miniature Schnauzers are overrepresented. Hypothyroidism, diabetes mellitus and hyperadrenocorticism are commonly reported co-morbidities with pancreatitis, perhaps due to alterations in serum lipid concentrations. Drugs that have been reported to cause/be associated with pancreatitis include azathioprine, chlorthiazine, hydrochlorthiazide, zinc, potassium bromide, vinblastine, sulphonamides, cisplatin, organophosphates, asparginase and 5-aminosalicylate. Note that the potential for glucocorticoids to directly cause pancreatitis in dogs is now largely dismissed, as corticosteroids increase nonspecific lipase activity but not canine pancreatic lipase (cPL) without causing pancreatic inflammation. Dietary risk factors include dietary indiscretion, high-fat low-protein diets, and high fat diets, but these risk factors remain unproven at a cellular level. Pancreatitis is reported after abdominal surgery, especially surgery for gastric-dilatation volvulus and adrenalectomy, likely related to hypotension and hypoxemia. One case control study found an interesting (if unexplained) association with pancreatitis in dogs (especially intact males) that had a previous surgery other than neutering. Despite the experimental association between premature trypsin activation and hypercalcemia, diseases (such as lymphoma) that cause hypercalcemia do not have a reported association with pancreatitis in dogs.

Risk factors: Cats

No age, gender or breed predisposition has been recognized in cats with pancreatitis and no relationship has been established with body condition score (most surveys associate it with underweight body condition, not obesity). A wide age range (5 weeks to 20 years) has been reported, but cats older than 7 years are more likely to be affected. In most cases, an underlying cause or instigating event cannot be determined, leading to classification as idiopathic. Abdominal trauma, infectious diseases (toxoplasmosis, liver flukes, FIP and FIV), lipodystrophy, and organophosphate administration have been associated with feline pancreatitis, but appear to account for a very small percentage of cases.

Hypercalcemia precipitated pancreatitis in one experimental study in cats and aspirin induced pancreatic cell damage in another. Evidence for glucocorticoid administration as a cause of acute pancreatic inflammation remains anecdotal in cats. The causal role of intercurrent inflammation in the billiary tract and/or intestine in the pathogenesis of pancreatitis remains the subject of speculation. Cholangitis is the most important type of biliary tract disease with which an association has been made.

Clinical presentation: Dogs

Common clinical signs in dogs are lethargy, anorexia, hunched stance, vomiting (± blood), diarrhea/hematochezia (33%), and increased respiratory rate. Physical examination findings are highly variable and include fever (32%), depression, dehydration, apparent abdominal pain, shock, petechiation, icterus and ascites. Vomiting is a relatively consistently reported clinical sign in dogs (90% of cases) and abdominal pain is common (58%), making pancreatitis relatively easy to recognize in this species. Some dogs with pancreatitis, however, exhibit few localizing clinical signs. Especially in such cases, diagnosis requires a high index of suspicion and use of additional diagnostic tests, particularly evaluation of sonographic findings, serum enzyme activities and cPL results, and careful exclusion of other diseases that may cause similar clinical signs. Occasionally diabetes mellitus will develop in conjunction with AP, either transiently while the pancreatic inflammation is active, or permanently, presumably due to destruction of a critical number of pancreatic beta cells.

Clinical Presentation: Cats

Lethargy (86-100%) and partial to complete anorexia (95-97%) are the most common clinical signs in cats diagnosed with acute necrotizing pancreatitis. All other clinical signs occur only sporadically. In particular, “textbook” signs of pancreatitis in dogs are usually absent – vomiting occurring in 35-52% of cats, abdominal pain in 25%, diarrhea in 15%, and fever in only 7%. Other reported physical examination findings are dehydration (92%), tachypnea (74%), hypothermia (68%), tachycardia (48%), and dyspnea (20%). Almost one-quarter of cats with pancreatitis (23%) have a palpable abdominal mass that may/may not appear painful and can be easily misdiagnosed as a lesion of another intra-abdominal structure. Some cases of AP are associated with severe clinical syndromes: shock, disseminated intravascular coagulation (DIC) and multi-organ failure. Both acute and chronic pancreatitis may be involved in the development of transient or permanent diabetes mellitus.

Laboratory findings: Dogs

Findings on the CBC are highly variable, ranging from mild neutrophilia and slightly increased hematocrit, through marked leukocytosis with a left shift, to thrombocytopenia, anemia and leukopenia with a degenerative left shift. If thrombocytopenia is detected, further coagulation testing is performed to rule out DIC. Serum biochemical abnormalities include azotemia (pre-renal and renal),

increased liver enzymes, hyperbilirubinemia, lipemia, hyperglycemia, hypoproteinemia, hypocalcemia, metabolic acidosis and variable alterations (usually decreases) in sodium, potassium and chloride. Obtaining a urinalysis enables azotemia to be better characterized as renal or pre-renal. Transient proteinuria occurs in some dogs with acute pancreatitis.

Measurement of serum amylase and/or lipase activities in dogs is meaningful in the diagnosis of pancreatitis, even though the sensitivity of these tests is relatively low, meaning that some dogs with confirmed pancreatitis have normal values of one or both enzymes. For example, in two case series of dogs with histologically confirmed pancreatitis, lipase was normal in 28 and 61% of dogs, and amylase was normal in 31 and 47% of dogs, respectively. Additionally, dogs with non-pancreatic disorders may have increased enzyme activities. Many different cell types in the body synthesize and secrete lipases and contribute to total lipase. Serum activities of some lipases may increase with non-pancreatic disorders including intestinal obstruction (amylase), corticosteroid administration (lipase) and azotemia (both enzymes).

The cPLI test was developed at Texas A&M University to provide a test that measures only lipase of pancreatic origin. Commercially available as the SNAP and Spec cPL tests (Idexx), estimates for cPL sensitivities and specificities, respectively, are 91.5 - 94.1% and 71.1 - 77.5% for SNAP and 71.7 - 77.8% and 80.5 – 88.0% for SPEC (cutoff of 400 mg/L). SNAP and SPEC cPL have higher sensitivity for diagnosing clinical AP than does serum amylase or lipase activity. A positive SPEC or SNAP has a good positive predictive value in populations likely to have acute pancreatitis and a good negative predictive value when there is low prevalence of disease. Test specificity of either the SNAP or Spec cPL indicate that, even in a dog with a positive cPL test, attention must be paid to ruling out other diseases that may produce similar clinical signs, such as intestinal foreign body. The effect of azotemia on the cPLI test was investigated and it was found that serum cPLI was significantly higher in dogs with experimentally induced chronic renal failure than in clinically healthy dogs, but most renal failure dogs still had concentrations within the reference range.

Laboratory Evaluation: Cats

Hematologic abnormalities in cats with pancreatitis are non-specific. In cats with APN, findings include non-regenerative anemia (26%), hemoconcentration (13%), leucocytosis (30%), and leukopenia (15%). Biochemical abnormalities in affected cats often reflect concurrent disease. High serum bilirubin concentrations and increases in liver enzyme activities are common. Serum glucose and cholesterol concentrations may be high, and azotemia and decreases in serum potassium and calcium concentrations are common. Low plasma ionized calcium concentration has been correlated with a poorer outcome in cats with APN.

Serum lipase activity is modestly increased very early in experimental feline pancreatitis but serum amylase actually decreases. Serum activities of both enzymes are frequently normal in cats with spontaneous pancreatitis. Increased

amylase and lipase are both associated with chronic malabsorption (chronic intestinal disease) and both may increase whenever the glomerular filtration rate is reduced. Therefore, neither serum lipase or amylase activities are of clinical value in the clinical diagnosis of pancreatitis in cats. The Spec fPL assay is a monoclonal ELISA that has recently become commercially available. A study presented in abstract form (ACVIM Forum 2009) estimated the sensitivity of this test for diagnosing pancreatitis at 79% and the specificity at 82% using a diagnostic cutoff of >= 5.4 µg/L. The SNAP fPL provides a useful point-of-care test that can be very helpful for ruling out pancreatitis. As with the Spec fPL, a positive test must be interpreted in light of other clinical information.

Diagnostic Imaging: Dogs

Radiographic signs of AP are nonspecific and don't often contribute to diagnosis except by eliminating the presence of intestinal obstruction. Radiographic findings may include loss of serosal detail, increased opacity in the right cranial quadrant of the abdomen, displacement of the duodenum ventrally and/or to the right, dilated hypomotile duodenum and caudal displacement of the transverse large intestine. Punctate calcification is occasionally identified due to saponification of mesenteric fat in the region of the pancreas. Thoracic radiographs may detect pleural fluid or pulmonary edema, both of which have been associated with acute pancreatitis, and pneumonia occasionally develops in dogs that are ill with pancreatitis.

Ultrasonographic evaluation of the abdomen may identify a pancreatic mass or an enlarged hypoechoic pancreas that may be surrounded by a hyperechoic rim, representing an increase in echogenicity of the peripancreatic fat. Pancreatic changes may be diffuse or involve one limb or region of the pancreas. Pancreatic cysts can also be identified. Ultrasound-guided fine needle aspiration of the pancreas for cytologic evaluation is being performed more commonly and can help confirm the diagnosis.

Diagnostic Imaging: Cats

As in dogs, exclusion of some of the other causes of vague gastrointestinal signs, is a major rationale for survey abdominal radiographs in cats with the clinical signs described above. The findings in cats with pancreatitis are similar to those listed for dogs.

Abdominal ultrasonography is a key diagnostic test in cats with suspected pancreatitis. Findings may include peritoneal effusion, a hypoechoic pancreas with hyperechoic peripancreatic fat and mesentery, cavitary lesions, a mass effect in the cranial abdomen, and/or biliary duct dilation. One feline study showed abdominal ultrasound had a sensitivity of 24% for detecting pancreatitis. This means that in some cats with biopsy-confirmed AP there will be no detectable abnormalities. Abnormal sonographic findings, however, are highly specific for pancreatitis, meaning that a cat with compatible clinical signs and changes in the pancreas on sonography is very likely to be correctly diagnosed

with pancreatitis. Ultrasound-guided fine needle aspirates of the pancreas and peri-pancreatic tissue and/or fluid may assist in the diagnosis of pancreatitis.

Biopsy

Pancreatic biopsy may be obtained by laparoscopy or exploratory laparotomy but is rarely indicated clinically and dogs and cats with AP are often poor anesthetic risks. Gross observation at the time of laparoscopy or exploratory laparotomy done primarily because of hepatic or intestinal disease may raise the index of suspicion of pancreatitis and warrant biopsy. Biopsies may be safely performed as long as blood flow is preserved. A single biopsy may be insufficient to exclude pancreatitis as inflammation may occur in discrete areas within the pancreas, and this may be sufficient to cause an increased cPL or fPL. Especially in cats, close inspection and possible biopsy of other viscera (e.g., intestine, biliary tract, liver) is of paramount importance because of the high rate of concurrent inflammation in these organs in cats. The clinical significance of lymphocytic inflammation in both species remains to be clarified, as it can be found at necropsy in patients with no history suggestive of pancreatic disease. However, it may also be compatible with chronic pancreatitis.

In studies on feline liver disease at the University of Minnesota, we reported that 83% of cats with cholangitis also had inflammatory changes in the bowel and 50% had evidence of concurrent chronic pancreatitis. Concurrent inflammation in these three organs has been termed “triaditis”. This association has been confirmed histologically in subsequent studies, but further investigation is warranted to determine the how often the clinical syndromes occur concurrently. Awareness of the association of these three disorders, however, may affect the diagnostic evaluation of individual patients.

Therapy: Dogs and Cats

Fluids and Electrolytes

The initial medical management of dogs and cats with acute pancreatitis must not be delayed until a diagnosis is confirmed. In experimental studies, one of the major factors in the progression of mild pancreatitis to severe pancreatitis is disturbed pancreatic microcirculation. Early intravenous fluid therapy with Lactated Ringers solution or 0.9% NaCl, supplemented with potassium and glucose as necessary, is recommended. One human study has shown that early fluid resuscitation (compared to fluid resuscitation 24 and 72 hours after the onset of pain) led to a better clinical outcome. Using LRS produced a better outcome that using normal saline.

Potassium supplementation (20-30 mEq/l KCl to start) is necessary to replace losses in diarrhea, vomitus, and urine and supplement the lack of food intake and should be based on serial measurement of serum potassium levels. Symptomatic hypocalcemia (tremors, seizure activity) is a possible complication of acute pancreatitis and requires that calcium gluconate be given at doses of 50-150 mg/kg intravenously over 12-24 hours and serum ionized calcium concentrations monitored during therapy. Insulin therapy is initiated in diabetic patients.

An experimental study in dogs with induced acute pancreatitis showed that dogs resuscitated with LRS alone required approximately 5L more fluid to maintain systemic pressures than dogs resuscitated with cystalloids and colloids. Colloids such as dextrans are also useful for hypoproteinemia and may have antithrombotic effects that help maintain the microcirculation. Plasma transfusion has been as been previously recommended to provide a fresh source of protease inhibitors and to provide coagulation factors, but its use in AP has been declining. There are no prospective studies examining the benefit of plasma transfusion in dogs or cats with naturally occurring pancreatitis. A report on a retrospective canine study indicated a significantly higher mortality (7/20) in dogs that received plasma than those that did not (6/57). Due to the retrospective nature of the study, there was no stratification based on disease severity nor control of any other treatments. The results, however, reflect much of the human literature on the same subject, and plasma adminsitration is not currently recommended.

Antiemetics and Gastroprotectants

Nausea and vomiting may be severe in patients with pancreatitis. The potent antiemetic, maropitant (Cerenia®), an NK_1 receptor antagonist, is very useful in controlling emesis associated with pancreatitis in both dogs and cats. It is administered in dogs at 2 mg/kg PO and 1 mg/kg SQ (refrigerate before administering) or IV once a day. In cats it is dosed at 1 mg/kg regardless of route of administration (SQ and PO use are extra-label). An alternative antiemetic for both species is a 5-HT_3 antagonist (ondansetron (Zofran®) 0.1-0.5 mg/kg IV *bid* or dolasetron (Anzemet®) 0.1-0.5 mg/kg IV *bid*). The dopaminergic antagonist, metoclopramide, may be useful to enhance motility in the upper gastrointestinal tract. It also acts as a weak peripherally-acting antiemetic in dogs but this effect is questionable in cats. Additionally, experimental rodent studies show benefit to dopamine infusion in acute pancreatitis, so there is a theoretical drawback to its use. The α_2 adrenergic antagonists are also effective antiemetics, including for cats; chlorpromazine (Thorazine®) is dosed at 0.2-0.4 mg/kg subcutaneously or intramuscularly every 8 hours, and Prochlorperazine (Compazine®) at 0.5 mg/kg *tid* SQ or IM.

Gastric acid suppression is commonly incorporated into the therapy of pancreatitis in both dogs and cats. The rationale includes protecting the esophagus from exposure to gastric acid during episodes of vomiting, protecting against gastric ulceration to which pancreatitis patients may be predisposed due to hypovolemia and local peritonitis, and that a higher gastric pH may reduce pancreatic secretion. Additionally, there may other benefits. A higher gastric pH may decrease exocrine pancreatic stimulation but remains undocumented as a treatment for pancreatitis. In human pancreatitis patients, nasogastric suctioning has failed to show any benefit in reducing pain or shortening hospitalization time. If gastric acid suppression is required, it is theoretically preferable to select a proton pump inhibitor (PPI) than an H_2-receptor antagonist. In addition to PPIs being more effective at reducing gastric acidity in dogs, an experimental study in rats showed that pantoprazole reduced inflammatory changes and leakage of pancreatic acinar cells.

Analgesics

Analgesia is an important aspect of treatment of pancreatitis. It can be easily overlooked in cats as they may not exhibit easily-recognized signs of pain. Analgesia can be provided using injectable opioids such as buprenorphine (cats: 0.005-0.01mg/kg SC or sublingual [transmucosal] q6-8hrs), butorphanol (dogs: 0.2-0.4 mg/kg SC q6hr) or oxymorphone (dogs: 0.1-0.2mg/kg IM, SC Q 1-3hrs). A transdermal fentanyl patch is a good way of providing a longer duration (72 hours) of analgesia but adequate fentanyl blood levels are not attained for about 24 hrs after application in dogs and about 12 hours in cats, so another analgesic should be administered during this period. Tramadol is usually avoided in cats as it can cause severe dysphoria. There is emerging evidence that the antiemetic, maropitant, also provides good visceral analgesia in dogs and cats.

Nutritional Support

In dogs and cats suspected of having acute pancreatitis, oral intake has historically been withheld for the initial 24-48h (or longer) and then gradually re-introduced as tolerated. The theory behind holding animals NPO (nothing by mouth) was to "rest the pancreas" by decreasing pancreatic stimulation. This rationale has come under close scrutiny in human and veterinary medicine and is no longer the standard of care. Currently, antiemetics are used immediately and as required to get vomiting controlled, and nasoesophageal feeding by slow infusion is begun as soon as possible (or gradual oral alimentation, if possible). This approach attempts to maintain enterocyte integrity and reduce the risk of bacterial translocation. Parenteral nutrition is indicated in feline patients only when vomiting precludes enteral support.

Recent studies in people indicate that enteral nutrition, administered via a naso-jejunostomy tube, can attenuate the systemic inflammatory response and may decrease complications. Due to technical difficulties associated with nasojejunal (NJ) feeding, human studies have assessed delivery into the stomach (nasogastric or NG). NG feeding was shown to be as well tolerated as NJ feeding, and there was no increase in pain upon feeding. This has been investigated in a prospective pilot study in dogs that demonstrated esophageal tube feeding was well tolerated in dogs with AP. This study compared enteral feeding to TPN, and was unable to show a statistically significant difference in outcome or other parameters. However, the enteral feeding group had significantly fewer episodes of vomiting and/or regurgitation.

In dogs and cats, as the appetite returns, small amounts of food can be frequently offered. In dogs, the diet selected is usually highly digestible and relatively low in fat, although there are no specific studies to support this choice. Boiled rice, rice with chicken, low fat cottage cheese, or prescription diets such as i/d® (Hills Pet Products), EN® (NestlePurina), or Gastrointestinal LF (Royal Canin) are often selected. The size of the meals should be slowly increased and the frequency of feeding decreased if vomiting does not recur. After about 3 days, the usual diet can be slowly re-introduced. Continued fat restriction is usually

recommended for dogs that have had pancreatitis.

In cats, a nasoesophageal tube is usually placed for short-term, in-hospital feeding. It can be replaced by a gastrostomy or esophagostomy tube for longer-term feeding in severe cases or in cats with concurrent diseases, such as hepatic lipidosis, that prolong their return to unassisted feeding. A low-fat diet is not thought to be of benefit in cats. The author's choice is to feed cats with a history of pancreatitis a diet high in antioxidants, and to provide SAMe (see below) as a supplement, based on preliminary human and canine evidence that antioxidant supplementation (selenium) is beneficial.

Antibiotics

Acute pancreatitis is thought to begin as a sterile process in dogs and reports of bacterial complications, such as pancreatic abscessation, are very uncommon. Prophylactic broad-spectrum antibiotics (e.g., amoxicillin ± enrofloxacin depending on severity) may be warranted in patients with shock, fever, or evidence of break down of the GI barrier but are not otherwise routinely used. Recent studies in cats using culture-independent methods suggest that greater consideration may need to be given to bacterial infection in cases of feline pancreatitis. Coliforms are the principal pathogens, as they are in bile cultures from cats with cholangitis. Broad-spectrum antibiotics may, therefore, be appropriate in cases of feline acute pancreatitis.

Surgery

Surgery is rarely needed to remove devitalized or infected tissue. Serum bilirubin may remain increased for weeks during apparent recovery from a bout of pancreatitis, especially in dogs, but only rarely is surgery required to relieve an obstruction of the common bile duct. Resection or surgical drainage of pancreatic pseudocysts is not usually necessary as these can resolve spontaneously or following ultrasound-guided percutaneous drainage. Surgery to treat pancreatic acute fluid collections in dogs has invariably resulted in a high mortality rate (> 50%), regardless of the technique used. Spontaneous resolutions of acute fluid collections have been reported, as well as good responses to percutaneous drainage, as noted above, suggesting non-invasive methods are preferable for managing this particular complication.

Glucocorticoids

Historical reluctance to use corticosteroids in dogs or cats with pancreatitis came from the presumption that corticosteroids could lead to pancreatitis. This concern may have arisen, in part, from an early canine study showing that dexamethasone increased serum activity of pancreatic enzyme concentrations, but it has been shown that there is no effect on pancreatic tissue. Corticosteroids are no longer considered high risk in human patients and are under evaluation in patients with acute pancreatitis. Corticosteroids exert a broad anti-inflammatory effect and, in addition, a specific role for corticosteroids in enhancing apoptosis

and increased production of pancreatitis-associated protein, which confers a protective effect against inflammation, has also been proposed. One other rationale for the use of corticosteroids in patients with pancreatitis is relative adrenal insufficiency (now termed critical illness-related corticosteroid insufficiency or CIRCI), a relative adrenal insufficiency along with tissue resistance to the effects of steroids due to a prolonged and severe severe proinflammatory state. For these reasons, the question of steroid use in dogs and cats with pancreatitis is being questioned but remains unexamined. Judicious use of corticosteroids is increasingly considered in animals with severe AP that are failing to respond to conventional therapies. Coexisting conditions, such as inflammatory liver disease and inflammatory bowel disease are common in cats with pancreatitis and must be managed concurrently. There is no evidence that steroid use is problematic in cats with apncratitis when necessary for controlling such problems. Additionally, anti-inflammatory doses of steroids are increasingly being used in cats with presumed chronic (or intermittent relapsing) pancreatitis, along with mirtazapine for appetite stimulation (and a theoretical antiemetic effect as well).

Other Therapies

Two drugs are of interest based on experimental data but they have not yet been investigated in clinical pancreatitis. Treatment with H_1 or H_2 histamine receptor antagonists protects against the development of hemorrhagic pancreatitis in these models. For this reason, and to mitigate the esophageal effects of vomiting acidic gastric contents, an H_2-receptor antagonist such as famotidine (0.5-1.0 mg/kg every 12-24 h) is usually administered. Although not in clinical use, low-dose dopamine infusion (5 µg/kg/min) improves pancreatic blood flow and reduces microvascular permeability in experimentally induced acute feline pancreatitis, even when it is given up to 12 hours after induction of the disease. Histamine and bradykinin-induced increases in microvascular permeability are associated with the development of hemorrhagic necrosis in experimental feline pancreatitis.

Based on experimental evidence and experience in human patients with pancreatitis, some referral centers are using hyperbaric oxygen treatments in dogs with severe pancreatitis. No outcome data is available at present.

Summary

In spite of advances in diagnostic capabilities, especially ultrasonography and cPL and fPL, the diagnosis of pancreatitis remains challenging in many cases, especially in cats. As the therapy for many causes of acute vomiting is similar to pancreatitis, misdiagnosing a case as having pancreatitis often does not have adverse consequences. However failure to perform additional diagnostic tests in cases with gastric or duodenal ulcer disease, foreign body intestinal obstruction, intussusception, or acute renal or liver failure, can have dramatic consequences. There is currently no single specific test for pancreatitis

and diagnosis is based on a combination of compatible clinical, clinicopathological and imaging findings. Further studies are needed that correlate laboratory findings with simultaneously obtained pancreatic biopsies. Improved diagnostic and management information about chronic pancreatitis in both species, but especially in cats, is urgently needed. Therapy is currently supportive with fluid and colloidal support, antiemetics, acid inhibition, analgesics, and enteral nutritional support (as soon as vomiting is controlled) providing the mainstays of therapy. Once the diagnostic hurdles are surmounted, further work on risk factors (to guide prevention strategies) and on treatment will be possible

Pancreatitis In Dogs Versus Cats

	CANINE	FELINE
Prevalence	1.0% of 9,342 dogs on necropsy >90% of cases undiagnosed (results on recent necropsy study)	0.6% of 6,504 cats on necropsy 67% of cats presented for necropsy (45% of healthy cats)
Classic Signalment	Age: Middle-aged to older Sex: Male or Female Breeds predisposed: Schnauzers, Yorkshire terriers, poodles	Age: Middle-aged to older Sex: Male or female Breeds predisposed: Possibly Siamese
Weight	Often obese	Often underweight or history of weight loss
Risk Factors	Drugs: Potassium bromide, azathioprine, furosemide, tetracycline, aspirin, sulfa drugs, L-Asparaginase, zinc toxicosis Diet: High-fat foods; dietary indiscretion Hyperlipidemia (e.g., familial in miniature schnauzers) Hypercalcemia Hypothyroidism Hyperadrenocorticism Blunt trauma	Drugs: Organophosphates infectious causes: Toxoplasma gondii, pancreatic fluke (Eurytrema procyonis), liver fluke (Amphimerus pseudofelineus); Viral – FIP, herpesvirus, VS-calicivirus Diet: High-fat foods not implicated in cats Hypertriglyceridemia Hypercalcemia Blunt trauma
Common Concurrent Diseases	Familial hyperlipidemia in miniature schnauzers Diabetes mellitus	Hepatic lipidosis Cholangitis Inflammatory bowel disease Diabetes mellitus
Clinical Signs*	Anorexia Vomiting	Lethargy Anorexia/decreased appetite

	Weakness Abdominal pain Dehydration Diarrhea	Dehydration Weight loss Icterus Vomiting Fever Abdominal pain Diarrhea Palpable abdominal mass
CBC*	Thrombocytopenia Neutrophilia with left shift Anemia Nonregenerative anemia Leukocytosis Leukopenia	Neutrophila Leukopenia Nonregenerative anemia Hemoconcentration Lipemia
Chemistry Profile*	Increased liver enzymes Azotemia Electrolyte imbalances Hyperbilirubinemia Hypoalbuminemia Hypercholesterolemia Hypoglycemia Hyperglycemia	Hypercholesterolemia Hyperbilirubinemia Increased liver enzymes Hyperglycemia Azotemia Electrolyte imbalances Hypoalbuminemia Hypocalcemia
Amylase and lipase	55% sensitive, 73% if 3X upper limit of reference interval Specific if 2-3X upper limit of the reference interval Trending increases utility Amylase: Sensitivity 52.4-56.0% Specificity 76.7-80.6% Lipase: Sensitivity 43.4-53.6% Specificity 89.3-92.5%	Neither amylase nor lipase shown to be useful
Radiographs	Nonspecific (24%) Identify obstruction, radiodense foreign bodies, etc.	Nonspecific Identify obstruction, identify radiodense and suspect linear foreign bodies, etc.
Abdominal Ultrasound	Up to 68% sensitive High specificity with experienced ultrasonographer	24-67% sensitive 73% specific
TLI**	33% sensitive 65% specific	28% sensitive 75% specific
Pancreas-	82% sensitive	67% overall sensitive

Specific lipases Spec cPL/SNAP cPL Spec fPl /SNAP fPL	>95% specific Spec cPL (> 400 mg/L) Sensitivity 71.7 - 77.8% Specificity 80.5 – 88.0% SNAP cPL Sensitivity 91.5 - 94.1% Specificity 71.1 - 77.5%	(54% in mild cases 100% in severe cases) 91% overall specificity (67% in symptomatic cats 100% in healthy cats) 79.4% sensitivity and 79.7% specificity in a recent study of 182 cats using a Spec cutoff of 5.4 ug/L.[a]

*Listed in order from most to least frequent findings.
** Note that serum TLI concentration remains the diagnostic test of choice for exocrine pancreatic insufficiency in both dogs and cats.
+ McCord K, et al. J Vet Intern Med 2012; 26:888-96.
[a] Forman MA, Armstrong PJ, Robertson J. J Vet Intern Med 2009;23:733-4 [abstract].

Selected References: Dogs

1. Mansfield C. Acute pancreatitis in dogs: Advances in Understanding, diagnostics and treatment. Topics in Compan An Med 2012;27:123-32.
2. Watson P. Chronic pancreatitis in dogs. Topics in Compan An Med 2012;27:133-9.
3. Furrow E, Armstrong PJ, Patterson EE. High prevalence of the c.74A>C SPINK1 variant in Miniature and Standard Schnauzers. J Vet Intern Med 2012;26(6); 1295-9.
4. Newman S, Steiner J, Woosley K, et al. Localization of pancreatic inflammation and necrosis in dogs. J Vet Intern Med 2004;18:488–93.
5. Newman SJ, Steiner JM, Woosley K, et al Histologic assessment and grading of the exocrine pancreas in the dog. J Vet Diagn Invest 2006; 18:115-8.
6. Mansfield CS, Anderson GA, O'Hara AJ. Association between canine pancreatic-specific lipase and histologic exocrine pancreatic inflammation in dogs: assessing specificity. J Vet Diag Invest 2012; 24(2):312-8.
7. Trivedi S, Marks SL, Kass PH, et al. Sensitivity and specificity of canine pancreas-specific lipase (cPL) and other markers for pancreatitis in 70 dogs with and without histological evidence of pancreatitis. J Vet Intern Med 2011;25:1241-
8. Neilson-Carley SC, Robertson JE, Newman SJ, et al. Specificity of a canine pancreas-specific lipase assay for diagnosing pancreatitis in dogs without clinical or histological evidence of the disease. Am J Vet Res 2011;72:302-7.
9. McCord K, Morley PS, Armstrong PJ, Simpson K, Rishniw M, Forman M, Biller D, Parnell N, Anrell K, Hill S, Avgeris S, Gittelman H, Moore M, Hitt M, Oswald G, Marks S, Burney D, Twedt D. A multi-institutional study evaluating the diagnostic utility of the Spec cPL™ and SNAP® cPL™ in clinical acute pancreatitis in 84 Dogs. J Vet Intern Med 2012; 26:888-96.
10. Hess RS, Saunders HM, Van Winkle TJ, et al. Clinical, clinicopathologic, radiographic, and ultrasonographic abnormalities in dogs with fatal acute

pancreatitis: 70 cases (1986–1995). J Am Vet Med Assoc 1998;213:665–70.
11. Warndorf MG, Kurtzman JT, Bartel MJ, et al: Early fluid resuscitation reduces morbidity among patients with acute pancreatitis. *Clin Gastroenterol Hepatol* 2011; 9:705-9.
12. Hackert T, Tudor S, Felix K, et al. Effects of pantoprazole in experimental acute pancreatitis. Life Sciences 2010;87:551-7.
13. Mansfield CS, James FE, Steiner J, et al. A pilot study to assess tolerability of early enteral nutrition via esophagostomy tube feeding in dogs with severe acute pancreatitis. J Vet Intern Med 2011;25:419-25.
13. Weatherton LK, Streeter EM. Evaluation of fresh frozen plasma in dogs with pancreatitis: 77 cases (1995-2005). J Vet Emerg Crit Care 2009; 19:617-22.

Selected References: Cats

1. Armstrong PJ and Williams DA. Pancreatitis in cats. Topics in Compan An Med 2012;27:140-7.
2.De Cock HE, Forman MA, Farver TB, et al. Prevalence and histopathologic characteristics of pancreatitis in cats. Vet Pathol 2007;44:39–49.
3. Forman MA, Marks SL, De Cock HE, et al. Evaluation of serum feline pancreatic lipase immunoreactivity and helical computed tomography versus conventional testing for the diagnosis of feline pancreatitis. J Vet Intern Med. 2004;18:807–15.
4. Ferrari JA, Hardam E, Kimmel SE, et al. Clinical differentiation of acute necrotizing from chronic nonsuppurative pancreatitis in cats: 63 cases (1996-2001). J Am vet Med Assoc 2002;223:469-74.
5. Gerhardt A, Steiner J, Williams D, et al. Comparison of the sensitivity of different diagnostic tests for pancreatitis in cats. J Vet Intern Med 2001;15:329–33.
6. Mansfield CS and Jones BR. Review of feline pancreatitis part two: clinical signs, diagnosis and treatment. J Fel Med Surg 2001;3:125-32.
7. Swift, NC; Marks SL, MacLachlan NJ, Norris CR. Evaluation of serum feline trypsin-like immunoreactivity for the diagnosis of pancreatitis in cats. J Am Vet Med Assoc. 2000;217:37–42.
8. Hill RC, Van Winkle TJ. Acute necrotizing pancreatitis and acute suppurative pancreatitis in the cat. A retrospective study of 40 cases (1976–1989). J Vet Intern Med. 1993;7:25–33.