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CANINE PANCREATITIS: DIAGNOSIS AND MANAGEMENT
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CLINICAL PRESENTATION
Middle aged to older dogs (>5yrs years old) who are overweight or obese appear at risk for developing acute pancreatitis. Miniature Schnauzers, Yorkshire and Silky Terriers, non-sporting breeds and perhaps miniature poodles may be at increased risk. There is no clear sex predisposition. Hypertriglyceridemia is a risk factor and may be one factor for why Miniature Schnauzers are overrepresented in studies on this disease. Analysis of the *SPINK1* gene (which encodes for pancreatic secretory trypsin inhibitor) in Miniature Schnauzers revealed 3 closely associated variants in healthy Miniature Schnauzers and Miniature Schnauzers with pancreatitis. In healthy dogs of other breeds, only 2 exon variants of this gene were identified, suggesting that variants of the *SPINK 1* gene may be associated with the development of pancreatitis in the Miniature Schnauzer. Hypothyroidism, diabetes mellitus and hyperadrenocorticism may also be risk factors for pancreatitis. The history may reveal a recent episode of dietary indiscretion or drug administration. Common clinical signs include lethargy, anorexia, hunched stance, vomiting (± blood), diarrhea (± blood), increased respiratory rate and painful abdomen.

Physical examination findings in dogs with acute pancreatitis are highly variable and include lethargy, dehydration, apparent abdominal pain, shock (tachycardia, prolonged capillary refill time, tacky mucous membranes, hypothermia), petechiation, icterus and ascites. An abdominal mass is palpated in some dogs. Some dogs with pancreatitis exhibit few localizing clinical signs. Especially in such cases, diagnosis requires a high index of suspicion. 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 are required to establish a clinical diagnosis.

LABORATORY FINDINGS
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, blood clotting tests (OSPT, APTT, FDP) are performed to determine if the patient has disseminated intravascular coagulopathy (DIC). Serum biochemical abnormalities are also variable and include azotemia (pre-renal and renal), increased liver enzymes (ALT, AST, ALP), 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. In dogs, the presence of glucosuria and/or ketonuria should prompt consideration of diabetes mellitus, which may be transient while the pancreatic inflammation is active or permanent, presumably due to destruction of a critical number of pancreatic beta cells.

Classically, increases in serum amylase and lipase activity have been used as indicators of pancreatic inflammation in dogs. These tests are not very accurate because dogs with non-pancreatic disorders may have elevated enzyme activities. Many different cell types in the body synthesize and secrete lipases. Serum activities of some lipases may increase with non-pancreatic disorders including intestinal obstruction (amylase), corticosteroid administration (lipase) and azotemia (both enzymes). Dogs with confirmed pancreatitis may also have normal amylase and lipase activities. 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. These limitations led to development of canine pancreatic lipase immunoreactivity (cPLI) with the goal of developing a more sensitive and specific blood test for pancreatitis. In comparisons of the different diagnostic tests in dogs with biopsy-proven pancreatitis, the sensitivity of serum TLI concentration was below 40% and that of serum lipase activity was about 60% (see table, below). (Note that serum cTLI concentration remains the diagnostic test of choice for exocrine pancreatic insufficiency). The sensitivity for serum cPLI for pancreatitis was above 80%, using a positive at >250 ug/L. The effect of azotemia on this 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 had serum cPLI concentrations within the reference range and none of the dogs had serum cPLI concentrations that were above 200 µg/L.

The cPLI test, developed at the Gastroenterology Laboratory at Texas A&M University, has now been made commercially available through Idexx Laboratories as the cPL test and as a semi-quantitative in-house SNAP test. Based on limited data, serum cPL appears to be quite sensitive for the diagnosis of canine pancreatitis (93% using a cutoff of >400 ug/L). Test specificity of 78% using <200 ug/L indicates that, even in a dog with a positive cPL test, attention must still be paid to ruling out other diseases that may produce similar clinical signs.

IMAGING RESULTS

Radiographic signs of acute pancreatitis are nonspecific and don't often contribute to diagnosis except by eliminating the presence of intestinal obstruction. Radiographic findings in dogs with acute pancreatitis 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 in dogs with pancreatitis due to saponification of mesenteric fat in the region of the pancreas. Thoracic radiographs may enable the detection of 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. Pancreatic neoplasia can also be detected by pancreatic cytology. Examination of peritoneal fluid (spontaneous or obtained by peritoneal lavage) may

aid the differential diagnosis of acute abdominal signs including pancreatitis, gastrointestinal perforation or ruptured bile duct.

Sensitivity of available diagnostic tests for pancreatitis in dogs

Lipase	TLI	cPL	Radiology	Ultrasound
54.5-73% using >3x upper limit of range	36.4% using >50ug/L	93% using >400 ug/L	24%	68%

THERAPY

The initial medical management of dogs with acute pancreatitis must not be delayed until a diagnosis is confirmed. Intravenous fluid therapy with Lactated Ringers solution or 0.9% NaCl, supplemented with potassium and glucose as necessary is usually required. Potassium supplementation is necessary to replace losses in diarrhea, vomitus, and urine and supplement the lack of food intake. Potassium supplementation (20-30 mEq/l KCl to start), should be based on 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 total or ionized calcium concentrations monitored during therapy.

Plasma transfusion (12-20 ml/kg) has been recommended to provide a fresh source of protease inhibitors and may be indicated in the presence of hypoproteinemia or shock and to treat DIC. Colloids such as hetastarch are also useful for hypoproteinemia and may also have antithrombotic effects that help maintain the microcirculation. Dextran 40 may increase micro-perfusion. Insulin therapy is initiated in diabetic patients.

Nausea and vomiting may be severe in dogs with pancreatitis. The potent antiemetic, maropitant (Cerenia®, Pfizer), an NK_1 receptor antagonist, administered at 1 mg/kg subcutaneously once a day is very useful in controlling emesis associated with pancreatitis. Alternatives are one of the 5-HT_3 antagonists (ondansetron 0.1-1.0 mg/kg or dolasetron 0.5-1.0 mg/kg, orally or intravenously every 12-24 hours). The dopaminergic antagonist, metoclopramide, is a relatively weak antiemetic, but may be a useful adjunct to therapy to enhance motility in the upper gastrointestinal tract. An H_2 antagonist, such as famotidine, is recommended to protect the esophagus from exposure to gastric acid during episodes of vomiting and may have other benefits.

Analgesia is an important aspect of treatment of pancreatitis. It can be provided using injectable opioids such as buprenorphine (0.005-0.01mg/kg SC q6-12hrs) or oxymorphone (0.1-0.2mg/kg IM, SC Q 1-3hrs). A transdermal fentanyl patch is a good way of providing a longer duration of analgesia (10-20kg dogs, 50µg/hr patch q 72hrs) but adequate fentanyl blood levels are not attained for about 24 hrs after application in dogs, so another analgesic

In dogs suspected of having acute pancreatitis, oral intake has traditionally been withheld for the initial 48h or longer and then gradually re-introduced as tolerated. The rationale for giving nothing by mouth was to "rest the pancreas" by decreasing pancreatic stimulation. This rationale is coming under close scrutiny in human medicine and requires re-examination in dogs. 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. Recent studies in people indicate that enteral nutrition, administered via a naso-jejunostomy tube, can attenuate the systemic inflammatory response and may decrease complications. As the dog's appetite returns, small amounts of a bland diet can be frequently offered. This diet should be highly digestible, and relatively low in fat. Boiled rice, rice with chicken, low fat cottage cheese, or prescription diets such as i/d® (Hills Pet Products), EN® (Ralston Purina), or Low Residue (Iams) are effective. 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 normal diet can be slowly added. Continued fat restriction is usually recommended for dogs that have had 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.

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. Surgery is occasionally needed to remove devitalized tissue in the unusual case with infected pancreatic necrosis or pancreatic abscess. Serum bilirubin may remain increased for weeks during apparent recovery from a bout of pancreatitis, but only rarely is surgery required to relieve an obstruction of the common bile duct. Resection or surgical drainage of pancreatic pseudocysts is not always necessary as these can resolve spontaneously or following ultrasound-guided percutaneous drainage.

PROGNOSIS

The majority of dogs with acute pancreatitis respond to symptomatic therapy, as outlined above. The prognosis for dogs with mild acute pancreatitis is good. Severe or recurrent pancreatitis is associated with a more guarded prognosis. The presence of shock or abnormalities such as oliguria, azotemia, icterus, markedly elevated transaminases, hypocalcemia, hypoglycemia, hypoproteinemia, acidosis, marked leukocytosis, marked decrease in hematocrit, thrombocytopenia and DIC should be considered likely indicators of severe pancreatitis. Permanent diabetes mellitus occasionally follows a severe and/or recurrent pancreatitis. Because the etiology is unclear, recurrent bouts of pancreatitis can occur. Prevention strategies are currently not evidence-based, but may include continuing a well-controlled, fat restricted diet, increasing the omega-3 content of the diet, and supplementation with antioxidants.

SUMMARY
Acute pancreatitis is a relatively common cause of vomiting in dogs but the severity of signs is highly variable. Some cases present with mild self-limiting vomiting that is similar to cases of dietary indiscretion. Other cases have life-threatening vomiting and require intensive therapy. Death occurs in some cases despite rigorous therapy. Acute pancreatitis is difficult to definitively diagnose. 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 in dogs and diagnosis is based on a combination of compatible clinical, clinicopathological and imaging findings. Classic findings of include: 1) acute vomiting, 2) cranial abdominal pain, 3) pyrexia, 4) leukocytosis with a left shift, 5) elevated serum amylase and lipase, and 6) ultrasonographic findings of an enlarged hypoechoic pancreas. Supportive findings include: 1) signalment 2) recent fatty meal or dietary indiscretion, 3) lipemia, 4) hypocalcemia, 5) elevated ALT, ALP, and bilirubin 6) hypercholesterolemia and 7) increased cPL. Amylase and lipase can be useful as long as the clinician is aware of the other causes of increased amylase and lipase and does not rule out pancreatitis based on normal enzyme concentrations. Abdominal ultrasound has assumed a major role in the diagnosis of pancreatitis and the differentiation of pancreatitis from other pancreatic disorders, but a normal appearing pancreas (or inability to image the pancreas) does not rule out pancreatitis. Therapy is supportive with fluid and colloidal support, antiemetics, analgesics, and enteral nutritional support (as soon as vomiting is controlled) providing the mainstays of therapy.

SELECTED READINGS
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