V155
Pancreatitis in the Dog
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OBJECTIVES OF THE PRESENTATION
- The attendee will know the many and varied presentations of pancreatitis in the dog.
- The attendee will know the problems of diagnosis and best way to quickly and efficiently obtain a diagnosis.
- The attendee will know the treatment and the problems with treatment of acute pancreatitis.

GENERAL KEY POINTS
- Many dogs with acute pancreatitis present identical to septic peritonitis and cannot be readily distinguished except at exploratory laparotomy.
- Some patients present as though they were in septic shock.
- Canine pancreatitis is almost always a sterile process (unless the pancreatitis is secondary to sepsis, which is rare).

KEY CLINICAL DIAGNOSTIC POINTS
- Ultrasound, even in the hands of an excellent ultrasonographer, is probably only 60–75% sensitive.
- The cPLI test is the most sensitive test we currently have, but it is still only about 80% sensitive, and there are some clinically normal patients with high cPLI values.
- Sometimes you cannot diagnose pancreatitis until you do an exploratory laparotomy.
- Anytime you have extra-hepatic biliary tract obstruction in a dog, you need to consider the possibility of pancreatitis.

KEY ETIOLOGIC AND PATHOPHYSIOLOGIC POINTS
- Fat appears to be the key factor causing most pancreatitis in dogs.
- Pancreatitis can be a post-operative complication of surgery done near the pancreas.
- Canine pancreatitis is very, very rarely due to sepsis, and very, very rarely does it become septic.

KEY THERAPEUTIC POINTS
- This area is a very contentious one, and nobody has good data showing that one treatment is clearly effective or clearly ineffective.
- Since fat is a major cause of canine pancreatitis, do not be in a hurry to start feeding. When you do feed, feed a zero fat diet (not a low fat diet, but a zero fat diet) such as potato or rice.
- It is better to treat too aggressively (i.e., fluids, NPO, etc) than to treat too casually and then have a severe relapse.

KEY PROGNOSTIC POINTS
- Prognosis is difficult to predict, but SIRS seems to be ominous.

OVERVIEW OF THE ISSUE
History and physical examination are helpful, but not as useful as we'd like for diagnosing pancreatitis. Schnauzers and Yorkies are famous for pancreatitis, but these breeds get a lot of other diseases that cause vomiting, and pancreatitis can be found in any breed of dog. Canine pancreatitis is classically considered to present with acute vomiting and anorexia. Abdominal pain is frequently present, but it is easy to miss during physical examination, and fever is occasionally seen. However, we are recognizing more and more "atypical" cases to the point that we are no longer sure what a "typical" case of canine pancreatitis is. We are now recognizing more and more cases of severe disease which present in shock due to

systemic inflammatory response syndrome (what used to be called septic shock, until we found out that you can have the same thing occur with any cause of massive inflammation); such patients may die very suddenly. We are also recognizing more and more dogs with acute pancreatitis that present as though they had an acute, septic abdomen. Some have substantial amounts of abdominal fluid. If acute pancreatitis is associated with or due to pancreatic carcinoma (rare), you may also see a dog that has widespread subcutaneous fat necrosis causing sterile abscesses that are typically painful and cause cutaneous discoloration. Most cases of canine pancreatitis are related to either ingestion of fat or lipemia associated with diabetic ketoacidosis. Trauma and drugs can also cause canine pancreatitis. Drugs that are suspected of causing pancreatitis in people and animals include azathioprine, sulfonamides, tetracycline, and potassium bromide.

CBC's often show an inflammatory leukogram, but 1) this is a relatively nonspecific finding and may be due to any number of problems and 2) not all animals with acute pancreatitis have a notable leukocytosis. Degenerative left shifts and substantial toxicity of circulating WBCs can be seen if the patient is in systemic inflammatory response syndrome. Likewise, thrombocytopenia due to DIC is not infrequent in severely affected patients. However, some animals with clinically severe disease have absolutely normal leukogram.

Serum biochemical panels are not as helpful as we would like. At the time of this writing, there is no readily available biochemical test that has good positive or negative predictive values. Serum lipase and amylase activities are insensitive (each is about 50%) and nonspecific for pancreatitis and should probably never be requested. Dogs with acute pancreatitis and even pancreatic abscesses have had normal serum lipase activities. We have also identified dogs with drastically increased serum lipase activities that have intestinal foreign objects or gastritis, but no gross evidence of acute pancreatitis. Lipase is produced by the canine gastric mucosa which explains why inflammation or damage to the stomach can result in excessive serum lipase activity. Canine TLI is a little more specific than amylase and lipase, but it is still not a sensitive test (approx. 35%)—it has very poor negative predictive value. We have seen plenty of dogs with pancreatitis that had normal serum TLI's.

Dr. Joerg Steiner at Texas A&M has developed an immunoreactive canine pancreatic lipase assay (i.e., cPLI) that appears to be more sensitive (approx 80%) and specific than any of the other tests available. There are still some false positive and negative results with this test, but it is clearly much, much better than any other blood test available, and looks like it will be a major benefit to the diagnosis of canine pancreatitis.

Blockage of the main pancreatic duct due to swelling due to generalized pancreatitis, an intrapancreatic granuloma, or an abscess that subsequently blocks the pancreatic duct may cause extrahepatic biliary tract obstruction with a notable increase in serum alkaline phosphatase and serum bilirubin. In fact, pancreatitis is probably the most common cause of extrahepatic biliary tract obstruction in the dog. However, while the triad of vomiting, abdominal pain, and icterus is consistent with acute pancreatitis (as well as many other diseases), relatively few dogs with acute pancreatitis evidence these changes. Furthermore, there are reasons for this triad of signs besides acute pancreatitis and extrahepatic biliary tract obstruction (e.g., cholangitis-cholangiohepatitis). Ultrasonographic evaluation of the abdomen (discussed below) is particularly helpful in these patients.

Plain abdominal radiographs help eliminate other diseases which may mimic acute pancreatitis. Not finding evidence of other abdominal disease (such as a foreign object) is helpful in eliminating obstruction and narrowing the list of differential diagnoses. Occasionally, one will find radiographic signs which specifically suggest acute pancreatitis: A sentinel loop (i.e., a dilated, air-filled segment) in the descending duodenum, lack of serosal detail in the upper right abdominal quadrant, lateral displacement of the descending duodenum on the ventro-dorsal projection, a mass medial to the descending duodenum (on the ventro-dorsal projection) and/or a mass just behind the liver and just below the pylorus (on the lateral projection) can be suggestive of pancreatitis. These findings are only meaningful if present; many dogs and cats with acute pancreatitis do not have these radiographic findings. Probably the greatest value of abdominal radiographs is that they help eliminate other diseases that could be causing signs similar to those caused by pancreatitis.

Abdominal ultrasonography often finds abnormalities that suggest or are consistent with pancreatitis as well as eliminate other potential causes of vomiting and abdominal pain. Depending upon the ultrasonographer, it can be about 60–70% sensitive in finding canine pancreatitis. One may sometimes detect hypoechogenicity surrounded by hyperechoic fat in the region of the pancreas that is due to pancreatitis. At other times, a markedly thickened pancreas may be found. One of the most diagnostic findings is an obvious pancreatic mass. Evidence of extrahepatic biliary tract obstruction (which requires seeing dilated bile ducts, not just a big gall bladder) is very suggestive of pancreatitis. Rarely, you will find dilated bile ducts due to inflammatory biliary tract disease, but this is not nearly as common a cause as is biliary tract obstruction. Any dog with extra-hepatic biliary tract obstruction and any vomiting/anorexia should be assumed to have pancreatitis until proven otherwise.

At this time, the combination of cPLI and abdominal ultrasound seems to be the best combination we have. The ultrasound can give you a quick answer, and failure to find pancreatitis on ultrasound is a good reason to submit a cPLI.

Diagnosing pancreatitis during exploratory abdominal surgery is the least desirable means of diagnosis. However, there are some patients that present as though they have acute septic peritonitis that are ultimately diagnosed as having non-septic pancreatitis at surgery. There is nothing wrong with doing an exploratory laparotomy in a patient in which septic abdomen is a major consideration, only to find out that the patient has non-septic pancreatitis. We very rarely have reason to biopsy a normal appearing canine pancreas, and obvious pancreatitis in the dog seldom requires a biopsy unless carcinoma is a possibility. However, you should never simply look at what appears to be an obviously neoplastic mass in the pancreas and make a diagnosis of carcinoma without biopsying it—no matter how extremely terrible it appears. Pancreatitis is much, much, much more common than pancreatic carcinoma, no matter how bad the pancreas looks or how many adhesions are present. If you do biopsy the pancreas, it is important that you obtain a deep biopsy that goes deeper than the superficial necrotic surface or adhesions. Cytology can be useful for making a presumptive diagnosis; however, I have seen at least one case in which cytology of a pancreatic mass was read out as carcinoma by two accomplished cytologists and yet multiple biopsies all came back as necrotic pancreatitis.

Chronic, recurrent pancreatitis (i.e., chronic pancreatitis with intermittent, relatively mild recurrences) can be challenging to diagnose. Dogs with episodic vomiting due to recurrent bouts of pancreatitis may not have any other signs of disease, and they invariably are admitted to your clinic for a work up after the last bout has run its course or is on the mend. Episodes of vomiting and anorexia due to recurrent pancreatitis can be random and unpredictable. In such patients, the previously mentioned diagnostics may be attempted, especially when acute exacerbations occur. The cPLI test seems to be particularly useful in these cases. Very rarely, upper gastrointestinal barium contrast radiographs may rarely reveal duodenal abnormalities (e.g., dilatation, stricture) which suggest that recurrent bouts of acute pancreatitis have caused scarring of the pancreas which in turn have compromised the maximum size of the duodenal lumen. Ultrasonographic changes are nice if they are present, but they can be minor, making it difficult to accurately interpret them. Feeding an ultralow fat diet for 3–4 times longer than what was previously the longest interval between episodes may be useful for making a presumptive diagnosis. If the episodic vomiting/anorexia does not recur while feeding such an ultra-low fat diet for an interval so long that you would have been sure to experience another episode, then we can often reasonably assume that the signs were due to pancreatitis (or perhaps some other dietary-responsive disease). Again, the cPLI test may be a great way to diagnose this form of pancreatitis.

Pancreatic abscess is a disease that we are diagnosing more frequently. These abscesses are invariably sterile in dogs. Affected dogs typically can have a much more chronic, smoldering course (e.g., vomiting for a month or more, mild loss of appetite) than most dogs with acute pancreatitis. We have even found one dog that had a large abscess and was completely asymptomatic. Abdominal pain seems to be uncommon. CBC and serum biochemistry findings cannot be predicted. Diagnosis requires ultrasound, and treatment seems to be surgical. However, percutaneous ultrasonographic drainage of the abscess should perhaps be considered in some cases.

Therapy

First, no body actually knows what is and what is not effective therapy for pancreatitis. As of this writing, there is not a single, well designed, prospective, stratified study on the treatment of pancreatitis. Therefore, all any of us has is opinions, period.

Nothing per os (NPO) still seems to have a place in the treatment of canine pancreatitis. While it is true that they feed people with pancreatitis earlier than we feed dogs, you must remember that people generally do not get pancreatitis from fat. People get pancreatitis from alcohol, trauma and MOF (multiple organ failure) as well as gall stones. In distinction, there appears to be a real difference with dogs; they seem to have a connection between eating fat and getting pancreatitis. It is possible that someday we will find out that fasting dogs is not helpful, but right now I am inclined to not be in a rush to feed dogs with pancreatitis. I like to see them not vomit for a couple of days before I start feeding, and then I avoid fat like the plague.

Fluid therapy is critical, and subcutaneous administration of fluids is clearly inferior to IV fluids for all but the mildly affected animals. IV fluid administration plus NPO is often sufficient, even in dogs in which a pancreatic granuloma has temporarily blocked the main bile duct. Adequate pancreatic circulation is probably necessary for healing of the damaged tissue; therefore, unless the patient has congestive heart failure or oliguric renal failure, it is far better to provide a little too much fluid rather than a little too little fluid. Remember that the abdominal viscera is not "first in line" to receive circulation when the patient is dehydrated, as most dogs with pancreatitis are when they come to your office. Obese and fat dogs (which describes a lot of dogs with pancreatitis) do not necessarily have skin tenting when they are dehydrated. Likewise, although you might expect dry, tacky oral mucus membranes, a nauseated animal may be salivating enough to make the mucus membranes moist even though it is dehydrated. If the dog is not eating or drinking and is vomiting, it is dehydrated regardless of how well hydrated it appears on physical examination. All that being said, if you give far too much crystalloid and dilute the serum protein concentrations, this could be detrimental.

One should monitor the serum albumin concentration during fluid therapy in these patients. If the serum albumin concentration decreases significantly, then the plasma oncotic pressure likewise decreases which diminishes the effective perfusion at the capillary level. Since perfusion is so critical to treating dogs with pancreatitis, one should probably become concerned whenever the serum albumin concentration falls below 2.0 gm/dl. The most common error in administering plasma is to administer too little to significantly raise the plasma albumin concentration. Remember that half of the albumin that you administer will end up extravascular instead of being in the intravascular compartment. If you are going to spend the money to administer plasma, you need to monitor the serum albumin concentration after administering the plasma to see if you have meaningfully affected the values. Hetastarch is probably helpful since it will improve plasma oncotic pressure and help microcirculation in patients that are becoming hypoproteinemic.

Administration of plasma might be more effective than administering hetastarch because plasma also restores circulating protease inhibitors and replenishes AT III (which is a treatment for DIC). This is a very contentious point. One retrospective study has shown that plasma did not help treat dogs with pancreatitis; however, this study suffers from the problems inherent in all retrospective studies.

Total parenteral nutrition (TPN) seems like it can be useful in patients with severe acute pancreatitis. However, it is expensive, labor-intensive, and can only be done in facilities where there is 24 hour coverage by trained individuals. In contrast, **partial parenteral nutrition** (PPN) is something that almost anyone can use in practice. The goal is to provide approximately ½ of the caloric requirement by using a combination of D5W, 8.5% amino acids plus electrolytes, and 20% lipid emulsion. One typically provides approximately 1/3 of the desired calories with each of the three ingredients, and then administers the solution through a peripheral catheter. Much less monitoring is required with PPN than with TPN. In general, PPN is used for 5–7 days to help the patient "get over the hump"; it is not usually intended to be used for more than a week. The best source of information on partial parenteral nutrition is: *Compendium of Continuing Education* 21: 512, 1999.

Enteral nutrition is another option that has advantages over parenteral nutrition: it is easier, less expensive, and less dangerous. In particular, it should be considered if an exploratory laparotomy was performed when the pancreatitis was diagnosed because a J-tube can be placed at that time. Alternatively, laparoscopy can also be used to place enterostomy tubes, which will hopefully cut down on surgery time and post-procedure morbidity. Supplying adequate nutrition seems to be very valuable, especially in cases requiring longer therapy.

Antiemetics are useful in patients that are so nauseated that they feel terrible. I prefer to only use antiemetics for short periods of time because I want to see if the patient is improving enough so that it no longer needs the antiemetic to stop vomiting. However, if the patient is vomiting multiple times per day or obvious feels terrible due to the nausea, then dolasetron (0.3–1.0 mg/kg qd) and ondansetron (0.25 mg/kg) are my favorite antiemetics in these patients.

H-2 receptor antagonists can also be used as drugs to treat dyspepsia (ulceration and erosion are exceedingly rare in most pancreatitis patients). I primarily use these drugs to help th antiemetics be more effective. I prefer famotidine (0.5 mg/kg qd) although some prefer ranitidine because it has prokinetic activity in addition to blocking H-2 receptors.

Antibiotics have been used to prevent infection of the inflamed pancreas which is supposed to be "fertile ground" for infection, but there is minimal evidence that infection is of any significance in canine pancreatitis.

Drugs designed to decrease pancreatic secretion have been disappointing, which is not surprising when one considers that acute pancreatitis may be associated with pancreatic hyposecretion instead of hypersecretion.

Corticosteroids are extremely controversial in the treatment of pancreatitis. First, they do not cause pancreatitis; they increase serum amylase and lipase activities but do not cause pancreatitis. It is possible that they may be useful in treating patients that are in Systemic Inflammatory Response Syndrome (i.e., SIRS, which used to be called "septic shock") due to the pancreatitis. This is not at all certain, and if done should probably be reserved only for the severely ill in which you are desperate to reduce inflammation. If this is done, warn the owners of the unknown nature of this therapy and the patient's poor prognosis (actually you should probably not even consider using steroids unless the patient is so severely ill that the prognosis is deemed very poor to begin with). If steroids are used, they are probably best used as a one-time or twice only therapy in these patients, but future work remains to confirm or deny this.

Although **heparin** therapy would seem to be helpful to treat early DIC (which can probably make acute pancreatitis worse), it has not been shown to be useful in treating acute pancreatitis. If DIC appears to be a major problem, aggressive administration of fresh frozen plasma to replace clotting factors and anti-thrombin III concentrations seems more effective than heparin in treating DIC.

Analgesics can be very useful in animals with substantial abdominal pain. In very severe cases, a constant rate infusion of fentanyl is very effective. For extreme cases, a constant rate infusion of fentanyl, lidocaine and ketamine appears to give the best analgesia. In less severe cases, buprenorphine given as needed may be used instead.

Whether or not to perform surgery on a dog with pancreatitis is probably one of the hardest therapeutic decisions in small animal internal medicine. Strict guidelines cannot be given, but some basic principals may be suggested. In general, one must realize that unless an abscess, pseudocyst, mass of necrotic tissue, and/or an obstructed gall bladder **with** a bacterial infection are found, surgery will probably not benefit the patient (and may even be detrimental—anesthesia is usually associated with some decrease in visceral perfusion unless great care is taken to maintain circulation). The basic idea is to try to find reasons why you should **not** do surgery, and only do surgery if you cannot find any good reason to avoid it. Ultrasonography usually finds the lesions that would be benefitted by surgery (i.e., abscess or pseudocyst). If one is uncertain whether or not a cyst or abscess might be present and might be responsible for appropriate medical therapy being ineffective, one may reasonably decide to explore the area surgically. However, this decision should be based on the finding that 5–7 days of excellent, aggressive supportive medical management has not been of any appreciable benefit. The best way to tell if the therapy has been of any benefit is to look at the patient; if the patient looks better but the blood tests do not, go with the clinical appearance.

Again, do not be in a hurry to take dogs with pancreatitis to surgery; but, if you need to do surgery, then you should do it without any further delay. That is why it is important to provide the best possible medical management when first confronted with the patient with suspected acute pancreatitis. I will usually try aggressive medical therapy for 5–8 days, depending upon how quickly the patient is decompensating. If I have no indication that optimal medical therapy is helping after 7–9 days, then I will seriously consider surgery. If the patient has an extrahepatic biliary tract obstruction, I generally will wait a long time (i.e., a week or more, assuming that the patient feels good) before I consider surgery to relieve the obstruction. It seems as though just about all of these patients will eventually have the extrahepatic biliary tract obstruction resolve if treated medically for long enough. If one thought that it was important to relieve extrahepatic biliary tract obstruction, then percutaneous drainage using ultrasound guidance might appropriate. Rarely a stent can be placed in the bile duct. If a pseudocyst or abscess is not found, lavaging the area and resecting obviously necrotic tissue might help the patient, but this is uncertain.

Prognosis is difficult to predict. Hyperbilirubinemia is not necessarily a poor prognostic sign; pancreatic granulomas causing icterus due to obstruction of the bile duct typically resolve if the patient receives appropriate supportive therapy. Hypocalcemia (used to prognosticate in people) is infrequently found in dogs and cannot be used to predict the outcome. Pancreatic abscesses are usually sterile. Finding a degenerative left shift and/or a marked thrombocytopenia (probably due to DIC) are not known to be prognosticators, but one intuitively fears that a poor outcome is more likely with such findings. Evidence of SIRS is probably the most important reason to give a poor prognosis.

When to send the patient home is the last question. The patient is sent home when it is doing well. Monitoring the ultrasonographic appearance or the cPLI or the lipase or whatever seems to be much less valuable than observing the patient. If the patient feels good and is eating and is not vomiting, then you can probably send it home regardless of what the ultrasound looks like or how high the cPLI is. When the dog is sent home, it should be on a very strict diet that is free of fat. If you tell them "fat free" and explain the hidden sources of fat in the diet, then maybe you will achieve "low fat". Also, if the dog ever gets sick again, they should come in and see you sooner rather than later, in case it is pancreatitis that is recurring.

KEY DRUGS, DOSAGES AND INDICATIONS

Key Drug	Drug Class	Dose Range	Frequency	Route	Indications
Dolasetron	5-HT3 antagonist	0.25 mg/kg	Once daily	IV	Vomiting
Famotidine	H-2 receptor antagonist	0.5 mg/kg	1–2 times daily	IV	Nausea
Maropitant	NK-1 antagonist	1 mg/kg 2 mg/kg	Once daily Once daily	IV PO	Nausea
Plasma	Colloid	5–10 ml/kg	As needed	IV	Hypoalbuminemia, DIC

SUMMARY
- Canine pancreatitis is more common than many people realize.
- Doing abdominal radiographs, abdominal ultrasound, and cPLI offers the best chance of making a pre-surgical or pre-necropsy diagnosis.

REFERENCES

1. VanEnkevort BA, O'Brien RT, Young KM. Pancreatic pseudocysts in 4 dogs and 2 cats: Ultrasonographic and clinicopathologic findings: *J Vet Int Med* 1999; 13: 309–313.
2. Ruaux CG, Atwell RB. A severity score for spontaneous canine acute pancreatitis: *Aust Vet J* 1999; 76: 804–808.
3. Hess RS, Kass PH, Shofer FS, *et al*. Evaluation of risk factors for fatal acute pancreatitis in dogs: *J Am Vet Med Assoc* 1999; 214: 46–51.
4. Logan JC, Callan MB, Drew K, *et al*. Clinical indications for use of fresh frozen plasma in dogs: 74 dogs (October through December 1999): *J Am Vet Med Assoc* 2001; 218: 1449–1455.
5. Herman B, Brawer R, Murtaugh R, *et al*. Therapeutic percutaneous ultrasound-guided cholecystocentisis in three dogs with extrahepatic biliary obstruction and pancreatitis: *J Am Vet Med Assoc* 2005; 227: 1782–1786.
6. Johnson M, Mann F. Treatment for pancreatic abscesses via omentalization with abdominal closure versus open peritoneal drainage in dogs: 15 cases (1994–2004): *J Am Vet Med Assoc* 2006; 228: 397–402.