Article #3

CE

Canine and Feline Pancreatitis

Jacqueline C. Whittemore, DVM, DACVIM (SAIM)
Vicki L. Campbell, DVM, DACVA, DACVECC
Colorado State University

ABSTRACT:

Pancreatitis is a multifactorial disease with a variable clinical course and outcome. An underlying cause is not commonly identified, but risk factors include breed, age, concurrent endocrine disease, obesity, drugs, and trauma. The clinical signs of the disease range from mild lethargy to severe vomiting, multiple-organ failure, and death. The diagnosis is often challenging and relies on a constellation of history, physical examination, and diagnostic findings. Treatment generally includes supportive care, pain control, nutritional support, and treatment of concurrent diseases. The outcome is variable, and the disease may recur without warning.

Pancreatitis is the result of inappropriate release of digestive enzymes within the pancreas. The inciting cause of canine and feline pancreatitis is not commonly identified, perhaps because of the complex nature of the disease or the subacute to chronic nature of many cases. Although an underlying cause is commonly not identified, risk factors include breed, age, concurrent endocrine disease, obesity, drugs, and trauma.

PHYSIOLOGY

The exocrine pancreas produces zymogens, pancreatic secretory trypsin inhibitor (PSTI), and active enzymes (i.e., lipase, amylase, and the procoenzyme procolipase).[1,2] The zymogens include trypsinogen, chymotrypsinogens, kallikreinogen, proelastases, procarboxypeptidases, and prophospholipase A_2.[2] Trypsin, the active form of protrypsinogen, is the only activated zymogen capable of activating itself or the other zymogens. This activation is controlled in large measure by local calcium concentration.[3] Interestingly, calcium has both inhibitory and activating effects on trypsinogen, depending on its concentration. At a low concentration, as is found within acinar cells, calcium binding protects the trypsinogen activation peptide from exposure. Increased calcium concentration, as is found in the ducts and intestine, increases the sensitivity of trypsinogen to activation by trypsin.[3] Ductular PSTI, also known as *serine protease inhibitor Kazal-type 1 (SPINK1)*, protects the pancreas by binding to the active site on trypsin in acinar cells and pancreatic ducts to prevent further zymogen activation and is packaged within zymogen granules.[3] Like most cells, exocrine pancreatic cells contain lysosomal granules important for cellular function; these contain proteases, including cathepsin B, that can activate zymogens on contact.

Protective mechanisms that decrease the risk of zymogen activation include the inclusion of PSTI with zymogens, the segregation of zymogens within lipid structures, and the maintenance of high alkaline ductular flushing. Alkalinity is maintained by bicarbonate secretion through the cystic fibrosis transmembrane conductance regulator (CFTR).[3] The association of pancreatitis with CFTR mutations in humans emphasizes the importance of ductular bicarbonate secretion

as a protective mechanism.[3] Zymogen granule secretion is the result of both neural and humoral mechanisms. The humoral mediators secretin and cholecystokinin are believed to be most important in stimulating zymogen secretion in dogs and cats.

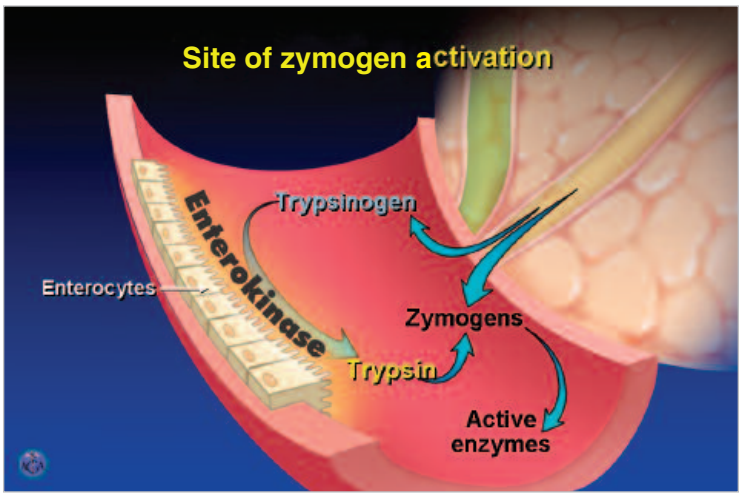
Duodenal brush border cells produce enterokinase, a strong protease responsible for zymogen activation within the intestinal lumen (Figure 1). Enterokinase is unique in that it is 2,000 times more effective at activating trypsinogen than trypsin itself.[4] Production of enterokinase in the intestine instead of the pancreas helps ensure efficient and effective activation of zymogens in the intestine while limiting the risk of zymogen activation within the pancreas. Enterokinase is not inactivated by PSTI and does not form complexes with antiproteases. Muscle sphincters in the pancreatic ducts help prevent reflux of enterokinase and duodenal contents into the pancreas.

Low levels of circulating exocrine pancreatic enzymes are commonly present in plasma, probably due to direct leakage into the bloodstream. They are commonly cleared through the kidneys. Circulating zymogens are bound by circulating enzyme inhibitors (i.e., α_1-antitrypsin, α_2-macroglobulin) that decrease their activity and increase monocyte–macrophage clearance, respectively.

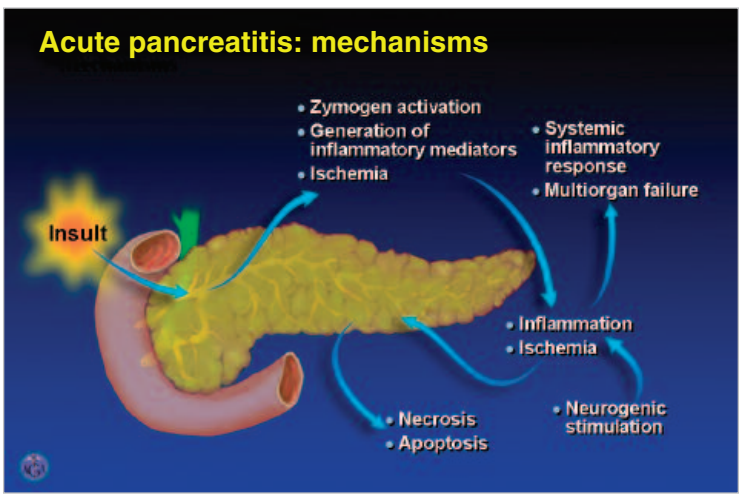
PATHOPHYSIOLOGY

Pancreatitis is a multifactorial and complex process that eventually culminates in inappropriate activation of zymogens within the pancreatic parenchyma. In most patients, this is likely the result of abnormal fusion of lysosomal and zymogen granules within the acinar cell.[1,2] A small subset of veterinary cases, like a large percentage of human cases, may be due to inappropriate duodenal reflux into the pancreas.[5] The activation of trypsinogen to trypsin furthers pancreatic damage by activating the other zymogens and trypsinogen. Once zymogen activation has occurred, damage is amplified by free radical–associated damage (e.g., lipid peroxidation) and increased capillary permeability due to endothelial membrane damage. This increase in permeability can lead to pancreatic edema, decreased microvascular circulation, increased free radical stasis, and local ischemia. The accumulation of free radicals and presence of local ischemia may lead to worsening inflammation and parenchymal damage (Figure 1).

Figure 1. Normal pancreatic function and consequences of abnormal zymogen release. (Reprinted with permission, © American Gastroenterological Association, Bethesda, MD)



Normal zymogen release into the duodenum with activation by enterokinase.

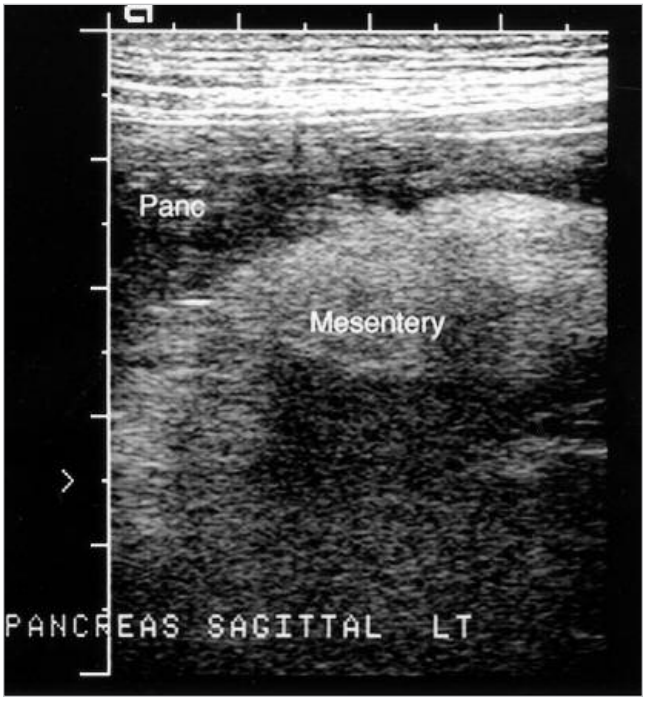


Local and systemic sequelae of pancreatic inflammation.

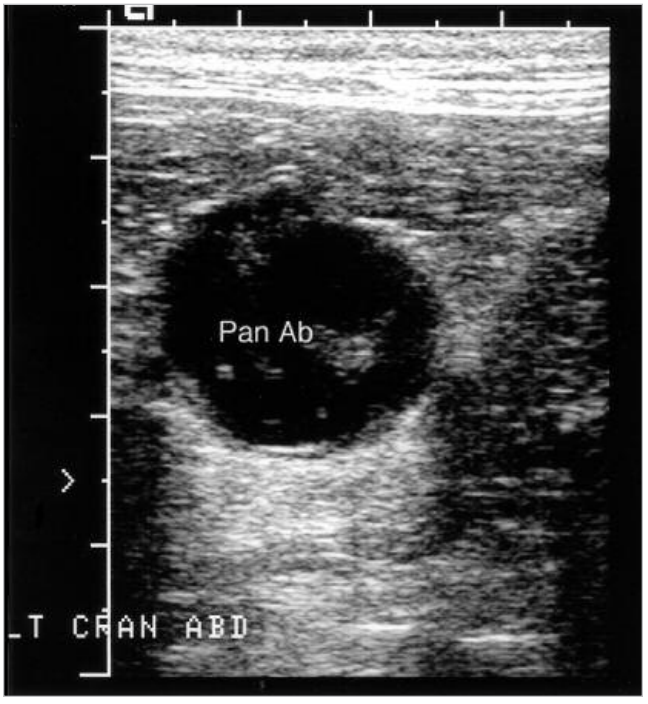
As proteolytic enzymes propagate, they may overwhelm the circulating antiproteases. Activation of inflammatory cascades, including complement, kinin, and coagulation systems, by proteases then occurs. This may lead to severe refractory hypotensive and vasoactive shock, disseminated intravascular coagulopathy (DIC), multiple organ dysfunction syndrome (MODS), and death.[2,6,7]

Pancreatitis can be acute or chronic and mild or severe. Acute pancreatitis may occur singly or recurrently. It can be mild or self-limiting. Severe cases may be associated with complications, including pancreatic abscessation or pseudocysts, hypotensive shock, acute renal failure,

Figure 2. Ultrasonographic findings associated with pancreatitis.



Mixed echogenicity of a pancreas *(Panc)* in a hyperechoic mesentery visualized via ultrasonography.



Hypoechoic focus in the pancreas consistent with a pancreatic abscess *(Pan Ab)* visualized using ultrasonography.

MODS, DIC, and death.[2,6,7] Pancreatic pseudocysts are collections of pancreatic secretions that form secondary to fibrosis or inflammation.[8,9] Pancreatic abscessation may also occur.[10,11] Although usually sterile, both pancreatic pseudocysts and abscesses may require surgical intervention for successful outcomes. Chronic pancreatitis may also be mild or severe. Mild cases are associated with minimal clinical signs and minimal morphologic or functional changes. Severe disease may lead to marked histologic abnormalities and may rarely be associated with development of exocrine pancreatic insufficiency or endocrine insufficiency (i.e., diabetes mellitus [DM]).

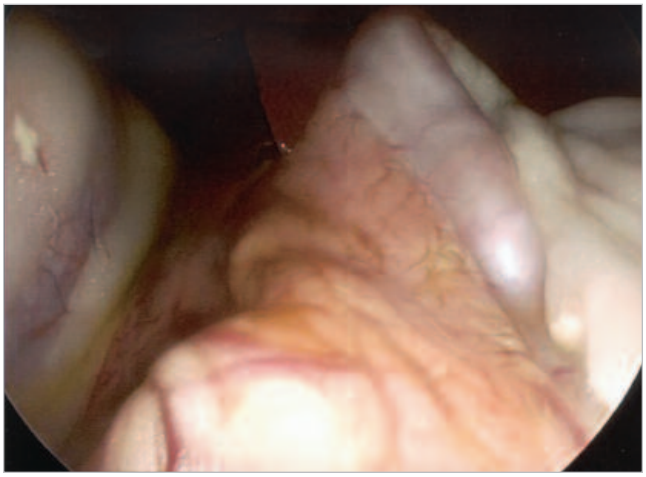
In humans, defects in the trypsinogen, SPINK1, and CFTR genes are associated with hereditary pancreatitis.[3] It is currently unknown whether there are specific hereditary causes of pancreatitis in dogs or cats, although terriers, miniature schnauzers, and Siamese cats are overrepresented.[12,13]

RISK FACTORS, CLINICAL SIGNS, AND PHYSICAL EXAMINATION FINDINGS

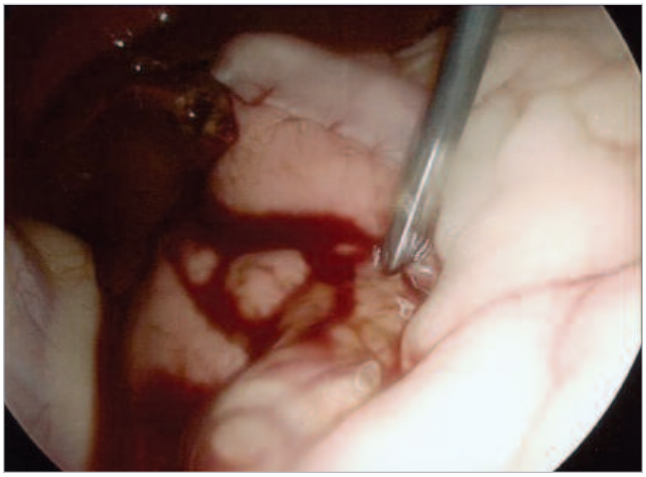
Known or suspected risk factors for canine pancreatitis include breed (i.e., terriers, miniature schnauzers), age (i.e., older than 5 years), concurrent endocrine disease (i.e., DM, hyperadrenocorticism, hypothyroidism, hypertriglyceridemia), hypercalcemia, obesity, gastrointestinal (GI) disease, drugs (i.e., sulfonamides, azathioprine), epilepsy, infection, and blunt abdominal trauma.[2,12,14–16] Glucocorticoids are no longer considered a risk factor for development of pancreatitis in humans. In addition, research does not support an association with pancreatitis in dogs or cats.[16] Risk factors in cats include breed (i.e., Siamese), age (i.e., older than 7 years), trauma, and concurrent disease (i.e., triaditis, hepatic lipidosis, DM).[5,17–20] The term *triaditis* is used by some veterinary gastroenterologists to refer to concurrent inflammatory bowel disease (IBD), cholangiohepatitis, and pancreatitis. Feline cases may be caused by FIP, toxoplasmosis, liver flukes, or pancreatic flukes.[5,21–24]

Clinical signs in dogs include anorexia, vomiting, diarrhea, abdominal pain, and fever.[2,16,25] Signs in cats include lethargy (100%), anorexia (97%), dehydration (92%), and jaundice (64%).[18,26] Vomiting (35%) and diarrhea (15%) are uncommonly associated with feline pancreatitis; mild weight loss or atypical behavior may be the only clinical sign.[18] Physical examination findings

Figure 3. **Laparoscopic evaluation of pancreatitis.**



Edematous pancreas with a focus of saponification visualized laparoscopically.



Laparoscopic biopsy of an inflamed and edematous pancreas.

include dehydration, abdominal pain, icterus, tachycardia, tachypnea, orthopnea, fever/hypothermia, or presence of an abdominal mass. In some animals, particularly cats, physical examination may be completely unremarkable.

DIAGNOSTICS

Nonspecific blood work abnormalities include nonregenerative anemia; an increased or decreased leukocyte count; an increased or decreased neutrophil count; an increased or decreased potassium or glucose concentration; a decreased calcium or albumin concentration; and an increased bilirubin, cholesterol, alanine aminotransferase, alkaline phosphatase, blood urea nitrogen, or creatinine concentration. Abnormalities in leukocytes, calcium, and potassium are associated with a poorer prognosis, especially in cats with hypocalcemia.[26]

The diagnosis of pancreatitis is complicated by the lack of a rapid, sensitive, and specific test. Although amylase and lipase serum values have been used as a diagnostic tool, they are not sensitive or specific and are believed to have no benefit in cats.[7,17,25,27,28] Values may be increased with renal disease, glucocorticoids (often greater than five times the normal level), GI disease or perforation, peritonitis, and dehydration.[13,29] Anecdotally, the diagnostic utility of measuring amylase and lipase may be increased when serum values are compared with those in abdominal fluid. Measurement in free fluid is ideal, although diagnostic peritoneal lavage fluid may be used.

Recently, there has been increased interest in using both the trypsin-like immunoreactivity (TLI) and pancreatic lipase immunoreactivity (PLI) tests to evaluate potential pancreatitis cases. The use of both tests is limited by turnaround time, depending on sample shipment date and geographic location, and nonaerofugable lipemia. Increased TLI is associated with pancreatitis in dogs but less so in cats because it is compromised by azotemia and GI disease.[30–32] Positive PLI test results are associated with disease in both dogs and cats, and the PLI test is now considered the test of choice.[33–35]

The sensitivity of radiography is very poor (i.e., 24%),[25] but radiography allows evaluation of the abdomen for concurrent disease and peritoneal effusion. Chest radiography may be used to evaluate severe cases for development of pleural effusion. The radiographic presence of a space-occupying lesion between the stomach and duodenum is consistent with a pancreatic mass. Other important radiographic findings include the reverse 7 sign, which is evidence of duodenal ileus.

Ultrasonography has better sensitivity (i.e., 68%) for detecting pancreatic abnormalities; allows evaluation of concurrent disease, biliary obstruction, or pancreatic pseudocyst; and may guide aspiration of fluid or tissue for further testing.[25,34,36] Ultrasonographic signs include a hypoechoic pancreas, a hypoechoic focus in the pancreas, a hyperechoic mesentery, and excessive corrugation of the duodenum (Figure 2).

Laparoscopy and laparotomy allow visualization and biopsy of the pancreas with or without debridement, visualization and biopsy of other abdominal organs, abdominal

Figure 4. Cat with an indwelling esophagostomy tube.

lavage, and placement of necessary feeding and therapeutic tubes (Figure 3). Biopsy samples can be submitted for histopathology and aerobic or anaerobic cultures.

TREATMENT

Treatment of pancreatitis is complex and requires attention to the many facets of disease. Although research in the human field has increasingly involved specific therapeutic targets such as somatostatin, clinical results to date remain disappointing, and treatment remains mostly symptomatic. Feeding is often the first question to be decided, and a number of nutritional support techniques can be used.[37] In general, the goals in treating pancreatitis are to feed early and enterally.

Common signs of canine pancreatitis include anorexia, vomiting, and diarrhea, whereas vomiting and diarrhea are uncommonly associated with feline pancreatitis.

NUTRITION

Nil per os (NPO; nothing by mouth) is beneficial because it rests the pancreas (pancreatic contraction is stimulated by the emptying of food and acid into the duodenum). Prolonged NPO leads to immunosuppression, decreased wound healing, increased bacterial translocation, sepsis, and decreased survival.[38–40] NPO should not last for more than 48 to 72 hours, including the time the patient was anorectic before presentation. Cats should not be fasted because fasting has not been shown to be beneficial and may exacerbate concurrent hepatic lipidosis.[18]

Parenteral nutrition should be considered if enteral feeding is not an immediate option or as a supplement to enteral feeding. When using parenteral nutrition, the formula should be adjusted daily based on changes in electrolytes, glucose, and degree of lipemia. To prevent inactivation of included vitamins (especially B complex vitamins) and bacterial complications, the bag should be shielded from light at all times and replaced daily, regardless of changes in formula, to protect against bacterial replication and propagation. A devoted catheter line is critical to limit bacterial contamination; this line should not be used for other fluids or treatments. One port on a multilumen catheter may be used for this purpose, leaving the other lumens free for fluids and intravenous injections. The parenteral nutrition line should be disconnected as infrequently as possible (ideally never) to prevent bacterial introduction. If complete nutrition is provided parenterally, a central venous line should be used because the high osmolality of the solution may cause irritation and sloughing of peripheral veins.

Benefits of enteral feeding include decreased bacterial translocation as well as improved enterocyte health and immune function.[38] An ideal enteral diet is bland, especially for dogs, and high in calories, especially for cats. Enteral feeding can be accomplished using a variety of feeding tubes. Considerations affecting feeding tube choice include necessary anesthesia time, wound-healing ability, the need for other diagnostics or therapeutics, and species of the patient.

Nasoesophageal and nasogastric tubes can be easily placed using a small amount of local anesthesia. They are useful for providing microenteral nutrition to maintain enterocyte health and decrease bacterial translocation, feeding dogs as disease resolves, and gastric suctioning to decrease vomiting. Given the small inner diameter of usable tubes, they have limited use in cats.

Esophagostomy tubes are useful primarily for feeding cats (Figure 4). Brief anesthesia is required for tube placement, and there are few complications with this procedure. To decrease the risk of a cat vomiting and thereby expelling the tube, a 20-Fr red rubber tube can

be used. Before placement, the tube should be measured to the level of the ninth rib to determine the ideal placement location. After tube placement, it is important to confirm that the tube does not extend past the lower esophageal sphincter.

Gastrostomy tubes can be placed percutaneously, endoscopically, or surgically. Anesthesia time for tube placement is generally brief, and this procedure may be coupled with diagnostic evaluation of the abdomen. Gastrostomy tubes are useful for feeding cats and gastric suctioning in dogs and cats.

Jejunostomy tubes can be placed surgically or laparoscopically and may be coupled with diagnostic evaluation of the abdomen. They are useful for feeding hospitalized dogs because the food bypasses the pancreas. Because feeding cannot be successfully administered as a bolus through jejunostomy tubes, they are not as useful for feeding after discharge.

PAIN CONTROL

Aggressive pain control is crucial for successful management of pancreatitis (Figure 5). Untreated or undertreated pain is associated with decreased immune function and may lead to decreased survival rate. In addition to increased use of standard pain medications, there are a number of new options for effective analgesia.

Opioids remain an excellent option for pain control. They are generally inexpensive, can be adjusted frequently, are reversible in cases of dysphoria or decompensation, and can be combined with other pain medications for balanced analgesia. Disadvantages include the development of ileus, constipation, and vomiting. Recommended options include fentanyl (an initial bolus of 2 to 4 µg/kg IV followed by a 1 to 4 µg/kg/hr constant-rate infusion [CRI]), morphine (0.05 to 0.1 mg/kg/hr CRI), hydromorphone (0.005 to 0.04 mg/kg/hr CRI), buprenorphine (0.01 mg/kg applied buccally [cats only] or 6 to 10 µg/kg IV, IM, or SC tid or qid), and butorphanol (0.1 to 0.2 mg/kg/hr CRI [CRI is necessary for adequate analgesia because of a short duration of action]; especially useful in cats). Considering the increased use of fentanyl patches in practice, it is important to remember that they do not achieve effective plasma levels for analgesia until 12 to 24 hours after application and should not be used as sole therapy.

Lidocaine is a new option for adjunctive pain control, may help prevent reperfusion injury associated with pancreatitis, and may indirectly improve GI motility by decreasing intraabdominal pain.[41] Lidocaine does not provide complete analgesia when used alone and is generally combined with an opioid, supplemental ketamine, or both. Lidocaine can cause significant toxicosis, especially in cats or in patients with concurrent intrathoracic blocks. The recommended dose of lidocaine is 20 to 30 µg/kg/min CRI. Ketamine used at subanesthetic doses decreases central wind-up and overall pain. It is appropriate as an adjunctive analgesic only; the recommended dose of ketamine is 2 to 5 µg/kg/min CRI.

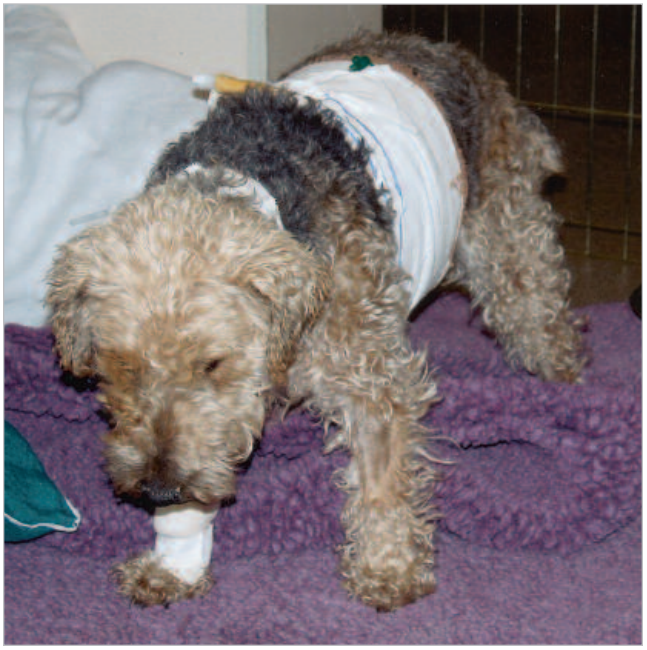


Figure 5. Welsh terrier in an orthopneic position because of uncontrolled abdominal pain.

Epidurals have limited benefit in long-term treatment of pancreatic pain. Local anesthetic agents should not be used because there is a risk of respiratory paralysis with a high epidural. It is generally difficult to achieve adequate rostral penetration with this technique, and repeat administration is impractical. In cases that benefit significantly from epidural analgesia, placement of an epidural catheter for epidural opioid administration can be considered, although the risks of infection and thromboembolic disease should be weighed. Intrathoracic (i.e., pleural) blocks can be very effective in treating pancreatic pain. Lidocaine and bupivacaine (1 mg/kg of each) should be combined in a single syringe and administered intrathoracically; this may be repeated every 6 to 8 hours as needed.

Acupuncture may be used to aid pain control and boost immune function.

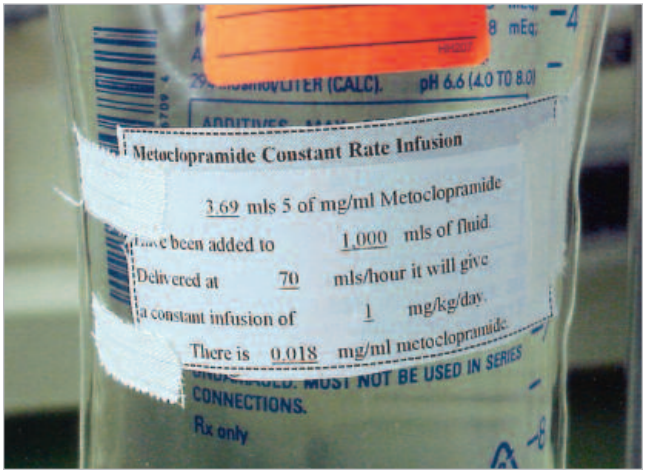


Figure 6. Bag labeled for metoclopramide CRI. Labels like this can be generated based on patient weight using a computer spreadsheet program.

BIOCHEMICAL CHANGES

Biochemical changes are unpredictable and common with pancreatitis. Most require little or no specific correction. Acidosis commonly occurs secondary to dehydration and vomiting. It usually improves with rehydration, although severe acidosis (i.e., pH < 7.2; bicarbonate ion [HCO_3^-] < 16 mEq/L) may require correction. Potassium abnormalities are common. Increased potassium is usually due to decreased glomerular filtration rate or tubular flow and acidosis and tends to correct with correction of acidosis and dehydration. Because most patients with pancreatitis have total body depletion of potassium, early supplementation is important. Frequent rechecking of electrolyte levels and the acid–base status is also important.

FLUID THERAPY

Adequate hydration is an important component of a balanced treatment protocol for pancreatitis. Animals that are severely hypovolemic may benefit from an initial fluid bolus (i.e., 45 to 90 ml/kg isotonic crystalloids divided into quarters and administered to effect). Isotonic polyionic fluids, such as 0.9% sodium chloride and Normosol-R (Abbott Laboratories), are usually recommended for initial replacement. Lactated Ringer's solution may also be helpful in cases without concurrent hepatic dysfunction. Initial replacement goals are calculated as follows:

$$\text{Replacement volume (ml)} = \text{Body weight (kg)} \times 1{,}000 \times \text{(Estimated \% dehydration} \div 100)$$

Initial replacement fluids should be administered over 12 to 24 hours, plus or minus initial shock fluids, concurrently with maintenance fluids (60 ml/kg/day) and ongoing losses. If more than one fluid type is needed, the rate for each need should be calculated separately. Patients with pancreatitis and prolonged vomiting leading to free water deficit (i.e., patients with increased serum sodium, and some patients with normal or decreased sodium)[42] may benefit from treatment with 0.45% sodium chloride with or without 2.5% or 5% dextrose.

Colloids are useful in treating patients with hypoproteinemia or decreased colloid osmotic pressure. Colloids may also decrease the effect of pancreatitis on renal blood flow.[43] It is important to keep in mind that they may increase bleeding times. The recommended daily dose is 10 to 20 ml/kg/day. The high osmotic pull of Oxyglobin (Biopure) makes it very useful as a colloid. Its other main benefit is that it may increase oxygen delivery to tissue by improving microvascular circulation.[44,45] Oxygen delivery is frequently compromised because of microthrombi, inflammation, and vasculitis. It is important to keep in mind that complications of overhydration may include development of pulmonary edema, especially in cats, if the fluid rate exceeds 5 to 10 ml/kg/hr.[46] The recommended dose of Oxyglobin is 10 to 30 ml/kg in dogs and 5 ml/kg in cats.

Prolonged fasting is associated with immunosuppression, decreased wound healing, increased bacterial translocation, sepsis, and decreased survival rate.

Plasma has been recommended as a provider of plasma protease inhibitors in cases of pancreatitis.[47,48] The theory is that plasma transfusion leads to replacement of depleted circulating plasma protease inhibitors and

decreases the progression of development of acute DIC, vasoactive shock, and death. Unfortunately, the evidence does not support this theory.[49] Although rat studies were promising, human studies[50–54] have shown no difference in survival or morbidity with treatment using plasma. To our knowledge, no studies in dogs or cats are currently evaluating this issue. Therefore, we consider the main use of plasma to be *part* of balanced colloid supplementation. The main uses of blood supplementation are similar to those of plasma. Realistically, the main use of blood is to provide oxygen-carrying capacity.

SUPPORTIVE CARE

Vomiting is common in canine pancreatitis and may occur in feline cases because of pain, stimulation of the chemoreceptor trigger zone, and ileus. Because intestinal disease is associated with high vagal tone, there is a reasonable risk of "vomit and die" syndrome if emesis is not controlled.

Metoclopramide is commonly used because it has limited side effects and is inexpensive and readily available. It acts directly in the brain on dopaminergic receptors in addition to increasing lower esophageal sphincter tone in dogs and enhancing intestinal motility. Efficacy appears to be increased when metoclopramide is administered via CRI (1 to 2 mg/kg/day); the CRI half-life is very short, and patients may begin vomiting within minutes of disconnection from it. Metoclopramide should be administered via a syringe pump so that the dose can be adjusted separately from that of the fluids. If metoclopramide is added to fluids, two fluid bags should be used so the bag containing metoclopramide can be used at a continuous rate and the fluid volume adjusted using the second bag (Figure 6). Because metoclopramide is light sensitive, fluid lines and bags should be shielded from light.[55]

Patients with severe cases may experience "breakthrough" vomiting. For these cases, it is worth considering the use of newer antiemetics. Ondansetron (0.1 to 1 mg/kg slow IV bid or tid [in dogs]) or dolasetron (0.6 to 3 mg/kg IV q24h [in dogs]) may be useful in these cases (feline doses are unknown). The main drawback to the newer antiemetics is the cost, especially in larger dogs. One of the more efficacious antiemetics is chlorpromazine, which is usually dosed at 0.11 mg/kg tid. It is light sensitive and can have sedative effects because it is a phenothiazine derivative.

GI ulceration secondary to deranged bicarbonate and digestive enzyme secretion is not uncommon. The mainstay of treatment is use of H_2-receptor blockers, of which famotidine and ranitidine are the most commonly used, with famotidine having the least P450 enzyme induction and fewest side effects. Because of the promotile effects of ranitidine, it may be a better choice in patients with ileus. Proton pump inhibitors are generally more effective for limiting intestinal ulceration and esophagitis, but their use has historically been limited by the need for oral administration. Parenteral proton pump inhibitors such as pantoprazole are now available from human hospitals. There are currently no published peer-refereed articles on veterinary pantoprazole use, but extrapolated dosages for dogs include 10 to 40 mg IV q24h or 0.7 to 1 mg/kg IV q24h.

Successful treatment hinges on identification and treatment of concurrent and underlying diseases.

Pancreatitis is almost always sterile in veterinary patients, even in those with pancreatic abscessation. However, bacterial translocation secondary to GI compromise is common in patients with prolonged NPO or severe disease. If GI compromise is suspected, antibiotic therapy should be targeted to the enteric population. A four-quadrant approach is not necessarily indicated. An antibiotic with good gram-negative and anaerobic bacterial coverage (e.g., cefoxitin) is generally an effective choice. However, when choosing an appropriate antibiotic, the entire clinical picture should be evaluated.

Vitamin B complex supplementation should be considered in all patients that have had prolonged NPO or anorexia. Supplementation is especially important in cats because concurrent intestinal disease or liver disease may further compromise a cat's ability to absorb vitamin B_{12}, leading to vitamin B_{12} deficiency. Cats often benefit from administration of steroid therapy at antiinflammatory doses. In addition, identification and treatment of underlying or concurrent disease are the cornerstone to essential pancreatitis management in cats and dogs.[19] This may include high-dose glucocorticoid therapy for

IBD or cholangiohepatitis, aggressive feeding with or without carnitine for idiopathic hepatic lipidosis, stabilization of concurrent endocrine disease, and control of hyperlipidemia and inflammation.

Patients should be evaluated frequently for impending DIC, MODS, or shock. If a patient is at increased risk for such complications, monitoring of one-stage prothrombin time, activated partial thromboplastin time, platelets, fibrin degradation products, D-dimers (the utility of D-dimers in evaluating cats for DIC has not been determined), fibrinogen, liver and kidney function, and systolic blood pressure may be indicated. Physical therapy (i.e., frequent walks, massage, passive range of motion exercises) should be performed because it may help mitigate increased risk of thromboembolism.[56–58] If testing suggests that the patient is developing thromboembolic disease, heparin therapy (100 to 200 U/kg SC tid) may be considered. Although treatment guidelines are poorly defined in veterinary medicine, significant work in humans suggests that heparin therapy should be started only if it can be continued for 6 weeks; otherwise, the risk of thrombi is probably greater than the benefit of treatment.[59] At the end of the treatment interval, patients receiving heparin therapy should be gradually weaned.

Dopamine has historically been recommended as a potential way to increase pancreatic microvascular circulation, leading to decreased progression of the disease. Data supporting dopamine use came from an experimental alcoholic cat model designed to simulate human alcoholic pancreatitis that has little relevance to veterinary pancreatitis.[60–62] In addition, dopamine infusion can lead to decreased organ blood flow—if α effects predominate—from increased systemic vascular resistance. This can be associated with development of MODS.

CONCLUSION

Pancreatitis is a complex disease that is often difficult to diagnose and challenging to treat. Pancreatitis in cats rarely has the key signs common to the disease in dogs. Serum amylase and lipase alone are not useful in reaching a diagnosis. A diagnosis may be obtained by comparison of serum and abdominal fluid amylase or lipase, serum PLI or TLI testing, abdominal ultrasonography, laparoscopy, or abdominal exploration. Treatment should focus on adequate nutritional supplementation, pain control, fluid therapy, and antiemetics. Concurrent disease should be identified and aggressively addressed to improve response to treatment. Patients should be monitored for shock, MODS, and DIC, and appropriate interventions should be undertaken early.

REFERENCES

1. Mansfield CS, Jones BR: Review of feline pancreatitis, part one: The normal feline pancreas, the pathophysiology, classification, prevalence and aetiologies of pancreatitis. *J Feline Med Surg* 3:117–124, 2001.
2. Williams DA: The pancreas, in Strombeck DR (ed): *Small Animal Gastroenterology*, ed 3. Philadelphia, WB Saunders, 1996, pp 381–410.
3. Whitcomb DC: Mechanisms of disease: Advances in understanding the mechanisms leading to chronic pancreatitis. *Nat Clin Pract Gastroenterol Hepatol* 1:46–52, 2004.
4. Rinderknecht H: Activation of pancreatic zymogens. Normal activation, premature intrapancreatic activation, protective mechanisms against inappropriate activation. *Dig Dis Sci* 31:314–321, 1986.
5. Weiss DJ, Gagne JM, Armstrong PJ: Relationship between inflammatory hepatic disease and inflammatory bowel disease, pancreatitis, and nephritis in cats. *JAVMA* 209:1114–1116, 1996.
6. Ruaux CG: Pathophysiology of organ failure in severe acute pancreatitis in dogs. *Compend Contin Educ Pract Vet* 22:531–542, 2000.
7. Ruaux CG, Atwell RB: A severity score for spontaneous canine acute pancreatitis. *Aust Vet J* 76:804–808, 1998.
8. Van Enkewort BA, O'Brien RT, Young KM: Pancreatic pseudocysts in 4 dogs and 2 cats: Ultrasonographic and clinical pathologic findings. *J Vet Intern Med* 13:309–313, 1999.
9. Hines BL, Salisbury SK, Jakovljevic S, et al: Pancreatic pseudocyst associated with chronic–active necrotizing pancreatitis in a cat. *JAAHA* 32:147–152, 1996.
10. Salisbury SK, Lantz GC, Nelson RW, et al: Pancreatic abscess in dogs: Six cases (1978–1986). *JAVMA* 193:1104–1108, 1988.
11. Stimson EL, Espada Y, Moon M, et al: Pancreatic abscess in nine dogs. *J Vet Intern Med* 9:202, 1998.
12. Hess RS, Kass PH, Shofer FS, et al: Evaluation of risk factors for fatal acute pancreatitis in dogs. *JAVMA* 214:46–51, 1999.
13. Mansfield CS, Jones BR: Review of feline pancreatitis part two: Clinical signs, diagnosis and treatment. *J Feline Med Surg* 3:125–132, 2001.
14. Whitney MS, Boon GD, Rebar AH, et al: Effects of acute pancreatitis on circulating lipids in dogs. *Am J Vet Res* 48:1492–1497, 1987.
15. Mohr AJ, Lobetti RG, van der Lugt JJ: Acute pancreatitis: A newly recognized potential complication of canine babesiosis. *J S Afr Vet Assoc* 71:232–239, 2000.
16. Williams DA, Steiner JM: Canine exocrine pancreatic disease, in Ettinger SJ, Feldman EC (eds): *Textbook of Veterinary Internal Medicine*, ed 6. St. Louis, WB Saunders, 2005, pp 1482–1488.
17. 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* 7:25–33, 1993.
18. Akol KG, Washabau RJ, Saunders HM, et al: Acute pancreatitis in cats with hepatic lipidosis. *J Vet Intern Med* 7:205–209, 1993.
19. Washabau RJ: Feline acute pancreatitis: Important species differences. *J Feline Med Surg* 3:95–98, 2001.
20. Ferreri JA, Hardam E, Kimmel SE, et al: Clinical differentiation of acute necrotizing from chronic nonsuppurative pancreatitis in cats: 63 cases (1996–2001). *JAVMA* 223:469–474, 2003.
21. Rothenbacher H, Lindquist WD: Liver cirrhosis and pancreatitis in a cat infected with *Amphimerus pseudofelineus*. *JAVMA* 143:1099–1102, 1963.
22. Roudebush P, Schmidt DA: Fenbendazole for treatment of pancreatic fluke infection in a cat. *JAVMA* 180:545–546, 1982.
23. Smart ME, Downey RS, Stockdale PH: Toxoplasmosis in a cat associated with cholangitis and progressive pancreatitis. *Can Vet J* 14:313–316, 1973.

24. Dubey JP, Carpenter JL: Histologically confirmed clinical toxoplasmosis in cats: 100 cases (1952–1990). *JAVMA* 203:1556–1566, 1993.
25. 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). *JAVMA* 213:665–670, 1998.
26. Kimmel SE, Washabau RJ, Drobatz KJ: Incidence and prognostic value of low plasma ionized calcium concentration in cats with acute pancreatitis: 46 cases (1996–1998). *JAVMA* 219:1105–1109, 2001.
27. Kitchell BE, Strombeck DR, Cullen J, et al: Clinical and pathologic changes in experimentally induced acute pancreatitis in cats. *Am J Vet Res* 47:1170–1173, 1986.
28. Parent C, Washabau RJ, Williams DA, et al: Serum trypsin-like immunoreactivity, amylase and lipase in the diagnosis of feline acute pancreatitis [abstract]. *J Vet Intern Med* 9:194, 1995.
29. Willard MD, Twedt DC: Gastrointestinal, pancreatic and hepatic disorders, in MD Willard, H Tvedten, GH Turnwald (eds): *Small Animal Clinical Diagnosis by Laboratory Methods*, ed 4. St. Louis, WB Saunders, 2004, pp 208–246.
30. Simpson KW: Feline pancreatitis. *J Feline Med Surg* 3:183–184, 2001.
31. Swift MC, Marks SL, MacLachlan NJ, et al: Evaluation of serum feline trypsin-like immunoreactivity for the diagnosis of pancreatitis in cats. *JAVMA* 217:37–42, 2000.
32. Gerhardt A, Steiner JM, Williams DA, et al: Comparison of the sensitivity of different diagnostic tests for pancreatitis in cats. *J Vet Intern Med* 15:329–333, 2001.
33. Williams DA, Steiner JM, Ruaux CG, et al: Increases in serum pancreatic lipase immunoreactivity (PLI) are greater and of longer duration than those of trypsin-like immunoreactivity (TLI) in cats with experimental pancreatitis [abstract]. *J Vet Intern Med* 17:445, 2003.
34. Forman MA, Marks SL, De Cock HE, et al: Evaluation of feline pancreatic lipase immunoreactivity and helical computed tomography versus conventional testing for the diagnosis of feline pancreatitis [abstract]. *J Vet Intern Med* 17:411, 2003.
35. Steiner JM, Broussard J, Mansfield CS, et al: Serum canine pancreatic lipase immunoreactivity (cPLI) concentrations in dogs with spontaneous pancreatitis [abstract]. *J Vet Intern Med* 15:274, 2001.
36. Saunders HM, VanWinkle TJ, Drobatz K, et al: Ultrasonographic findings in cats with clinical, gross pathologic, and histologic evidence of acute pancreatic necrosis: 20 cases (1994–2001). *JAVMA* 221:1724–1730, 2002.
37. Freeman LM, Labato MA, Rush JE, et al: Nutritional support in pancreatitis: A retrospective study. *J Vet Emerg Crit Care* 5:32–40, 1995.
38. Zhao G, Wang CY, Wang F, et al: Clinical study on nutrition support in patients with severe acute pancreatitis. *World J Gastrenterol* 9:2105–2108, 2003.
39. Remillard RL: Nutritional support in critical care patients. *Vet Clin Small Anim* 32:1145–1165, 2002.
40. McClave SA, Greene LM, Snider HL, et al: Comparison of the safety of early enteral vs parenteral nutrition in mild acute pancreatitis. *J Parenter Enteral Nutr* 21:14–20, 1997.
41. Cassutto BH, Gfeller RW: Use of intravenous lidocaine to prevent reperfusion injury and subsequent multiple organ dysfunction syndrome. *J Vet Emerg Crit Care* 13:137–148, 2003.
42. Adrogue HJ, Madias NE: Hyponatremia. *N Engl J Med* 342:1581–1589, 2000.
43. Wells AD, Schenk WG: Effectiveness of normal saline solution, dextran 40 or dextran 75, and aprotinin (Trasylol) on renal blood flow preservation during acute canine pancreatitis. *Am J Surg* 148:624–629, 1984.
44. Driessen B, Jahr JS, Lurie F, et al: Effects of haemoglobin-based oxygen carrier hemoglobin glutamer-200 (bovine) on intestinal perfusion and oxygenation in a canine hypovolaemia model. *Br J Anaesth* 86:683–692, 2000.
45. Driessen B, Jahr JS, Lurie F, et al: Arterial oxygenation and oxygen delivery after hemoglobin-based oxygen carrier infusion in canine hypovolemic shock: A dose-response study. *Crit Care Med* 31:1771–1779, 2003.
46. Gibson GR, Callan MB, Hoffman V, et al: Use of a hemoglobin-based oxygen-carrying solution in cats: 72 cases (1998–2000). *JAVMA* 221:96–102, 2002.
47. Logan JC, Callan MB, Drew K, et al: Clinical indications for use of fresh frozen plasma in dogs: 74 dogs (October through December 1999). *JAVMA* 218:1449–1455, 2001.
48. Murtaugh RK, Jacobs RM: Serum antiproteases concentrations in dogs with spontaneous and experimentally induced acute pancreatitis. *Am J Vet Res* 46:80–83, 1985.
49. Silverstein D: Plasma therapy for pancreatitis: What does the evidence say? *Proc Int Vet Emerg Crit Care* 8:190–194, 2002.
50. Cuschieri A, Wood RA, Cumming JR, et al: Treatment of acute pancreatitis with fresh-frozen plasma. *Br J Surg* 70:710–712, 1983.
51. Leese T, Holliday M, Heath D, et al: Multicentre clinical trial of low volume fresh-frozen plasma therapy in acute pancreatitis. *Br J Surg* 74:907–911, 1987.
52. Goodman AJ, Bird NC, Johnson AG: Antiprotease capacity in acute pancreatitis. *Br J Surg* 73:796–798, 1986.
53. Leese T, West KP, Morton DB, et al: Fresh-frozen plasma therapy in acute pancreatitis: An experimental study. *Int J Pancreatol* 3:437–477, 1988.
54. Leese T, Holliday M, Watkins M, et al: A multicentre controlled clinical trial of high-volume fresh-frozen plasma therapy in prognostically severe acute pancreatitis. *Ann R Coll Surg Engl* 73:207–214, 1991.
55. Plumb DC: Metoclopramide, in *Plumb's Veterinary Drug Handbook*, ed 5. Ames, IA, Blackwell, 2005, pp 519–521.
56. Turpie AGG, Chin BSP, Lip GYH: Venous thromboembolism: Pathophysiology, clinical features, and prevention. *BMJ* 325:887–890, 2002.
57. Wolfe WG: Pulmonary embolism. *Ann Surg* 238:S67–S71, 2003.
58. Dalen JE: Pulmonary embolism: What have we learned since Virchow? *Chest* 122:1801–1817, 2002.
59. Kearon C: Duration of therapy for acute venous thromboembolism. *Clin Chest Med* 24:63–72, 2003.
60. Karanjia ND, Widdison AL, Lutrin FJ, et al: The anti-inflammatory effect of dopamine in alcoholic hemorrhagic pancreatitis in cats. *Gastroenterology* 101:1635–1641, 1991.
61. Karanjia ND, Lutrin FJ, Chang YB, et al: Low-dose dopamine protects against hemorrhagic pancreatitis in cats. *J Surg Res* 48:440–443, 1990.
62. Karanjia ND, Widdison AL, Lutrin FJ, et al: Dopamine in models of alcoholic acute pancreatitis. *Gut* 35:547–551, 1994.

ARTICLE #3 CE TEST

This article qualifies for 2 contact hours of continuing education credit from the Auburn University College of Veterinary Medicine. Subscribers may purchase individual CE tests or sign up for our annual CE program. Those who wish to apply this credit to fulfill state relicensure requirements should consult their respective state authorities regarding the applicability of this program. To participate, fill out the test form inserted at the end of this issue or take CE tests online and get real-time scores at ***CompendiumVet.com****.*

1. Most cases of pancreatitis are the result of

a. inappropriate duodenal reflux into the pancreas.
b. pancreatic and liver flukes.
c. abnormal fusion of lysosomal and zymogen granules within the pancreas.
d. toxoplasmosis.

2. Which is not a risk factor for pancreatitis?

a. DM
b. obesity
c. trauma
d. steroid administration

3. Which laboratory abnormality is associated with decreased survival in cats?

a. an increased alanine aminotransferase concentration
b. hypocalcemia
c. an increased creatinine concentration
d. hyperglycemia

4. Which is not affected by renal disease in cats?

a. amylase
b. lipase
c. trypsin-like immunoreactivity
d. pancreatic lipase immunoreactivity

5. Prolonged NPO is associated with

a. immunosuppression.
b. increased bacterial translocation.
c. decreased survival.
d. all of the above

6. Which is associated with adequate analgesia?

a. improved immune function
b. decreased vomiting
c. increased survival
d. all of the above

7. Which is an appropriate first-line treatment for vomiting?

a. metoclopramide
b. famotidine
c. omeprazole
d. pantoprazole

8. Antibiotics are commonly used in cases of pancreatitis because

a. the disease is often bacterial in origin.
b. pancreatic abscesses are difficult to diagnose and require antibiotic therapy.
c. animals have increased risk of bacterial translocation and sepsis secondary to prolonged NPO and mucosal breakdown.
d. antibiotics prevent sepsis in patients receiving parenteral nutrition.

9. Treatment of feline pancreatitis often relies on treating concurrent diseases. Which is not common with feline pancreatitis?

a. IBD
b. cholangiohepatitis
c. idiopathic hepatic lipidosis
d. urinary tract infection

10. Which is a risk of dopamine use in treating pancreatitis?

a. decreased organ blood flow from increased systemic vascular resistance
b. hypotension
c. bradycardia
d. thromboembolic disease

Test answers now available at CompendiumVet.com