Chapter 67

Acute and Chronic Pancreatitis

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"What do you want–an adorable pancreas?"
Jean Kerr, The Snake Has All the Lines

CLINICAL IMPORTANCE

Pancreatitis has been recognized as a clinical entity in dogs for more than a century (Simpson, 1993). In dogs, acute pancreatitis is an important differential diagnosis for vomiting and abdominal pain. Because of difficulties in diagnosis, pancreatitis is a less common diagnosis in cats. Based on clinical and pathologic reports, diagnosis of feline pancreatitis is apparently increasing (Akol et al, 1993; Hill and Van Winkle, 1993; Steiner and Williams, 1997; Hines et al, 1996; De Cock et al, 2007; Maddison, 2008). One study reported an incidence of 0.57 to 3.5% in cats (Mansfield and Jones, 2001). Another pathology study reported that exocrine pancreatic lesions are present in approximately 1.5% of patients presented for necropsy and that 59% of dogs and 46% of cats with exocrine pancreatic lesions had evidence of pancreatitis (Hanichen and Minkus, 1990).

PATIENT ASSESSMENT

History and Physical Examination

As many as 90% of dogs with pancreatitis present with acute vomiting (Hess et al, 1998). Vomiting may be sporadic and mild or very severe. Other clinical signs include abdominal pain, depression, anorexia, fever and diarrhea. Icterus and pale-colored stools may be reported if pancreatic inflammation and edema are severe enough to result in common bile duct obstruction. If present, diarrhea is usually of large bowel origin because the transverse colon passes dorsal to the pancreas and is susceptible to local inflammation at that site.

An episode of dietary indiscretion often occurs during the 24 hours before the onset of vomiting. The owner commonly relates consumption of high-fat human food. Occasionally, the onset of clinical signs is preceded by administration of drugs associated with pancreatitis. Corticosteroids, in particular, have been linked to pancreatitis in dogs (Simpson, 1993).

Cats with pancreatitis have highly variable clinical signs. In some cats, the disease may mimic the typical canine presentation (i.e., acute vomiting, lethargy, anorexia, diarrhea and abdominal pain). In others, a more indolent, smoldering course occurs, resulting in a mild chronic illness (Steiner and Williams, 1997). The most common clinical signs in cats are anorexia, lethargy, dehydration and weight loss. Abdominal pain may be difficult to recognize and vomiting occurs in fewer than 50% of cases (Washabau, 2001). Other cats may present with a palpable abdominal mass. In some cats, pancreatitis may be linked to diabetes mellitus and clinical signs may include

polydipsia/polyuria and weight loss (Steiner and Williams, 1997). In others, hepatic lipidosis or cholangiohepatitis may occur concurrently resulting in icterus (Akol et al, 1993; Weiss et al, 1996). In some cats, pancreatitis, cholangiohepatitis and inflammatory bowel disease (IBD) may be present simultaneously (triaditis).

Depression, fever and dehydration may be the most prominent physical examination findings. Abdominal palpation may elicit splinting and discomfort that can be localized to the right cranial quadrant. Icterus, shock and coagulopathies may be detected in severe cases.

Clinical manifestations are variable in chronic pancreatitis. Weight loss and poor body condition may be the only signs noted in cats. An abnormal thickening or hardness of the falciform fat pad may be palpated in some cats, suggesting saponification and fat necrosis.

Laboratory and Other Clinical Information

The laboratory diagnosis of acute and chronic pancreatitis can be very frustrating. Diagnosis is hampered by the poor specificity of available laboratory tests and the inaccessibility of tissue for cytologic or histopathologic examination. Serum amylase and lipase activities are the most commonly used laboratory tests for the diagnosis of pancreatitis in dogs and cats. Unfortunately, these tests are not very specific because they are influenced by a number of other disease conditions (e.g., renal failure, dehydration, hyperlipidemia). In addition, the short half-life of amylase and lipase often precludes their use as diagnostic aids unless the patient is presented promptly after the onset of clinical signs. If present, hyperamylasemia and hyperlipasemia support a diagnosis of pancreatitis if azotemia and hyperlipidemia are not present. In cats, pancreatic amylase secretion is only 10% of that in dogs and serum amylase is usually low in cats with pancreatitis (Zoran, 2007).

Serum trypsin-like immunoreactivity (TLI) concentration has been suggested as a diagnostic aid for evaluating dogs and cats with suspected pancreatitis. Because TLI is specifically pancreatic in origin, high serum TLI concentrations were hoped to be a more reliable indicator of clinical pancreatitis than high amylase or lipase activities (Simpson et al, 1989). However, the sensitivity of TLI assays in dogs and cats with acute pancreatitis appears to be very low (30 to 60%) (Williams, 2006).

More recently, assays for canine and feline specific pancreatic lipase have come into clinical use. In healthy dogs and cats, very little pancreatic lipase is present in blood. In pancreatitis, the inflamed organ leaks larger amounts of lipase into the blood, which is measurable by immunoassay. These species-specific assays appear to be more sensitive (>80%) than TLI concentrations for the diagnosis of pancreatitis in dogs and cats (Steiner, 2006; Forman et al, 2002). Additionally, these assays are not falsely elevated in renal disease (Steiner et al, 2001) or by corticosteroid administration (Steiner et al, 2003).

A complete blood cell count, serum biochemistry profile and urinalysis should be done for any dog or cat suspected to have pancreatitis to rule out other potential causes for the clinical signs. Additionally, these tests may aid in the diagnosis of concurrent medical conditions such as diabetes mellitus, hepatic lipidosis, interstitial nephritis and cholangiohepatitis.

Anorectic or vomiting canine and feline patients with pancreatitis may become hypokalemic. In one retrospective study, hypocalcemia was recognized in 40% of cats with acute pancreatitis and was considered indicative of a poor prognosis (Kimmel et al, 2001). Hypocalcemia may be attributable to conditions such as hypoalbuminemia, parathormone resistance or to the saponification of calcium by fatty acids (Kimmel et al, 2001; Washabau, 2001).

An inflammatory leukogram is typically identified in patients with pancreatitis. A degenerative left shift may indicate severe necrotic pancreatitis. In cats, leukopenia appears to occur more commonly than in dogs and is associated with a poor prognosis (Washabau, 2001). If thrombocytopenia is noted on the hemogram, a complete coagulation screen should be performed to rule out disseminated intravascular coagulation.

Imaging can be useful for diagnosing pancreatitis in dogs and cats. Findings consistent with pancreatic inflammation on survey abdominal radiographs may include haziness and widening of the gastroduodenal angle in the right cranial quadrant. Often, segmental gas distention of the proximal duodenum is noted. In the hands of an experienced operator, abdominal ultrasonography appears to be a sensitive test for the diagnosis of acute pancreatitis in dogs (Mansfield et al, 2008). Typical findings include enlargement of the pancreas, hypoechogenicity, dilatation of the pancreatic duct and hyperechogenicity of the mesentery. Peripancreatic fluid accumulation is a common finding in dogs and cats (Williams, 2006). Ultrasonography may reveal fluid-filled cysts, pseudocysts or abscesses within the pancreatic parenchyma and can be used to guide needle aspiration of pancreatic masses (Salisbury et al, 1988; VanEnkevort et al, 1999). In cats, the reported sensitivity of abdominal ultrasonography ranges from 20 to 67% (Rademacher et al, 2008). Typical ultrasonographic findings in cats are similar to those described in dogs. More sophisticated contrast-enhanced power and color Doppler ultrasonographic procedures also distinguish between normal cats and cats with pancreatitis (Rademacher et al, 2008). When coupled with measurement of serum pancreatic lipase immunoreactivity, abdominal ultrasonography was more sensitive than computed tomography in the diagnosis of acute pancreatitis in cats (Forman et al, 2004).

The gold standard for diagnosing acute and chronic pancreatitis is histopathology. Unfortunately, pancreatic biopsies are rarely performed because of the invasive nature of the procedure and because many patients with pancreatitis are poor anesthetic risks. However, laparoscopic techniques for the diagnosis of pancreatic disease in dogs and cats have been described; these provide a minimally invasive method for collection of pancreatic biopsy specimens (Marmoinen et al, 2002; Webb and Trott, 2008). Unfortunately, laparoscopy does not provide good visualization of the entire pancreas, which can result in failure to biopsy affected areas of the organ (Steiner, 2008).

Risk Factors

Several risk factors have been associated with pancreatitis in dogs and cats (**Table 67-1**). Most patients with these risk factors, however, do not develop pancreatitis.

A number of endocrinopathies such as diabetes mellitus, hypothyroidism and hyperadrenocorticism have been linked to pancreatitis in dogs (Hess et al, 1999). These endocrine conditions are often associated with hyperlipidemia and obesity, two other risk factors for acute pancreatitis.

An association has been made between hyperlipidemia and acute pancreatitis in dogs and people that has led to speculation that disturbances in lipid metabolism may be involved (Simpson, 1993). The exact relationship is unknown in dogs and cats and information is often extracted from human cases. Hyperlipidemia is thought to precede and cause the development of pancreatitis; however, it can also be evident during and after such episodes (Simpson, 1993). The rate of hyperlipidemia in people with pancreatitis has been estimated between 3 and 12% when alcoholics are not included in the case study. The incidence of hyperlipidemia in dogs or cats with pancreatitis is generally thought to be high. In a retrospective study of fatal acute pancreatitis in dogs, 26% of patients were hyperlipidemic (Hess et al, 1998). However, experimentally induced pancreatitis in dogs has not resulted in lipemia or hypertriglyceridemia (Bass et al, 1976; Whitney et al, 1987). Hypertriglyceridemia is present in some but not all naturally occurring cases of canine pancreatitis as determined by serum lipid and electrophoretic patterns (Whitney et al, 1987; Rogers et al, 1975). Most people with pancreatitis do not have hyperlipidemia; however, those that do and who are not alcoholics more often have preexisting hyperlipoproteinemia types I and V; more specifically hypertriglyceridemia. Serum triglyceride levels (>900 mg/dl) increase the risk of pancreatitis in dogs (Xenoulis et al, 2006).

Several pet breeds are predisposed to pancreatitis (e.g., miniature schnauzers, briards, Shetland sheepdogs, Siamese cats). This predisposition may be attributed to the fact that these breeds are also frequently hypertriglyceridemic. Recently, mutations in the pancreatic secretory trypsin-inhibitor gene (SPINK gene) have been described in miniature schnauzers, which may explain this breed's increased risk for pancreatitis (Bishop et al, 2007; Steiner, 2008). A number of other breeds also appear to be at risk for pancreatitis including boxers, cavalier King Charles spaniels, cocker spaniels, collies and Yorkshire terriers (Watson et al, 2007; Hess et al, 1999; Lem et al, 2008). Feeding a high-fat (>20% dry matter [DM]) food, treat or human food has often been associated with the onset of acute pancreatitis and a history of dietary indiscretion of high-fat human foods increases the risk of acute pancreatitis (Steiner, 2008). Ingestion of table scraps, garbage and new/unusual foods has been linked to pancreatitis in a case control study (Lem et al, 2008). Experimentally, feeding high-fat, low-protein foods was associated with the development of pancreatitis and hepatic lipidic changes in dogs (Lindsay et al, 1948; Goodhead, 1971). The most widely repeated explanation for the association between hypertriglyceridemia and acute pancreatitis is that hydrolysis of serum triglycerides by lipase within the pancreatic microvasculature releases free fatty acids locally. Free fatty acids cause microthrombi and/or bind with calcium to cause further capillary damage, which, in turn, releases more pancreatic lipase (Havel, 1969). Consumption of calorically dense, high-fat foods also contributes to obesity in pets, which is also considered a risk factor for pancreatitis (Lem et al, 2008). In one report, 43% of dogs with acute pancreatitis were considered overweight or obese (Hess et al, 1998). Obese patients develop more severe experimental pancreatitis than dogs with lower body condition scores (Relford et al, 2006).

Pancreatitis has been associated with hypercalcemia in several dogs with hyperparathyroidism or cancer and in a dog receiving a calcium infusion (Simpson, 1993; Relford et al, 2006). Experimentally, elevated ionized calcium concentrations can induce pancreatitis in cats (Frick et al, 1990). The pathophysiologic mechanism for pancreatitis in association with hypercalcemia has not been determined.

Drug-induced pancreatitis in people is very common; alcohol consumption is recognized as the most common cause of the disease. Reports of drug-induced pancreatitis in companion animals are uncommon but the following compounds have been implicated: calcium, azathioprine, vinca alkaloids, l-asparaginase, phenobarbital and potassium bromide in dogs and tetracyclines, sulfonamides and organophosphates in cats.

Anecdotal reports suggest that corticosteroids are the most common drug associated with pancreatitis in dogs. Pancreatitis

Table 67-1. Risk factors for pancreatitis in dogs and cats.

Breed
Boxer
Briard
Cavalier King Charles spaniel
Cocker spaniel
Collie
Miniature schnauzer
Sheltie
Yorkshire terrier
Himalayan cat
Dietary factors
High-fat, low-protein foods
Ingestion of garbage or table scraps
Drug administration
Azathioprine
Corticosteroids
L-asparaginase
Organophosphate insecticides (cats)
Fasting hyperlipidemia
Gender
Castrated males
Spayed females
Hepatobiliary disease
Feline suppurative cholangiohepatitis
Triaditis (IBD, cholangiohepatitis, pancreatitis)
Hypercalcemia
Hyperparathyroidism
Intravenous calcium infusion
Increasing age
Intervertebral disk disease
Ischemia or reperfusion
Postgastric dilatation-volvulus
Obesity

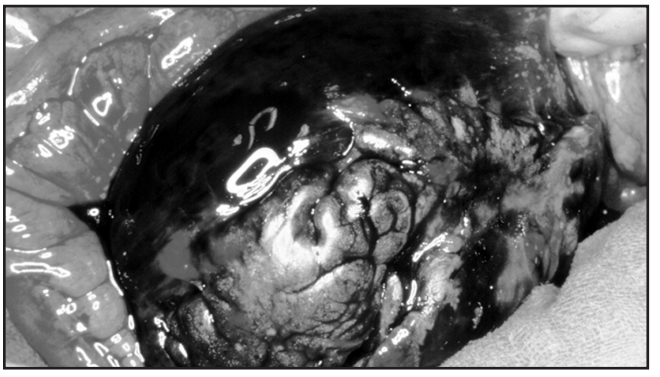

Figure 67-1. Intraoperative photograph of a dog with acute necrotizing pancreatitis. (Courtesy Dr. Dan Smeak, College of Veterinary Medicine, The Ohio State University, Columbus.)

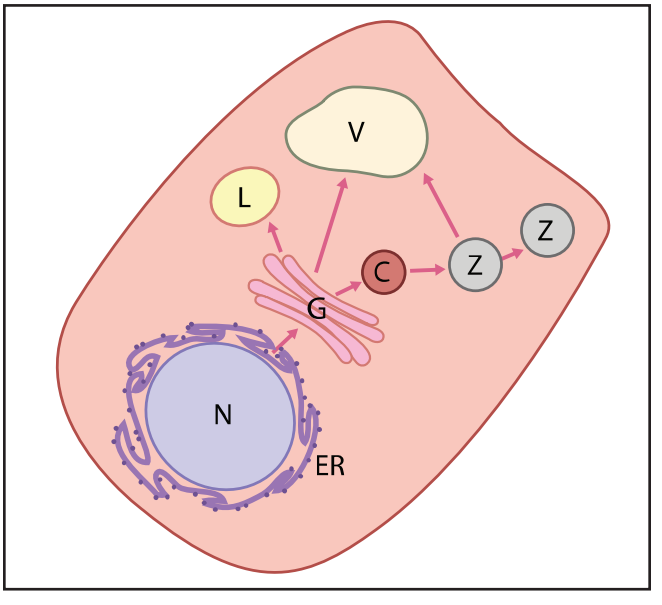

Figure 67-2. Schematic representation of zymogen and lysosomal fusion in acute pancreatitis. Digestive and lysosomal enzymes are synthesized in the rough endoplasmic reticulum (ER) and transferred to the Golgi apparatus (G) next to the nucleus (N). Normally, digestive and lysosomal enzymes are separated. Digestive enzymes are concentrated in zymogen granules within acinar cells and lysosomal enzymes are stored separately in lysosomes (L). Digestive enzymes are concentrated in condensing vacuoles (C) and in zymogen granules (Z) that fuse with luminal-plasma membranes. Hyperstimulation of the pancreas results in mixing of lysosomal and digestive enzymes in large vacuoles (V). (Adapted from Simpson KW. Current concepts of the pathogenesis and pathophysiology of acute pancreatitis in the dog and cat. Compendium on Continuing Education for the Practicing Veterinarian 1993; 15: 247-254.)

is common in dogs with hyperadrenocorticism and in dogs receiving corticosteroids for management of intervertebral disk disease (Moore and Withrow, 1982). Experimentally, corticosteroids increase the sensitivity of dispersed acinar cells to cholecystokinin and stimulate proliferation of the pancreatic ductular epithelium (Simpson, 1993). However direct evidence is lacking for a role of corticosteroids in the development of pancreatitis in dogs and cats (Steiner, 2008).

In dogs, potassium bromide and phenobarbital administration has been associated with elevations in serum pancreatic lipase immunoreactivity and acute pancreatitis (Podell and Fenner, 1993; Gaskill and Cribb, 2000; Steiner et al, 2008). Pancreatitis occurs in as many as 6 to 7% of dogs treated for seizures with potassium bromide.

Ischemia and reperfusion injury have been linked to acute pancreatitis (Williams, 1996; Simpson, 1993). Hypovolemic shock, gastric dilatation-volvulus and abdominal trauma have been reported to precede acute pancreatitis (Williams, 1996; Simpson, 1993). In addition, abdominal surgery marked by inept manipulation of the pancreas can result in pancreatitis (Williams, 1996; Simpson, 1993).

In cats, pancreatitis does not seem linked to obesity, hyperlipidemia, hypertriglyceridemia or to dietary triggers (Mansfield and Jones, 2001; Zoran, 2007). Instead, a number of infectious diseases have been implicated including calicivirus, toxoplasmosis, feline infectious peritonitis, feline immunodeficiency virus, panleukopenia, the fluke, *Amphimerus pseudofelieus*, (Relford et al, 2006) and enterococci (Lapointe et al, 2000).

Etiopathogenesis

Acute pancreatitis is the sudden onset of inflammation of the pancreatic acinar tissue. Typically, the primary histopathologic lesion is edema. After resolution, there is usually no residual pancreatic lesion. However, in more severe cases, the pancreatic lesion may become hemorrhagic or may progress to necrosis (**Figure 67-1**). Mortality is high in acute necrotizing pancreatitis. Acute edematous or hemorrhagic pancreatitis may occur as a singular or recurrent event in dogs and cats.

Pancreatitis occurs as a consequence of intracellular pancreatic acinar enzymatic activation and resultant autodigestion of the pancreas. In the normal pancreas, safeguards ensure that harmful pancreatic enzymes are not activated until they reach the intestinal lumen (**Table 67-2**) (Stewart, 1994). Pancreatic enzymes are synthesized in endoplasmic reticuli, modified in Golgi apparatuses and stored in zymogen granules within acinar cells. Evidence suggests that intracellular pancreatic enzyme activation occurs as a result of abnormal zymogen activation. Normally, zymogens and lysosomes are segregated intracellularly. In pancreatitis, lysosomes containing proteases fuse with zymogen granules (**Figure 67-2**) (Simpson, 1993). The lysosomal contents (e.g., proteases such as cathepsin B) activate trypsinogen. In addition, the acidic environment of lysosomes interferes with self-regulating trypsin inhibitors stored with pancreatic enzymes in zymogen granules.

Cholecystokinin and acetylcholine are widely recognized as the principal physiologic mediators of pancreatic enzyme secretion (Simpson, 1993). Normally, these substances initiate fusion of zymogen granules with the acinar cell membrane. Hyperstimulation of the pancreas with supraphysiologic doses of cholecystokinin appears to cause pancreatitis in experimental animals by interfering with the intracellular movement of zymogens resulting in fusion of zymogens and lysosomes (Simpson, 1993). The lysosomal enzyme cathepsin B is then thought to activate trypsinogen and precipitate pancreatitis

(Simpson, 1993). Pancreatic duct obstruction also appears to facilitate fusion of zymogens and lysosomal enzymes. Foods high in fat and protein (particularly the amino acid arginine) stimulate production and release of cholecystokinin, gastrin and secretin (Simpson, 1993). Organophosphate insecticides and intravenous calcium infusions are hypothesized to cause hyperstimulation via cholecystokinin (Simpson, 1993).

Bile acid and enteric reflux into the pancreatic duct can also activate pancreatic enzymes interstitially (i.e., within the pancreatic duct system and interstitium) (Simpson, 1993). This mechanism is thought to be involved in the development of pancreatitis in cats in conjunction with suppurative cholangiohepatitis and enteritis (Simpson, 1993). The anatomic configuration of the common bile duct and pancreatic duct in cats facilitates this mechanism. Experimentally, free fatty acids generated by the action of lipase on triglycerides damage acinar cell membranes, releasing lecithin, which causes marked necrosis of acinar cells when converted to lysolecithin by phospholipase A_2 (Simpson, 1993).

Regardless of the initiating cause, active pancreatic enzymes (trypsin, phospholipase, collagenase and elastase) and inflammatory mediators are released into the pancreatic tissues and blood vessels. These factors apparently activate coagulation, fibrinolytic, kinin and complement cascades (Simpson, 1993). Circulating defense mechanisms include α_1-antitrypsin and α_2-macroglobulin, which bind to active enzymes to contain local damage and prevent systemic damage (Simpson, 1993). After these defenses are overwhelmed, increased pancreatic permeability leads to fluid loss into the pancreas and the abdomen, a decline in pancreatic blood flow and an increase in the local concentrations of pancreatic enzymes and inflammatory mediators (Simpson, 1993). Large numbers of leukocytes migrate to the inflamed pancreas and serve as a source of free radicals, inflammatory mediators and enzymes (Simpson, 1993). This vicious, self-perpetuating cycle may ultimately lead to thrombosis of pancreatic blood vessels and pancreatic necrosis. Systemic complications may develop, including hypovolemic shock and disseminated intravascular coagulation.

Chronic pancreatitis is less commonly recognized in companion animals vs. people in whom alcohol can serve as a constant stimulus for smoldering acinar inflammation. Some authors suggest that chronic mild interstitial pancreatitis is the most common form of pancreatitis recognized in cats (Williams, 1996; Maddison, 2008). Histopathologic examination of tissues from dogs and cats with chronic pancreatitis reveals irreversible fibrotic changes resulting from the persistent inflammatory condition. Chronic and recurrent pancreatitis may result in acquired exocrine pancreatic insufficiency.

Table 67-2. Protection against pancreatic autodigestion.

Enterokinase, produced by the duodenal brush border, is required for activation of proenzymes
Pancreatic enzymes are synthesized as proenzymes (zymogens)
Serum protease inhibitors bind free trypsin
The pancreas secretes a trypsin inhibitor in pancreatic juice that binds free trypsin
Zymogens and lysosomal enzymes are stored in different intracytoplasmic membranes

Table 67-3. Key nutritional factors for foods for canine and feline patients with pancreatitis.*

Factors	Recommended levels
Fat	≤15% for non-obese and non-hypertriglyceridemic dogs
	≤ 25% for non-obese and non-hypertriglyceridemic cats
	≤10% for obese and/or hypertriglyceridemic dogs
	≤15% for obese and/or hypertriglyceridemic cats
Protein	15 to 30% for dogs
	30 to 40% for cats

*Nutrients expressed on a dry matter basis.

Key Nutritional Factors

Key nutritional factors for patients with pancreatitis are listed in **Table 67-3** and discussed in more detail below.

Water

Water is the most important nutrient in patients with acute vomiting because of the potential for life-threatening dehydration due to excessive fluid loss and inability of patients to replace those losses. Moderate to severe dehydration should be corrected with appropriate parenteral fluid therapy rather than using the oral route. Further nutritional support should be postponed until electrolyte, fluid and acid-base abnormalities have been corrected.

Protein

Free amino acids (i.e., phenylalanine, tryptophan and valine) in the duodenum are a strong stimulus for pancreatic secretion, in fact, more so than fat (Go et al, 1970). Therefore, excess dietary protein should be avoided, while providing adequate protein for recovery and tissue repair. DM protein levels of 15 to 30% for dogs and 30 to 40% for cats are appropriate.

Fat

Obese and hypertriglyceridemic patients recovering from pancreatitis should receive low-fat foods (≤10 and ≤15% DM for dog and cat foods, respectively). Other patients can be fed moderate-fat foods (≤15 and ≤25% DM for dog and cat foods, respectively). The most clinically relevant form of hypertriglyceridemia in veterinary patients is hyperchylomicronemia because triglycerides make up 84 to 89% of the lipids in chylomicrons (Chapter 28). Plasma chylomicrons are derived from two sources. Large (12-carbon) triglycerides are present for a few hours after ingestion of dietary fat, whereas smaller triglycerides, secreted from the liver, are always present and independent of dietary fat intake.

Other Nutritional Factors

Antioxidants

Recently, results of a randomized controlled clinical trial in people with chronic pancreatitis demonstrated a 50% reduction

in painful days per month with oral antioxidant administration as compared to placebo (Bhardwaj et al, 2009). One third of patients receiving an antioxidant preparation containing selenium, vitamin C, vitamin E, β-carotene and methionine became pain free as compared to 12% of those receiving placebo. Markers of oxidative stress including lipid peroxidation products were higher in chronic pancreatitis than in healthy patients and improved after antioxidant administration. Similar trials have not been performed in chronic or acute pancreatitis in veterinary patients.

Cobalamin

Assessment of serum cobalamin is recommended in cats with pancreatitis complicated by IBD or triaditis. If levels are depleted, parenteral supplementation is recommended. Cats should receive weekly subcutaneous parenteral cobalamin therapy (250 μg/cat) for four to six weeks or until serum levels return to the normal range (Ruaux et al, 2005). Once or twice monthly therapy may be required for longer-term maintenance.

FEEDING PLAN

Dietary management goals for patients with pancreatitis are to decrease stimuli to pancreatic secretion (thus preventing pancreatic autodigestion) and still provide adequate nutrient levels to support tissue repair and recovery. Acute hemorrhagic or necrotizing pancreatitis should be considered a medical emergency. Initially, appropriate parenteral fluid therapy should be provided to correct dehydration and electrolyte and acid-base disturbances.

Oral food intake stimulates pancreatic secretions by several mechanisms. Likewise, the physical presence of food in the stomach stimulates gastrin, which in turn stimulates pancreatic secretion. In addition, many patients with pancreatitis will exhibit abdominal pain and/or vomit when fed, which increases the risk of aspiration. Therefore, nothing per os (NPO) therapy is the initial treatment of choice for a limited time period (≤ three days including days of anorexia pre-presentation). The advent of potent antiemetics (e.g., dolansetron, ondansetron) has led some clinicians to initiate immediate enteral nutritional support (Relford et al, 2006).

Therapy used in conjunction with the feeding plan includes intravenous fluids, antiemetics, plasma transfusions, nasogastric suctioning of gastric secretions and air, control of gastric acidity with H_2-receptor blockers or proton pump inhibitors, anticholinergic agents, somatostatin analogues (octreotide), antibiotics and surgical exploration of the abdomen for extirpation or drainage of pancreatic abscesses or pseudocysts (Johnson and Mann, 2006). Aggressive pain control with single agents or combination therapy with opioids, lidocaine, ketamine or epidurals is also recommended for canine and feline patients with pancreatitis (Whittemore and Campbell, 2005).

Assess and Select the Food

Levels of protein and fat should be evaluated in foods currently fed to patients with pancreatitis and compared with recommended levels. Information from this aspect of assessment is essential for making any changes to foods currently provided. Changing to a more appropriate food is indicated if protein and fat levels in the food currently fed do not match recommended levels. Owners of dogs at risk for acute pancreatitis fed struvite litholytic foods should be counseled about potential adverse events that require medical attention (Chapter 43).

Small amounts of water, ice cubes, oral rehydration solutions or monomeric foods can be offered after vomiting and abdominal discomfort subside. Monomeric foods are liquid foods containing nutrients in their simplest absorbable form. Thus, nutrients in these foods minimally stimulate pancreatic secretion (Green and Guan, 1993). Some monomeric products also contain glutamine to stimulate enterocyte hyperplasia after several days of NPO therapy, which may have induced intestinal mucosal atrophy. In general, 1 to 2 ml/kg body weight q.i.d. are well tolerated and rarely induce vomiting.

If liquids are well tolerated for one to two days, solid food may be slowly reintroduced. Highly digestible, commercial veterinary therapeutic foods designed for patients with gastrointestinal (GI) disease are often used initially (**Tables 67-4** and **67-5**, for dogs and cats, respectively). These foods also contain moderate levels of protein and fat. If vomiting recurs, NPO therapy should be reinstituted and feeding attempted again after 12 to 24 hours. A veterinary therapeutic food formulated for patients with GI diseases should be fed for another seven to 10 days before reintroducing the patient's regular food, if it is to be used at all.

Low-fat (<10% DM fat) foods are often used if obesity or hyperlipidemia was a contributing factor (**Tables 67-6** and **67-7**, for dogs and cats, respectively). High-fat commercial foods (>20% DM fat), table foods and snacks should be avoided. It may be necessary to remind clients of this around the holiday season, when many owners succumb to the desire to share family meals with pets.

Assess and Determine the Feeding Method

Because the feeding method is often altered in patients with pancreatitis, a thorough assessment should include verification of the feeding method currently being used. Items to consider include feeding frequency, amount fed, how the food is offered, access to other food sources including human food and garbage and who feeds the pet. All of this information should have been gathered when the dietary history was obtained. In cases in which acute pancreatitis is associated with eating garbage or other inappropriate foods (most often during a holiday), strict avoidance of foods other than the pet's regular food is recommended.

Discontinuing oral intake of food and water (NPO) has been the cornerstone of initial therapy for acute pancreatitis. Factors (GI distention and hormone release [gastrin, secretin, cholecystokinin]) that would normally stimulate pancreatic secretions, nausea, vomiting and abdominal discomfort are reduced when food and water are withheld. Most patients respond within two to three days. After vomiting and abdominal discomfort resolve or lessen in severity, liquids and food can be reintroduced grad-

Table 67-4. Key nutritional factors in selected commercial veterinary therapeutic foods for dogs with pancreatitis compared to recommended levels.* (See **Table 67-6** if patient is obese or hypertriglyceridemic.)

Moist foods	**Fat (%)**	**Protein (%)**
Recommended levels	**≤15**	**15-30**
Hill's Prescription Diet i/d Canine	14.9	25.0
Iams Veterinary Formula Intestinal Low-Residue	13.2	35.9
Medi-Cal Gastro Formula	11.7	22.1
Purina Veterinary Diets EN GastroENteric Formula	13.8	30.5
Royal Canin Veterinary Diet Digestive Low Fat LF	6.9	31.9
Royal Canin Veterinary Diet Intestinal HE	11.8	23.1
Dry foods	**Fat (%)**	**Protein (%)**
Recommended levels	**≤15**	**15-30**
Hill's Prescription Diet i/d Canine	14.1	26.2
Iams Veterinary Formula Intestinal Low-Residue	10.7	24.6
Medi-Cal Gastro Formula	13.9	22.9
Purina Veterinary Diets EN GastroENteric Formula	12.6	27.0
Royal Canin Veterinary Diet Digestive Low Fat LF 20	6.6	24.2
Royal Canin Veterinary Diet Intestinal HE 28	22.0	33.0

*Manufacturers' published values. Nutrients expressed as % dry matter.

Table 67-5. Key nutritional factors in selected commercial veterinary therapeutic foods for cats with pancreatitis compared to recommended levels.* (See **Table 67-7** if patient is obese or hypertriglyceridemic.)

Moist foods	**Fat (%)**	**Protein (%)**
Recommended levels	**≤25**	**30-40**
Hill's Prescription Diet i/d Feline	24.1	37.6
Iams Veterinary Formula Intestinal Low-Residue	11.7	38.4
Medi-Cal HYPOallergenic/Gastro	35.9	35.5
Medi-Cal Sensitivity CR	35.1	34.5
Dry foods	**Fat (%)**	**Protein (%)**
Recommended levels	**≤25**	**30-40**
Hill's Prescription Diet i/d Feline	20.2	40.3
Iams Veterinary Formula Intestinal Low-Residue	13.7	35.8
Medi-Cal HYPOallergenic/Gastro	11.5	29.8
Purina Veterinary Diets EN GastroENteric	18.4	56.2
Royal Canin Veterinary Diet Intestinal HE 30	23.7	34.4

*Manufacturers' published values. Nutrients expressed as % dry matter.

ually over several days. Normal feeding methods can be reintroduced after several days without clinical signs, unless dietary indiscretion or inappropriate foods or feeding methods initially contributed to the problem.

After three days (including periods of inappetence before admission) of the NPO protocol, patients with severe pancreatitis should receive enteral or parenteral nutritional support. The method deemed most desirable is the least invasive, supports the patient nutritionally and minimally stimulates pancreatic secretions. Some clinicians suggest feeding anorectic cats even earlier because of the risk of hepatic lipidosis (Zoran, 2007).

Protracted cases of pancreatitis with intractable vomiting often require parenteral nutrition to meet the patient's energy, protein, electrolyte and B-vitamin requirements while minimizing pancreatic secretions (Chapter 26). This is particularly true for patients for which the general anesthesia required for tube placement is considered too risky. Parenteral administration of nutritional solutions (including lipid solutions) has been associated with pancreatic atrophy; thus, pancreatic stimulation is minimal or nonexistent (Relly and Nahrwold, 1976; Betzhold and Howard, 1986). Both total parenteral and partial parenteral nutritional feeding have been used in patients with pancreatitis (Zsombor-Murray and Freeman, 1999; Zoran, 2007). In one review, pancreatitis was the most common diagnosis in hospitalized patients receiving partial parenteral nutrition (Chan et al, 2002). Intravenous administration of nutrients to support patients with pancreatitis through a five- to 14-day course of vomiting is possible, safe and economical in most practices (Chapter 26). Parenteral solutions are of particular benefit for managing pancreatitis in cats, especially when complicated by hepatic disorders, IBD or interstitial nephritis (Akol et al, 1993; Weiss et al, 1996).

Selection of parenteral solutions for feeding patients with pancreatitis is controversial because of the association between hyperlipidemia and pancreatitis. Some authors suggest that selection of parenteral solutions be based on amino acid and dextrose content only, whereas others advocate the use of lipid solutions in the admixture if the patient is not hyperlipidemic.

Table 67-6. Key nutritional factors in selected commercial veterinary therapeutic foods for obese or hypertriglyceridemic dogs with pancreatitis compared to recommended levels.*

Moist foods	**Fat (%)**	**Protein (%)**
Recommended levels	**≤10**	**15-30**
Hill's Prescription Diet w/d Canine	12.7	17.9
Medi-Cal Fibre Formula	9.1	24.8
Purina Veterinary Diets OM Overweight Management Formula	8.4	44.1
Dry foods	**Fat (%)**	**Protein (%)**
Recommended levels	**≤10**	**15-30**
Hill's Prescription Diet w/d Canine	9.0	18.9
Medi-Cal Fibre Formula	10.6	26.2
Purina Veterinary Diets DCO Dual Fiber Control	12.4	25.3
Purina Veterinary Diets OM Overweight Management Formula	7.2	31.1
Royal Canin Veterinary Diet Calorie Control CC 26 High Fiber	10.4	30.9
Royal Canin Veterinary Diet Diabetic HF 18	9.9	22

*Manufacturers' published values. Nutrients expressed as % dry matter.

People with pancreatitis have a decreased capacity to oxidize glucose, peripheral resistance to insulin and hyperglycemia. Administering glucose as the sole nonprotein energy source perpetuates hyperglycemia and increases the risk of hepatic steatosis (Helton, 1993). Lipids in total nutrient admixtures (Chapter 26) have been used successfully in dogs and cats with pancreatitis.[a] Lipid emulsions administered intravenously are synthetic 0.5-μm chylomicrons that appear to be well used by rats, people and dogs with pancreatitis (Raasch et al, 1983; Silberman et al, 1982; Kawaura et al, 1976; Zieve, 1968). People with pancreatitis and concurrent hypertriglyceridemia or hyperlipoproteinemia types I and V are not given lipids intravenously until levels of these parameters have decreased (Helton, 1993). Plasma lipid data from dogs with naturally occurring pancreatitis are sparse; however, not all canine patients with pancreatitis are hypertriglyceridemic (Whitney et al, 1987; Rogers et al, 1975). Therefore, serum triglyceride levels should be assessed before lipids are administered intravenously. Although isolated cases of pancreatitis in people have been linked to lipid infusion, these cases are considered rare and were complicated by concurrent diseases such as alcoholism and IBD (Wolfe and Ney, 1986). Second, respiratory quotients in people with pancreatitis are between 0.76 and 0.91, indicating mixed fuel (glucose and lipid) use. Finally, adding fat to dextrose infusions improves nitrogen balance (Sitzmann et al, 1989). Although respiratory quotients have not been measured in dogs and cats with pancreatitis, lipid administration is well tolerated, most likely because the liver would be using endogenous fat stores if lipid were not supplied exogenously as in people.

Enteral nutritional support by nasoesophageal, esophagostomy, gastrostomy or jejunostomy tubes should also be considered in prolonged cases of pancreatitis. Human reports suggest that enteral feeding after a short period of NPO (two days) may be superior to parenteral feeding in acute pancreatitis. Intra-jejunal feeding reduced complications and shortened hospital stays as compared to total parenteral nutrition (Windsor et al, 1998; Meier and Beglinger, 2006). Similar findings have been reported in experimental canine pancreatitis; enteral feeding was found to improve gut barrier function without increasing enteric hormone release (Qin et al, 2002, 2007). Studies have not been performed in spontaneous pancreatitis in dogs or when enteral routes proximal to the jejunum were used (Watson, 2007; Mansfield, 2007).

Jejunostomy tubes bypass the stomach and duodenum but are best placed when patients must undergo general anesthesia and abdominal surgery for other reasons (Swann et al, 1997). Studies have demonstrated the efficacy of nasojejunal feeding in people with mild and complicated acute pancreatitis (McClave et al, 1997; Kudsk et al, 1990). Jejunal feedings in people and dogs stimulate pancreatic secretion no more than parenteral feedings (Ragins et al, 1973; Cassim and Allardyce, 1974). In veterinary patients, however, a practical technique for nasojejunal feeding has not been developed; thus, jejunal feeding requires abdominal surgery. For that reason, some clinicians prefer parenteral feeding or the use of minimally invasive techniques such as nasoesophageal or percutaneous gastrostomy tube placement in patients with prolonged, refractory pancreatitis (Zoran, 2007).

Monomeric liquid foods infused directly into the duodenum of dogs stimulate some pancreatic output, whereas oral administration of the same monomeric foods stimulated a greater volume of pancreatic secretion (Relly and Nahrwold, 1976). If jejunal tube feeding is selected, a liquid food supplemented with glutamine to maintain intestinal integrity that minimally stimulates the pancreas and meets the patient's resting energy requirement (RER) is most suitable. Directly infusing a readily absorbable monomeric liquid food (vs. a polymeric product) into the jejunum should also reduce pancreatic secretions because whole nutrients elicit a greater response from the pancreas than monomeric nutrient forms. Monomeric liquid foods may be infused into the jejunum by slow continuous gravity drip (1 to 2 ml/kg body weight/hour) or, preferably, by an enteral pump. This rate of enteral feeding meets the RER of most patients and precludes other forms of nutritional support until oral intake is possible. If patients tolerate this rate of administration, solid food in small frequent meals may be given

Table 67-7. Key nutritional factors in selected commercial veterinary therapeutic foods for obese or hypertriglyceridemic cats with pancreatitis compared to recommended levels.*

Moist foods	**Fat (%)**	**Protein (%)**
Recommended levels	**≤15**	**30-40**
Hill's Prescription Diet w/d Feline with Chicken	16.6	39.6
Medi-Cal Fibre Formula	17.1	40.0
Purina Veterinary Diets OM Overweight Management Formula	14.6	44.6
Royal Canin Veterinary Diets Calorie Control CC High Fiber	21.3	33.5
Dry foods	**Fat (%)**	**Protein (%)**
Recommended levels	**≤15**	**30-40**
Hill's Prescription Diet w/d Feline	9.8	39.0
Hill's Prescription Diet w/d Feline with Chicken	9.9	39.9
Medi-Cal Fibre Formula	12.2	34.2
Purina Veterinary Diets OM Overweight Management Formula	8.5	56.2
Royal Canin Veterinary Diets Calorie Control CC 29 High Fiber	10.2	33.5

*Manufacturers' published values. Nutrients expressed as % dry matter.

for several days in addition to the liquid feedings. Liquid feedings may cease and the number of oral meals per day increased when solid food is well tolerated. Hydrolyzed or novel protein foods may be of value in cats with concurrent pancreatitis and inflammatory bowel disease (Zoran, 2009). These foods are typically highly digestible and may be beneficial for managing intestinal and pancreatic disorders (Chapter 31).

REASSESSMENT

Hospitalized patients with pancreatitis should be assessed frequently. Assessment of body weight and condition are recommended to ensure adequate hydration and caloric intake, if feeding is instituted. Electrolyte and acid-base status should be monitored to assess adequacy of therapy. If parenteral nutrition is used, daily monitoring of electrolytes, glucose and triglycerides is necessary to allow adjustment of parenteral solution composition (Whittemore and Campbell, 2005). Certain laboratory parameters (leukogram and serum concentrations of amylase, lipase, pancreatic lipase immunoreactivity and bilirubin) are helpful markers of progress. However, the patient's attitude, appetite and presence or absence of vomiting and abdominal pain are often the most important predictors of progress. In addition, it is imperative that sera be evaluated for triglyceride concentration initially and then monitored daily for lipemia. It is important to distinguish between lipemia from endogenous sources vs. exogenous fat emulsions when parenteral nutrition is administered.

Discharged patients should be reevaluated in a number of weeks. If a low-fat, high-fiber food was recommended to control obesity or hyperlipidemia, body weights should be recorded and serum triglyceride concentrations determined (or the sample should be inspected visually for lipemia) to assess compliance with the dietary management program. Regaining or maintaining optimal body weight and condition, normal activity level and absence of clinical signs are measures of successful dietary management.

Patients that relapse should be reevaluated and assessed for evidence of pancreatic pseudocysts, pancreatic necrosis or abscesses because these are potential sequelae to acute pancreatitis (Coleman and Robson, 2005).

ENDNOTE

a. Remillard RL. Personal experience. 1999.

REFERENCES

The references for **Chapter 67** can be found at www.markmorris.org.

CASE 67-1

Anorexia in a German Shepherd Crossbred Dog

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Patient Assessment

A five-year-old neutered male German shepherd crossbred dog was examined on an emergency basis for acute onset of anorexia and depression. The owners found the dog outside hiding under a large shrub. The dog seemed lethargic and refused food and water. Past clinical problems included multiple seizures, hyperlipidemia and recurrent superficial staphylococcal pyoderma. The dog was receiving phenobarbital for seizures and had just completed six weeks of therapy with cephalexin for superficial pyoderma.

Physical examination revealed a very depressed, febrile (rectal temperature 40.0°C [104.0°F]) dog. Pain was elicited when the cranial abdomen was palpated and the dog vomited a small amount of clear liquid. Oral mucous membranes were brick red. The dog was overweight (body condition score [BCS] 4/5, body weight 45 kg).

Blood was drawn for a complete blood count and serum biochemistry profile. Therapy for shock was initiated with intravenous fluids, antibiotics and corticosteroids. Results of diagnostic studies included leukocytosis with a marked left shift (**Table 1**, Day 1) and very lipemic serum. Fluid therapy and antibiotics were continued through the night.

Intermittent vomiting continued. The next morning, abdominal radiographs were taken. Loss of serosal detail in the cranial abdomen consistent with focal fluid accumulation or peritonitis was noted. Results of a complete blood count were still consistent with severe inflammation (**Table 1**, Day 2) and the serum was still lipemic. Results of a serum biochemistry profile included increased serum amylase and lipase activities and increased liver enzyme activity (**Table 1**, Day 2). Fluid recovered by abdominal lavage was evaluated cytologically. The abdominal lavage fluid contained many nondegenerative neutrophils with no evidence of bacteria. Pancreatitis with non-septic peritonitis was diagnosed.

Assess the Food and Feeding Method

The dog was fed a commercial dry premium brand dog food free choice plus a variety of leftover foods from the owner's meals.

Questions

1. What are potential complications of pancreatitis?
2. What are the key nutritional factors for this patient?
3. Outline a short-term (i.e., next few days) and long-term (i.e., next several months) treatment and feeding plan for this dog.

Answers and Discussion

1. Life-threatening complications of pancreatitis include shock, pulmonary edema, cardiac dysrhythmias, peritonitis, sepsis, disseminated intravascular coagulopathy, hepatic lipidosis (cats) and extrahepatic bile duct obstruction. Other complications include diabetes mellitus and exocrine pancreatic insufficiency.
2. Key nutritional factors for patients with pancreatitis include water, protein and fat. Aggressive intravenous fluid therapy to correct water, electrolyte and acid-base deficits is a cornerstone of successful treatment for acute pancreatitis. Potassium supplementation in fluids is often indicated because of potassium losses in vomitus. Dietary protein and fat are the major stimuli for pancreatic secretions; therefore, excessive levels should be avoided. Excess dietary fat should also be avoided in patients with hyperlipidemia.
3. Initially, oral food and water are withheld for three to five days to minimize pancreatic secretions and help control vomiting. Parenteral fluid therapy is used to correct fluid deficits and electrolyte and acid-base disturbances and to meet maintenance water requirements. Colloids (e.g., dextrans, hetastarch) may be needed initially to maintain blood volume and pancreatic microcirculation. After replacement of deficits, additional fluids are given to match the patient's maintenance requirements and ongoing losses. Drug therapy usually includes corticosteroids (only in shock), antiemetics, antibiotics and analgesics. Food and water are gradually introduced in multiple small feedings while clinical signs, especially vomiting, are monitored. Foods for patients with pancreatitis should avoid excessive levels of protein and fat, and contain balanced levels of other nutrients. Some clinicians suggest using a "bland," low-protein, low-fat, high-carbohydrate food such as cooked rice for the initial few days of feeding. Parenteral nutritional support should be considered if clinical signs persist beyond five days (Chapter 26). Long-term use of foods that avoid excess dietary fat (i.e., <10% dry matter fat) may be especially important in this overweight dog with a history of hyperlipidemia (Chapter 28).

Table 1. Selected laboratory parameters from a dog with pancreatitis.

Parameters	Day 1	Day 2	Day 6	Day 107	Day 121	Day 154	Reference values
Packed cell volume (%)	68	57	53	45	45	56	37-55
Total white blood cells (/μl)	20,900	22,500	12,900	12,500	10,800	26,200	8,000-17,000
Total segmented neutrophils (/μl)	9,614	9,450	11,868	8,750	7,236	19,388	3,600-13,100
Total band neutrophils (/μl)	5,852	8,775	258	0	1,944	1,834	0-400
Total juvenile neutrophils (/μl)	1,254	112	0	0	0	0	0
Amylase (IU/l)	ND	1,608	563	897	2,340	2,640	350-1,200
Lipase (U/l)	ND	107	133	64	ND	260	0-100
ALT (IU/l)	ND	99	77	42	ND	120	0-75
Alkaline phosphatase (IU/l)	ND	333	309	30	ND	757	0-80

Key: ND = not done, ALT = alanine aminotransferase.

Progress Notes

Intravenous fluids, antibiotics and phenobarbital were continued for several days. The dog apparently felt much better by the sixth day of hospitalization and the hemogram indicated that the peripheral inflammatory response had improved (**Table 1**, Day 6). No vomiting had occurred for 24 hours and the dog readily ate cooked rice. The dog continued to improve and was released to the owner's care four days later.

A commercial low-fat, moderate-fiber veterinary therapeutic food (Prescription Diet w/d Canine[a]) was dispensed for use at home. The dog began eating this food during its last two days in the hospital. The daily energy requirement (DER) was calculated to achieve mild weight loss (1.2 x resting energy requirement [RER] [RER = $30Wt_{kg}+70$] for an ideal body weight of 39 kg) while supporting recovery from pancreatitis and peritonitis. DER equals approximately 1,500 kcal (6.28 MJ), which was met by feeding three and one-half cups of food twice daily. The owners were asked to eliminate table food and other snacks from the diet.

Three months later, the dog was examined for recurrent pyoderma. Blood parameters were normal and the serum was not lipemic (**Table 1**, Day 107). The dog's weight remained stable. Antibiotics were dispensed, oral phenobarbital was continued and the amount of food offered was reduced to two and two-thirds cups of food twice daily. Two weeks later, the dog developed anorexia, vomiting and mild abdominal pain after eating fried chicken. Serum was lipemic and blood parameters were consistent with recurrent pancreatitis (**Table 1**, Day 121). Five days of therapy with intravenous fluids, antibiotics and nothing per os resulted in clinical improvement. The dog was released to the owner's care with instructions to strictly follow the previously developed feeding plan.

A month later, the dog was again examined for anorexia, vomiting, icterus and severe cranial abdominal pain. Laboratory parameters were consistent with pancreatitis and bile duct obstruction (**Table 1**, Day 154). Exploratory celiotomy revealed severe, chronic, fibrosing pancreatitis with entrapment and compression of the extrahepatic bile duct. The fibrotic portion of the pancreas was excised and the gallbladder was attached to the duodenum (cholecystoduodenostomy). The dog recovered uneventfully from anesthesia and surgery and was released from the hospital seven days later. The low-fat, moderate-fiber food was fed for the next three years until the dog died from other causes. Significant weight loss did not occur but body weight was stabilized at 43 kg and there was no evidence of hyperlipidemia or further pancreatitis.

Endnote

a. Hill's Pet Nutrition Inc., Topeka, KS, USA.

Bibliography

Williams DA. Acute pancreatitis. In: Kirk RW, Bonagura JD, eds. Current Veterinary Therapy XI. Philadelphia, PA: WB Saunders Co, 1992; 631-639.