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INTRODUCTION

Disorders of the digestive tract occur commonly in dogs and cats. The clinical signs involving diseases of the liver, pancreas, and bowel can show considerable overlap. This makes an accurate diagnosis a formidable challenge to the small animal practitioner.

Most experienced internists will attest that there is seldom anything pathognomonic about acute pancreatitis. Therefore, if a diagnosis is to be made, a thorough review of all of the available clinical findings is necessary.

ACUTE PANCREATITIS

Definition/overview Of the various clinical disorders treated by the small animal practitioner, there is probably none more difficult and frustrating to treat than acute pancreatitis. Despite the continuing acquisition of new knowledge regarding pancreatic physiology and pathophysiology, there is still no miracle treatment that can directly counteract the ravages of acute necrotizing pancreatitis. However, the optimal therapeutic outcome depends to a great extent on the clinician's working knowledge of the physiology, pathophysiology,

clinical features, and medical and surgical treatments for this disorder in the dog and cat.

Etiology Fortunately, the dog and cat are spared from many of the causes of pancreatitis that affect humans (Table 10.1). However, there are several general mechanisms that should be considered such as obstruction to the pancreatic duct, dietary factors, infectious agents, trauma, toxic drug reactions, metabolic abnormalities, and vascular alterations.

Pathophysiology At the cellular level the calcium-dependent intra-acinar cell activation of pancreatic digestive zymogens, particularly proteases, is an early event in the initiation of acute pancreatitis. Activation of transcription factor NF- κ B also occurs early in experimental pancreatitis. Early pathologic Ca²⁺ mobilization into acinar cells has a central role in the pathogenesis of acute pancreatitis. Another early acinar cell event is thought to be a decrease in compartmental pH. Other contributing factors to pathogenesis include neurally mediated inflammation and the production of large amounts of reactive oxygen species along with the simultaneous depletion of antioxidants.

TABLE 10.1 SOME CAUSES OF ACUTE PANCREATITIS IN HUMANS

Biliary tract disease*	Carcinoma of the pancreas*
Ethanol abuse	Hyperlipoproteinemias (type I, IV, and V in humans)*
Infectious agents (viral, bacterial, toxoplasmosis)	Hypotensive shock*
Peptic ulcer*	Hypercalcemia*
Methanol	Ductal obstruction by tumors*
Trauma, surgery	Drugs*
Scorpion bites (Trinidad)	High fat diet – dogs only*
Vascular factors – ischemia, thrombosis*	Hereditary pancreatitis, pancreas divisum

*Those which have been implicated in dogs and cats

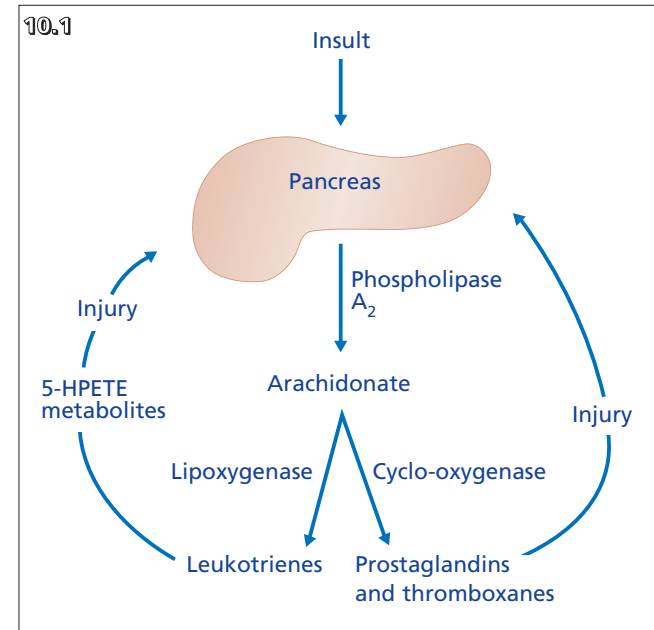
Prostaglandins are thought to have a key role in the pathogenesis of acute pancreatitis (10.1). Suspected mechanisms for these cyclo-oxygenase-2 effects include regulating heat shock protein 70 expression, inducible nitric oxide synthase activity, release of substance P, and neutrophil function. A number of factors that can cause the described disturbances of cellular metabolism will cause increased permeability of cellular lipoprotein membranes surrounding the lysosomal hydrolases in

the acinar cells, with resultant inappropriate proenzyme activation and autodigestion. At first the antiproteases will attempt to counteract the released proteases, but eventually the activation of the pancreatic proteolytic enzyme cascade will prevail and cause clinical acute pancreatitis. The characteristics of activated pancreatic enzymes and their effects on the pancreas and other tissues are shown in Table 10.2 and illustrated pathologically in 10.2–10.21.

TABLE 10.2 CHARACTERISTICS OF THE PANCREATIC ENZYMES*

Enzyme	Substrate	Effects
Lipase	Triglyceride	Fat necrosis Hypocalcemia Cell membrane damage
Phospholipase A ₂	Cell membranes	Lysophosphatide formation
	Phosphatides	Membrane destruction Vascular leakage Acute respiratory distress syndrome (ARDS)
Trypsin	Other proenzymes Kallikreinogen Scleroproteins	Coagulation necrosis
		Vascular leakage, shock
		Proteolysis Coagulopathy Kinin release
Chymotrypsin/ carboxypeptidase	Scleroproteins	Coagulation necrosis
		Proteolysis Vascular leakage
Elastase	Scleroproteins Elastic/collagen fibers of blood vessels	Coagulation necrosis Elastocollagenolysis Proteolysis Vascular leakage Hemorrhage
Kallikrein	Kinins	Kinin release

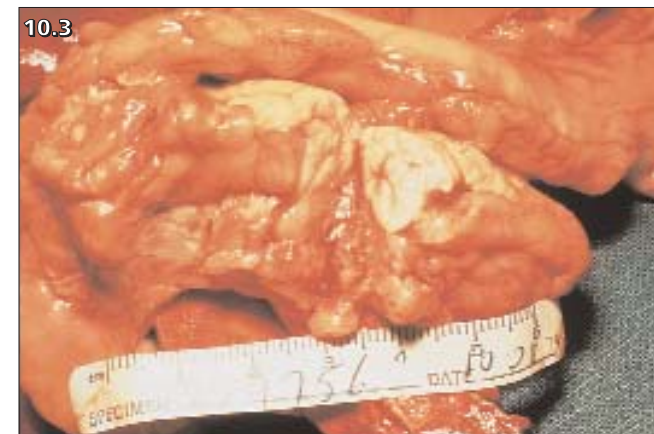
*Modified from Büchler MW, Uhl W, Malfertheiner P, Sarr MG (2004) (eds) *Diseases of the Pancreas*. Karger, Basel.



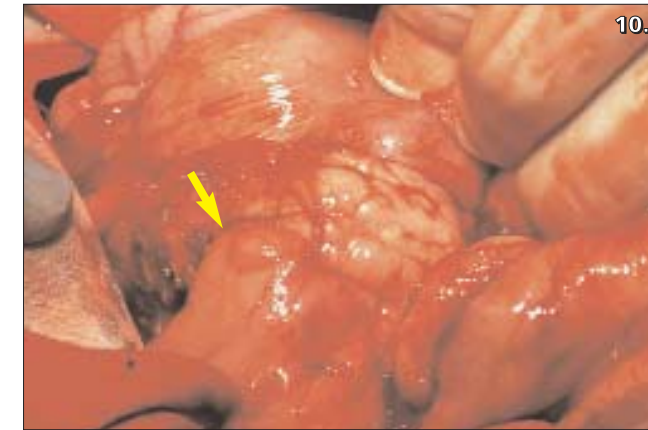
10.1 The role of prostaglandins in acute pancreatitis. Arachidonic acid metabolites are important mediators of inflammation in acute pancreatitis. 5HPETE, 5-hydroperoxyeicosatetraenoic acid. (Adapted from Nager AB, Gorelick FS (2004) Acute pancreatitis. *Current Opinions in Gastroenterology* 20(5):439–443.)



10.2 This seven-year-old male Poodle was taken to surgery after a 5–7 day period of medical treatment accompanied by persistent vomiting. Shown is edematous pancreatitis.



10.3 Postmortem specimen illustrating edematous pancreatitis and extensive peripancreatic fat necrosis. The patient was a four-year-old female Yorkshire Terrier that also had diabetic ketoacidosis and renal failure.



10.4 Surgical view of hemorrhagic necrotic pancreatitis in a ten-year-old male Wirehaired Fox Terrier. Note how one half of the pancreas is hemorrhagic and the other half is edematous (arrows).



10.5 Radiograph taken from the dog in 10.4 is typical of acute pancreatitis, showing increased fluid density in the right upper abdominal quadrant (arrow) and lateral displacement of the duodenum.



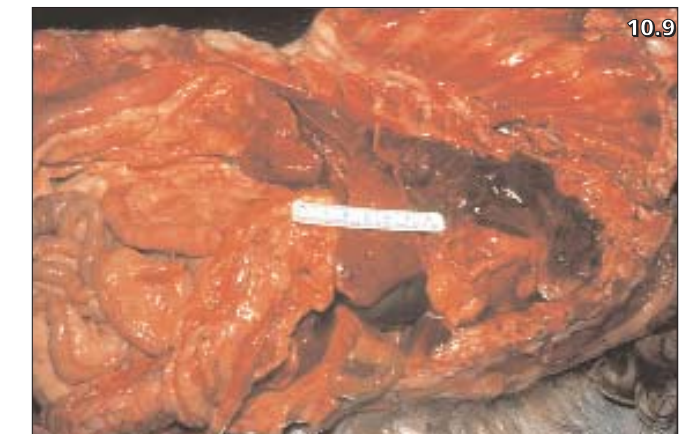
10.6 Over the ensuing year, the dog in 10.4 and 10.5 had several episodes of relapsing pancreatitis that eventually terminated with renal shutdown. This postmortem specimen shows chronic pancreatic scarring along with recent necrotic changes.



10.7 Postmortem view of the abdomen of a 13-year-old female Lhasa Apso showing diffuse edematous pancreatitis accompanied by diffuse calcium soap deposition (arrows) throughout the mesentery and omentum.



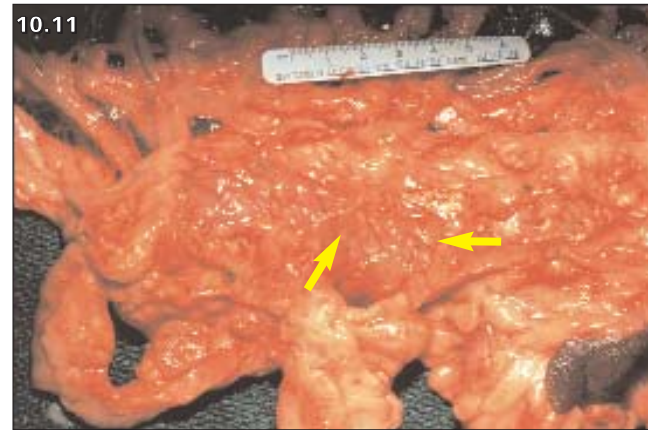
10.8 Another view of the specimen shown in 10.7. This calcium soap formation is one of the accepted explanations for the lowered serum calcium level that can accompany acute pancreatitis.



10.9 This 14-year-old male Dachshund had pleural effusion along with acute pancreatitis. Shown is the serosanguineous pleural effusion that is accompanied by calcium soap deposits on the pleural membranes underlying the thoracic viscera.



10.10 The same dog as in **10.9**, showing the intercostal muscles with calcium soap deposits (arrow).



10.11 The dog in **10.9** and **10.10** had edematous pancreatitis (arrows).



10.12 Postmortem findings of severe hemorrhagic pancreatitis complicated by pathologic coagulation causing infarction to the duodenum (arrow) and omentum.



10.13 Marked pancreatic necrosis in the specimen shown in **10.12**. The peripancreatic lymph node is markedly enlarged from hemorrhagic necrosis.



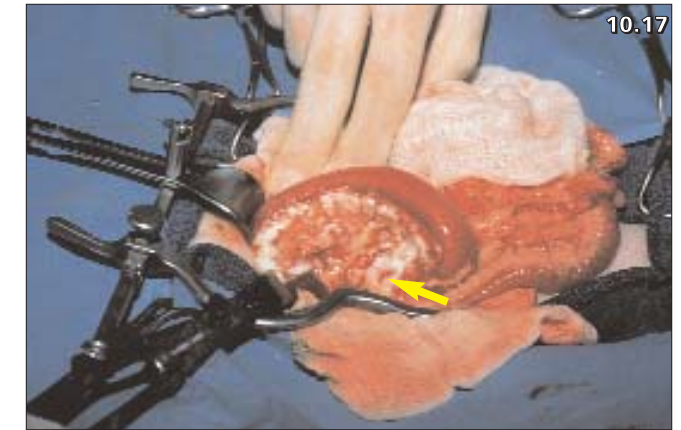
10.14 Multiple splenic infarcts in the nine-year-old dog in **10.12** and **10.13**. It was taken to surgery where it expired. DIC was the cause of the hypercoagulable state.



10.15 Surgical view of a 16-year-old cat with chronic active pancreatitis. This cat had been hospitalized three years earlier with acute pancreatitis, which responded well to conservative treatment.



10.16 This ten-year-old cat was taken to surgery for the primary problems of vomiting, depression, and a hemorrhagic abdominal effusion. Shown is hemorrhagic pancreatitis. Copious surgical lavage and the insertion of abdominal drains until 2–3 days postoperatively would be the usual surgical measures for this type of pathology.



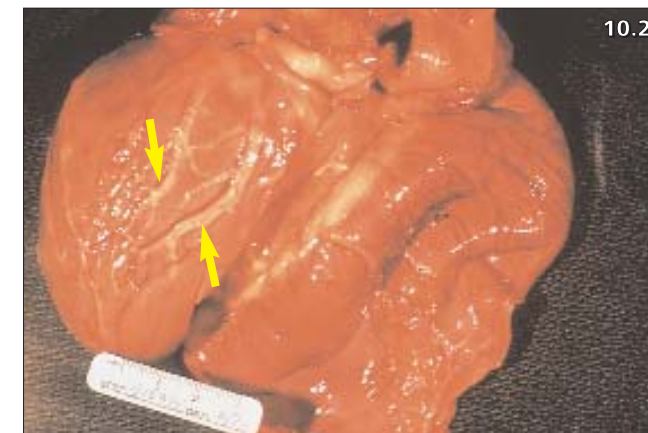
10.17 After seven days of medical therapy, this 12-year-old female cat was taken to surgery because it showed no signs of improvement. Shown is hemorrhagic pancreatitis accompanied by extensive peripancreatic and mesenteric calcium soap formation (arrow). Postoperatively, nutrition was provided through a jejunostomy tube that was inserted at the time of surgery. This cat survived after three weeks of illness.



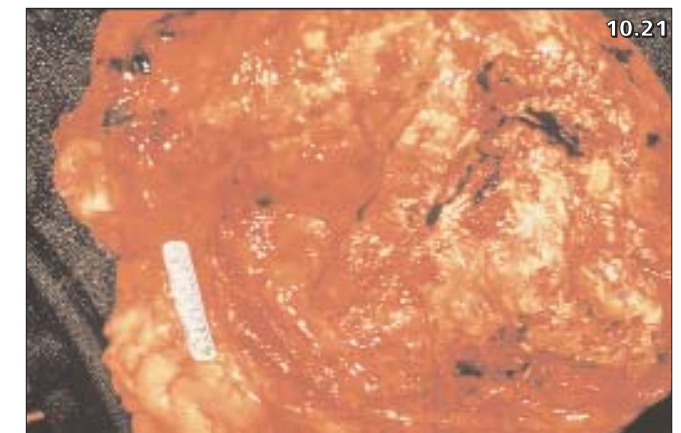
10.18 This five-year-old male Labrador Retriever had vomiting, fever, depression, and abdominal pain.



10.19 Blood samples taken initially from the dog shown in **10.18** were markedly lipemic. The patient died despite intensive medical efforts.



10.20 Postmortem examination of the dog in **10.18** showed diffuse thyroid atrophy. The severe atherosclerotic vascular lesions shown here involved the coronary arteries (arrows).



10.21 There was also extensive pancreatic phlegmon formation in the dog shown in **10.18**. The pathogenesis of this dog's pancreatitis was the hypothyroidism, which caused marked hyperlipidemia; this, in turn, could have triggered the acute pancreatitis. Hyperlipidemia is a well-known common cause of acute pancreatitis in humans.

Marked hypotension can be observed in dogs and cats with acute pancreatitis, and it is probably the main contributing factor to their demise. Studies of the hemodynamic consequences of severe pancreatitis in humans demonstrate that the cardiac index is increased and the systemic vascular resistance is decreased; these findings are similar to those in patients with sepsis. The mechanisms responsible for these effects involve various inflammatory mediators including IL-1, IL-2, IL-6, IL-8, TNF, platelet activating factor (PAF), and interferon gamma. Circulating vasoactive compounds, such as bradykinin and myocardial depressant factor (in the dog) resulting from pancreatic necrosis, also contribute to the vasomotor instability. The low blood pressure may also be due to sequestration of fluid from the plasma space into the 'third spaces' of the peritoneal cavity and retroperitoneum. Experiments in the dog have shown that approximately 35% of the total plasma volume can be lost from the circulation four hours after the induction of acute pancreatitis. The local and systemic effects of acute pancreatitis are shown (10.22).

Clinical presentation Most occurrences of acute pancreatitis in the dog involve middle-aged, obese females; however, dogs with normal weight and male dogs can also be affected. The most common historical signs involve a sudden onset of vomiting, anorexia, and mental depression. Some occurrences reportedly follow the ingestion of a fatty meal, although this might not be a consistent finding. Initially, the vomitus might contain partially undigested food and this may be followed subsequently by vomitus consisting of bile and watery mucus. After the initial vomiting, the dog might show regurgitant movements only because of nausea. Its attitude will vary from mild to marked depression, and its posture will either be normal, upright with abdominal tucking, or lateral recumbency depending on the degree of pain and hypovolemia (10.23–10.27). Diarrhea might occasionally occur, but scant or absent feces is more common due to the peritonitis-induced ileus.

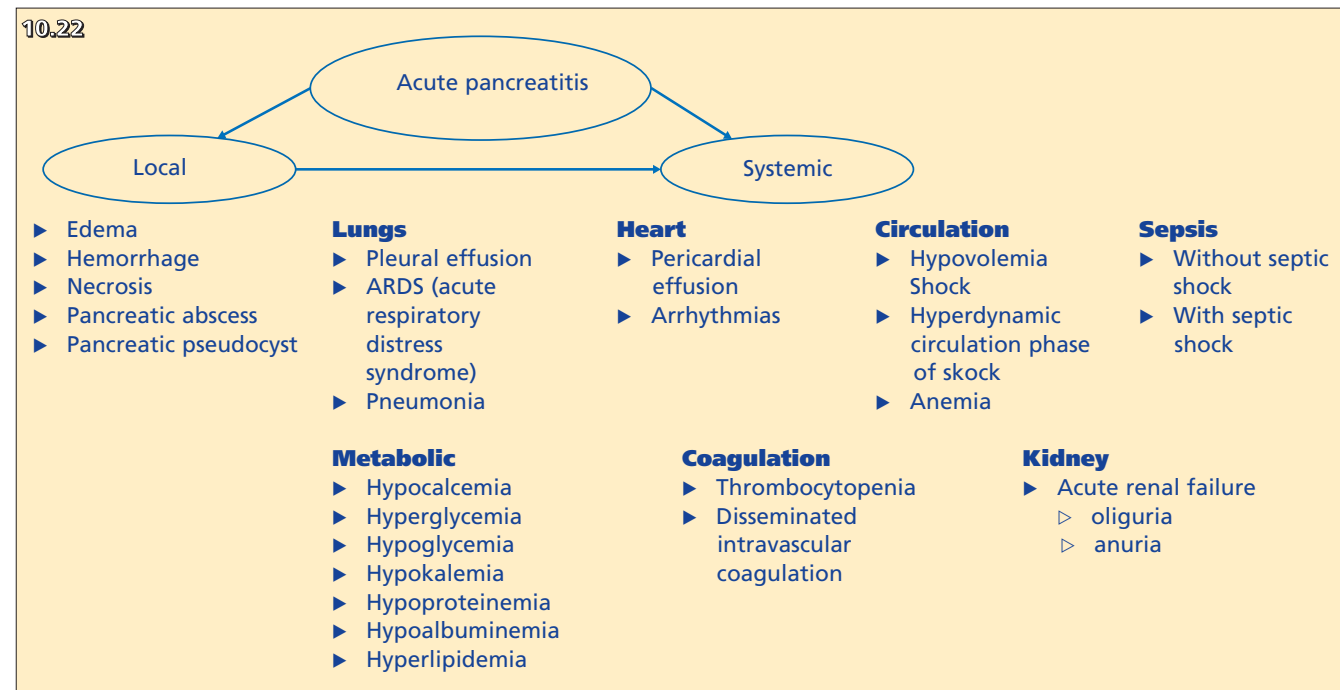
The age of cats affected with acute pancreatitis can range from young to old, although in one study the majority of the



10.23, 10.24 This five-year-old male Doberman Pinscher dog displays abnormal posturing from abdominal pain caused by acute pancreatitis. After three days of treatment the dog is pain free and postures normally.



10.25 The clinical signs of acute pancreatitis can vary from mild to marked. This 13-year-old female Poodle had acute vomiting, mental depression, and marked abdominal pain peracutely immediately after dinner. Despite the use of intensive fluid therapy, the dog died from hemorrhagic necrotic pancreatitis.



10.22 Pathophysiologic consequences of acute pancreatitis. The adverse effects of acute pancreatitis are far reaching with involvements of several organ systems. In many cases this can lead to multiple organ dysfunction and the patient's demise. (Modified from Büchler MW, Uhl W, Malfertheiner P, Sarr MG (2004) *Diseases of the Pancreas*. Karger, Basel.)



10.26 Postmortem examination on the dog in 10.25. Shown here are calcium soap deposits (arrowheads) on the abdominal fat and pancreatic ascites.



10.27 Severe hemorrhagic pancreatic necrosis (arrow) in the postmortem examination of the dog shown in 10.25.

TABLE 10.3 PRACTICAL SEVERITY SCORING IN DOGS

Disease severity	Score*	Prognosis	Clinical presentation and typical therapy
Mild	0	Excellent	Often resolves spontaneously. Recovery is uncomplicated. Managed as an outpatient, if hydration status is good. Intravenous fluids can be given, if necessary. Pancreatic rest and/or pain control is usually all that is required.
Moderate	1	Good to fair	Usually dehydrated – the renal system is most often compromised (prerenal failure). Treatment involves the administration of crystalloids at twice the maintenance rate together with electrolytes. NPO until vomiting stops, with analgesia as appropriate. Recovery is usually uncomplicated provided adequate fluid therapy is given. If anorexia lasts for more than two days, consider additional nutritional support.
	2	Fair to poor	Dehydrated, hypovolemic, often prerenal failure and degenerative left shift leucocytosis. Animals usually recover with intensive therapy, but may have to be euthanized for financial reasons. Intravenous crystalloids (initially administered as per treatment for shock) followed by colloids, with or without plasma in many cases. Monitor urine output, renal function, and lung sounds. Control pain and consider special nutritional support. Monitor coagulation status carefully and intervene early with fresh frozen plasma and heparin, if necessary. May need referral if there is a poor response to initial therapy.
Severe	3	Poor	Extensive therapy and life support is required with constant monitoring. Early referral is advised. Surgical intervention and peritoneal lavage may be necessary. Ventilatory support, central venous pressure monitoring, and high volume fluid therapy is usually needed. Jejunostomy feeding or total parenteral nutrition are often required. Most patients die and euthanasia may have to be considered.
	4	Grave	

From Ruaux and Atwell (1998) and Ruaux (2000)

*The severity scoring system is based on the number of organ systems apart from the pancreas that show evidence of failure or compromise at initial presentation.

cats were older than eight years. Many have normal body weight. The clinical signs are similar to the dog, although vomiting might be occasionally absent (10.28, 10.29).

The physical examination findings vary with the severity of the problem. Dogs and cats with mild pancreatitis might only show mild mental depression, normal vital signs, and equivocal palpable abdominal tenderness. Signs associated with the hemorrhagic necrotic form include marked mental depression; fever; hypotension with accompanying tachypnea, tachycardia, and weak femoral pulse; a painful abdomen; and a moderate to marked degree of dehydration. Abdominal palpation in the cat can sometimes detect bowel adhesions (10.30). One retrospective study involving 40 cats reported the most common signs being severe lethargy, anorexia, and dehydration. Histopathology identified acute necrotizing pancreatitis and acute pancreatic necrosis as the two main types.

Clinically detectable icterus will not occur initially with pancreatitis, but it might be evident by the third day and usually results from cholestasis; bile duct obstruction occurs rarely. Abdominal distension can result from paralytic ileus. A reddish-brown colored ascitic fluid (pancreatic ascites) can sometimes accumulate with hemorrhagic necrotic pancreatitis. A guarded to grave prognosis should always be given to those pancreatitis patients that assume lateral recumbent posture, mental dullness, oliguria/anuria, and hypotension that is resistant to treatment. A more detailed and practical severity scoring system is provided in Table 10.3.

Differential diagnosis The initial differential diagnosis of acute pancreatitis includes a variety of clinical disorders

TABLE 10.4 DIFFERENTIAL DIAGNOSIS OF ACUTE PANCREATITIS IN THE DOG AND CAT

Acute gastroenteritis	Intestinal ischemia and infarction
Intoxications	
Blunt abdominal trauma	Emphysematous cholecystitis
GI obstruction	Ruptured organs (i.e. uterus, urinary bladder, gallbladder)
GI perforation	Acute renal failure
Intestinal volvulus	Acute hepatopathy

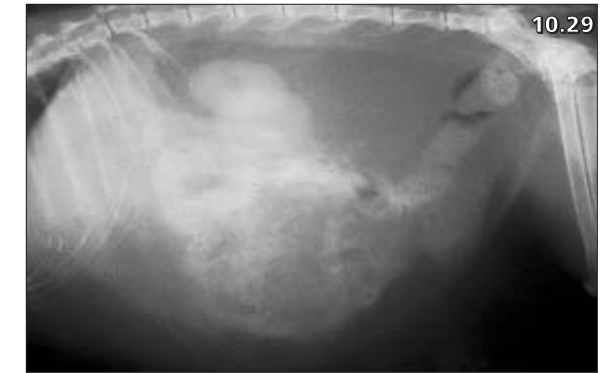
(Table 10.4). The list is extensive because the signs mimic any number of acute abdominal syndromes. Several are surgical emergencies that require rapid diagnosis and treatment.

Diagnosis

Imaging findings The two most commonly used modalities are radiology and ultrasonography. Abdominal radiographs of dogs and cats with acute pancreatitis can show several abnormalities. In the mild edematous form the findings can range from normal to mild ileus involving the stomach and duodenum. The more severe forms cause the following changes as a result of the peritonitis: increased fluid density with loss of visceral detail in the anterior abdomen, right-sided lateral displacement of a gas-distended duodenum, and gastric distension. In addition to these classic findings, acute pancreatitis can also cause radiographically demonstrable pleural effusion and pulmonary fluid accumulations (10.9–10.11, 10.29, 10.31–10.33). In cats, pleural and pericardial effusions have been described.



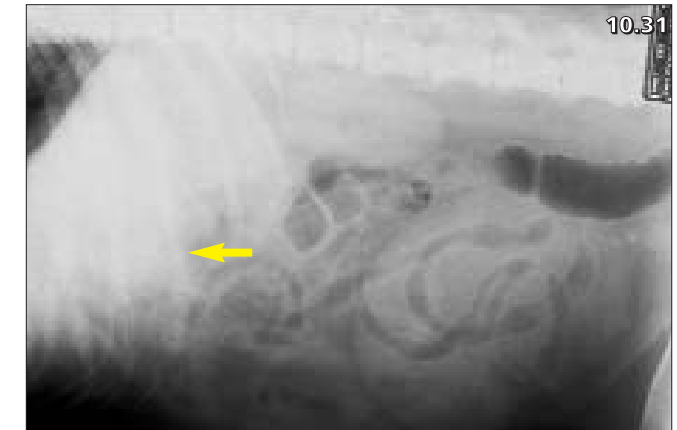
10.28 Pancreatitis in cats is typically accompanied by anorexia, mental depression, and marked inactivity. Although many cats will vomit, there are those who will not. Most cats with pancreatitis will show abdominal tenderness and varying degrees of radiographic pathology. A definitive diagnosis can only be obtained by visualizing the pancreas grossly with or without biopsy and histopathology.



10.29 Lateral abdominal radiograph of the cat in 10.28, which presented with acute pancreatitis, showing a diffuse abdominal effusion and a 'gathering effect' of the small bowel. These lesions were evident at surgery (see 10.30). The abundant amount of retroperitoneal fat causes ventral depression of the descending colon.



10.30 This surgical view of a 16-year-old female DSH cat shows small bowel adhesions, which were detectable on abdominal palpation. Also shown are diffuse calcium soap deposits on the parietal and visceral peritoneal surfaces. These deposits are pathognomonic of acute pancreatitis.



10.31, 10.32 Lateral and ventrodorsal abdominal radiographs of a dog illustrating several abnormalities indicative of acute pancreatitis. The lateral projection (10.31) shows a loss of detail in the anterior mid abdomen and an increased fluid density in the anterior abdomen just caudal to the liver (arrow). The ventral dorsal view (10.32) shows an increased right upper abdominal fluid density along with duodenal ileus and lateralization (arrow).



10.33 This lateral thoracic radiograph from an adult Labrador Retriever shows a pleural effusion as well as pulmonary infiltrate. The dog had hemorrhagic necrotic pancreatitis and secondary acute respiratory distress syndrome.

Ultrasonography is very useful in detecting pathology associated with pancreatitis in the dog and cat. While the normal pancreas is seldom visualized, the inflamed organ in the dog acquires an increased hypoechogenicity. In the presence of peripancreatic fat inflammation, the perimeter of the pancreas becomes hyperechogenic. Additional findings in the dog include pancreatic enlargement and irregularity, peritoneal effusion, and evidence of extrahepatic biliary obstruction. Inflammation of the right pancreatic limb can cause the duodenum to appear thickened. One study describing the ultrasonographic findings of acute pancreatitis in cats included hypoechogenic pancreas, hyperechoic peripancreatic mesentery, peritoneal effusion, pancreatic enlargement, hyperechoic hepatomegaly, and mixed hypo- and hyperpancreatic echogenicity. Pancreatic anechoic pseudocyst and abscess formation, and pancreatic ascites, can also be detected with ultrasonography (10.34, 10.35). Overlying distended bowel loops are the major limitation to this imaging technique (10.36–10.39).

Clinicopathologic findings The characteristic laboratory test abnormalities of acute pancreatitis in dogs and cats have been described. These are listed in Table 10.5 and illustrated in 10.40. In cats the serum biochemical profile is variable, ranging from normal to abnormalities involving renal, liver, glucose, protein, and electrolyte parameters. The hemogram often indicates an inflammatory response. One study in 46 cats with pancreatitis suggests that low plasma ionized calcium concentration is common and is associated with a guarded to grave prognosis, especially when ionized calcium concentrations are ≤ 1.00 mmol/l. The choice between the selection of amylase or lipase as a

diagnostic test has been a subject of controversy for several years, because both enzyme levels can be normal or elevated from other conditions despite the presence of acute pancreatitis, thus causing them to lack both sensitivity and specificity. Increases in serum amylase levels to 3–5 times normal are strongly suspicious of acute pancreatitis in the appropriate clinical setting.

The serum lipase level has been reported to be more reliable than amylase for diagnosing acute pancreatitis in the dog. However, lipase as well as amylase may be elevated in patients with serious abdominal illnesses such as hepatopathies and renal and neoplastic disease. Serum amylase and lipase activities can be normal or even decreased despite the presence of serious pancreatic damage. The interpretation of serum amylase and lipase results should always be made solely within the context of the patient's other ongoing clinical findings.

In feline pancreatitis the appearance of abnormally elevated serum amylase and lipase levels are typically variable and should never be the sole criteria for diagnosis. Normal levels of both enzymes commonly occur in the cat despite the presence of acute pancreatitis. A two-fold or more increase in serum amylase and lipase activity in the presence of normal renal function is suggestive of acute pancreatitis when used with other supportive clinical findings.

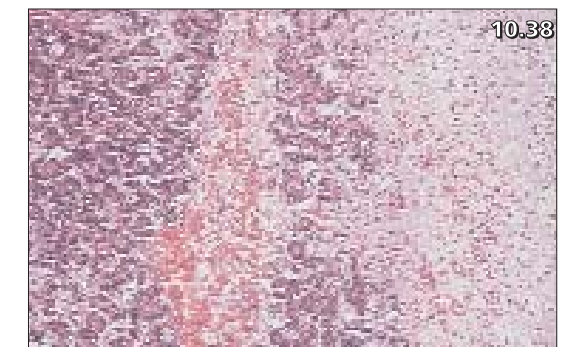
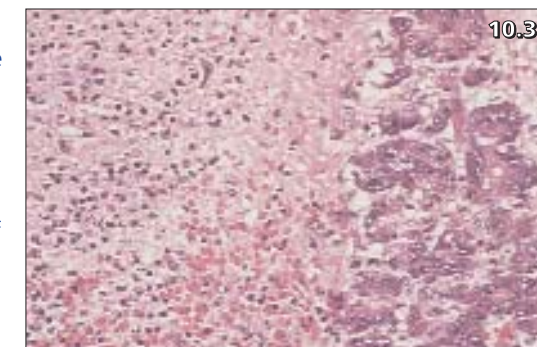
When the feline TLI concentration test first became available, there was a false dependence on its proposed accuracy. It is no longer recommended as a diagnostic test for acute pancreatitis in cats.

In dogs the canine pancreatic lipase immunoreactivity (PLI) test is supposed to be fairly sensitive for diagnosing acute pancreatitis. The diagnostic cut-off value is 200 $\mu\text{g/l}$. This test

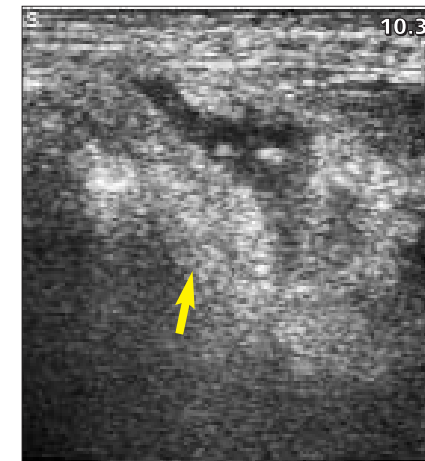
10.36 Abdominal ultrasound examination of a seven-year-old male English Cocker Spaniel showing lesions typical of acute pancreatitis, including hypoechogenicity of the pancreatic parenchyma (arrowhead) and prominent hyperechogenicity of the inflamed peripancreatic fat, which contained ample calcium soap deposits (arrow). This dog was also in an Addisonian crisis. He went anuric and was subsequently euthanized. The postmortem findings included acute necrotizing pancreatitis (similar to 10.26, 10.27), bilateral adrenocortical atrophy, and thyroid atrophy. It was thought that the untreated hypothyroidism caused hyperlipidemia, which could have predisposed the dog to acute pancreatitis. The adrenal and thyroid conditions could have been associated with an autoimmune polyhypoendocrinopathy condition.



10.37, 10.38 Histopathology of the pancreas of the dog in 10.36 showing glandular necrosis, hemorrhage, edema, and inflammatory infiltrate consisting of neutrophils and macrophages. (H&E) (Photomicrographs courtesy P Ginn)



10.39 Cats can also have typical ultrasonographic signs of acute pancreatitis, as evidenced by parenchymal hypoechogenicity and a 'rim' of hyperechogenicity (arrow). This seven-year-old male cat was also a ketoacidotic diabetic who gradually improved with three weeks of intensive medical treatment alone. He eventually became cured of both diseases.



10.40	
Glucose	48.6 mmol/l (884 mg/dl)
BUN (urea)	35.7 mmol/l (100 mg/dl)
Creatinine	424 $\mu\text{mol/l}$ (4.8 mg/dl)
Cholesterol	7.8 mmol/l (300 mg/dl)
Total bilirubin	61.5 $\mu\text{mol/l}$ (3.6 mg/dl)
Total protein	74 g/l (7.4 g/dl)
Albumin	26 g/l (2.6 g/dl)
ALP	492 U/l
Calcium	2.2 mmol/l (8.8 mg/dl)
Phosphorus	1.5 mmol/l (4.7 mg/dl)
AST	110 U/l
ALT	46 U/l
Globulin	48 g/l (4.8 g/dl)
Chloride	103 mmol/l (103 mEq/l)
Sodium	130 mmol/l (130 mEq/l)
Potassium	4.4 mmol/l (4.4 mEq/l)
Total CO ₂	12 mmol/l (12 mEq/l)
Amylase	3,000 U/l
Lipase	2.0 U/l
Osmolality	360 mOsmol/kg

10.40 Example of marked serum biochemical abnormalities taken from the dog in 10.3. These results support the additional clinical diagnoses of hyperosmolar diabetic ketoacidosis and renal failure. The serum amylase and lipase exceeded the upper limits of normal by twofold, thus supporting the main clinical diagnosis of acute pancreatitis. The lowered serum calcium level is attributed to calcium soap formation. The elevated liver enzymes are likely due to hepatic lipidosis and cholangiostasis, while the hyponatremia could have been due to losses from impaired renal tubular sodium reabsorption, osmotic diuresis, and vomiting. Pseudohyponatremia could have also been present from hyperlipidemia or marked hyperglycemia. The low total CO₂ reflects metabolic acidosis, and the hyperosmolality is due to the marked hyperglycemia.



10.34, 10.35 These abdominal ultrasonograms are from a five-year-old male Irish Setter taken two weeks after a bout of acute pancreatitis. 10.34 is a general orientation of the dog's upper abdomen showing an anechoic area in the pancreas. 10.35 shows a more detailed view of the pancreatic cavitation. The transabdominal fine needle aspiration yielded a dark colored fluid that was composed of sterile amorphous debris. All of the 'cystic' fluid was removed by aspiration and the dog recovered well.