

Acute pancreatitis in dogs: a review article

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SUMMARY

Canine acute pancreatitis is a relatively common disease, but it is often misdiagnosed. The most common causes of acute pancreatitis in dogs include malnutrition, drug administration, infection, trauma, reflux of duodenum contents into the pancreatic duct and ischaemia. Idiopathic causes have also been encountered. The clinical signs of the disease are not specific and are often associated with a number of life-threatening, severe systemic complications. Despite the continuing new knowledge of pancreatic pathophysiology, the aetiopathogenesis of canine pancreatitis is still unclear and subsequently treatment is supportive.

Key words: Exocrine pancreas; Canine; Aetiology; Pathogenesis

Definition and Incidence

According to the Atlanta Symposium, acute pancreatitis (AP) is defined as an acute inflammatory process of the pancreas with variable involvement of other regional tissues or remote organ systems [1]. The above definition refers to humans, but it also characterizes the disease in dogs. Based on the patient's condition, it is classified as mild, moderate or severe, and non - fatal or fatal [2, 3]. Histopathological criteria for AP include pancreatic oedema and necrosis, infiltration of mononuclear and polymorphonuclear cells, peripancreatic fat necrosis and thrombosis, but without permanent disruption of the pancreatic architecture. In humans, AP is usually complicated by pancreatic pseudocyst formation, abscesses and acute intraabdominal fluid collection [2, 3], which are rather rare in dogs. Several terms related to AP have been replaced or abandoned in human medicine. *Infected pseudocyst* is replaced by *pancreatic abscess*, and *persistent acute pancreatitis* is replaced by *interstitial or necrotizing pancreatitis*. *Haemorrhagic pancreatitis* was abandoned, because most cases of pancreatic necrosis occur without gross intraglandular haemorrhage [4].

Although AP is a common disease in dogs, it is often misdiagnosed, especially in its mild forms, because of the lack of pathognomonic clinical signs, and diagnostic tests with high sensitivity and specificity [3].

Outline of anatomy and physiology of the pancreas

The pancreas lies in the cranioventral abdomen and consists of right and left lobes with a small central body. The right lobe lies in contact or in close proximity to the descending duodenum and contains most of the pancreatic polypeptide-producing cells, while the left lobe lies between the greater curvature of the stomach and the transverse colon and contains glucagon-secreting cells. Each pancreatic lobule is composed mainly of acinar cells that synthesize the digestive enzymes in the form of proenzymes and store them in zymogen granules. The pancreas of the dog usually has two ducts by which secretions are transported from the organ to the descending duodenum [5]. The pancreas also contains endocrine tissue, the islets of Langerhans, accounting for one to two percent of the gland [3].

The main function of the exocrine pancreas is the secretion by the acinar cells of a fluid rich in digestive enzymes involved in the initial degradation of proteins, lipids, and polysaccharides [6]. Exocrine pancreatic proteases include trypsin, chymotrypsin, elastase, carboxypeptidase A and B, and Phospholipase A.

The principal inorganic components of exocrine pancreatic secretions include water, sodium, potassium, chloride, bicarbonate. The exocrine pancreatic secretions facilitate delivery

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of digestive enzymes to the lumen of the duodenum and neutralize acidic content coming from the stomach [7]. Colipase, contained in the pancreatic fluid, facilitates the breakdown of fats by the pancreatic lipase [8]. The pancreatic juice also contains factors that enable the absorption of cobalamin (vitamin B₁₂) and zinc, as well as antibacterial agents, and "trophic agents" for the small intestinal mucosa [9].

Several mechanisms protect the normal pancreas against autodigestion. The proteolytic enzymes are synthesized and secreted by the pancreas in an inactive form (zymogens) into the duodenum. The enterocytes lining the duodenal mucosa are responsible for the synthesis of an enzyme called *enteropeptidase* that converts inactive trypsinogen to active trypsin. Trypsin, in turn, activates the remaining digestive enzymes [9-11]. Another protective mechanism against early trypsin activity is the synthesis and secretion of pancreatic secretory trypsin inhibitor (PSTI) by the acinar cells [9-11, 12]. Moreover, blood plasma contains several antiproteases, such as α 1-proteinase inhibitor, α 2-macroglobulin and antichymotrypsin, which limit intrapancreatic proenzyme activation [10]. Additional protective mechanisms include the sequestration of pancreatic enzymes within the intracellular compartments of the acinar cells during synthesis and transport, and the separation of digestive enzymes from lysosomal hydrolases as they pass through the Golgi apparatus (Figure 1) [3].

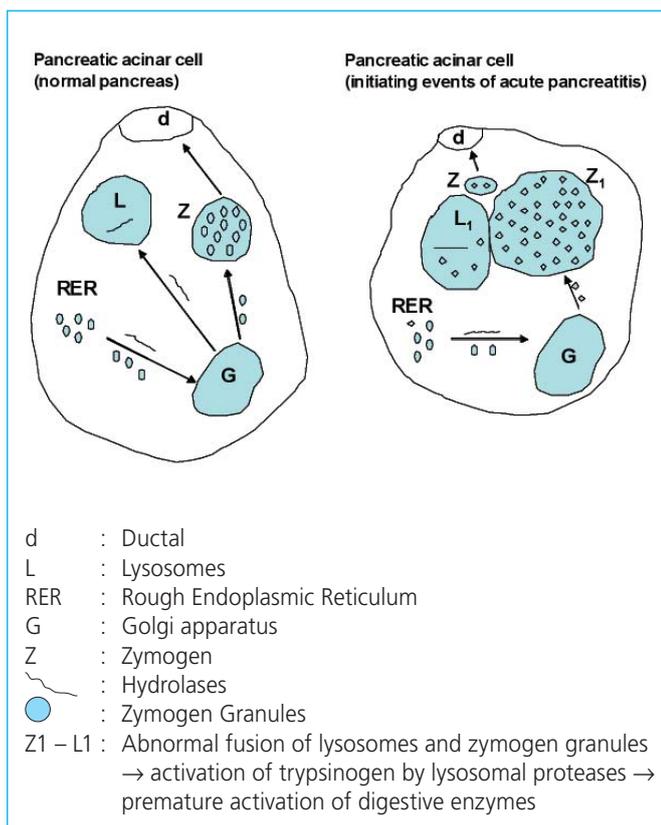
Pathogenesis

It is believed that AP develops because of premature activation of the digestive zymogens within the acinar cell (Figure 1). Premature activation of trypsin results in further activation of all

zymogens, which contributes to pancreatic inflammation, acinar necrosis and peripancreatic fat necrosis [9-11].

Normally, free plasma protease inhibitors inactivate the proteolytic enzymes released into the circulation. Consequently, α 1-proteinase inhibitor, which serves as a transient inhibitor, passes the proteases on to α 2-macroglobulins. Finally, the enzyme-macroglobulin complex is cleared from the plasma by the monocyte-macrophage system [9-11]. During an episode of AP, excessive trypsin causes depletion of the trypsin inhibitors in the pancreas and plasma [9, 11-13]. Furthermore the barrier, which normally inhibits the translocation of bacteria from the intestine into the systemic circulation, breaks down. Under condition of stress, such as acute inflammation, the pancreas becomes vulnerable to bacterial infections. In canine experimental pancreatitis luminal *Escherichia coli* translocates to mesenteric lymph nodes and remote organs [14]. These pathophysiologic events may produce systemic inflammatory response syndrome (SIRS), acute respiratory distress (ARDS) and multiorgan failure. In experimental pancreatitis in rats, activation of trypsin occurs within 10 minutes, and large amounts of trypsin and increased concentrations of trypsinogen activation peptide (TAP) accumulate within the pancreas [15]. TAP is produced when trypsinogen is activated to trypsin and serum or urine concentration of TAP correlates with the severity of pancreatic inflammatory response [16]. While enzyme synthesis continues, early blockage of pancreatic secretion may produce AP [4]. AP produces microcirculatory injury, leukocyte chemoattraction and release of cytokines, oxidative stress and bacterial translocation [4]. The release of pancreatic enzymes damages the vascular endothelium and the acinar cells, producing microcirculatory changes, vasoconstriction, capillary stasis, progressive ischaemia and oedema of the pancreas. Pancreatic damage may lead to the release of free radicals and inflammatory cytokines into the circulation, which could cause further multiorgan failure. In cases of AP, active granulocytes and macrophages release proinflammatory cytokines (TNF- α , IL-1, IL-6, IL-8), arachidonic acid metabolites (prostaglandins, PAF and leukotrienes) and reactive oxygen metabolites. These substances also interact with the pancreatic microcirculation and increase vascular permeability, which in turn induces thrombosis and haemorrhage (Figure 2) [4].

Figure 1: Initiating events of acute pancreatitis.



Aetiology

The inciting cause of canine AP usually remains unclear. However, the following trigger factors should be considered:

Diet: low-protein, high-fat diets seem to induce pancreatitis probably by stimulating oversecretion [9-11]. It is still indefinite whether hyperlipidaemia causes AP or it is the result of AP [9-11, 17, 18].

Drugs: the drugs most commonly used in veterinary practice and suspected of causing canine AP are azathioprine, oestrogens, tetracycline, chlorthiazides, thiazide diuretics, furosemide, L-asparaginase, potassium bromide and organophosphates [9-12]. The role of steroids in the aetiopathogenesis of AP is controversial. It has been found that steroid administration is related with high serum lipase activity. However, there is still no evidence of steroids inducing pancreatitis [19, 20].

Duodenal fluid reflux: conditions, such as vomiting or

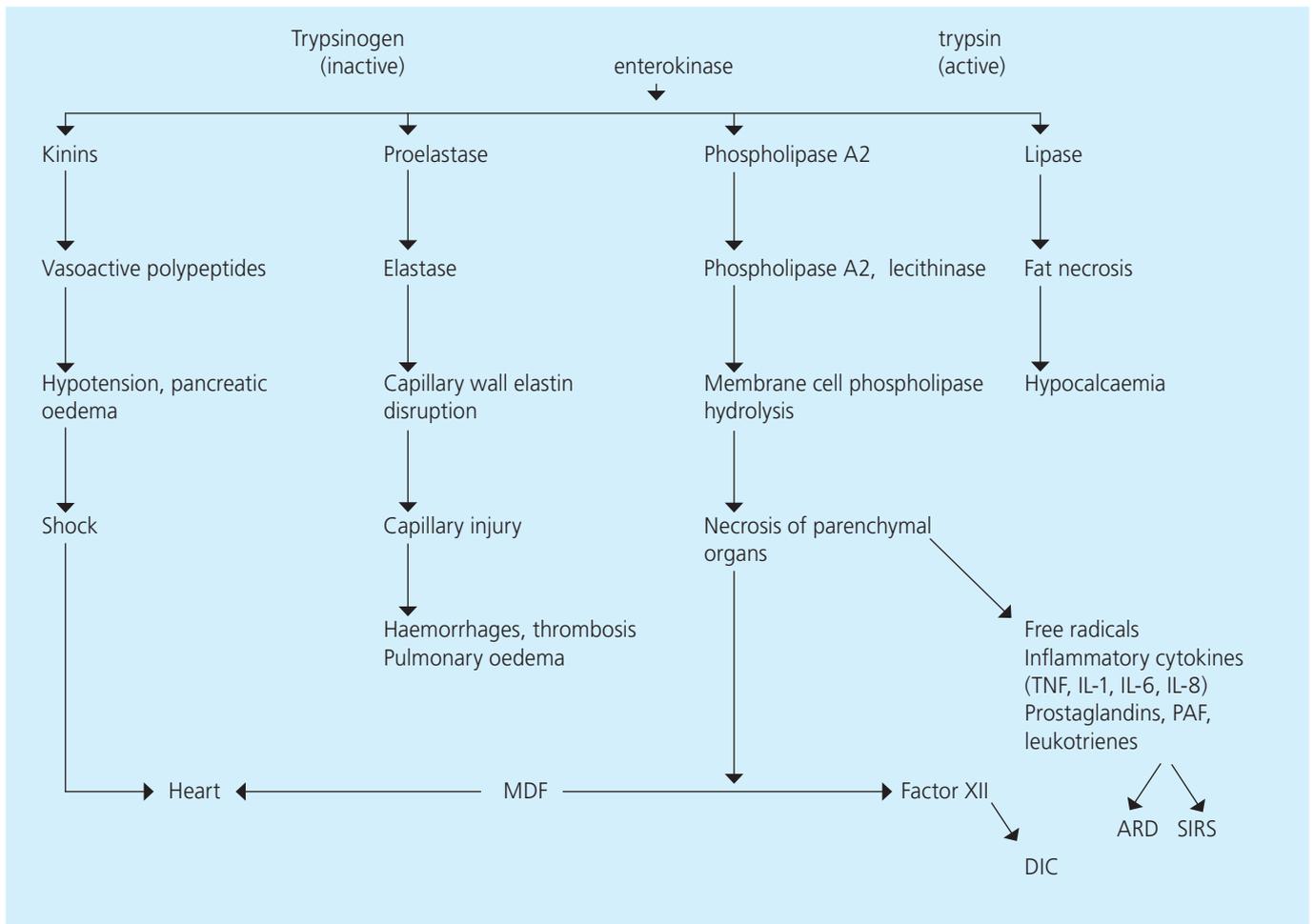


Figure 2. Pathophysiology of systemic complications of AP (neutralization of protective mechanisms).

MDF: Myocardial Depressant Factor
 DIC: Disseminated Intravascular Coagulation
 ARD: Acute Respiratory Distress
 SIRS: Systemic Inflammatory Response Syndrome
 TNF: Tumor Necrosis Factor
 IL: Interleukin
 PAF: Platelet Activating Factor

altered intestinal motility, disorganise the antireflux protective mechanism of the high-pressure system of the sphincter of Oddi and the pancreatic duct. Duodenal contents (active pancreatic enzymes, bacteria and bile) reflux into the pancreatic ducts contributes to the development of AP [9, 11, 12, 18].

Pancreatic trauma/ischaemia: intraabdominal surgical procedures and manipulations, including biopsy of the pancreas, or accidental trauma could be the inciting cause of AP [9-11, 18]. According to our experience, in a total of 47 cases, surgical pancreatic biopsies did not produce AP (unpublished data). Moreover, ischaemia of the pancreas due to shock, severe anaemia, and hypotension may also lead to the onset of AP [9, 11, 18].

Hypercalcaemia: it is a rather uncommon finding in dogs with AP. However, it is suspected to have a fundamental role in the pathogenesis of AP on a cellular basis. Exposure of acinar cells to free radicals causes increased calcium concentration. This abnormal increase can trigger trypsin activation, acinar cell damage and AP [21].

Infectious agents: while some infectious agents (Feline Infectious Peritonitis Virus, *Toxoplasma gondii*) and liver flukes are considered as potential causes of AP in cats [9, 18], there is no such evidence in dogs. However, canine babesiosis can cause AP either primarily or as a complication to SIRS [22].

History, Risk Factors and Clinical Signs

Most affected dogs are middle-aged or older [23]. Miniature schnauzers, Yorkshire terriers and Skye terriers may be at increased risk of developing pancreatitis. Recent data suggest that mutations of PSTI gene might be associated with pancreatitis in Miniature schnauzers [24]. Males and neutered females appear to be in a high-risk group of developing the severe form of AP [23]. Concurrent diseases, such as diabetes mellitus, hyperadrenocorticism, hypothyroidism and epilepsy are related to a poorer prognosis [23]. However, epileptic dogs receiving a combination of potassium bromide and phenobarbital may be at high risk of developing AP [25].

Dogs with AP are usually presented with a sudden onset of widely varied clinical signs, such as pyrexia, anorexia, vomiting, weakness, and diarrhoea, as well as adoption of "praying" position that indicates cranial abdominal pain. In severely affected dogs, hemorrhagic diarrhoea, shock, and even sudden death may be seen. Most animals are mildly to moderately dehydrated and the palpation of a mass in the cranial abdomen may be

a possible clinical finding. Jaundice, bleeding disorders, ARDS, and cardiac arrhythmias, as a result of systemic complications of severe AP and multi-organ failure, may rarely be observed [9, 26].

Due to the vague clinical signs of AP, differential diagnosis should include all the conditions causing acute abdomen syndrome:

- Acute enteritis or gastroenteritis (*Parvo-virus*, syndrome of acute gastroenteritis)
- Exacerbation of inflammatory bowel disease
- Intestinal obstruction, particularly due to foreign bodies or intussusception
- Peritonitis
- Acute renal failure
- Acute hepatitis/acute hepatic failure
- Pyometra
- Ruptured abdominal organs
- Acute prostatitis

Complications of acute pancreatitis

The most commonly seen complications of AP are diabetes mellitus, diabetic ketoacidosis, intestinal obstruction, bile duct obstruction, renal failure and pulmonary oedema; rare complications of acute pancreatitis include pleural effusion, pancreatic abscess and pseudocyst formation, cardiac arrhythmia, disseminated intravascular coagulation (DIC), bacteraemia and acute respiratory distress (ARD) [27, 28].

Pathophysiology of systemic complications of acute pancreatitis

In the presence of severe AP, hyperproduction of proinflammatory cytokines, such as tumor necrosis factor- α (TNF- α) and interleukin (IL-6), is noticed, resulting in upregulation of the immune system. These substances, and especially TNF- α , stimulate the accumulation of neutrophils mainly at the site of inflammation (pancreatic tissue) and pulmonary parenchyma, which in turn are degranulated resulting in the secretion of proteolytic enzymes and oxidative substances causing endothelial damage, cellular dysfunction, DIC, formation of emboli and finally multiple organ failure syndrome (Figure 2) [17, 27-30].

Diabetes mellitus / Diabetic ketoacidosis

During an episode of AP, transient or permanent hyperglycaemia may be the result of progressive islet cell destruction. Alternatively, autoantibodies directed against insulin secreting cells might trigger generalized pancreatic inflammation. Diabetic ketoacidosis may also occur [28, 31]. It should be mentioned that human patients with diabetic ketoacidosis without suffering from AP might show signs of abdominal pain and increased values of serum glucose and amylase [28].

Acute renal failure

Aetiologic factors for acute renal failure are hypovolaemia / ischaemia, release of proteolytic enzymes from the inflamed pancreas and the presence of intravascular coagulopathy [28, 29].

Coagulation abnormalities / SIRS/ Cardiac arrhythmia

The extrinsic coagulation pathway is stimulated and DIC is established [27]. In a retrospective study, 61% of the dogs with severe AP showed prolonged partial thromboplastin time (PTT), and 43% prolonged prothrombin time (PT) [26]. Therefore, performing coagulation function tests is recommended in all dogs having or being suspected of having AP.

Severe AP promotes bacterial translocation into the circulation resulting in septicaemia [27, 32]. It is the authors' impression that this might be the same mechanism as the one that produces spontaneous peritonitis in humans.

In the presence of AP, trypsin stimulates the formation of a bradykinin that increases vascular permeability, while acinar cells produce the myocardial depressant factor (MDF). The exact role of MDF is not known, but in experimental pancreatectomy in animals the amount of MDF was decreased [27].

Acute respiratory distress syndrome / Pulmonary oedema / Pleural effusion

Monocytes and macrophages are believed to be the main source of TNF- α production, and in the presence of large numbers of alveolar macrophages the early development of ARD may be explained [27]. In addition, one of the main pancreatic enzymes involved in pulmonary surfactant degradation and development of ARD is considered to be phospholipase (lecithinase) [33]. Lecithin is an essential component for normal pulmonary function, and its degradation may be responsible for alveolar collapse in AP [28]. Pleural effusion may be present in patients suffering from AP due to altered vascular permeability [27].

Pancreatic abscess / pseudocyst formation

Pancreatic abscess is defined as the collection of pus with little or no pancreatic necrosis, usually associated with superinfection of a pseudocyst by the enteric flora, from which bacterial cultivation is possible [34, 35]. Pancreatic pseudocyst is defined as the collection of sterile pancreatic juice surrounded by a capsule of fibrous or granulation tissue [34, 35]. Both pancreatic abscess and pseudocyst are uncommon complications of AP but should be suspected in any case where clinical signs do not resolve [35].

Diagnostic approach to acute pancreatitis

The diagnostic approach to a dog suspected of having AP should include a complete blood count (CBC), serum biochemistry profile, urinalysis and diagnostic imaging. However, the changes seen are non-specific.

Complete blood count

Evidence of dehydration with high packed cell volume (PCV) and plasma protein concentration is a common finding. On the other hand, anaemia is possible in some cases and can be explained either by the shortened life span due to azotemia and decreased production of the red blood cells in AP or due to the presence of bloody diarrhoea [18, 36]. Some dogs may have pancreatic ascites characterized by a serosanguineous fluid that may also contribute to the low PCV [36]. Leukocytosis characterized by a neutrophilia with a left shift is expected, especially in the

cases where significant inflammation is present (i.e., peritonitis, pancreatic abscess) [18, 36]. Additional tests of haemostasis, e.g. PT, APTT, fibrinogen, D-dimer, and/or FDPs, must be performed in cases of thrombocytopenia in dogs having or being suspected of having AP.

Serum biochemistry profile

Increased blood urea nitrogen (BUN) and creatinine concentrations in dogs unable to eat or drink may be due to prerenal azotemia, or it may be the result of acute renal failure [9, 11, 18]. Urine analysis, prior to fluid therapy, could help to differentiate prerenal and renal azotemia based on the urine specific gravity.

Elevation of serum liver enzyme levels reflect hepatic inflammation either due to the close anatomical proximity of the pancreas or due to the inflammation caused by the pancreatic enzymes delivered from the pancreas in portal circulation or due to cholestasis [18]. Hyperbilirubinaemia usually indicates bile duct obstruction secondary to pancreatic oedema/inflammation [18].

Hyponatraemia and hypokalaemia are frequently seen and associated with anorexia, gastrointestinal electrolyte loss, osmotic diuresis and aldosterone stimulation secondary to hypovolaemia [18, 36].

During an episode of AP hyperglycaemia is expected and is associated with hyperglucagonaemia, hypoinsulinaemia due to islet cell destruction and elevation of gluconeogenic hormones (catecholamines and cortisol) [9, 18, 28, 36].

Proposed explanations for the hypocalcaemia seen in AP are hypomagnesaemia, calcium soap deposition, hyperglucagonaemia resulting in increased calcitonin secretion and decreased parathormone secretion [28, 36]. Dogs with AP are often hypoalbuminaemic and since approximately half of the circulating calcium is bound to albumin, total calcium measurements may be correspondingly low [26, 28, 36]. Ideally, ionized calcium should be measured to detect hypocalcaemia, or the total serum calcium should be corrected for the degree of hypoalbuminaemia based on the following formula:

Corrected calcium (mg/dl) = Serum calcium (mg/dl) - Serum albumin (g/dl) + 3.5

Pancreas specific enzymes

Classically, increased activities of serum amylase and lipase have been used as indicators of pancreatic inflammation in dogs. However, elevation of these enzymes may be observed in diseases of other organ systems or other disorders of the pancreas, such as renal failure, hepatic disease, GI neoplasia, pancreatic neoplasia-abscess and duct obstruction [37-39]. Serum lipase activity was found to be increased in young dogs with enteritis or gastroenteritis [40]. It has been shown that the sensitivity/specificity for amylase is 62%/57%, and for lipase 73%/55%, respectively [41]. In a recent study of 23 dogs with macroscopic and histological evidence of pancreatic inflammation, serum lipase had the lowest sensitivity (13%), followed by serum amylase activity (17.4%) [42]. Furthermore, corticosteroid administration may increase serum lipase activity up to five-fold without histologic evidence of pancreatitis [19, 20]. In contrast, the administration of corticosteroids appears to decrease serum amylase activity [19, 20]. In summary, serum

amylase and lipase activities are of limited clinical value in dogs with AP.

Trypsin-like immunoreactivity (TLI) is specific for exocrine pancreatic function in dogs. According to experimental studies, TLI declines to the lower limit after pancreatectomy in dogs [43] and increases after pancreatic duct ligation [44]. It is suggested, that TLI is an early indicator of AP, because peak concentrations are noticed more rapidly than amylase and lipase [44, 45], but its early decline to normal values indicates that we cannot rule out AP if TLI concentration is normal [44]. Serum TLI concentrations are increased in experimentally induced pancreatitis. However, these elevations are observed in less than 40% of dogs with spontaneous pancreatitis, making it a suboptimal diagnostic test for pancreatitis in dogs [46]. According to recent data, the sensitivity of TLI appears to be approximately 34.8% [42].

Limitations in the sensitivity and specificity of TLI led to the development of a new diagnostic test. An enzyme-linked immunosorbent assay (ELISA) for the determination of canine pancreatic lipase immunoreactivity (cPLI) was developed [47]. The use of immunoassays allows for the specific measurement of lipase activity originating from the exocrine pancreas and is specific for assessing exocrine pancreatic function. Serum cPLI concentrations were significantly decreased in dogs with exocrine pancreatic insufficiency [48], while were found to be normal in 24/25 dogs with biopsy proven gastritis, indicating that serum cPLI concentration originates from the exocrine pancreas and is specific for exocrine pancreatic function determination. In another study serum cPLI was evaluated in dogs with experimentally induced chronic renal failure, where none of the dogs had serum cPLI concentrations above the cut-off value for pancreatitis [49]. Further studies showed that serum cPLI is sensitive (81.8%) for the diagnosis of AP in dogs [46]. Thus, serum cPLI is not only a specific marker for exocrine pancreatic function but is also highly sensitive for the diagnosis of canine pancreatitis.

Trypsinogen activation peptide (TAP) is a small peptide that derives from further activation of trypsinogen that sometimes occurs during an episode of AP and therefore is measurable in plasma and urine [50]. Measurement of serum TAP and/or urine TAP to creatinine ratio (UTCR) seems to be of more importance in severe, necrotizing pancreatitis and may be a better prognostic than a diagnostic indicator of pancreatic inflammation [41, 50]. Peritoneal fluid lipase activity may be a more sensitive and specific marker than serum lipase activity. It is suggested that a two-fold increase of lipase activity in peritoneal fluid over serum activity may be indicative of pancreatic inflammation [51]. Controlled trials are needed to substantiate this hypothesis.

Radiographic studies

The main radiographic abnormalities associated with AP are increased radiopacity and loss of detail in the right cranial quadrant, gas filling and displacement of descending duodenum and/or stomach, widening of gastric/duodenal angle, and abdominal fluid leading to local increased opacity [37]. The described changes are not always present and are non-specific. However, abdominal radiographs are a valuable tool in ruling out other gastrointestinal diseases.

Ultrasonography

Ultrasonographic findings associated with AP include hypoechoic pancreatic parenchyma, hyperechoic mesentery, pancreatic enlargement, peritoneal effusion, and identification of pancreatic cysts, pseudocysts, or masses [37, 52]. One study in dogs with fatal acute pancreatitis indicated that ultrasonographic examination supported a diagnosis of pancreatitis in 23/34 dogs (68% sensitivity) [26].

Computerized Tomography (CT)

CT of the abdomen is a routine procedure for the diagnosis of AP in humans. In small animals the use of CT is limited because of the expense, the expertise skills required and the need for general anaesthesia; however there are sedation protocols that allow the performance of CT in dogs without the need for general anaesthesia [53].

Histopathology

Pancreatic histopathological examination is considered to be the most definitive method for diagnosis of pancreatitis. In both clinical and experimental canine AP the macroscopic findings include generalized peritonitis, massive adhesions to adjacent organs, extensive necrosis, haemorrhage, fat necrosis and areas of abscessation [54]. Lack of macroscopic findings does not exclude histologic pancreatitis [55]. The main histopathological findings are extensive necrosis of pancreatic acinar cells, haemorrhage, inflammatory cell infiltration of pancreatic tissue, pancreatic and peripancreatic fat necrosis, and saponification, acinar atrophy, and fibroplasias [54]. Pancreatitis lesions are often focal, and multiple sections of pancreas should be taken in vivo if AP is suspected. In a recent study pancreata were sectioned every 2 cm. In half of the dogs with pancreatitis evidence of pancreatic inflammation was found in less than 25% of all sections [55].

Treatment

Main treatment strategies of AP are listed in Table 1 and include:

- Removal of the inciting cause, if known
- Maintenance of fluid and electrolyte balance
- Relief of pain
- Management of complications
- Constant monitoring

In order to correct dehydration, hypovolaemia or shock, parenteral administration of balanced electrolyte solutions (e.g., Lactated Ringer's) is proposed. The rate of administration depends on the estimated degree of dehydration and shock. Continuous monitoring of the patient is necessary and includes the control of body weight, urine output and careful auscultation in order to avoid pulmonary overhydration.

Serum creatinine and/or blood urea nitrogen (BUN) should be monitored in order to evaluate renal function. Blood glucose monitoring is essential since hyperglycaemia is common. Serum potassium should be determined on a daily basis since anorectic, vomiting patients tend to be hypokalaemic, and supplemental potassium chloride should be added to the IV fluids as necessary (the rate of 0.5 mmol/kg/hour should never be exceeded) [9].

Correction of suspected acid-base imbalances with the

Conventional treatment

- Parenteral administration of electrolyte solutions (44-66 ml/kg + % dehydration x B.W. x 1000) ml
- Correction of metabolic acidosis (bicarbonate 1-2 mmol/kg IV)
- Correction of hypokalaemia (Scott's scale)

Serum K (mmol/L)	mmol/L of administered solution
<2	80
2.1-2.5	60
2.6-3.0	40
3.1-3.5	28
>3.5 <5.0	20

- Antiemetic agents (metoclopramide [0.2 - 0.4 mg/kg SC every 6 to 8 hours or 1 mg/kg/day by continuous intravenous infusion], ondansetron [0.05 mg/kg IV every 8 to 12 hours], maropitant [1mg/kg SC every 24 hours])
- H2 blockers (ranitidine [2-4 mg/kg IV every 12 hours])
- Antibiotics (enrofloxacin [2.5-5 mg/kg SC every 12 hours, trimethoprim-sulphathiazine [15 mg/kg IV every 12 hours])*
- Plasma or blood transfusion (10-20 ml/kg B.W.)
- Analgesics (meperidine hydrochloride [5-10 mg/kg IM or SC every 2 to 4 hours], butorphanol [0.2 - 0.4 mg/kg SC every 6 hours], morphine [0.5-2 mg/kg SC or IM every 3-4 hours], diadermic phentanyl patches)

Treatment recommendations of questionable usefulness

- Vasoactive agents (vasopressin, dopamine, terbutaline)
- Pancreatic antisecretory agents
 - anticholinergic agents (atropine, propantheline)
 - other agents (glucagon, somatostatin, octreotide)
- Pancreatic enzyme inhibitors (aprotinin)
- Glucocorticosteroids (shock)
- Peritoneal lavage
- Surgical intervention (rarely and under certain circumstances)

* The routine use of antibiotics in canine AP is not recommended since infectious complications are rather uncommon. However, in cases with evidence of pancreatic infection or in cases of AP failing to respond to supportive measures, antibiotic use is justified.

Table 1. Treatment of acute pancreatitis

administration of bicarbonate should not be blinded, without prior blood gas determination, since patients may be acidotic or alkalotic [9, 18].

In the presence of severe hypoproteinaemia the administration of plasma or another volume expander is required. Plasma transfusion is beneficial by replacing α 1-antitrypsin and α 2-macroglobulin and by providing clotting factors in patients at high risk of DIC [9, 12].

Treatment recommendations in dogs suffering from AP traditionally included withholding food, water and per os medications for 24-48 hours, in order to reduce the stimuli for pancreatic enzyme synthesis and secretion. Results of recent studies have led to some changes in the former nutritional strategy. It is true that patients with pancreatitis should be offered nothing per os (NPO) if vomiting is profuse for a

period of up to 48 hours. Current evidence in both dogs with experimental pancreatitis and humans with pancreatitis, suggest that enteral feeding is not contraindicated, and may even be beneficial; pancreatic secretion from enteral nutrients decreases as the feeding site moves down the bowel. Consequently, early institution of intrajejunal feeding may have beneficial effects in dogs with AP. This is attributed to the maintenance of intestinal integrity and reduced bacterial translocation from the intestine and a reduced systemic inflammatory response [56]. Oesophagostomy, gastrostomy, or jejunostomy (distal to the site of pancreatic stimulation) tubes are useful for nutritional management of anorectic dogs. In non-vomiting dogs feeding by naso-oesophageal or gastrostomy tube may be beneficial.

In cases with signs indicative of severe abdominal pain, analgaesic therapy should be given to provide relief. Analgaesic agents recommended are meperidine hydrochloride, butorphanol tartrate, morphine or diadermic phentanyl patches [57].

Antiemetics, such as metoclopramide hydrochloride should be given only in cases with frequent and uncontrolled vomiting, since its cessation may indicate improvement of the patient's condition [56]. In cases where metoclopramide administration is not effective, slow intravenous administration of ondansetron is recommended. A new antiemetic, maropitant, has recently become available and seems to have antiemetic efficacy in dogs [58].

Appropriate antibiotic therapy is based on the ability of the drug to penetrate the pancreas and on its effectiveness against bacteria known to cause pancreatic infection. However, the beneficial effects of antibiotic treatment in any case of AP are still controversial. In contrast to what has been demonstrated in humans with AP, infectious complications are rather uncommon in dogs with naturally occurring AP [59, 60, 61]. Consequently, the routine use of antibiotics in canine AP is not recommended.

However, in cases with evidence of pancreatic infection or in cases of AP failing to respond to supportive measures, antibiotic use is justified [59,60]. Clindamycin, metronidazole, chloramphenicol, and ciprofloxacin are substances with high pancreatic tissue concentrations in canine models of AP [17].

The use of pancreatic antisecretory agents is not yet recommended. Administration of somatostatin, dopamine and octreotide in experimental AP cases in both dogs and cats seems to improve the severity of symptoms and duration of the disease [9]. The use of proinflammatory cytokines (TNF α /IL6) and free radicals inhibitors may aid in the future treatment of AP.

Surgical treatment may be beneficial in cases of obstructive jaundice, intestinal obstruction or in the presence of pancreatic abscess and severe necrosis of the pancreas [59, 60]; however, further studies are warranted to evaluate the efficacy of surgical intervention in dogs with AP.

Peritoneal lavage in order to remove toxic substances as trypsin and kinins is recommended in cases where exploratory laparotomy is performed or in patients that fail to respond to medical treatment [9, 10, 12, 17, 18]. However, there are no studies specifically evaluating the beneficial effects of peritoneal lavage in canine AP and given the potential risks (e.g. peritonitis), this procedure should be carefully considered.

Prognosis

Stratifying the severity of AP is necessary in order to decide how aggressive the medical and nutritional support should be. Mild pancreatitis often responds to symptomatic treatment and has a good prognosis, whereas severe pancreatitis requires aggressive therapy and prognosis is guarded. Early diagnosis and treatment of the disease and the absence of systemic complications are factors that result in a better outcome. A scoring system

Table 2. Systems considered and criteria for compromise of organs, as used in the "severity of illness" score applied to spontaneous canine acute pancreatitis.

System	Criterion	Laboratory reference range
Lymphoid	> 10% band neutrophils or white cell count > 24 x 10 ⁹ /L	0.0 – 0.2 x 10 ⁹ /L band neutrophils 4.5 – 17.0 x 10 ⁹ /L WCC
Renal	Serum urea concentration > 14 mmol/L or creatinine concentration > 0.3 mmol/L	2.5 – 9.5 mmol/L urea 0.06 – 0.18 mmol/L creatinine
Hepatic	Any of ALP, AST or ALT > 3 x reference range	0 – 140 IU/L ALP 15 – 80 IU/L AST 15 – 80 IU/L ALT
Acid/base buffering^a	Bicarbonate concentration < 13 or > 26 mmol/L and/or anion gap < 15 or > 38 mmol/L	15 – 24 mmol/L bicarbonate 17 – 35 mmol/L anion gap
Endocrine pancreas^a	Blood glucose > 13 mmol/L and/or β -OH butyrate > 1 mmol/L	3.3 – 6.8 mmol/L glucose 0.0 – 0.6 mmol/L β -OH butyrate

The score is the total count of organ systems showing compromise under these criteria (Ruaux and Atwell 1998)

a : if hyperglycaemia, butyrate and acidosis coexist, count as one system

WCC: white cell count

ALP: alkaline phosphatase

AST: aspartate aminotransferase

ALT: alanine aminotransferase

Disease severity	Score	Prognosis	Mortality rate (%)
Mild	0	Excellent	0
Moderate	1	Good to fair	11.1
	2	Fair to guarded	20
Severe	3	Poor	66.6
	4	Grave	100

Ruaux and Atwell 1998, Ruaux 2000

Table 3. Scoring system – prognosis and mortality rate (%) in canine acute pancreatitis cases according to the number of organ systems showing evidence of failure based on Table 2.

has been suggested reflecting the severity of canine AP [62] (Tables 2, 3). This system is a scale of 1 to 4, indicating the number of organs other than the pancreas showing evidence of compromise or failure.

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