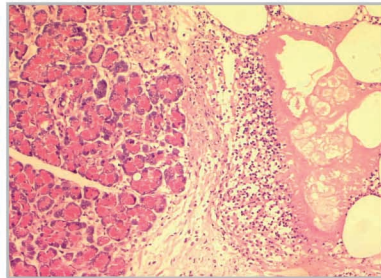


VETERINARY **focus**

Special edition

The worldwide journal for the companion animal veterinarian



Main pitfalls in the management of pancreatitis



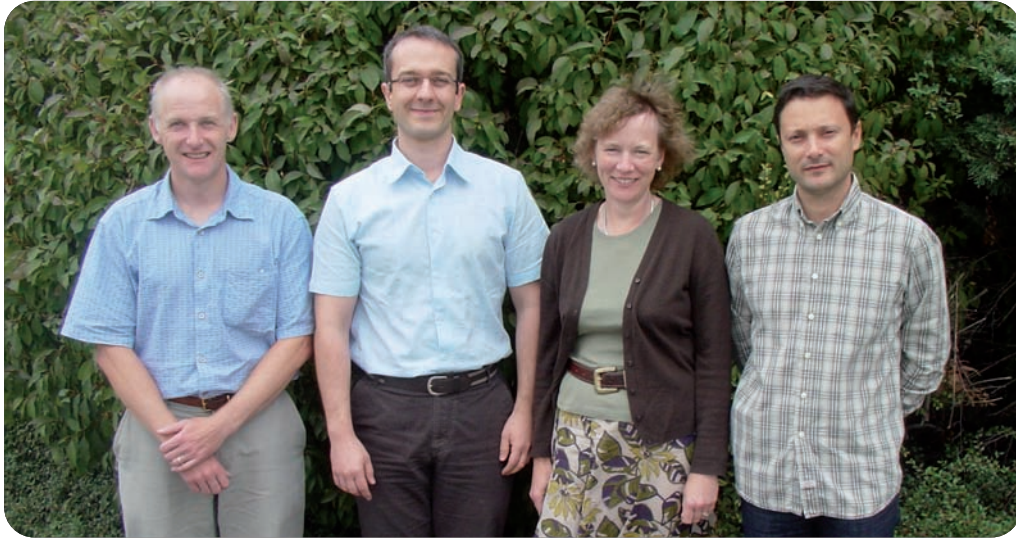
Juan Hernandez
Josep Pastor
Kenny Simpson
Penny Watson

Main pitfalls in the management of pancreatitis

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Introduction



C. Renner

What traps should be avoided in the diagnosis, treatment and nutritional management of dogs and cats affected by pancreatitis? That is the subject of this Focus special edition which has been carried out by a team of four international specialists, who gathered on two occasions to combine the most recent and most relevant clinical knowledge on this pathology.

Pancreatitis is a serious illness which develops quickly. Unfortunately, it is often fatal and needs immediate and precise management. Generally speaking, veterinary practitioners have a tendency to overdiagnose acute pancreatitis and underdiagnose chronic pancreatitis. But the first trap to be avoided is to understand that the concepts of acute and chronic pancreatitis are not necessarily the same from a histological and clinical perspective!

Another trap is relying too much on blood tests which are never 100% specific nor sensitive.

We wanted this Focus to be concrete and immediately applicable within your daily practice. We are sensitive to your expectations and wanted to help you save time with a global and educational presentation, illustrated with clinical cases to make it easier to commit to memory.

We hope that after reading these 50 pages, pancreatitis will no longer hold any secrets for you!

Philippe Marniquet,
DVM, dipl. ESSEC
Royal Canin

A stylized, handwritten signature in black ink, appearing to read 'Philippe Marniquet'.

1. What is canine pancreatitis?

> SUMMARY

Pancreatitis, both acute and chronic, is a common disease in dogs. The clinical signs vary from mild and non-specific to severe and potentially fatal. It is impossible to differentiate acute from chronic disease on clinical signs alone, but this is not important for emergency, short term management. In the longer term, if the animal recovers, acute pancreatitis is completely reversible whereas chronic pancreatitis can lead to progressive loss of exocrine and/or endocrine tissue resulting in the development of exocrine pancreatic insufficiency and/or diabetes mellitus. The causes of canine acute and chronic pancreatitis are usually unknown, although cocker spaniels may suffer from an autoimmune form of the disease.

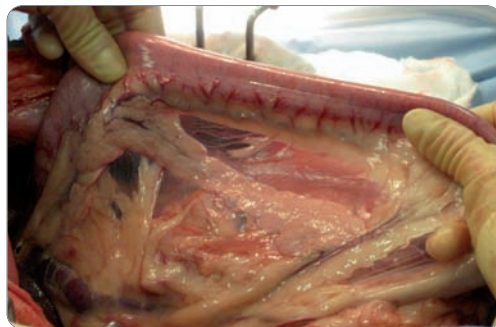
Introduction: anatomy and function of the canine pancreas

In dogs, the pancreas is a rather poorly circumscribed organ with important exocrine and endocrine functions which sits in the cranial abdomen caudal to the stomach. It has a left limb or lobe, which lies behind the greater curvature of the stomach and adjacent to the cranial aspect of the transverse colon; a right limb or lobe which lies just medial to the proximal duodenum (**Figures 1 and 2**) and a body between these two limbs. The exocrine pancreas secretes important digestive enzymes, bicarbonate, and intrinsic factor (IF) into the proximal duodenum and makes up about 98% of the pancreatic mass. The enzymes are secreted into the small intestine from secretory acini via two pancreatic ducts in most dogs (whereas most humans and cats have only one pancreatic duct). The largest pancreatic duct in the dog is actually equivalent to the accessory duct in humans and it enters the duodenum at the minor duodenal papilla. The smaller duct is the pancreatic duct which enters the duodenum approximately 28 mm cranial to the accessory duct and in close proximity to the bile duct at the major

duodenal papilla. The pancreatic duct and bile duct run close together but do not join in dogs.

The endocrine islets secrete insulin, glucagon and other hormones involved in metabolism and make up only 2% of the pancreatic mass (**Figure 3**). The close anatomical association between acini and islets allows subtle signalling between them to coordinate digestion and metabolism but also means that there is a complex cause-and-effect relationship between diabetes mellitus and pancreatitis.

Figure 1. Gross appearance of a normal canine pancreas at surgery (right, duodenal limb).



Courtesy of Jackie Demetriou, Surgery Department, Queen's Veterinary School Hospital, University of Cambridge

Figure 2. Histological section of normal pancreas in a dog showing acini containing enzymes within lobules and two pancreatic ducts. Haematoxylin and eosin stain.

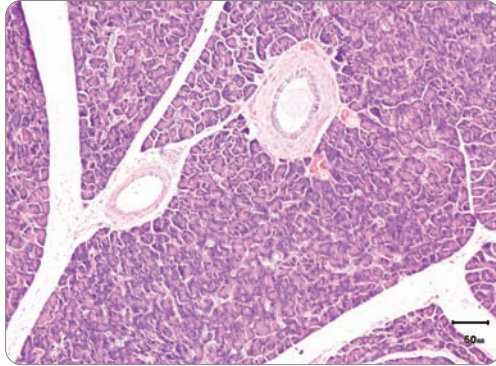
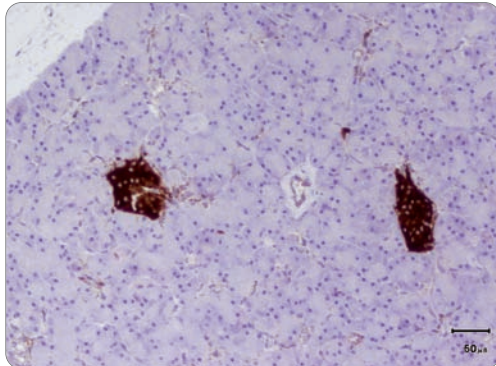


Figure 3. Histological section of pancreas from normal dog stained immunohistochemically with synaptophysin to demonstrate the islets (stained brown).



Pancreatic enzymes are responsible for the initial digestion of larger food molecules and require an alkaline pH to function, hence pancreatic duct cells concurrently secrete bicarbonate. The pancreas secretes several proteases, phospholipases, ribonucleases, and deoxyribonucleases as inactive precursors (zymogens) and also α -amylase and lipase as intact molecules. The pancreas is the only significant source of lipase, and therefore steatorrhea (fatty faeces) is a prominent sign of exocrine pancreatic insufficiency (EPI).

In the normal animal, pancreatic secretion is triggered by the thought of food and stomach filling, and most

potently by the presence of fat and protein in the small intestinal lumen. The vagus nerve and the hormones secretin and cholecystokinin released from the small intestine stimulate pancreatic secretion. Trypsinogen is activated within the small intestine by the brush border enzyme enterokinase, which cleaves a peptide (the 'trypsin-activation peptide' TAP) from trypsinogen. Activated trypsin then activates the other zymogens within the intestinal lumen. IF, which is necessary for cobalamin absorption in the ileum, is secreted predominantly by the pancreas in the dog, but a small amount is also secreted by the gastric mucosa. This contrasts with humans, where IF is secreted entirely by the stomach and the cat, where IF is secreted entirely by the pancreas and there is no gastric source.

1/ What is pancreatitis?

Pancreatitis is the inflammation of the pancreas which is usually sterile. It can further be defined as acute pancreatitis or chronic pancreatitis. It is very important to realise that, as in other organs such as the liver and kidneys, these definitions are histological NOT clinical (**Figures 4 and Table 1**). A dog with underlying chronic pancreatitis could present with apparent classical 'acute' pancreatitis, whereas a dog with acute disease could have recurrent episodes mimicking chronic pancreatitis (**Figure 5**). Furthermore, there is a tendency for dogs with chronic pancreatitis to have a long period of subclinical, clinically silent disease culminating in an acute presentation, by which time there is already a significant loss of pancreatic function (**Figure 6**). In a clinical case series of 14 cases of histologically confirmed chronic pancreatitis in dogs, most dogs had recurrent, low grade gastrointestinal signs but three cases presented with acute exacerbation of gastrointestinal signs, two presented with acute post-hepatic jaundice and one dog presented with acute diabetic ketoacidosis as its first clinical sign (Watson PJ, 2010).

Deciding whether the case is truly 'acute' or 'chronic' is not important for immediate treatment of the dog because the treatment is symptomatic. However, it does affect the long term management and it is also important to recognise the difference because the aetiologies of acute and chronic disease may be different. Chronic

pancreatitis is defined as a continuing inflammatory disease of the pancreas characterised by the progressive destruction of pancreatic parenchyma and progressive loss of function. Eventually, dogs with chronic pancreatitis may develop exocrine pancreatic insufficiency (EPI) due to loss of exocrine tissue and/or diabetes mellitus (DM) due to loss of islets, but because of the large pancreatic functional reserve, these represent end stage disease after 80-90% of pancreatic tissue has been lost. Acute pancreatitis, by contrast, is potentially completely reversible, provided the animal recovers, and would never lead to EPI. Animals with acute pancreatitis may however suffer from DM because the cause and effect relationship between DM and pancreatitis is complex: DM predisposes to fatal acute pancreatitis in dogs (Hess RS, 1999), as well as chronic pancreatitis apparently causing DM as a result of loss of pancreatic mass. Chronic pancreatitis has been proposed as the cause in up to 30% of canine cases of DM (Hoenig M, 2002).

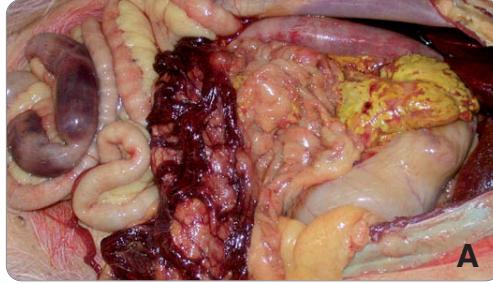
2/ How common is canine pancreatitis?

The true prevalence of canine pancreatitis is unknown. It is very difficult to do studies on a disease in which the 'gold standard' for diagnosis is pancreatic histopathology, which is rarely performed or indicated. No other diagnostic tests have 100% sensitivity or specificity. Veterinary surgeons frequently recognise and treat acute pancreatitis in dogs in practice, so it appears to be a common disease. Published studies of the prevalence of acute pancreatitis have usually reported only fatal cases (where there is histopathological confirmation) and are also very biased to second opinion populations. In a study of 70 dogs with fatal acute pancreatitis, 40% of the cases were actually acute exacerbations of chronic disease (Hess RS, 1998).

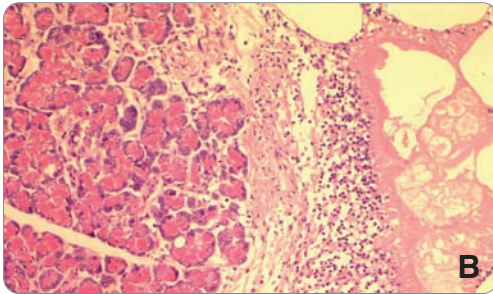
Chronic pancreatitis appears to be remarkably common in dogs. A recent post mortem study reported that 25% of old dogs euthanized for a variety of 'old dog' diseases in first opinion practice had histologically confirmed chronic pancreatitis (Watson PJ, 2007). A similar pathology study in the USA looking at second opinion and intensive care cases also found that histological lesions of chronic

Figures 4. Acute and chronic pancreatitis.

Appearance of fatal acute necrotising pancreatitis in a dog at post mortem.



Histological appearance of acute fatal pancreatitis in a dog. Note inflammatory cell infiltrate, oedema and fat necrosis but absence of fibrosis. If this dog had recovered, the pancreas would have returned to a histologically normal appearance.



Histological appearance of end stage chronic pancreatitis in a cavalier king charles spaniel. Large areas of pancreatic parenchyma have been replaced by fibrous tissue (stained light purple) and only small islands of acini remain (stained dark purple in the right hand side). This dog was also diabetic and no islets were visible in the remaining pancreatic tissue.

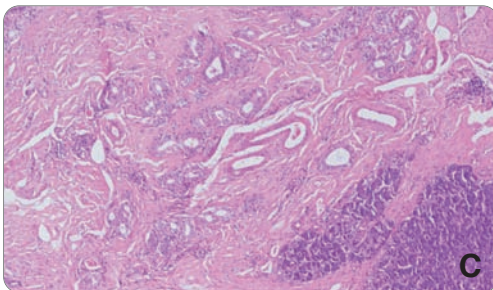


Figure 5. Both acute and chronic pancreatitis can show a spectrum of clinical signs from mild to severe.

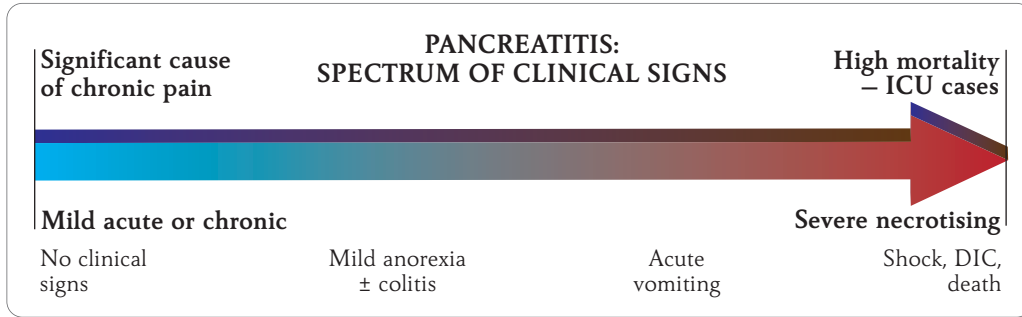


Figure 6. Diagrammatic representation of the typical clinical presentation of chronic pancreatitis in dogs: the first clinical bout often occurs after a long pre-clinical period of pancreatic inflammation.

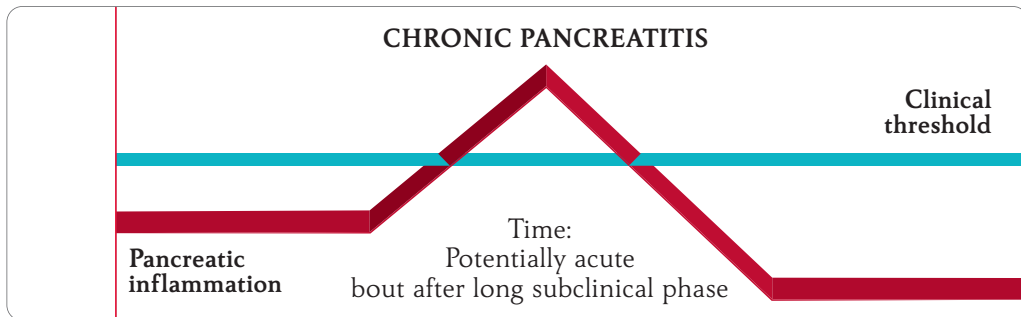


Table 1. Definitions of acute and chronic pancreatitis.

	Acute pancreatitis	Chronic pancreatitis
Histological definition	Pancreatic necrosis often with a neutrophilic infiltrate but without any underlying fibrosis or chronic inflammation i.e. potentially completely reversible.	Mononuclear (usually lymphocytic) or mixed mononuclear and polymorphonuclear (acute-on-chronic) inflammatory infiltrate in the pancreas with or without fibrosis which disrupts the normal architecture of the pancreas. Most cases have fibrosis in addition to a mononuclear infiltrate. Histological changes are irreversible and tend to be progressive.
Clinical definition NB : Acute and chronic pancreatitis cannot be differentiated reliably on clinical signs alone – histology is required for definitive diagnosis.	An acute inflammatory process of the pancreas that can involve peripancreatic tissues or remote organ systems, or both. It may occur as an isolated attack or recur in distinct episodes BUT by definition, acute pancreatitis is reversible.	A continuing inflammatory disease of the pancreas characterised by irreversible morphological changes that typically cause pain and permanent, progressive loss of exocrine and endocrine function. It can be clinically mild or clinically severe and indistinguishable from ‘acute’ pancreatitis.

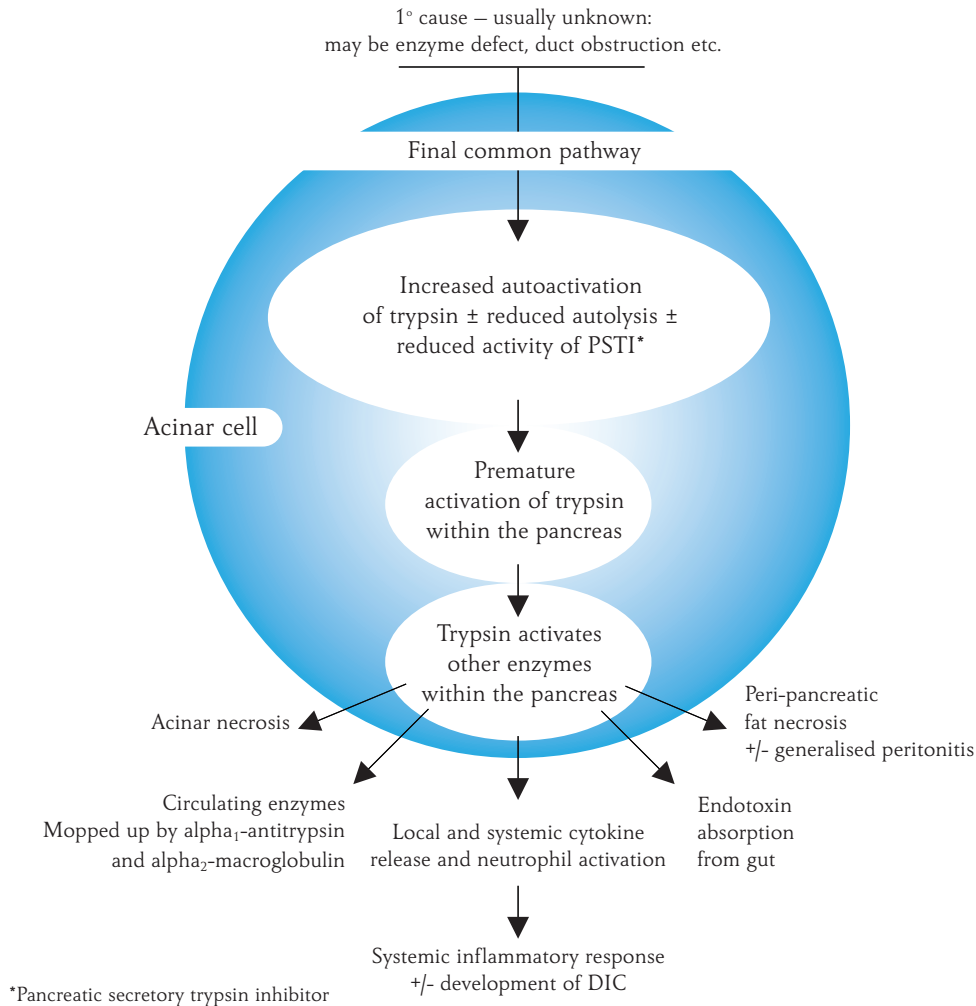


Figure 7. Diagrammatic representation of the pathophysiology of pancreatitis.

pancreatitis were common in dogs (Newman S, 2004). Pancreatitis is therefore undoubtedly a common disease in dogs, although it is unclear how many of these translate into clinical disease.

3/ Why do dogs get pancreatitis?

Inappropriate early activation of the zymogen trypsinogen to trypsin within the pancreatic acini, with resultant 'digestion' of the organ, is believed to be the final common pathway triggering pancreatic inflammation in most cases (Figure 7). This leads on to peri-pancreatic fat necrosis, systemic inflammation and potentially the development of systemic inflammatory response syndrome (SIRS) and

disseminated intravascular coagulation (DIC). Even mild cases of pancreatitis have some signs of a systemic inflammatory response. In addition to early activation of trypsin, other factors can be involved in triggering pancreatitis, particularly in chronic disease, where immune-mediated disease and duct destruction become more important (see below and Tables 2 and 3).

The reason WHY trypsin activates early within the pancreas is often unknown in dogs. In humans, many cases have a known cause and few are now idiopathic (Table 2). There are strong genetic predispositions, even to alcoholic pancreatitis. Heavy drinking is a risk factor for pancreatitis in humans, but only about 10% of heavy drinkers suffer from pancreatitis (Etamad B, 2001) – it is now clear that this is due to an underlying genetic susceptibility in some humans. It is likely that there is an inherited element to pancreatitis in dogs: certain breeds



Should I breed from my dog which has had pancreatitis?

This is a difficult question! We know that certain breeds are more likely to get pancreatitis than others – for example, terrier breeds are predisposed to acute pancreatitis and spaniel breeds are more likely to get chronic pancreatitis than other breeds. The increased prevalence of a disease in certain breeds suggests that it is at least partly inherited. However, we don't yet know anything about the inheritance of pancreatitis in dogs or how many and what genes are involved: it is very likely that the risk of pancreatitis in dogs involves a number of genes and complex inheritance, as in humans. These genes would then interact with the environment the dog lives in to determine whether it contracts the disease. For example, you could have a dog at moderate genetic risk which shows no signs until they eat a big meal of very fatty food. To make things even more complicated, many dogs with low grade chronic pancreatitis have the disease all their lives without ever being diagnosed.

Therefore, at the current state of our knowledge of the inheritance of pancreatitis, we would not usually advise breeders to avoid breeding from affected dogs. However, if a particular pedigree dog breeder began to see a lot of related individuals in their line developing pancreatitis, it would be wise to consider either not breeding from affected dogs or out-crossing to a different line.

Table 2. Causes of pancreatitis in humans and dogs

Humans	Dogs
Idiopathic: 10%	Idiopathic: 90%
Gall stones	Not recognised
Alcoholism	Not recognised
Cystic fibrosis	Not recognised
Hereditary/familial <ul style="list-style-type: none"> • Enzyme mutations • Pancreatic secretory trypsin-inhibitor mutations • Others 	Likely but not described
Autoimmune	Not previously recognised – perhaps cocker spaniels (see text)

are repeatedly recognised to suffer from the disease whereas others (such as greyhounds) very rarely suffer from pancreatitis. Acute pancreatitis is more commonly reported in small breed dogs, particularly terriers and

chronic pancreatitis has been recognised more frequently in Cavalier King Charles spaniels, cocker spaniels, boxers and collies in the United Kingdom (**Figure 8**) (Watson PJ, 2007). A number of 'risk factors' have been suggested for pancreatitis in dogs (**Table 3**) – but many of these may in fact be triggers in an already genetically susceptible individual. In humans, some genetic mutations are sufficient alone to cause recurrent pancreatitis without any external trigger. These are most often mutations in the cationic trypsinogen gene which change the three-dimensional structure of the trypsin molecule making it resistant to hydrolysis once activated within the pancreas. Candidate gene studies on one dog breed (Miniature schnauzers) have failed so far to identify a mutation in either the cationic or anionic trypsinogen gene. A mutation in the pancreatic secretory trypsin inhibitor has been found in some miniature schnauzers but in humans, mutations in this enzyme are not sufficient alone to cause pancreatitis but have to be combined with another risk factor.

A form of chronic pancreatitis has recently been reported in cocker spaniels in the UK which is distinctive clinically, on diagnostic imaging and histologically (Watson PJ,

Table 3. Triggers for pancreatitis in dogs

All of these have been reported, either clinically or experimentally, but their relative importance is unclear. Some may be true 'causes' but many are likely 'triggers' in susceptible dogs

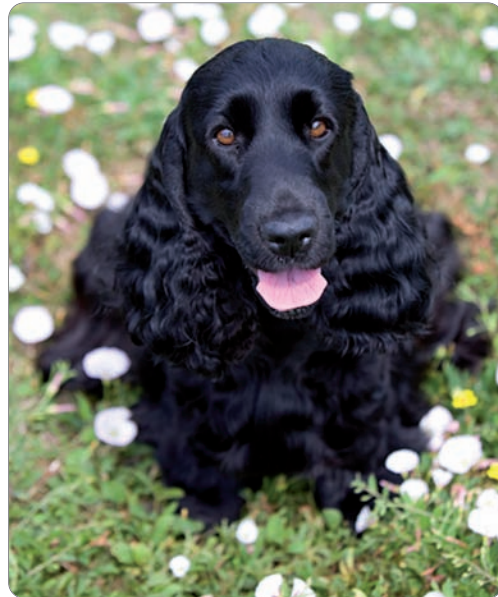
- Duct obstruction + increased secretion ± bile reflux
 - Neoplasia
 - Chronic pancreatitis
 - Cholangitis/inflammatory bowel disease – more in cats than dogs
- Hypertriglyceridaemia
 - Inherent e.g. miniature schnauzers
 - Secondary to endocrine disease: diabetes mellitus, hyperadrenocorticism, hypothyroidism – **Important** associations with fatal acute disease (Hess, 1998)
- Pancreatic ischaemia
 - Surgery
 - GDV
 - Shock
 - Severe anaemia
- Hypercalcaemia (Experimental. Clinical significance unclear)
 - Less common in dogs than cats
- Obesity
 - Is this a true risk factor or co-segregating in high risk breeds?
- High fat diets, if predisposed
- Drugs/toxins
 - Organophosphates, azathioprine, thiazides, oestrogens, furosemide, sulphas, tetracycline, procainamide, asparaginase, bromide, clompiramine
 - (Steroids have been suggested but never proven)
 - Propofol infusions have been suggested in dogs and reported in humans (likely due to lipid vehicle)
- (Infections can involve the pancreas but pancreatitis is rarely the most significant sign of these eg. Toxoplasma; parvo virus)

2006). It is a duct destructive disease which bears a striking resemblance to human autoimmune chronic pancreatitis, where T lymphocytes selectively attack pancreatic ducts. It often occurs concurrently with keratoconjunctivitis sicca, another 'duct-centred' immune-mediated disease. This opens the possibility of more specific treatment in these dogs with immunosuppressive medication. However, chronic pancreatitis in most other dog breeds does NOT have this pattern and it is likely that other breeds suffer from other forms of disease such as primary enzyme mutations which would not respond to immunosuppressive medication.

4/ Conclusions

Pancreatitis, both acute and chronic, is therefore a common disease in dogs with potentially severe, even fatal, clinical consequences. A number of trigger factors have been identified and Cocker spaniels may suffer from an immune-mediated form of chronic pancreatitis. However, in the majority of dogs, the cause remains unknown. ■

Figure 8. The cocker spaniel is a breed at risk of chronic pancreatitis



Frédéric Dhayer

2. When to suspect pancreatitis and how to confirm it in dogs

> SUMMARY

The diagnosis of pancreatitis does not only depend on laboratory test results, but also on careful interpretation of the animal's symptoms, results of physical examination, presence of predisposing factors, correct interpretation of changes in laboratory tests, and diagnostic imaging findings, especially ultrasound. Vomiting and cranial abdominal pain are the most common presentations for animals with acute pancreatitis. However milder cases of pancreatitis may not necessarily present with vomiting or abdominal pain. Nowadays, cPLI and ultrasound are the most useful tests to detect pancreatitis, but not all animals with pancreatitis have abnormalities detected on these studies. Biopsy remains the golden standard for the diagnosis of pancreatitis, but on the other hand, not all animals are good candidates for biopsies. Cytology is more helpful in the diagnosis of neoplasia than pancreatitis.



1/ Clinical presentation

The clinical presentation of pancreatitis in animals varies enormously according to the degree of pancreatic disease. In the mildest cases there may be sub-clinical and self-limiting signs. If the disease is recurrent, this may lead to chronic pancreatitis in time. Animals with more severe pancreatitis mainly present with anorexia (91% of cases), vomiting (90%), weakness (79%), abdominal pain (58%), dehydration (46%) and diarrhoea (33%) (Hess, 1998). The most severe cases also usually present with fever, respiratory distress, jaundice and cardiovascular shock. In some cases cutaneous signs of panniculitis develop associated with pancreatitis although panniculitis has also been associated with pancreatic neoplasia and not just pancreatitis (Steiner, 2003).

In cases of chronic pancreatitis, clinical signs may result from endocrine or exocrine dysfunction, i.e., apart from abdominal pain, diabetes mellitus or exocrine pancreatic insufficiency may also be observed (Watson, 2003).

A) Medical history

Pancreatitis can affect dogs of any age, although the incidence appears to be higher in overweight and adult dogs. The medical history should always include current medication (for example, if the dog is being treated with anti-seizure medication, particularly in the case of phenobarbital or potassium bromide), current diet (because there is a higher incidence in animals on fatty diets or with food imbalances), and other predisposing factors such as

Key point

Although pancreatitis symptoms may be very non-specific, dogs with severe pancreatitis usually present with vomiting and cranial abdominal pain. Pancreatitis should be suspected in animals presenting with these clinical signs. Milder cases of pancreatitis may not necessarily present with vomiting or abdominal pain.

Figure 1. Specific position called praying position that has been associated with the presence of cranial abdominal pain.



Figure 2. Abdominal palpation to find evidence of abdominal pain in the pancreatic zone.



concomitant disease (a worse outcome has been reported in animals with hyperadrenocorticism, hypothyroidism or diabetes mellitus) or breed (Hess, 1999).

In some animals, owners may report a specific position called praying position, characterised by limbs stretched out on the floor, the sternum on the floor and the back legs lifted up (**Figure 1**). This position has been associated with the presence of abdominal pain.

2/ Physical examination

Recently, different indices have been published to facilitate a prognosis and define the severity of the pancreatitis (Mansfield, 2008; Ruaux, 1998). According to these indices, the factors that have the biggest impact on pancreatitis severity and evolution are the clinical signs associated with the involvement of different organs and systems. For this reason, it is essential that the medical history and physical examination includes not only a general physical examination (mucous membrane colour, capillary refill time, temperature, etc.) but also a special assessment should be made of the following organs and systems:

- Cardiovascular system: special attention should be paid to the presence of tachycardia or ventricular tachycardia with ectopic ventricular complexes, and therefore peripheral pulse deficits. Also, the presence of hypotension, peripheral oedema or signs of dehydration.
- Respiratory system: check for the presence of tachypnoea (more than 40 breaths per minute), dyspnoea or respiratory distress. In some cases heart and lung sounds are reduced on auscultation due to the presence of fluid in the pleural cavity or there are lung crackles suggesting the presence of oedema or pneumonia.
- Intestinal condition: Intestinal sounds can be heard on auscultation (absence of these sounds is related to paralytic ileus). Digital rectal examination is performed to find evidence of fresh blood, melaena or diarrhoea.
- Abdominal palpation: This is essential in all animals with suspected pancreatitis. In many animals it is possible to palpate abdominal pain (**Figure 2**) or the presence of a cranial abdominal mass (which may be inflammatory rather than neoplastic). In some cases the presence of small amounts of abdominal free fluid can be found.
- Hepato-biliary system: The presence of jaundice may suggest liver disease or oedema in proximity with the common bile duct, and therefore obstruction of this duct.
- Presence of disseminated intravascular coagulation: petechiae, ecchymoses in mucous membranes or skin, acute respiratory distress.

Key point

The involvement of different organs and systems is associated with more severe pancreatitis and therefore with a worse prognosis.

Test	Sensitivity (%)
cTLI	33
Lipase	55
Amylase	57
Abdominal ultrasound	68
cPLI	>80

Table 1. Approximate sensitivity of diagnostic tests for pancreatitis ordered from lowest to highest. Sensitivity of a diagnostic test is the frequency with which a test is positive in patients that have the disease of interest. Specificity is the frequency with which a test is negative in patients that do not have the disease of interest.

A) Blood count and biochemistry

In general these tests are not specific for pancreatitis, although they are useful to assess the animal's general condition and to rule out other possible causes of abdominal pain and vomiting. Biochemical abnormalities vary according to the degree of pancreatic inflammation, and so there is no single presentation.

The blood count may show changes that are compatible with an acute inflammatory response. Leukocytosis with a left shift can be observed in 55% of cases of severe pancreatitis. However, it is also possible to observe leukopenia due to neutrophil sequestration in the inflamed zone or in abdominal fluid (Hess, 1998). Thrombocytopenia can be found in a similar percentage of cases (59%) and anaemia can also be found, indicating disseminated intravascular coagulation.

Elevated acute-phase proteins such as C-reactive protein have been reported secondary to pancreatic inflammation, and it has been suggested that this is useful for monitoring the evolution of pancreatitis (Mansfield, 2008).

Disseminated intravascular coagulation may be triggered in more severe cases of pancreatitis. In these cases the following may be observed: prolonged coagulation times (prothrombin time and activated partial thromboplastin time), reduced fibrinogen levels and increased D-dimers. (Hess, 1998, 1999). However, a decrease in platelet count together with high fibrinogen values and increased D-dimers can be an early indication of DIC and these animals need to be treated aggressively.

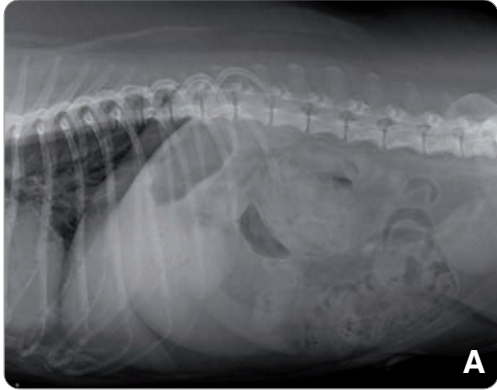
Blood biochemistry usually shows moderate elevations of pancreatic enzymes (lipase, amylase), electrolyte changes (compatible with dehydration and vomiting), azotemia, hypoalbuminaemia, hypocalcaemia (due to calcium deposits in necrotic areas) and hyperglycaemia (Steiner, 2009). Lipase has been reported to be a useful test in the diagnosis of pancreatitis, but it has major limitations (**Table 1**), and it is suggested that a 3 to 5-fold increase above the reference range should be observed in order to consider pancreatitis. A sensitivity of 73% and specificity of 55% have been reported for lipase (Steiner, 2003). Amylase is fairly similar, since sensitivity (62%) and specificity (57%) are not optimum. Therefore, it is felt that lipase and amylase alone are not very reliable tests to diagnose pancreatitis, and increased lipase and amylase levels are not reliable indicators of prognosis (Ruau, 1998). Other blood biochemistry changes that are related to the consequences of and/or that cause pancreatitis are hypertriglyceridaemia, hypercholesterolaemia, hypercalcaemia and hyperglycaemia.

TLI is another test that has been used to diagnose pancreatitis, where it may be elevated. It has a low sensitivity and is not considered as having much advantage

Key points

- The degree of elevations of lipase and amylase do not correlate with severity of pancreatitis.
- At present, pancreatic lipase (cPLI) is the most sensitive biochemistry test for diagnosing canine pancreatitis.
- Laboratory changes in animals with pancreatitis depend on the severity of the condition, and vary greatly between one animal and another.

Figures 3. X-ray images of pancreatitis showing very mild changes.



Juan Hernandez

over other tests in the diagnosis of pancreatitis. Low TLI may be found in cases of chronic pancreatitis with weight loss and diarrhoea, due to development of exocrine pancreatic insufficiency (Watson 2003; Xenoulis, 2008). Serum vitamin B12 may also be low in these cases. However, a transient low TLI may also be observed in animals with acute pancreatitis and the test needs to be repeated to confirm the presence of EPI.

A specific pancreatic lipase assay (cPLI) has recently been brought onto the market and is available for the majority of veterinary surgeons. It is marketed as a Snap® test and also in quantitative form. Pancreatitis should be suspected if blood values are over 400 µg/l. This test has very good sensitivity (83%) (Steiner, 2001). Also, if CPLI is lower than 100 µg/l it is unlikely that the dog has acute pancreatitis. However, increased serum concentrations have been reported in cases of gastritis, chronic inflammatory bowel disease, chronic renal failure and possibly induced by anti-seizure drugs (bromide and phenobarbital) (Steiner, 2003, 2009; Kathrani, 2009).

Urine analysis shows elevated urine specific gravity secondary to dehydration. However, in cases of renal failure, urine may not be concentrated, and there may be casts in sediment and proteinuria (Steiner, 2003).

In some animals abdominal fluid may be observed. Exudates have been reported in animals with pancreatitis, containing proteins at over 2.5 mg/dl and non-degenerate neutrophils. However transudates have also been described. If lipase

and amylase are tested in the abdominal fluid, they usually have higher values than in plasma.

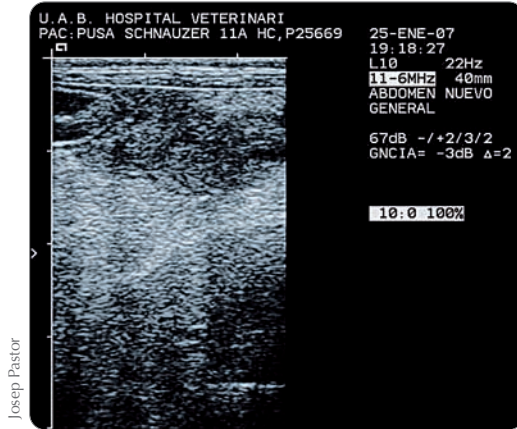
B) Diagnostic imaging techniques

Abdominal X-rays may show loss of detail in the cranial abdomen (**Figures 3**), and in some cases this may be compatible with a cranial abdominal mass. Characteristic radiographic signs are lateral shift of the duodenum and caudal shift of the transverse colon. However, these are subjective changes and on their own they do not contribute to confirming a diagnosis of pancreatitis (Steiner, 2009).

Chest X-rays are usually normal, although a pleural effusion has been reported in animals with severe pancreatitis.

Abdominal ultrasound is considered as being very specific in detecting pancreatitis. However 1/3 of animals with pancreatitis may have normal abdominal ultrasound. Pancreatitis cannot be diagnosed simply by observing hypochoic lesion in the pancreas, because the same appearance is found in animals with portal hypertension

Figure 4. Typical ultrasound image of pancreatitis.



and hypoalbuminaemia (Lamb, 1999). Pancreatitis has many different appearances on ultrasound, depending on severity, duration and spread of pancreatic and peri-pancreatic tissue inflammation. If there is necrosis, the pancreas usually shows decreased echogenicity and is surrounded by an area of increased echogenicity because of the necrotic peri-pancreatic fat and a zone of decreased echogenicity due to accumulation of fluids and oedema. The sensitivity of ultrasound clearly depends on the equipment used and the sonographer's skill, but it is estimated that it has high sensitivity (68%) in diagnosing pancreatitis. The body of the pancreas can be examined on ultrasound from the ventral zone or right side, with the animal in a dorsal recumbency or lateral (left or right) recumbency, moving the scanned plane to a position that is cranio-medial to the proximal descending duodenum and caudal to the pyloric antrum. The vena porta serves as a sound anatomical reference point as it is positioned

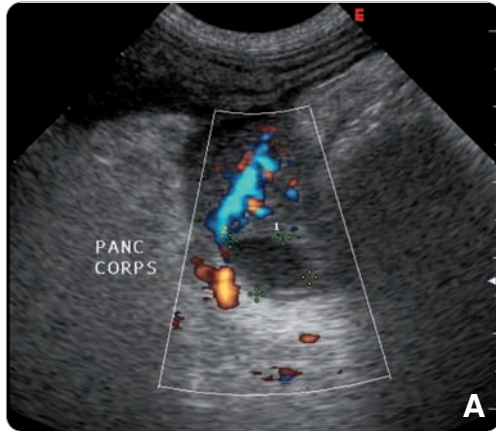
dorsally and to the left of the body of the pancreas. The left pancreatic lobe is harder to examine in dogs because of interference from gas in the adjacent stomach and in the transverse colon (**Figure 4**) Sometimes pancreatic fluid collections can be observed on ultrasound, such as: (1) Pseudocysts, which are fluid collections caused by pancreatitis, surrounded by a fibrous tissue capsule. The fluid is composed of pancreatic secretions that come from broken ducts. (2) Retention cysts, formed by an obstructed pancreatic duct. (3) Pancreatic abscesses (**Figures 5**), which are circumscribed collections of pus, are generally located in or directly adjacent to the pancreas and may be sterile or infected. On ultrasound it is impossible to distinguish between these different types of pancreatic fluid collections.

Biliary obstruction secondary to pancreatic inflammation and subsequent fibrosis can cause gallbladder and bile duct distension. Exocrine pancreatic tumours such as adenocarcinoma originate in acinar cells or in the ductal epithelium. Although these tumours are very rare, they are the most commonly-observed type of pancreatic tumour in dogs and cats. They generally develop in the central part of the gland. As they grow, they can compress the common bile duct and invade adjacent gastric and duodenal segments, and frequently lead to metastases in the liver and regional lymph nodes, very often in the form of nodules or masses with decreased echogenicity. Other pancreatic tumours which have been reported in dogs and cats include cystadenoma, metastatic carcinoma and lymphoma. Endocrine pancreatic tumours such as glucagonomas, insulinomas and gastrinomas are rare and are often not detected on ultrasound. Of this group, insulinomas are reported most in dogs. Although pancreatic tumours usually present as focal nodules or masses, they cannot be reliably distinguished from pancreatitis or ultrasound evidence of nodular hyperplasia (Hecht, 2008).

Key points

- Pancreatitis has many different appearances on ultrasound, depending on severity, duration and spread of pancreatic and peri-pancreatic tissue inflammation.
- The best combination for the specific diagnosis of pancreatitis in dogs is elevated cPLI and ultrasound findings compatible with pancreatitis (Steiner, 2008).
- A normal cPLI and/or normal ultrasound does not rule out pancreatitis.

Figures 5. Ultrasound image of a pancreatic abscess (A) and fluid obtained from the abscess (B).



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C) Biopsy and cytology

Biopsy is considered as being the most definitive test in the diagnosis of pancreatitis. Although pancreatitis may be suspected because of the macroscopic appearance of the pancreas during an exploratory laparotomy, biopsies are usually necessary to confirm the diagnosis. Pancreas size is not indicative of absence of disease. In cases of pancreatitis, the biopsy may not always be diagnosed because it depends on the site where the sample is taken in order to observe the characteristic changes (**Figure 6**). ■

Figure 6. Laparoscopic view of an enlarged, red pancreas with white plaques. The appearance is consistent with acute necrotizing pancreatitis. Pancreatic biopsy can be performed under direct visualization to confirm the diagnosis

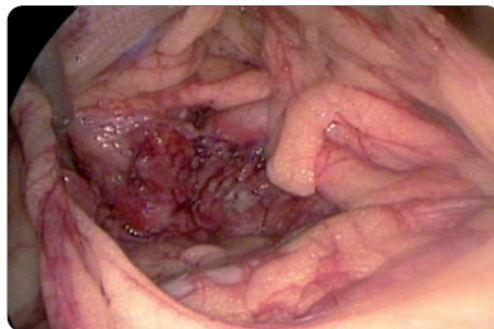


Image courtesy of Dr. David Twedt, Colorado State University

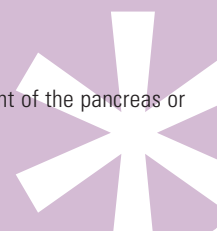
Key points

- Histopathological results of pancreatic biopsy depend on the site where the sample is taken, especially in the case of chronic pancreatitis. Cytology is a useful technique if a pancreatic tumour is suspected, especially in the case of adenocarcinoma. Cytology can also be used to study cystic cavities in the pancreas, because degenerate neutrophils may be observed on a protein background, suggesting pancreatic abscess or pancreatic cyst (Raskin, 2009).
- Cytology is useful for assessing abdominal effusions and pancreatic aspirates especially to rule out neoplasia.

3. Treatment of pancreatitis in dogs

> SUMMARY

- Appropriate medical intensive care (intravenous fluids, analgesia, control of vomiting and nutritional support) is essential in the treatment of acute pancreatitis in dogs.
- Early and progressive enteral feeding is mandatory in acute pancreatitis.
- Plasma transfusion and heparin therapy is indicated in severe pancreatitis.
- Persistent biliary obstruction, abscess formation, suspicion of necrosis of a segment of the pancreas or suspicion of tumour are indications for exploratory laparotomy.



1/ Resolve any predisposing factors

Although the majority of cases of pancreatitis in dogs arise spontaneously, there are several recognized risk factors (chapter I). These should therefore be identified and ruled out.

- A diet that is too rich in fats should be corrected. This is particularly important in animals with hypertriglyceridemia (**Figure 1**) or underlying endocrinopathy.
- Certain drugs can trigger pancreatitis, these should be discontinued: azathioprine, potassium bromide, L-asparaginase, etc. Corticosteroids do not appear to be clearly implicated in the onset of pancreatitis.
- It is also important to correct hypercalcaemia.

2/ Maintain vascular filling

The maintenance of adequate intravascular volume via the administration of appropriate intravenous fluid therapy is essential (Heinrich, 2006 ; Steiner, 2009). The perfusion (type of solution, flow rate) should be adapted to the animal's hydration, acid-base, electrolyte, and

cardiovascular status. Maintenance requirements (40 to 60 ml/kg/day) should be covered. Then add the volume needed to correct dehydration and compensate for any estimated losses (vomiting). This is usually equivalent to 1,5-2 x maintenance rate in the absence of shock. Potassium supplementation is based on the serum potassium concentration (**Table 1**). Although metabolic acidosis is common, it cannot be corrected unless the pH, pCO₂, and bicarbonate have been measured. If this is impossible, a lactated Ringers solution with additional potassium should be chosen.

Table 1. Intravenous potassium supplementation based on the measured serum potassium concentration.

Serum potassium concentration (mmol/l)	Supplementation (mmol of potassium per litre of infusion - maximum 0.5 mmol/kg/h)
3.7-5.0	10-20
3.0-3.7	20-30
2.5-3.0	30-40
2.0-2.5	40-60
<2.0	60-70

3/ Pain relief

This is also an essential part of the treatment; apart from the animal's comfort, major visceral pain can exacerbate the state of shock and provoke cardiac rhythm disorders. Analgesia is therefore systematically administered for acute pancreatitis. Opioids are often needed (**Table 2**). Non steroidal anti-inflammatories should be avoided due to the risk of gastroduodenal ulceration. If the animal is in severe pain, a continuous intravenous infusion of Morphine/Lidocaine/Ketamine may be required (**Table 3**) (Heinrich, 2006; Steiner, 2009).

4/ Control vomiting

Although commonly used, metoclopramide may reduce pancreatic perfusion due to its anti-dopaminergic properties. Maropitant (an antagonist of neurokinin 1) or dolasetron or ondansetron (serotonin antagonists) or chlorpromazine (phenothiazine) are recommended for the symptomatic treatment of vomiting (**Table 4**).

5/ Treat any bacterial complications

The use of antibiotics remains controversial in veterinary medicine since the etiology of pancreatic inflammation

Figure 1. Typical appearance of the serum of a dog with severe hypertriglyceridemia.



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has been shown to be chemical rather than septic. However, the authors all recommend the implementation of antibiotic treatment to treat any possible gastrointestinal bacterial translocation. The administration of a betalactam antibiotic (amoxicillin, ampicillin, cephalexin, etc.) and metronidazole is the most commonly used combination (**Table 5**). Fluoroquinolones or aminoglycosides should be reserved for suspected cases of bacteraemia that could result in a state of septic shock (Heinrich, 2006).

Table 2. Dosage of the principal analgesics used in canine pancreatitis.

Drug	Brand name	Dose rate
Ketamine	Imalgène (V**), Ketamine (V)	CRI*: 0.1 to 0.5 mg/kg/h IV
Tramadol	Tramadol (H***)	2 to 10 mg/kg/d PO
Butorphanol	Dolorex (V)	0.2 to 0.5 mg/kg IV, IM, SC or PO every 6 hours
Morphine	Morphine	0.1 to 0.5 mg/kg SC or IV every 6 hours
Buprenorphine	Vetergesic (V), Buprecare (V)	0.01-0.03 mg SC, IM or IV every 8 hours
Paracetamol	Doliprane (H), Pardale V (V)	15 mg/kg PO every 8 hours
Fentanyl (infusion)		2-6 µg/kg/hour
Fentanyl (patch)	Durogesic (H) *Constant rate infusion **Veterinary licence *** Licensed for humans	<ul style="list-style-type: none"> • 5 to 10 kg dog: 25 µg/h patch • 10 to 20 kg dog: 50 µg/h patch • 20 to 30 kg dog: 75 µg/h patch • Dogs over 30 kg: 100 µg/h patch

Table 3. Administration of Morphine/Lidocaine/Ketamine (MLK) infusion for the control of severe visceral pain.

The solution is prepared as follows: add the following volumes of morphine, lidocaine, and ketamine to 100 ml of 0.9% NaCl:
1.2 ml of morphine (10 mg/ml vial)
7.5 ml of lidocaine (20 mg/ml bottle)
0.3 ml of ketamine (100 mg/ml bottle)
This solution is administered intravenously using an electric syringe pump at a rate of 1 to 2 ml/kg/h (total solution) to give final infusion rates of 0.24 mg/kg/h morphine; 3 mg/kg/h lidocaine and 0.6 mg/kg/h ketamine.

Table 4. Doses of the principal antiemetics used in the treatment of canine pancreatitis.

Drug	Brand name	Dose rate
Chlorpromazine	Largactil (H)	0.2 to 0.4 mg/kg PO, IM, SC 2 to 3 times per day
Dolasetron	Anzemet (H)	0.6-1.0 mg/kg PO or IV once daily
Domperidone	Motilium Vet (V), Motilum (H)	0.3 mg/kg PO, twice daily
Granisetron	Kytril (H)	0.1 to 0.5 mg/kg PO or IV, twice daily
Maropitant	Cerenia (V)	1 mg/kg/d SC or 2 mg/kg/d PO
Metoclopramide Use controversial due to its anti-dopaminergic properties	Primperid (V), Primperan (H), Maxalon (H)	0.2 to 0.5 mg/kg PO, IM, SC or IV, 2 to 4 times per day CRI: 0.08 mg/kg/h
Ondansetron	Zophren (H)	0.1 to 0.2 mg/kg IV 2 to 4 times daily or 0.5 to 1 mg/kg PO 1 to 2 times daily

Table 5. Doses of the principal antibiotics used in the treatment of canine pancreatitis.

Drug	Brand name	Dose rate
Amoxicillin	Clamoxil (H), Amoxycare (V), Duphamox (V)	10 to 20 mg/kg IV, SC or IM three times daily
Ampicillin	Albipen (V), Ampicat (V), Ampidog (V), Kalampi (V), Totapen (H), Ampicare (V)	10 to 20 mg/kg IV, SC or IM three times daily
Ceftiofur	Excenel (V)	2.2 to 4.4 mg/kg IV, SC, or IM twice daily
Cephalexin	Rilexine (V), Therios (V)	10 to 30 mg/kg IV, SC, or IM 2 to 3 times daily
Enrofloxacin	Baytril (V)	Dog: 2.5 to 20 mg/kg PO in 1 inj; Cat: 5 mg/kg PO in 1 inj
Gentamycin	Septigen 10 and 40, Gentalline 10, 20 and 40(H)	Dog: 6-8 mg/kg IV once daily; Cat: 5-8 mg/kg IV once daily
Marbofloxacin	Marbocyl (V)	2 mg/kg/d, once daily
Metronidazole	Flagyl (H)	7.5 to 15 mg/kg PO or IV, twice daily

6/ Reintroducing food: when and how?

A) When should food be reintroduced?

Food should be reintroduced as soon as possible (Qin, 2002; Qin, 2007). It has been clearly demonstrated that starvation induces a reduction in the total thickness of the intestinal mucosa and the height of the villi. Intestinal permeability is increased, exposing the animal to septic complications via bacterial translocation. Ideally, food should be reintroduced at the same time as the instigation of the other treatments (fluid therapy, analgesia, etc.). The limiting factor being the presence of vomiting and gastroduodenal ileus, which are both common during acute pancreatitis. Food is therefore often withheld for 12 to 24 hours until the medical treatments have started to take effect.

B) How should food be reintroduced?

Food should be reintroduced very progressively in terms of calories, lipids, and proteins, so as to avoid stimulating pancreatic secretion via the secretion of secretin and cholecystokinin (Qin, 2002; Qin, 2007). In practice, the ration given on the first day corresponds to 1/5 of the maintenance requirements for the current or optimal weight.

It is difficult to make any general recommendations concerning the route of administration (oral, naso-oesophageal tube, parenteral) in cases of acute pancreatitis. To clarify the problem, the authors have defined a classification system for acute pancreatitis using a mild, moderate or severe clinical severity index (Mansfield, 2008). These are only guidelines and the recommendations should be adjusted to the clinical presentation of the dog.

- Acute pancreatitis with mild clinical signs and minimal vomiting:

Food can be reintroduced immediately or after 12 to 24 hours if the vomiting requires pharmacological control (maropitant, dolasetron, etc.). If the animal is eating on

Figure 2. Naso-oesophageal tube placement in a dog with mild acute pancreatitis.



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its own, an appropriate diet in terms of protein and lipid content should be fed in 2 or 3 portions per day.

If the patient is not feeding, a naso-oesophageal tube should be placed (**Figure 2**). When reintroducing food via a nasoesophageal tube, the protein and lipid content of the food can be higher than the moderate values sought, given that the dog is being given very few calories (progressive reintroduction of food). However this should be changed to a more appropriate diet as soon as possible and especially as soon as the totality of the dog's energy requirements are met.

- Acute pancreatitis with moderate clinical signs and / or persistent vomiting:
 - Food can be reintroduced immediately or after 12 to 24 hours if the vomiting requires pharmacological control.
 - If the vomiting persists despite medical treatment or if significant gastroduodenal ileus is detected on ultrasound, the naso-oesophageal route cannot be used due to the risk of rejection of the tube. The authors advise the endoscopic placement of a gastrostomy tube (PEG) (**Figures 3 and 4**), with the introduction of another smaller tube via the first; the latter is then guided into the distal duodenum (**Figure 5**) (Jergens, 2007). The dog is thus fed directly into the jejunum, which has the advantage of preserving digestive integrity and preventing the gastric and digestive phases of pancreatic stimulation.



What shall I feed my dog with pancreatitis?

The answer to this question depends on whether your dog had a single bout of acute pancreatitis caused by a definite 'triggering' event, or whether your dog is having repeated bouts of acute or chronic pancreatitis independent of any trigger.

If your dog has had just one bout of acute pancreatitis triggered by, for example, engorging on an unusual food or raiding a dustbin, there is no need to change its regular diet. It is however very wise to take greater care in future not to feed your pet on high fat tit-bits and not to let your pet scavenge, because any one bout of acute pancreatitis can be severe and fatal.

If, on the other hand, your dog is predisposed to repeated bouts of pancreatitis, even if these are only clinically mild (perhaps shown as occasional bouts of anorexia and diarrhoea) you should change your dog's diet to a low fat diet, such as Royal Canin Intestinal Low Fat* or Chappie. There is strong evidence in humans with chronic pancreatitis that feeding a low fat diet reduces the pain associated with the disease (Gachago and Draganov, 2008), and this appears to be true in dogs too.

*New brand name since 2010: Gastro-intestinal Low Fat

- Acute pancreatitis with severe clinical signs:
The clinical status of these dogs may not allow assisted enteral nutrition, as the vomiting and / or gastroduodenal ileus are severe.
The placement of a PEG or a jejunostomy tube is delayed for 12 to 72 hours as general anaesthesia is usually deemed to be too risky. Transpyloric and naso-jejuno-stomy tube shows promise. The dog should be stabilised first (intravenous fluids, analgesia, antiemesis, etc.).

The authors recommend starting with PPN (partial parenteral nutrition) as soon as possible to at least partially cover nutritional requirements and reverse the catabolic state. PPN is a mixture of a source of carbohydrates, amino acids, and lipids, and must be prepared under strictly aseptic conditions.

Unlike TPN, it does not cover all of the animal's requirements. However, when implemented early on, it limits catabolism. It is complimented with progressive enteral nutrition as soon as possible, which is always preferable for the maintenance of gastrointestinal function.

The solution is preferably administered via a central venous line as administration via a peripheral vein often induces phlebitis.

7/ Other treatments

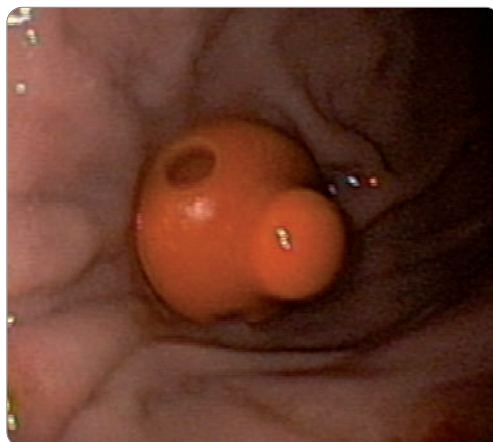
A) Corticosteroids

The use of corticosteroids in pancreatitis has been heavily debated. Their use is not as deleterious as was once thought (Heinrich, 2006). However, their hyperlipemic and anti-insulin actions mean that they should be avoided. Identification of lymphoplasmocytic pancreatitis (Cocker spaniel pancreatitis) suggests that immunosuppressive treatment may be indicated in some cases. This diagnosis can only be established by the histological analysis of pancreatic biopsies, which can be taken via laparotomy or laparoscopy. The loading dose of prednisolone is 1 to 2 mg/kg/day. The dose is then reduced incrementally.

Figure 3. Gastrostomy tube placement in a dog with moderate acute pancreatitis.



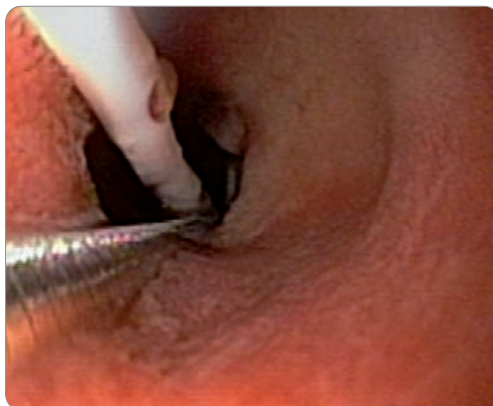
Figure 4. Endoscopic view of the gastrostomy tube.



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Some authors use glucocorticoids to treat the state of shock. In this case, the treatment is short (1 or 2 IV doses of methylprednisolone or dexamethasone) and is used as a complement to the other therapies for shock (intravenous fluids, etc.).

Figure 5. A small tube is inserted via the gastrostomy tube and guided into the distal duodenum for jejunal feeding.



B) Antacids

Antacids are indicated as erosive gastroduodenal lesions are commonly found in cases of pancreatitis. H2 receptor inhibitors are the most widely used as they can be administered by injection (**Table 6**).

C) Plasma transfusion and heparin therapy

Fresh plasma transfusion provides numerous potentially beneficial elements for the treatment of dogs with acute pancreatitis:

- Alpha-macroglobulin is an anti-protease that is naturally present in the blood stream. Its plasma concentration falls in animals with pancreatitis. It is therefore plausible to consider that the provision of alpha-macroglobulins would have an inhibitory effect on the proteases that are activated within the pancreas. This benefit has yet to be proven.
- Albumin, which helps to maintain oncotic pressure.

- Numerous coagulation factors that help to prevent the development of disseminated intravascular coagulation (DIC). If Antithrombin or platelet depletion and elevated D-dimer are detected on laboratory results, plasma transfusion is mandatory to try to reverse DIC.

Although no studies have proven the prognostic benefit of a plasma transfusion (Weatherton, 2009), the authors all recommend its use in the treatment of severe acute pancreatitis. A volume of 10 to 20 ml/kg IV is administered over a period of 4 to 6 hours. The volume and speed of perfusion are adjusted to the cardiovascular status of the dog.

Table 6. Doses of the principal antacids used in the treatment of canine pancreatitis.

Drug	Brand name	Dose rate
Cimetidine	Zitac (V), Tagamet (H)	5 to 10 mg/kg PO or IV, 3 to 4 times daily
Famotidine	Peptide (H), Pepcidac (H)	0.5 mg/kg PO, IV, SC, or IM 1 to 2 times daily
Omeprazole Per os only	Mopral (H), Zoltum (H)	0.7 mg/kg PO once in the evening
Pantoprazole Per os only	Eupantol (H), Inipomp (H)	1.5 mg/kg PO once in the evening
Ranitidine	Azantac (H), Raniplex (H)	0.5 to 2 mg/kg PO or IV, 2 to 3 times daily

Heparin therapy is indicated to prevent or treat DIC. Furthermore, heparin activates endothelial lipoprotein lipase, which may decrease triglyceridemia in hyperlipemic animals. Unfractionated heparin is used at 75 to 150 IU/kg SC every 8 hours in severe cases of acute pancreatitis.

D) The use of antiproteases

Aprotinin has been used in the treatment of acute pancreatitis for its inhibitory effects on pancreatic proteases (trypsin, chymotrypsin). The objective is to stop the autolysis process initiated by the intra-tissue activation of enzymes.

Clinical trials performed in humans and experimental data from the dog have given disappointing results (Bassi, 1989). Their use has now been abandoned since we know that the proteolytic process plays a significant role in the initiation of the disease but a minor role in its maintenance. By the time that the pancreatitis has become clinically apparent, it is essentially the inflammatory process that is responsible for the disease and not the activation of proteases.

The authors do not recommend their use in the treatment of pancreatitis in the dog or cat.

E) Treatment of diabetic ketoacidosis

When diabetic ketoacidosis is diagnosed, one should automatically look for a triggering factor. Acute

pancreatitis is one of the most common causes (together with other triggers such as urinary infection, cholangiohepatitis, etc.).

The treatment of acute pancreatitis associated with diabetic ketoacidosis should include 4 essential elements (in addition to the treatment for the pancreatitis):

1. Intravenous fluids to restore circulating volume using a 0.9% NaCl or Ringer Lactate solution depending on blood sodium levels.
2. Administration of fast-acting insulin (Actrapid®) via IM, IV, or SC injection as a function of the protocols described (Bassi, 1989).
3. Correction of electrolyte deficits (potassium, magnesium, phosphorous).
4. Correction of severe metabolic acidosis (pH < 7.1).

F) Supplementation with pancreatic enzymes

Some cases of chronic pancreatitis can result in the progressive destruction of the acinar cells leading to exocrine pancreatic insufficiency. The administration of pancreatic extracts is thus indicated with each meal and may be given in several forms:

- When available (abattoir or local butcher), fresh bovine pancreas is very effective. In the dog, 90 to 120 g of pancreas are needed per meal. The pancreas retains its enzymatic activities after freezing and thawing.
- Several human or veterinary products contain synthetic pancreatic extracts. The most widely used

are Canizyme® (1 dose/10 kg), Eurobiol 25,000® or Creon 25,000® (2 capsules/25 kg), or Tryplase® (2 to 3 capsules/25 kg) or Lypex® (1 capsule with each meal for dogs over 10 kg; half a capsule with each meal for cats and dogs under 10 kg). It is not necessary to pre-incubate the feed with the enzymes.

Only in proven cases of exocrine pancreatic insufficiency, enzyme supplementation is indicated. Recent metanalysis in people shows that the exogenous supply of pancreatic enzymes does not inhibit the natural secretions and does not reduce pain in pancreatitis (Robles, 1982).

G) When is surgery indicated?

The surgical resection of diseased pancreatic tissue (inflamed or even necrotic) has been studied in man. These studies did not show any improvement in the survival rate. Surgery should therefore be avoided in the

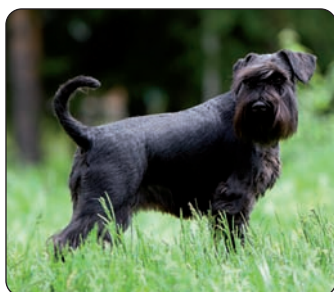
majority of cases. This is even more important given that the majority of animals with severe pancreatitis are haemodynamically unstable making anaesthesia more risky. However, certain specific indications still justify surgical exploration (Thompson, 2009):

- Biliary obstruction due to significant oedema around the bile duct and its opening. Cholecystoduodenostomy may then enable biliary drainage. Nevertheless, most biliary obstruction will resolve spontaneously if time is given.
- The formation of an abscess cavity requiring drainage and omentalization.
- Ultrasonographic suspicion of necrosis of a segment of the pancreas that may require resection (necrosectomy).
- A suspected tumour within the inflamed tissue for excision or biopsy.

The dog should be monitored in intensive care during the postoperative period. ■

4. Clinical cases (dogs)

1/ Miniature Schnauzer



A 7-year-old spayed female miniature Schnauzer presented for consultation with a history of apathy and anorexia. The owner also reported the onset of polyuria/polydipsia. There was a previous medical history of recurrent urinary tract infections, hypercholesterolaemia and hypertriglyceridaemia. When these abnormalities were observed, a complete list of differential diagnoses was drawn up and investigated (**Table 1**), ruling out all secondary causes of the hypertriglyceridaemia. The animal was diagnosed with idiopathic hyperlipidaemia of miniature Schnauzers and was being treated with a low-fat diet with increased omega-3 fatty acids.

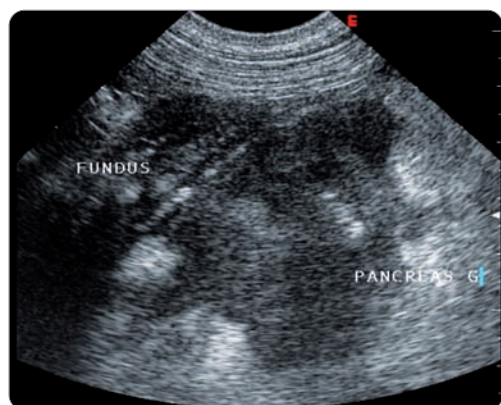
On physical examination, the animal was found to be depressed, with tachycardia (120 beats per minute), tachypnoea (40 breaths per minute), weak peripheral pulses, 8% dehydration, prolonged capillary refill time (2 seconds) and mild pain on cranial abdominal palpation.

A list of problems was drawn up that included anorexia, possible polyuria/polydipsia (PU/PD), shock and dehydration, hypertriglyceridaemia and hypercholesterolaemia. A thorough list of differential diagnoses was drawn up, including the causes of elevated triglycerides and its consequences (**Table 2**).

The diagnostic work-up included a complete blood count, complete biochemistry (**Table 3**), thoracic radiograph survey and abdominal ultrasound. The thoracic radiographs did not show evidence of abnormalities, and the laboratory tests showed leukocytosis with a mild left shift, severe hypertriglyceridaemia, hypercholesterolaemia, hyperglycaemia, elevated lipase, alkaline phosphatase and hypoalbuminaemia. The abdominal ultrasound showed a significant increase in pancreas size starting at the base of the right kidney and occupying the whole of the cranial abdomen (**Figure 1**).

Treatment was commenced with analgesia, antiemetics, fluid therapy, diet and insulin. The outcome was satisfactory. The animal recovered and the pancreatic abdominal mass disappeared completely.

Figure 1. Cranial abdominal ultrasound. The pancreas can be observed as a mass of reduced echogenicity adjacent to the duodenum and extending as far as the right kidney. Observe the large-sized pancreas in this animal.



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Table 2. Haematology and biochemistry.

Parameter	Value (+ normal range) traditional units	Value (+ normal range) SI units
Red blood cell count	6.28 ($\times 10^6/\mu\text{l}$) (5.5-8.5)	6.28 ($\times 10^{12}/\text{l}$) (5.5-8.5)
Haemoglobin	13.8 (g/dl) (12-18)	8.56 (mmol/l) (7.45-11.20)
Haematocrit	39 (%) (35-55)	0.39 (l/l) (0.35-0.55)
MCV	62.1 (fl) (60-70)	62.1 (fl)
MCH	35.4 (g/dl) (33-36)	354 (g/l) (330-360)
White blood cell count	21.470 ($\times 10^3/\mu\text{l}$) (6-17)	21.470 ($10^9/\text{l}$) (6-17)
Lymphocytes	3.006 ($\times 10^3/\mu\text{l}$) (1.0-4.8)	3.006 ($10^9/\text{l}$) (1.0-4.8)
Monocytes	0.429 ($\times 10^3/\mu\text{l}$) (0.150-1.35)	0.429 ($10^9/\text{l}$) (0.15-1.35)
Neutrophil band	0.215 ($\times 10^3/\mu\text{l}$) (<0.3)	0.215 ($10^9/\text{l}$) (<0.3)
Segmented neutrophils	17.391 ($\times 10^3/\mu\text{l}$) (<13.864)	17.391 ($10^9/\text{l}$) (<13.864)
Eosinophils	0.429 ($\times 10^3/\mu\text{l}$) (0.1-1.5)	0.429 ($10^9/\text{l}$) (0.1-1.5)
Platelet count	196 ($\times 10^3/\mu\text{l}$) (200-500)	196 ($10^9/\text{l}$) (200-500)
Creatinine	1.08 (mg/dl) (0.5-1.5)	95.47 ($\mu\text{mol/l}$) (44.2-136.6)
Urea	20 (mg/dl) (20-60)	7.14 (mmol/l) (7.14-21.42)
Cholesterol	535 (mg/dl) (135-270)	13.84 (mmol/l) (3.49-6.9)
Triglycerides	1078 (mg/dl) (50-100)	12.17 (mmol/l) (0.26-1.13)
Glucose	357.8 (mg/dl) (6-118)	19.87 (mmol/l) (0.34-6.55)
Total proteins	5.24 (g/dl) (5.5-7.5)	52.4 (g/l) (55-75)
Alb	1.6 (2.6-3.3)	16 (g/l) (26-33)
Alpha 1	0.15 (0.2-0.5)	1.5 (g/l) (2-5)
Alpha 2	1.31 (0.3-1.1)	13.1 (g/l) (3-11)
Beta	1.86 (0.9-1.6)	18.6 (g/l) (9-16)
Gamma globulin	0.33 (0.3-0.8)	3.3 (g/l) (3-8)
Total bilirubin	0.09 (mg/dl) (0.1-0.5)	1.54 ($\mu\text{mol/l}$) (1.71-8.55)
Alkaline phosphatase	3946.3 (UI/l) (20-156)	3946.3 (U/l) (20-156)
GGT	3 (UI/l) (1.2-6.4)	3 (U/l) (1.2-6.4)
ALT	61 (UI/l) (21-102)	61 (U/l) (21-102)
Calcium	9.1 (mg/dl) (9-11.3)	2.27 ($\mu\text{mol/l}$) (2.25-2.82)
K	3.74 (mmol/l) (4.37-5.35)	3.74 (mmol/l) (4.37-5.35)
NA	138 (mmol/l) (141-152)	138 (mmol/l) (141-152)
Cl	107.8 (mmol/l) (105-115)	107.8 (mmol/l) (105-115)
Phosphorus	5.09 (mg/dl) (2.6-6.2)	1.64 (mmol/l) (0.84-2.01)
Lipase	577 (UI/l) (13-200)	577 (U/l) (13-200)
cPLI	1200 ($\mu\text{g/l}$) (0-200)	1200 ($\mu\text{g/l}$) (0-200)

Table 1. Causes of increased triglycerides in serum and clinical presentation.

Causes of increase	
• Secondary Postprandial	- Obesity
• Primary	- Idiopathic hyperlipidaemia of Schnauzers and Beagles
• Secondary	- Diabetes mellitus
	- Hyperadrenocorticism
	- Hypothyroidism
	- Nephrotic syndrome
	- Cholestasis
	- Pancreatitis

Clinical consequences of hypertriglyceridaemia	
• Acute and/or chronic pancreatitis	- Anorexia, vomiting, diarrhoea, abdominal pain, fever
• Ocular changes	- Corneal lipid deposit, uveitis signs, retinal lipid deposit, blindness (lipid keratopathy, uveitis, retinopathy)
• Dermatological complications	- Pruritus, alopecia, cutaneous xanthomas
• Neurological changes	- Behavioural changes, seizures

Table 3. Hyperlipidaemia interference in laboratory tests.

Total and conjugated bilirubin	Elevated
Total proteins	Elevated
Calcium	Elevated
Inorganic phosphorus	Elevated
Alkaline phosphatase	Elevated
Glycaemia	Elevated
Fructosamine	Elevated
Creatinine	Reduced
Amylase	Reduced
Lipase	Reduced
Chloride	Reduced
Sodium	Reduced
Potassium	Reduced

Questions

1) Is hypertriglyceridaemia primary or secondary to the pancreatitis?

Animals with pancreatitis often present with hyperlipidaemia. It is normally evident in plasma and animals do not necessarily have to have eaten food recently. The section on pathophysiology and predisposing factors explains the implications of hyperlipidaemia. However, in these animals it is often necessary to prescribe a low-fat diet. If the hyperlipidaemia is not controlled with diet, gemfibrozil or another lipid-regulating agent can be used.

2) What false laboratory abnormalities have been reported with hyperlipidaemia?

Table 3 summarises the laboratory changes reported in animals due to hyperlipidaemia in plasma.

3) What is the cause of the hyperglycaemia?

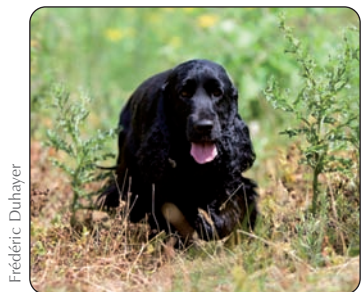
Can insulin secretion be normalised?

In animals with pancreatitis, hyperglycaemia may be due to various factors: (1) hyperglucagononaemia, (2) stress-induced, increasing catecholamine and cortisol levels, and (3) the destruction of endocrine cells in the pancreas due to inflammation. Not all animals develop diabetes mellitus, and an assessment should be made of the animal's progress in order to decide whether it will be able to produce adequate levels of insulin. In this case, the animal recovered normal insulin levels 15 days after discharge, and so it was possible to discontinue the insulin treatment. However, one year later, the animal became an insulin-dependent diabetic because of recurrent chronic pancreatitis. This abnormality and exocrine pancreatic insufficiency are the most common complications associated with chronic pancreatitis.

4) Is pancreas size on ultrasound a prognostic factor?

Pancreas size on ultrasound has not been associated with the prognosis. Some animals present with a very large pancreas associated with pancreatitis, as in this case report. In general primary pancreatic tumours are not large in size, and often already have metastases in the liver and other abdominal organs or in the chest at the time of diagnosis. Cytology can identify neoplasia, and a successful diagnosis is reported in 25% of cases. Therefore, if neoplasia is suspected, it is often necessary to perform a pancreatic biopsy in order to obtain a specific diagnosis.

2/ Cocker Spaniel



Frédéric Dubayer

A 7-year-old entire male Cocker spaniel presented with a 3 day history of anorexia and vomiting. The owner reported it was triggered by the dog eating pork. The dog had a 2-month history of mild bouts of vomiting undigested food an hour after feeding and intermittent yellow, smelly diarrhoea which were not severe enough to be presented to the vet. He used to be an obese dog but the owner reported that he had recently lost weight. The owner noted that the dog had started drinking a lot in the last 24 hours.

Clinical examination revealed the dog to be in normal body condition but rather depressed with a dry, flaky coat. He was not clinically dehydrated and thoracic auscultation was unremarkable. However, there was pain on cranial abdominal palpation. The rectal temperature was normal and the prostate was moderately enlarged but symmetrical and non-painful on rectal palpation. The conjunctiva of both eyes appeared inflamed and there was a tacky, mucopurulent ocular discharge bilaterally. The breath smelt of ketones. Schirmer tear tests confirmed bilateral keratoconjunctivitis sicca (KCS).

Blood samples were taken (**Table 1**). A urine sample was positive for ketones but blood pH was normal.

Abdominal ultrasound showed a large mass-like lesion in the pancreas adjacent to the duodenum with evidence of surrounding pancreatic oedema. This mass resolved on subsequent examinations, confirming it was inflammatory rather than neoplastic.

A definite diagnosis of diabetic ketosis (but not yet ketoacidosis) was made with concurrent KCS and a presumptive diagnosis of concurrent pancreatitis and the dog was stabilised with intravenous fluids, opiate analgesics and soluble insulin, followed by twice daily Lente. The dog was fed twice daily Royal Canin Intestinal low-fat diet and topical optimmune was used in the eyes. The recent weight loss and dry coat gave a suspicion of developing exocrine pancreatic insufficiency (EPI), so the dog was also given pancreatic enzyme supplementation in the food. The TLI had fallen to 1.8 ng/ml on re-examination 2 months later and remained consistently low after that, confirming the development of EPI. The dog did well for 2 years and finally was euthanized for end stage chronic hepatitis. End stage chronic pancreatitis with very little remaining exocrine tissue and no visible islets was confirmed at post mortem. ■

Table 1. Haematology and biochemistry.

Parameter	Normal range SI (and traditional)	Case (SI + traditional)
Glucose mmol/l (mg/dl)	3.4-5.3 (61-95)	22 (450)
Alkaline phosphatase iu/l	3-142	365
Alanine aminotransferase iu/l	21-59	74
Amylase iu/l	500-1500	934
Lipase iu/l	0-250	1160
Blood urea mmol/l (mg/dl)	3.3-6.7 (20-48)	3.1 (19)
Creatinine mmol/l (mg/dl)	70-170 (0.5-1.7)	51 (0.6)
Sodium mmol/l	135-155	148
Potassium mmol/l	3.7-5.8	4.3
cPLI ng/ml	2.2-102 (>200 pancreatitis; 102-200 indeterminate)	276
TLI ng/ml	>5.0 (2.5-5.0 indeterminate)	5.4

5. Feline pancreatitis

> SUMMARY

- The most common clinical findings in cats with acute pancreatitis are lethargy, anorexia, and weight loss.
- A specific cause for pancreatitis is not apparent in the majority of cats.
- There is no single test that will accurately diagnose pancreatitis in all affected cats.
- Cats with pancreatitis often have inter-current disease involving the liver and small intestines.
- Medical treatment is based on maintaining or restoring adequate tissue perfusion, limiting bacterial translocation, inhibiting inflammatory mediators and pancreatic enzymes and providing enteral nutritional support.
- Surgical treatment consists of restoring biliary outflow, removing infected necrotic pancreatic tissue, or coping with sequela such as pseudocysts.

The prognosis for acute pancreatitis in cats is always considered guarded, and is particularly poor for suppurative pancreatitis.



Introduction

Since its initial description in 1989 (Macy, 1989) feline pancreatitis has emerged as an important and potentially life-threatening disease. Despite increased awareness an underlying cause is usually not identified, diagnosis is challenging, and surgical biopsy is often required to confirm a diagnosis, and facilitate detection of intercurrent disease. Treatment is symptomatic and typically involves aggressive nutritional support. This chapter reviews the diagnosis and management of acute pancreatitis in cats.

1/ The spectrum of pancreatic inflammation in cats

The gross and histological appearance of the inflamed feline pancreas is variable and there is not yet a consensus on the interpretation of pancreatic histopathology. In general, histopathology is reported according to the predominant features as acute

pancreatitis associated with necrosis and/or suppurative inflammation, or chronic non-suppurative pancreatitis (lymphocytic/plasmacytic inflammation and fibrosis, \pm acinar atrophy) (Ferreri, 2003; Gerhardt, 2001; Hill, 1993; Macy, 1989; Saunders, 2002; Simpson, 1994; Simpson, 2001; Swift, 2000; Weiss, 1996; De Cock, 2007) (**Figure 1**). Whether these histologic types indicate a distinct etiology or some form of progression is unclear. At the present time there is no reliable way to noninvasively distinguish acute pancreatitis from chronic non-suppurative pancreatitis (Ferreri, 2003; De Cock, 2007). Uncommon sequelae to pancreatitis include abscesses/infected necrosis and cystic accumulations of fluid (Simpson, 1994).

2/ When should I suspect pancreatitis?

Acute pancreatitis has been reported in cats aged from 4 weeks to eighteen years old. Domestic Short- and Long-hair cats are most commonly affected. Siamese cats have

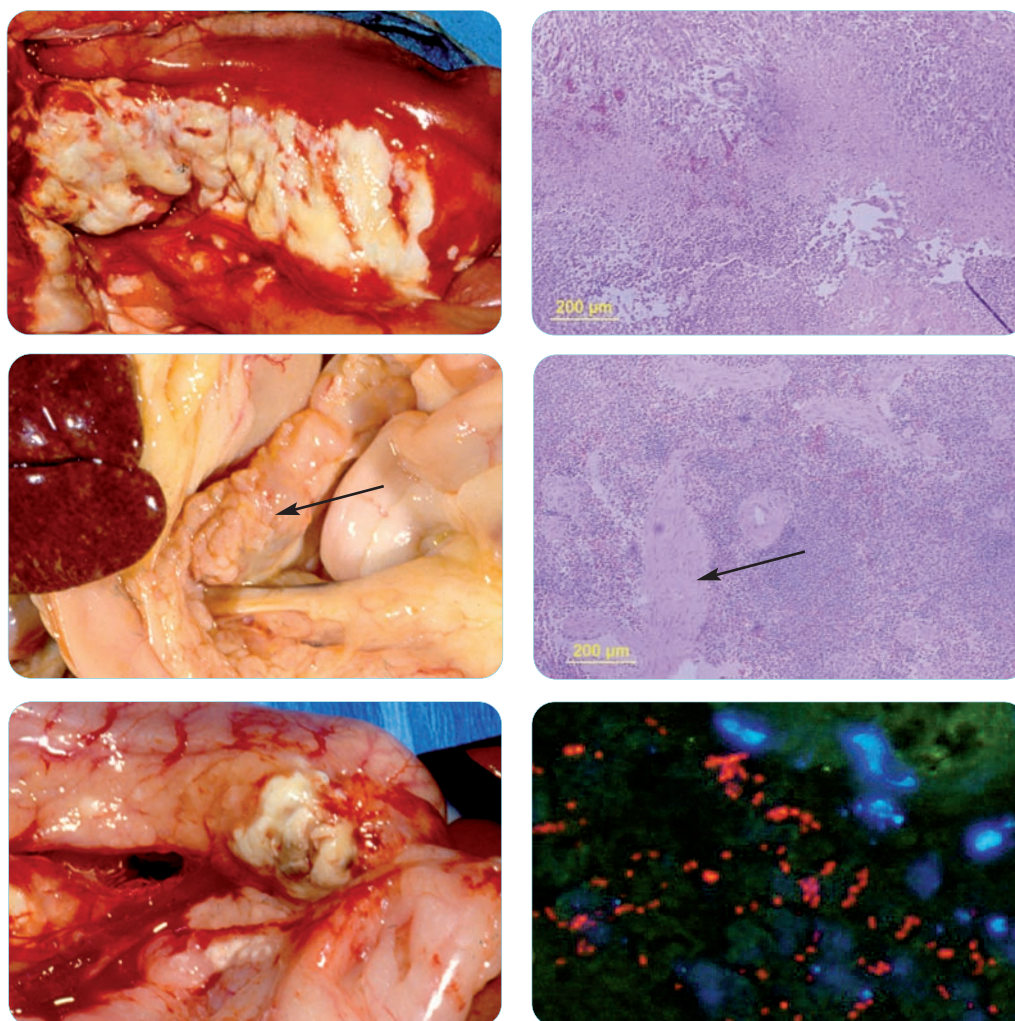


Figure 1. Left row (top to bottom): acute pancreatitis (note saponified fat and inflamed duodenum), chronic pancreatitis with fluid filled cyst (arrow), pancreatic abscess. Right row: Histopathology of pancreatitis (top to bottom): acute suppurative pancreatitis, chronic pancreatitis with extensive fibrosis (arrow) and lymphocytic infiltrates fibrosis, intra-pancreatic bacteria (red) visualized with eubacterial fluorescence in situ hybridization.

been over-represented in some series. No sex bias has been demonstrated.

A small number of cases have been associated with trauma, *Toxoplasma gondii*, pancreatic and liver flukes (Vyhna, 2008), FIP, calicivirus (virulent variant) and lipodystrophy. Usually there are no obvious associated factors (**Table 1**). The most common clinical findings in cats with acute

pancreatitis are lethargy, anorexia, and weight loss. Vomiting diarrhoea, constipation, icterus, dehydration, ascites and dyspnoea are more variably present. Polyuria and polydipsia have been encountered in some cats with diabetes mellitus and pancreatitis. The duration of clinical signs until presentation varies from less than 3 days to 12 weeks.

Table 1: When should I suspect pancreatitis?

- The most common clinical findings in cats with acute pancreatitis are lethargy, anorexia, and weight loss.
- Vomiting diarrhoea, constipation, icterus, dehydration, ascites and dyspnea are more variably present.
- Polyuria and polydipsia can be associated with concurrent diabetes mellitus and pancreatitis.
- Increased liver enzymes, increased bilirubin, low albumin and decreased calcium raise the possibility of pancreatitis.

Physical examination

Dehydration and hypothermia are commonly reported. Icterus may also be present. Abdominal pain is infrequently elicited. The presence of a palpable cranial abdominal mass or abdominal pain has been reported in a quarter to a third of cats in some clinical series and cats with experimental and trauma-induced pancreatitis.

3/ Diagnostic approach and differential diagnosis

A) General points

Lethargy anorexia and weight loss are the most common presenting complaints. Localizing signs or findings such as vomiting, icterus, diarrhoea, abdominal pain, abdominal mass, polyuria or polydipsia should be pursued if present.

Where vomiting is present it is approached by pursuing localizing findings such as abdominal pain or masses and by ruling out infectious, parasitic, metabolic and gastrointestinal causes. Hyperthyroidism should be ruled out in cats > 5 years-old by measuring serum total T₄ concentration. Elevated liver enzymes, hyperbilirubinemia, hyperglycemia, and glucosuria are frequently encountered in

cats with acute pancreatitis so pancreatitis should be strongly considered in these cats.

The diagnostic approach to feline jaundice is to first rule out pre-hepatic causes i.e hemolysis, and then to pursue hepatic or post-hepatic causes. Acute pancreatitis in combination with hepatic lipidosis is associated with increased mortality. Concurrent pancreatitis, cholangio-hepatitis and inflammatory bowel disease (triaditis) has been shown in some studies (e.g. Akol, 1993; Forman, 2004; Simpson, 2001; Weiss, 1996; De Cock, 2007). A high index of suspicion should be adopted for pancreatitis in cats with hepatic, biliary or intestinal disease. Cats with a confirmed diagnosis of hepatic lipidosis who have a peritoneal effusion should also be strongly suspected of having pancreatitis (Akol, 1993).

Pancreatitis may be the cause of diabetes mellitus in some cats, but the true association between these diseases is unclear. One study suggests that cats with pancreatitis and diabetes mellitus are very sensitive to insulin. Transient euglycemia and reduced insulin requirements after removal of a pancreatic abscess suggest that pancreatic inflammation or infection can exacerbate diabetes mellitus in cats. Transient diabetes mellitus has also been reported in a cat that was suspected of having pancreatitis.

Where a high index of suspicion for pancreatitis is present ultrasonography and determination of pancreatic markers (e.g. pancreas specific lipase) should initially be employed to help detect pancreatic inflammation. However, given the spectrum of inter-current disease in cats with pancreatitis a well performed exploratory laparotomy with biopsy of the pancreas, liver, intestines and mesenteric lymph nodes is often required to generate an accurate diagnosis and enable feeding-tube placement. The diagnostic approach to cats with suspected pancreatitis is illustrated in the **Clinical case** and is summarized in **Table 2**.

B) Laboratory findings

Routine clinicopathological tests:

Hematology

A mild anemia that may be non-regenerative, and leukocytosis, often without a left-shift, are common in cats with pancreatitis. Leukopenia is present in some cats and

suggests a poorer prognosis.

Serum biochemistry

Increased ALT, SAP, bilirubin, cholesterol and glucose, and hypokalemia and hypocalcemia (total and ionized) are most frequently observed. Azotemia is variably present.

Hypocalcemia

Hypocalcemia, present in about 50% of cases, is perhaps the most helpful finding for raising the probability of a diagnosis of pancreatitis (Kimmel, 2001). Pancreatitis-associated hypocalcemia may be a consequence of saponification of fat, soft tissue accumulation and changes in PTH homeostasis. The presence of ionized hypocalcemia (< 1 mmol/l) carries a poor prognosis (Kimmel, 2001). Hypocobalaminemia is present in some cats with pancreatitis and is thought to reflect concurrent intestinal disease, rather than exocrine pancreatic insufficiency (Simpson, 2001).

Urinalysis

Urinalysis enables azotemia to be characterized as renal or pre-renal. The presence of glucose or ketonuria should prompt consideration of diabetes mellitus.

Pancreas specific enzymes

Classically, elevations in serum amylase and lipase activity have been used as indicators of pancreatic inflammation in dogs. In cats it seems fair to state that total serum amylase and lipase are of no utility for diagnosing acute pancreatitis.

These limitations have stimulated the development of assays for enzymes or "markers" considered pancreatic in origin. Tests for trypsin-like immunoreactivity (TLI), trypsinogen activation peptide (TAP) and pancreas specific lipase have been evaluated in cats.

Feline Trypsin like immunoreactivity (fTLI)

Immunoreactive trypsin has been shown to enable the reliable detection of feline exocrine pancreatic insufficiency. It is much less useful as an indicator of pancreatic inflammation (Forman, 2004; Gerhardt, 2001; Simpson 2001; Swift, 2000) (see **Clinical case**). Its sensitivity has been reported to be as low as 28%, and cats with fatal acute pancreatitis frequently have values within the normal range. Specificity is somewhat better, approx. 66-75%. The poor sensitivity, particularly in cats

Table 2: How do I accurately diagnose pancreatitis?

- There is no single non-invasive test that accurately identifies all cats with pancreatitis.
- Measurement of serum amylase, lipase and TLI is not reliable for confirming a diagnosis of acute pancreatitis.
- Pancreas specific lipase shows promise with a sensitivity estimated at 67% sensitivity, 91% specificity for fPLI. For the Spec fPL assay (a commercialized version of fPLI) using 5.4 µg/l as the diagnostic cut off, yielded a sensitivity of 79% and the specificity of 82%.
- Abdominal ultrasound has a sensitivity of 35-67% and specificity of approx. 73%.
- Cats with pancreatitis may have normal fPLI/SpecfPL and ultrasonographic findings.
- Pancreatic biopsy enables confirmation and distinction between histological subtypes of pancreatitis, pancreatic hyperplasia and pancreatic cancer.
- An exploratory laparotomy enables diagnosis of intercurrent disease in the liver and small intestine.

with severe acute pancreatitis, strongly suggests down regulation of TLI in the inflamed pancreas, similar to that observed in dogs with pancreatitis. Altered renal clearance in cats with renal failure can impact the specificity, as can the finding of normal pancreatic histology in cats with high TLI and intestinal disease.

Pancreas specific lipase immunoreactivity (fPLI, SpecfPL)

Given the limitations of fTLI tests to measure feline pancreas-specific immunoreactive lipase have recently been developed (Steiner, 2004). Clinical utility is still being ascertained. However the initial results for fPLI are a lot more promising than fTLI, with sensitivity for pancreatitis reported as 67%, and specificity at 91% (Forman, 2004). Preliminary evaluation of the commercial version of the fPLI test, Spec fPL using 5.4 µg/l as the diagnostic cut-off, yielded a sensitivity of 79% and the specificity of 82% (Forman et al, unpublished observations).

Trypsinogen activation peptide

Trypsinogen activation peptide (TAP), is a peptide generated by the activation of trypsinogen (Karanjia, 1993). In health, TAP is not detected in the circulation or urine. However the intrapancreatic activation of trypsinogen liberates TAP that can be measured in EDTA plasma and urine. Experimental studies have shown that TAP generation can be detected in cats with oedematous and hemorrhagic pancreatitis, with higher levels generated in those with hemorrhagic pancreatitis (Karanjia, 1993). Unfortunately, clinical application is unlikely as the assay is generally unavailable.

4/ Diagnostic imaging

A) Radiography

Radiographic findings in cats with acute pancreatitis may include loss of serosal detail, increased opacity in the right cranial quadrant of the abdomen, displacement of the duodenum ventrally and/or to the right, dilated hypomotile duodenum and caudal displacement of the transverse large intestine. Although radiographic signs often are absent, non-specific radiography is a logical first choice imaging modality for animals with gastrointestinal signs. Negative or equivocal radiographic findings may be followed up with ultrasonography or an upper gastrointestinal contrast study. Thoracic radiographs may enable the detection of pleural fluid, oedema or pneumonia which has been associated with pancreatitis in dogs and cats (Hill, 1993; Saunders, 2002). The high rate of pulmonary thromboembolism associated with feline pancreatitis may explain some of the thoracic radiographic abnormalities (Schermerhorn, 2004).

B) Ultrasonography

Ultrasonographic findings include enlarged, hypoechoic pancreas, cavitory lesions such as abscess or pseudocyst, dilated pancreatic duct, swollen hypomotile duodenum, biliary dilatation and peritoneal fluid (Ferreri, 2003; Gerhardt, 2001; Saunders, 2002, Simpson 1994; Swift, 2000). Findings in cats indicate that ultrasound will detect

from 35 to 67 % of cats with pancreatitis, with a specificity of approx. 73% (Forman 2004; Gerhardt, 2001; Saunders, 2002; Swift, 2000). This clearly means that a normal ultrasound does not rule out pancreatitis, and that diseases other than pancreatitis (e.g. pancreatic hyperplasia, pancreatic neoplasia) should be considered when an abnormal pancreas is visualized.

The clinician should also be careful to consider differential diagnoses of enlarged peri-pancreatic structures, which can have an identical ultrasonographic appearance to pancreatitis. Fine needle aspirates of cavitory lesions may be useful to distinguish abscess from pseudocyst, neoplasia from inflammation etc. (Simpson, 1994).

Computed tomography

Contrast enhanced computed tomography (CE-CT) is the diagnostic test of choice for diagnosing pancreatitis in people. Studies in cats have been disappointing, ranging from a failure to detect the pancreas to no differences visualized in cats with pancreatitis compared with normal cats (Forman, 2004; Gerhardt, 2001).

Abdominal paracentesis

Examination of peritoneal fluid may aid the detection of various causes of acute abdominal signs such as pancreatitis, gastrointestinal perforation or ruptured bile duct. The accumulation of fluid in the abdomen or the pleural cavity has been variably encountered in cats with acute pancreatitis. Effusion in the abdomen or chest was present in 17/40 cats in one study, in the abdomen of 5/5 cats with hepatic lipidosis and pancreatitis, and the abdomen of 2/8 cats another.

5/ Prognostic indicators

The presence of shock or abnormalities such as oliguria, azotemia, icterus, markedly elevated transaminases, ionized hypocalcaemia (< 1 mmol/l), hypoglycemia, hypoproteinemia, acidosis, leukopenia, falling hematocrit, thrombocytopenia and DIC should be considered likely indicators of severe pancreatitis in the cat

A) Pancreatic biopsy and histology

The pancreas can be biopsied surgically or laparoscopically. Current recommendations, based on the patchy distribution of pancreatic inflammation, suggest taking biopsies from parts that look or feel abnormal, and from the left and right limbs and the body. Histological findings are variable and there is not yet a consensus on their interpretation (**Figure 1**). In general histopathology is reported according to the predominant features as acute necrotizing (necrosis predominates), acute suppurative (neutrophils predominate) or chronic non-suppurative (lymphocytic/plasmacytic inflammation and fibrosis) (Ferreri, 2003; Gerhardt, 2001; Hill, 1993; Macy, 1989; Saunders, 2002; Simpson 2001; Simpson, 1994; Swift, 2000; Weiss, 1996; De Cock, 2007). Whether these histologic types indicate a distinct etiology or some form of progression is unclear. The prognosis for suppurative pancreatitis is poor (Hill, 1993).

6/ How do I treat pancreatitis?

A) Medical management

Medical treatment is based on maintaining or restoring adequate pancreatic perfusion, limiting bacterial translocation and inhibiting inflammatory mediators and pancreatic enzymes; surgical treatment consists principally of restoring biliary outflow, removing infected necrotic pancreatic tissue, or coping with sequela such as pseudocysts (**Table 3**). No studies have critically evaluated treatment modalities in cats with naturally occurring pancreatitis.

The initial medical management is usually initiated before a diagnosis is confirmed, and is based on the presenting clinical findings and initial laboratory data. Dehydration or hypovolemia are supported with intravenous fluid therapy. Lactated Ringers solution or 0.9% NaCl are common first choices. Potassium and glucose should be supplemented where necessary. The type of fluid should be tailored on the basis of electrolyte and pH measurements to restore normal electrolytes and acid-base balance. Ionized hypocalcemia is a common finding in cats with acute pancreatitis and impacts prognosis (Kimmel, 2001). However, it is not clear if

Table 3: How do I treat pancreatitis?

No studies have critically evaluated treatment modalities in cats with naturally occurring pancreatitis.

Medical therapy:

- Maintain or restore adequate pancreatic perfusion,
- provide analgesia,
- limit bacterial translocation,
- inhibit inflammatory mediators and pancreatic enzymes,
- provide enteral nutritional support (**Figure 2**),
- surgical treatment,
- restore biliary outflow,
- remove infected necrotic pancreatic tissue cope with sequelae such as pseudocysts.

treatment of hypocalcemia, which is not usually associated with fasciculations, tetany or seizures, will impact outcome.

Plasma (20m l/kg i.v.) or colloids (10-20 ml/kg/day i.v.) may be indicated in the presence of hypoproteinemia or shock. Colloids such as dextran 70 and hetastarch may also have antithrombotic effects that help maintain the microcirculation.

Insulin therapy is initiated in diabetic patients. Stress hyperglycemia has to be differentiated from diabetes mellitus (i.e. stress hyperglycemia is characterized by absence of ketones, normal fructosamine, transient hyperglycemia).

Where vomiting is a persistent problem antiemetics (chlorpromazine 0.2-0.4 mg/kg administered subcutaneously or intramuscularly every 8 hours) and antacids (e.g. famotidine 0.5-1 mg/kg) may be beneficial.

Prophylactic broad-spectrum antibiotics (e.g. amoxicillin ± fluoroquinolone depending on severity) may be warranted in patients with shock, fever, diabetes mellitus or evidence of breakdown of the GI barrier. Bacterial translocation has been demonstrated in feline pancreatitis using distinct *E.coli* placed in the colon, and other sites e.g. bile, and colonization was prevented with cefotaxime (50 mg/kg TID) (Widdison, 1994; Widdison, 1994). We have recently observed bacteria within the feline pancreas (**Figure 1**) but the frequency of translocation remains to be determined.

Analgesia is an important aspect of caring for animals with pancreatitis. It can be provided using injectable opioids such as buprenorphine (0.005-0.01 mg/kg SC q 6-12 hours) or oxymorphone (0.05-0.1 mg/kg cats IM, SC Q 1-3 hours). It may be necessary to administer low dose sedation with acepromazine (0.01 mg/kg IM) to patients who become dysphoric after opioids. Buprenorphine is a partial agonist and may antagonize the administration of more potent analgesics in animals with severe pain. A transdermal fentanyl patch (Duragesic, Janssen) applied to a clipped clean area of skin provides longer duration of analgesia (25 µg/hr patch). Adequate fentanyl levels are not attained for between 6-48 hours after application, so another analgesic should be administered in the short term. This author does not use non-steroidal anti-inflammatory drugs to provide analgesia to cats with suspected pancreatitis.

Once a diagnosis of pancreatitis is confirmed potentially more specific therapy may be employed.

The specific treatment of pancreatitis has evolved along two lines:

1. Stopping further pancreatitis from occurring
2. Limiting the local and systemic consequences of pancreatitis

The lack of success with inhibiting the progression of spontaneous pancreatitis has led to increased emphasis on damage limitation; ameliorating the effects of inflammatory mediators or pancreatic enzymes on the patient and maintaining pancreatic perfusion.

Coagulation abnormalities should be pursued and treatment with parenteral vitamin K can be assessed. Where a coagulopathy e.g. DIC, or hypoproteinemia are present, or the patient with pancreatitis is deteriorating, fresh frozen

plasma (10-20 ml/kg) may be beneficial in alleviating the coagulopathy, hypoproteinemia and restoring a more normal protease-antiprotease balance. The administration of heparin (75-150 IU/kg TID) may be potentially useful in ameliorating DIC, promoting adequate microcirculation in the pancreas and clearing lipemic serum. In experimental pancreatitis isovolemic rehydration with dextran has also been shown to promote pancreatic microcirculation in dogs. A dopamine infusion (5 µg/kg/min) had a protective effect when administered to cats within 12 hours of induction of pancreatitis (Karanjia, 1990). H₁ and H₂- antagonists blocked the progression of oedematous to hemorrhagic pancreatitis in experimental cats and may be beneficial in patients (Harvey, 1987).

In the future therapy to directly abrogate the systemic inflammatory response e.g. antagonists of PAF (e.g. lexipafant), IL-1 and TNF-α may prove to be beneficial (Raraty, 2004).

Oral pancreatic enzyme extracts have been reported to reduce pain in humans with chronic pancreatitis, though this is controversial. The presence of a protease mediated negative feedback system has not been described in cats.

B) Dietary management

In contrast to dogs, where vomiting and abdominal pain predominate, pancreatitis in cats is usually associated with anorexia and weight loss. The presence of anorexia and weight loss in cats with pancreatitis may be a significant contributing factor to their poor prognosis. Prolonged fasting (> 3 days) to avoid pancreatic stimulation may only serve to compound malnutrition. The clinician is faced with the dilemma of having to provide nutritional support to prevent or reverse malnutrition and hepatic lipidosis, and fasting the patient to prevent "pancreatic stimulation".

Current dogma and catma suggest that oral intake be avoided in patients with pancreatitis who are vomiting or have abdominal pain, and that enteral nutrition should avoid nutrients that stimulate the pancreas (though the protein requirements of cats makes this unachievable).

However, there is growing evidence in people, and animals, that enteral nutrition is superior to parenteral nutrition in the

treatment of acute pancreatitis (Qin, 2002; Windsor, 1998). Jejunal feeding (distal to the site of pancreatic stimulation) does not exacerbate acute pancreatitis in people or experimental animals. People with acute pancreatitis fed via jejunostomy tubes (these can be oral transpyloric tubes), have lower morbidity, shorter hospital stay, and less cost than those treated with TPN (total parenteral nutrition) (Windsor, 1998). As it is now feasible to place jejunostomy tubes non-surgically in cats and dogs, through the nose, oesophagus or stomach, clinical application of this feeding strategy is not restricted by a surgical procedure. However, it remains open whether cats with acute pancreatitis really require jejunal delivery of nutrients. Good responses have been observed at referral centres employing nasogastric, nasooesophageal, oesophagostomy or gastrostomy tube feeding of enteral diets (e.g. Clinicare) containing approximately 50% calories as fat (Figure 2). One recent publication using nasogastric feeding showed a continuously infused liquid enteral diet was well tolerated in cats with suspected pancreatitis with 91% of cats surviving > 28 days (Klaus, 2006). These results seem consistent with findings in people and experimental dogs that show the major benefits of enteral support in acute pancreatitis are due to reductions in the systemic inflammatory response and the translocation of enteric bacteria rather than a reduction in pancreatic stimulation (Kalfarentzos, 1997; Qin, 2002; Windsor, 1998).

C) Patient monitoring

Patients with suspected or confirmed pancreatitis should be monitored to enable early detection of shock or other systemic abnormalities. Minimal monitoring for stable patients includes regular assessment of vital signs and fluid and electrolyte balance. In those with systemic abnormalities, monitoring should be more aggressive and may include vital signs, weight, hematocrit, total protein, fluid intake and output, blood pressure (central venous and arterial), electrolytes and glucose, acid-base status, platelets and coagulation status. Ultrasound-guided fine needle aspiration of the pancreas may enable infected pancreatic necrosis to be detected (Simpson, 1994). Ultrasonography may also enable detection of delayed consequences of acute pancreatitis such as pancreatic abscessation, pseudocyst formation and biliary obstruction.

D) Surgery

Surgery is often necessary to confirm a diagnosis of acute pancreatitis in cats and also enables feeding tube placement. The increasing accuracy of ultrasonography and markers of pancreatic inflammation (e.g. pancreas specific lipase) may lead to a reduced dependency on surgery in cats with high pancreatic lipase and sonographic abnormalities, but at present time up to a third of cats with pancreatitis will have normal sonography and pancreatic lipase. It should also be stressed that cats with



Can a cat with normal pancreatic enzymes and pancreatic ultrasonography still have pancreatitis?

Yes. There is currently no single non-invasive test that accurately identifies cats with pancreatitis. Measurement of serum amylase, lipase and TLI is not reliable for confirming a diagnosis of acute pancreatitis. Pancreas specific lipase shows promise with a sensitivity estimated at 67% to 79% but this means up to 33% of cats with pancreatitis could have a normal pancreatic lipase value. Abdominal ultrasound has a sensitivity that varies from 35-67%, which again translates to at least a third of cats with pancreatitis having a normal ultrasound. Where there is a high index of suspicion for pancreatitis in the face of normal enzymology and imaging, an exploratory laparotomy enables pancreatic biopsy and detection of intercurrent diseases that frequently accompany pancreatitis e.g. in the liver and intestine.



Figure 2. An oesophagostomy tube (top left) is an effective means of delivering enteral nutritional support to anorexic cats with pancreatitis, where nutritional support is likely to be required for more than five days (A nasoesophageal tube may be used for short term support). The cat is anaesthetized and placed in right lateral recumbency and a closed pair of curved forceps are inserted into the proximal oesophagus (bottom left). The forceps are pushed firmly laterally to move any overlying structures out of the way and an incision is made over the tip of the forceps. The forceps are pushed through the incision and a 15Fr polyvinyl feeding tube is grasped in the open jaws and retracted towards the mouth. The tip of the feeding tube is then repositioned and directed down the oesophagus. The tube is premarked to denote the position of the 7th or 8th intercostal space. It should not pass through the lower oesophageal sphincter. The tube is secured with a Chinese finger trap suture (top and bottom right). Tube position is confirmed radiographically (radiograph). Feeding is typically started once the cat has fully recovered from anesthesia, and is increased in a stepwise fashion feeding 1-third, 2-thirds and 3-thirds of caloric requirements (approximately 60 kCal/kg) over three days. A liquid enteral diet is frequently used in the initial stages, but blenderized watered down cat food can be fed in the longer term.

pancreatitis often have concurrent abnormalities in other organ systems e.g liver and gut, and biopsy of these organs and the pancreas may be indicated to optimize diagnosis and treatment. Transient euglycemia and reduced insulin requirements were noted after the removal of a pancreatic abscess in one cat. This suggests that surgical intervention may be beneficial in these cases. Surgery is potentially indicated for infected pancreatic necrosis, abscess drainage, and to investigate and relieve persistent biliary obstruction. Resection or surgical drainage of pancreatic pseudocysts is not always necessary as these can resolve spontaneously or following percutaneous drainage.

E) Prognosis

The prognosis for acute pancreatitis in cats is usually considered guarded. Extensive hepatic lipidosis, suppurative pancreatitis, leucopenia and ionized hypocalcemia < 1 mmol/l are associated with a poor prognosis (Akol, 1993; Hill 1993; Kimmel, 2001). ■

6. Clinical case (cat)

Clinical presentation

4-year-old neutered male domestic shorthaired "Joey"

Presenting complaints: Vomiting, Anorexia, Lethargy

History: 7-day history of clinical signs

Physical examination: HR 230bpm; T 101.7; 7.1kg; Body condition score 4/5; Overweight, otherwise normal physical

Differential Diagnosis: Vomiting

Diagnostic investigations

CBC:

• Packed cell volume	49 (32-52 %)
• Mean corpuscular volume	51 (40-52 fl)
• White blood cell count	10.5 (5.3-16.6 x10 ⁹ /μl)
• Neutrophils	6.7 (2.3-11 x10 ⁹ /μl)
• Band neutrophils	0 (0-0.1 x10 ⁹ /μl)
• Lymphocytes	1.8 (1.2-6.9 x10 ⁹ /μl)
• Monocytes	0.6 (0-1.1 x10 ⁹ /μl)
• Eosinophils	1.4 (0.1-2.3 x10 ⁹ /μl)
• Platelets	adequate - clumping
• Total protein	8.7 (5.9-7.5 g/dl)

Clinical Chemistry:

• Na	149 (146-156 mEq/l)
• K	3.7 (3.8-5.6 mEq/l)
• Cl	116 (112-123 mEq/l)
• HCO ₃	17 (12-21 mEq/l)
• Urea	15 (17-35 mg/dl)
• Creatinine	1.4 (0.7-2.1 mg/dl)
• Ca	9.4 (8.2-11.5 mg/dl)
• PO ₄	3.5 (3.6-6.6 mg/dl)
• Total protein	6.8 (6.7-8.5 g/dl)
• Albumine	3.6 (2.9-4.3 g/dl)
• Globulin	3.2 (3.1-5.1 g/dl)
• Glucose	157 (63-140 mg/dl)
• ALT	1195 (29-186 U/l)
• AST	302 (13-46 U/l)
• ALP	28 (15-96 U/l)
• GGT	3 (0-3 U/l)
• Bilirubin	0.6 (0-0.2 mg/dl)
• Amylase	1071 (489-2100 U/l)
• Cholesterol	248 (73-265 mg/dl)
• CK	759 (71-502 U/l)

Interpretation

Increased liver enzymes (hepatocellular enzymes) and hyperbilirubinemia in the absence of anemia indicate liver disease (e.g. cholangiohepatitis, hepatic lipidosis) or biliary disease (e.g. cholangitis, partial biliary obstruction should be considered by stones or pancreatitis).

Intercurrent disease in the intestines and pancreas should be considered i.e. "triaditis".

Diagnostic imaging

Ultrasound - **see picture below.**

Abdominal sonography:

- Mild dilation cystic duct
- Pancreas is hypoechoic surrounded by hyperechoic fat
- Mild lymphadenopathy adjacent to colon

Cytology

Fine needle aspirate of liver: non-diagnostic, no

Figure 1. Cranial abdominal ultrasound. The pancreas is hypoechoic surrounded by hyperechoic fat.



hepatocytes detected

Fine needle aspirate of lymph node: reactive hyperplasia

These findings suggest pancreatitis. Reactive hyperplasia of abdominal lymph nodes suggestive of intestinal disease

- Prominent irregular pancreas (**see photo A**)
- Pale liver (**see photo B**)
- Increased colonic LN (**see photo C**)
- Culture liver and bile

Histopathology

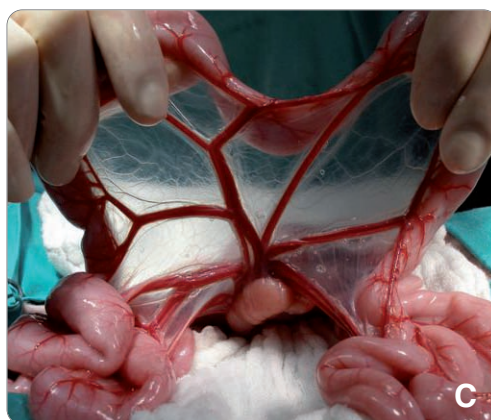
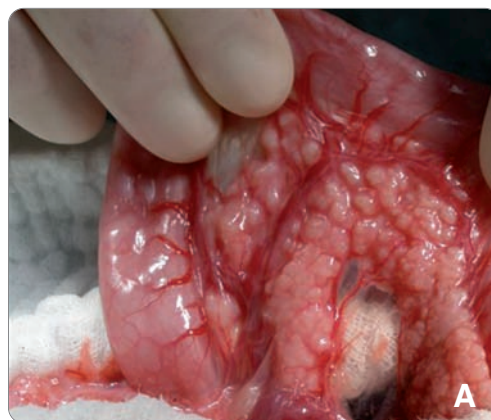
- **Pancreas:** within lobular septae small numbers of neutrophils, macrophages plasma cells and mild oedema

Further evaluation of pancreatic inflammation and intestinal function

PLI: 100.7 (2-6.8 µg/l) **FTLI:** 66.7 (12-82µg/l)

Cobalamin: 1617 (>900 pg/ml)
Folate 16 ng/ml (12-20 ng/ml)

Interpretation: Elevated PLI consistent with pancreatitis, note TLI is normal. Normal cobalamin and folate do not support the presence of severe concurrent small intestinal disease.



Therapeutic plan

Symptomatic and supportive care was administered:

- IV fluids with additional KCL
- Famotidine
- Ampicillin
- Metronidazole
- Metoclopramide
- Assisted feeding (e.g. clinicare) with syringe, or nasogastric tube feeding, if that is unsuccessful

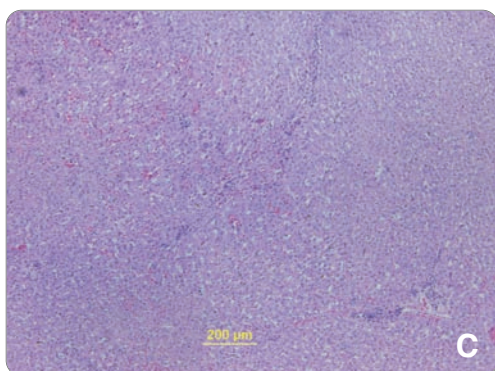
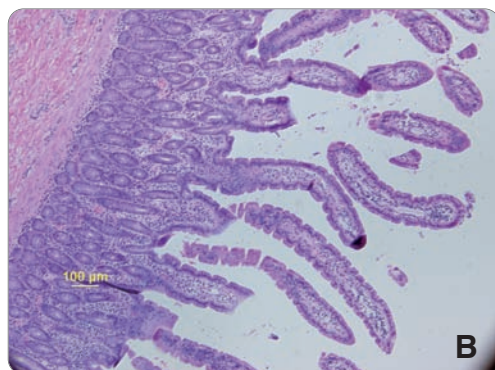
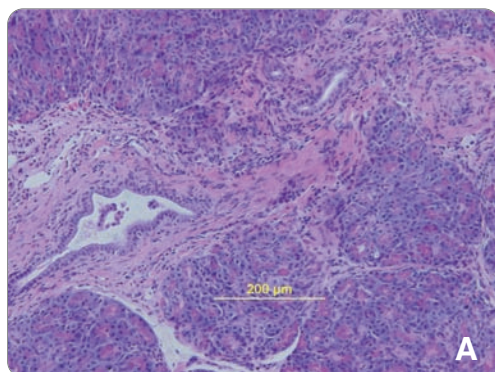
Vomiting resolved, appetite picked-up and the cat was discharged.

Follow-up

Cat represented 6 days later with recurrence of vomiting. Abdominal palpation revealed thickened intestine. Abdominal radiograph showed mineral opaque tubular foreign body and distended loop of small intestine (18mm).

Surgery

- Circular foreign body in proximal jejunum



(see photomicrograph)

- **Duodenum:** small to moderate numbers of plasma cells, eosinophils, lymphocytes, occasional transmigrating neutrophils (see photomicrograph)
- **Liver:** occasional large portal triads have bile duct hyperplasia. Occasional hepatocellular vacuolation

Diagnosis: mild chronic pancreatitis, mild duodenitis, mild reactive lymphoid hyperplasia

The cat was discharged after surgery on antibiotics and supportive feeding, with transition back to a normal balanced cat food. Increases in liver enzymes and bilirubin resolved and the cat has not re-presented.

The principal diagnosis was pancreatitis - the clinical picture, results of diagnostic imaging and PLI supported this diagnosis which was confirmed by surgical biopsy. It is suspected that the increased liver enzymes and bilirubin were secondary to pancreatitis-induced acute inflammation and possibly concurrent intestinal damage next to the pancreas (increased translocation into the portal system). It is noteworthy that the TLI and amylase values were within the normal range, the foreign body is thought to have been swallowed when the cat went home after hospitalization. ■

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