Diagnosis of pancreatitis in dogs and cats

P. G. Xenoulis

Clinic of Medicine, Faculty of Veterinary Medicine, University of Thessaly, Karditsa 43100, Greece
Animal Medical Center of Athens, Athens, Greece

Pancreatitis is the most common disorder of the exocrine pancreas in both dogs and cats. Ante-mortem diagnosis of canine and feline pancreatitis can be challenging. The clinical picture of dogs and cats with pancreatitis varies greatly (from very mild to severe or even fatal) and is characterised by non-specific findings. Complete blood count, serum biochemistry profile and urinalysis should always be performed in dogs and cats suspected of having pancreatitis, although findings are not-specific for pancreatitis. Serum amylase and lipase activities and trypsin-like immunoreactivity (TLI) concentrations have no or only limited clinical value for the diagnosis of pancreatitis in either dogs or cats. Conversely, serum pancreatic lipase immunoreactivity (PLI) concentration is currently considered to be the clinicopathological test of choice for the diagnosis of canine and feline pancreatitis. Abdominal radiography is a useful diagnostic tool for the exclusion of other diseases that may cause similar clinical signs to those of pancreatitis. Abdominal ultrasonography can be very useful for the diagnosis of pancreatitis, but this depends largely on the clinician’s experience. Histopathological examination of the pancreas is considered the gold standard for the diagnosis and classification of pancreatitis, but it is not without limitations. In clinical practice, a combination of careful evaluation of the animal’s history, serum PLI concentration and abdominal ultrasonography, together with pancreatic cytology or histopathology when indicated or possible, is considered to be the most practical and reliable means for an accurate diagnosis or exclusion of pancreatitis compared with other diagnostic modalities.

INTRODUCTION

Exocrine pancreatic disorders are common in clinical practice and pancreatitis is by far the most common disorder of the exocrine pancreas in both dogs and cats. Strictly speaking, pancreatitis refers to inflammation (i.e. infiltration with inflammatory cells) of the exocrine pancreas. However, the term pancreatitis is commonly expanded to also include diseases of the exocrine pancreas characterised mainly by necrosis (necrotising pancreatitis) or irreversible structural changes such as fibrosis (chronic pancreatitis), sometimes with only minimal inflammatory component. Pancreatitis is generally divided into acute and chronic forms based on the absence or presence of permanent histopathological lesions, respectively, such as pancreatic fibrosis and/or atrophy (Xenoulis et al. 2008). The categorisation of pancreatitis into acute and chronic has potential diagnostic, therapeutic, and prognostic implications.

Despite recent advances in diagnostics, it is increasingly recognised that accurate clinical diagnosis of pancreatitis can be challenging. New diagnostic modalities as well as new knowledge regarding older diagnostic modalities are becoming available with increasing frequency. Proper use and correct interpretation of the results of these diagnostic modalities is crucial for a correct diagnosis. Although the diagnostic evaluation of dogs and cats suspected of having pancreatitis should always take into account the signalment, clinical presentation and general clinicopathological findings, this review will mainly focus on the diagnostic modalities that are used to specifically evaluate pancreatic structure, function and pathology.
SIGNALMENT AND RISK FACTORS

Dogs and cats of any age, breed or sex can develop pancreatitis. Certain age groups and breeds might be predisposed. Most dogs and cats that are presented with pancreatitis are middle aged to old (usually >5 years of age), although the age range is from a few months to >15 years (Akol et al. 1993, Cook et al. 1993, Hess et al. 1998, Ferreri et al. 2003, Watson et al. 2010). With regard to breed predisposition, differences likely exist in different geographic regions. Miniature schnauzers and terrier breeds (especially Yorkshire terriers) are considered to be at increased risk mainly in the USA (Cook et al. 1993, Hess et al. 1998, Lem et al. 2008). Cocker spaniels, Cavalier King Charles spaniels, Border collies and boxers have been reported to be at increased risk for chronic pancreatitis in the UK (Watson et al. 2007). No significant breed predisposition has been identified in cats (Akol et al. 1993, Hill & Van Winkle 1993, Ferreri et al. 2003, De Cock et al. 2007).

In the majority of cases, pancreatitis is considered idiopathic in both dogs and cats. However, several pathological conditions (e.g. hypertriglyceridaemia, endocrine disease, adverse drug reactions, prior infections; infections and dietary factors) have all been identified as potential risk factors for pancreatitis in dogs, while in cats risk factors are even less clear. Although a cause-and-effect relationship has not been established for most of those factors, their presence along with compatible clinical signs should raise the suspicion for pancreatitis. The pathophysiology, causes and risk factors for pancreatitis are discussed elsewhere in this issue as well as in other recent publications (Mansfield 2012a,b, Watson 2012, Xenoulis & Steiner 2013).

CLINICAL SIGNS AND PHYSICAL EXAMINATION FINDINGS

The perception of the clinical presentation of dogs and cats with pancreatitis has changed dramatically over the last decade. It is now widely accepted that the clinical presentation of dogs and cats with pancreatitis varies greatly. There is mounting evidence that many dogs and cats with pancreatitis, especially chronic pancreatitis, have subclinical disease, whereas others might only display mild and non-specific clinical signs such as intermittent anorexia and weakness with no gastrointestinal signs. Diagnosis of pancreatitis is often missed in those animals mainly due to low level of suspicion for the disease. On the other hand, dogs and cats with severe acute pancreatitis might be presented with cardiovascular shock, disseminated intravascular coagulation (DIC) or multi-organ failure and die within hours of the development of clinical signs.

There is no single clinical sign or combination of clinical signs that is pathognomonic for pancreatitis in dogs. Dogs with severe acute pancreatitis are typically presented with an acute onset of anorexia, weakness, vomiting, diarrhoea and/or abdominal pain (Hess et al. 1998, Weatherton & Streeter 2009). Dogs may display one or more of these clinical signs and in various combinations.

Dehydration, abdominal pain, icterus, fever or hypothermia, bleeding diathesis or ascites may be identified in some dogs on physical examination (Hess et al. 1998). Severe systemic complications (e.g. cardiovascular shock, DIC or multi-organ failure) might occur in patients with severe pancreatitis (Ruaux 2000, Weatherton & Streeter 2009). Dogs with chronic pancreatitis are typically presented with intermittent clinical signs that are less specific and milder than those of dogs with acute pancreatitis. These usually include anorexia and weakness, while sometimes weight loss, vomiting, diarrhoea or abdominal pain may also be present (Watson et al. 2010, Bostrom et al. 2013). It is important to note that additional clinical signs are often present as a consequence of concurrent or complicating diseases (e.g. polyuria/polydipsia in animals with diabetes mellitus or polyphagia and weight loss in dogs with exocrine pancreatic insufficiency) (Hess et al. 1998, Watson et al. 2010, Bostrom et al. 2013). This is of particular importance especially in dogs with mild or chronic pancreatitis because clinical signs caused by pancreatitis per se are often subtle or absent, while clinical signs of concurrent diseases predominate and may mislead the clinician.

Clinical signs in cats with pancreatitis are similar to those described in dogs. An important difference is that the majority of cats with pancreatitis are presented for anorexia and/or lethargy. Gastrointestinal clinical signs are seen less commonly and include vomiting, weight loss and diarrhoea (Akol et al. 1993, Hill & Van Winkle 1993, Kimmel et al. 2001). The most common physical examination findings include dehydration, pallor and icterus. Tachypnoea and/or dyspnoea, hypothermia or fever, tachycardia, signs of abdominal pain and a palpable abdominal mass may also be noted (Akol et al. 1993, Hill & Van Winkle 1993, Kimmel et al. 2001). Similar to dogs, severe systemic complications (e.g. DIC, pulmonary thromboembolism, cardiovascular shock and multi-organ failure) may occasionally be seen in cats with severe pancreatitis (Schermerhorn et al. 2004).

ROUTINE CLINICAL PATHOLOGY

Results of complete blood count (CBC), serum biochemistry profile and urinalysis in dogs and cats with pancreatitis are non-specific and therefore non-diagnostic. However, these tests should always be performed in animals with suspected pancreatitis because they are useful for the diagnosis or exclusion of other diseases, and also give important information about the general condition of the patient. In addition, routine clinical pathology may help estimate the severity of pancreatitis to determine the optimal therapeutic plan for each individual patient.

The results of the CBC, serum biochemistry profile and urinalysis are often within normal limits in dogs and cats with pancreatitis, especially in mild cases. On the other hand, animals with pancreatitis can be presented with almost any kind of haematological abnormality, including anaemia or haemoconcentration, leukocytosis or leucopenia and thrombocytopenia (Akol et al. 1993, Hill & Van Winkle 1993, Hess et al. 1998, Kimmel et al. 2001, Ferreri et al. 2003). Clinico pathological abnormalities, when present, are variable and unpredictable (Akol et al. 1993,
The PLI assays are currently considered the most sensitive and specific serum marker for pancreatitis in dogs and cats. The advantages of the PLI assays over the traditional lipase activity assays rely on two facts: (1) pancreatic lipase is exclusively of pancreatic origin and (2) in contrast to the traditional activity assays for lipase, which indiscriminately measure the activities of lipases of multiple origins, immunoassays used to measure pancreatic lipase concentration in serum (i.e. the PLI assays) quantify exclusively lipase of pancreatic origin based on its unique structure (Steiner 2000, Steiner et al. 2002, 2006, Hoffmann 2008, Neilson-Carley et al. 2011). Therefore, the PLI assays have inherent advantages over the traditional serum lipase activity assays that make them more suitable for specific evaluation of the exocrine pancreas in dogs and cats.

The originally developed and analytically validated immunoassays for the specific measurement of serum pancreatic lipase in dogs (canine PLI) and cats (feline PLI) (Steiner et al. 2003, 2004, Steiner & Williams 2003) have been replaced by more widely available immunoassays (Spec cPL® for dogs and Spec fPL® for cats) that demonstrate a similar clinical performance with the original PLI assays (Steiner et al. 2008, Huth et al. 2010). The reference interval for Spec cPL is 0 to 200 µg/L and for Spec fPL 0 to 3-5 µg/L. Both assays incorporate a gray zone in the interpretation of the results (201 to 399 µg/L for Spec cPL and 3-6 to 5-3 µg/L for Spec fPL); values in the gray zone are non-diagnostic and further testing or retesting is recommended. Concentrations ≥400 µg/L (Spec cPL) or ≥5-4 µg/L (Spec fPL) are considered highly suggestive of pancreatitis. It needs to be mentioned that the implementation of cut-off values for the Spec PL assays was originally somewhat arbitrary but these cut-off values have now been used in several studies and are considered clinically useful.

**Canine PLI:** Both clinical (McCord et al. 2012) and histopathological (Steiner et al. 2008, Watson et al. 2010, Trivedi et al. 2011) studies on the sensitivity of cPLI for canine pancreatitis have been published and all generally agree that serum cPLI is the most sensitive and specific serum marker for pancreatitis in dogs (Table 1). In the only multi-institutional clinical study on the sensitivity of serum cPLI (Spec cPL) currently available that included 84 dogs, the sensitivity of cPLI was reported to range between 72 and 78% (McCord et al. 2012). Three necropsy studies have also determined the sensitivity of cPLI (Steiner et al. 2008, Watson et al. 2010, Trivedi et al. 2011). However, it is more challenging to accurately interpret and determine the clinical significance of the results of those studies, because the diagnosis of pancreatitis was primarily based on histopathological criteria. Therefore, clinically healthy dogs with histopathological lesions of the pancreas but clinically insignificant disease were also included in those studies (Steiner et al. 2008, Trivedi et al. 2011). It is of note that in the most recent of those studies (Trivedi et al. 2011), in which 70 dogs euthanased for a variety of reasons were examined, 56 (89%) of 63 dogs that had histopathological evidence of pancreatitis had only mild lesions. In these three necropsy studies, the sensitivity of cPLI ranged from 21% for mild (and most likely clinically insignificant) pancreatitis to 71% for histopathologically moderate to severe pancreatitis (Table 1). The wide overall range of sensitivities reported for cPLI (21 to 78%) is also seen with other markers for pancreatitis and cats.

**Serum tests for pancreatic function and pathology**

The search for a sensitive and specific serum test for pancreatitis started over 5 decades ago. Several serum tests have been developed and evaluated since then, but most have shown no or only limited usefulness for the diagnosis of pancreatitis in dogs and cats. It needs to be mentioned that the evaluation of the diagnostic accuracy of new diagnostic tests is always predicated upon having an acceptable gold standard. Although histopathology of the pancreas is often used as a gold standard for the diagnosis of canine and feline pancreatitis, it cannot be considered an ideal gold standard (see section on histopathology) (Xenoulis & Steiner 2012). Therefore, the results of the studies discussed in the following sections should be interpreted with caution and the understanding that they rely upon an imperfect gold standard. It also needs to be mentioned that it is particularly difficult to determine a single number that corresponds to the exact sensitivity of a diagnostic test for pancreatitis, because this varies depending upon several factors, including the type of study, the criteria for pancreatitis used (i.e. based on histopathological confirmation, ultrasonographic findings, or overall clinical information available), the type of pancreatitis (i.e. acute or chronic, mild or severe), the cut-off values used, etc. Therefore, direct comparison of the results among different studies is often challenging. Table 1 provides an overview of selected studies evaluating the sensitivity and/or specificity of different laboratory tests for the diagnosis of pancreatitis in dogs and cats.

**Pancreatic lipase immunoreactivity (PLI) assays**

The PLI assays are currently considered the most sensitive and specific serum tests for the diagnosis of pancreatitis in both dogs and cats. The PLI assays have inherently advantages over the traditional serum lipase activity assays that make them more suitable for specific evaluation of the exocrine pancreas in dogs and cats.

The originally developed and analytically validated immunoassays for the specific measurement of serum pancreatic lipase in dogs (canine PLI) and cats (feline PLI) (Steiner et al. 2003, 2004, Steiner & Williams 2003) have been replaced by more widely available immunoassays (Spec cPL® for dogs and Spec fPL® for cats) that demonstrate a similar clinical performance with the original PLI assays (Steiner et al. 2008, Huth et al. 2010). The reference interval for Spec cPL is 0 to 200 µg/L and for Spec fPL 0 to 3-5 µg/L. Both assays incorporate a gray zone in the interpretation of the results (201 to 399 µg/L for Spec cPL and 3-6 to 5-3 µg/L for Spec fPL); values in the gray zone are non-diagnostic and further testing or retesting is recommended. Concentrations ≥400 µg/L (Spec cPL) or ≥5-4 µg/L (Spec fPL) are considered highly suggestive of pancreatitis. It needs to be mentioned that the implementation of cut-off values for the Spec PL assays was originally somewhat arbitrary but these cut-off values have now been used in several studies and are considered clinically useful.
<table>
<thead>
<tr>
<th>Study</th>
<th>Species</th>
<th>Number of animals</th>
<th>Gold standard</th>
<th>Spec PL</th>
<th>Lipase</th>
<th>Amylase</th>
<th>TLI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Sensitivity (%) Specificity (%)</td>
<td>Sensitivity (%) Specificity (%)</td>
<td>Sensitivity (%) Specificity (%)</td>
<td>Sensitivity (%) Specificity (%)</td>
<td></td>
</tr>
<tr>
<td>Steiner et al.</td>
<td>Canine</td>
<td>22</td>
<td>Pathologic findings</td>
<td>64/73</td>
<td>–</td>
<td>14/32</td>
<td>18/41</td>
</tr>
<tr>
<td>(2008)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Watson et al.</td>
<td>Canine</td>
<td>14</td>
<td>Histopathology</td>
<td>26/58</td>
<td>–</td>
<td>28/44</td>
<td>14/67</td>
</tr>
<tr>
<td>(2010)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trivedi et al.</td>
<td>Canine</td>
<td>70</td>
<td>Histopathology – mild pancreatitis</td>
<td>21/43</td>
<td>100/86</td>
<td>54</td>
<td>43</td>
</tr>
<tr>
<td>(2011)</td>
<td></td>
<td></td>
<td>Moderate/severe pancreatitis</td>
<td>71/71</td>
<td>71</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Neilson-Carley et al. (2011)</td>
<td>Canine</td>
<td>40</td>
<td>Histopathology</td>
<td>–</td>
<td>98/95</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>McCord et al.</td>
<td>Canine</td>
<td>84</td>
<td>Clinical criteria</td>
<td>72 to 78/87</td>
<td>81 to 88/66</td>
<td>52 to 56</td>
<td>77 to 81</td>
</tr>
<tr>
<td>(2012)</td>
<td></td>
<td></td>
<td></td>
<td>94</td>
<td>77</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Mansfield et al.</td>
<td>Canine</td>
<td>32</td>
<td>Histopathology</td>
<td>33/58</td>
<td>90/80</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>(2012)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Forman et al.</td>
<td>Feline</td>
<td>29</td>
<td>Histopathology – mild pancreatitis</td>
<td>54</td>
<td>67 to 100%</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>(2004)</td>
<td></td>
<td></td>
<td>Moderate/severe pancreatitis</td>
<td>100</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Forman et al.</td>
<td>Feline</td>
<td>182</td>
<td>Clinical criteria</td>
<td>79</td>
<td>82</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>(2009)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

PL: Pancreatic lipase, TLI: Trypsin-like immunoreactivity
Spec cPL: Whenever two values are separated by a slash, the first value represents the cut-off for pancreatitis (200 for cPL) and the second value represents the upper limit of the reference interval (102.1 for cPL and 200 for Spec cPL)
Amylase and lipase: Whenever two values are separated by a slash, the first value represents a suggested cut-off for pancreatitis that is three times the upper limit of the reference interval and the second value represents the upper limit of the reference interval.
reflects the inherent differences in the study design, the methodology and the dog population used in each study. However, in the above-mentioned studies, cPLI consistently showed the best performance (sensitivity and specificity) compared with other serum markers evaluated (Steiner et al. 2008, Watson et al. 2010, Trivedi et al. 2011, McCord et al. 2012).

Based on some evidence from recent studies (Steiner et al. 2008, Watson et al. 2010, Trivedi et al. 2011) and the fact that histopathological lesions associated with chronic pancreatitis such as pancreatic fibrosis and atrophy are not expected to be associated with leakage of pancreatic enzymes (Neilson-Carley et al. 2011), the sensitivity of cPLI is believed to be lower for chronic pancreatitis than for acute pancreatitis. In one study of 14 dogs with chronic pancreatitis (Watson et al. 2010), the sensitivity of cPLI ranged between 26 and 58% (depending on the cut-off value), further supporting this hypothesis. However, the clinical significance of chronic pancreatitis in those cases is questionable as the majority of dogs had concurrent diseases and were evaluated for reasons that were likely unrelated to clinical disease resulting from chronic pancreatitis.

Similar to its sensitivity, serum cPLI is considered to have the highest specificity for pancreatitis compared with any other serum test currently available, with specificities ranging between 81 and 100% (Strombeck et al. 1981, Simpson et al. 1989, Mansfield & Jones 2000a, Steiner et al. 2001b, 2009, Neilson-Carley et al. 2011, Trivedi et al. 2011, Mansfield et al. 2012, McCord et al. 2012). In the multi-institutional clinical study mentioned earlier, the specificity of this assay in a cohort of dogs with a clinical presentation consistent with pancreatitis was reported to range between 81 and 88% (McCord et al. 2012). However, this study may have underestimated specificity because a result was judged to be false positive if there were no other clinical supporting data available, yet histopathology of multiple sections of the pancreas was not available. In two necropsy studies that included dogs that died or were euthanased for a variety of reasons and had a normal pancreas on histopathology, serum Spec cPL showed a specificity of 100% (Trivedi et al. 2011) and 90% (Mansfield et al. 2012) using the recommended cut-off of 400 µg/L. In another necropsy study, in which 40 dogs were euthanased for a variety of reasons and had a normal pancreas on histopathology, the specificity of Spec cPL using the recommended cut-off of 400 µg/L was 98% (Neilson-Carley et al. 2011). It is important to note, however, that dogs included in the above-mentioned necropsy studies did not all have clinical signs of or a clinical suspicion for pancreatitis, and therefore, many of these dogs would not normally undergo diagnostic testing for pancreatitis. In another study of 25 dogs with clinical signs compatible with pancreatitis (i.e. vomiting) that ended up having gastritis, only 1 dog had a possible false positive result, suggesting a specificity of 96% (Steiner 2000). Experimentally induced chronic renal failure (Steinet et al. 2001b) and long-term prednisone administration (Steinet et al. 2009) were not found to have any clinically significant effect on serum cPLI concentration. Similarly, pancreatic sampling by ultrasound-guided fine-needle aspiration (FNA) or surgical biopsy did not cause any increase in serum cPLI concentrations in healthy dogs (Cordner et al. 2010). It remains to be determined whether pancreatic sampling of a diseased pancreas would also have no effect and it is currently recommended that determination of serum cPLI concentration is best performed before sampling of pancreatic tissue. Finally, there have been anecdotal concerns that high cPLI concentrations might occasionally be associated with pancreatic inflammation that is not clinically important or in cases where pancreatitis is not the problem of primary clinical significance (e.g. when a foreign body is present in the proximal small intestine). Therefore, it remains to be determined whether serum cPLI concentration can detect histopathologically mild pancreatitis that might be of minor clinical importance. In either case, a final diagnosis of pancreatitis should ideally not be based solely on the results of PLI, but rather, on a careful consideration of the general clinical and clinicopathological picture of the animal and the results of ultrasonography, pancreatic cytology or histopathology.

Canine SNAP PL: A rapid, in-clinic, semi-quantitative, visually read test for the estimation of canine pancreatic lipase in serum has recently been developed (Beall et al. 2011). This test incorporates a reference spot that corresponds to the upper limit of the reference interval and a sample spot that is visually compared with the reference spot (Beall et al. 2011). Therefore, the results of this rapid assay are considered either normal (less intense than the reference spot) or abnormal (equally to or more intense than the reference spot). In the latter case, the actual PLI concentration may be in the gray zone (200 to 400 µg/L) or consistent with the diagnosis of pancreatitis (>400 µg/L for Spec cPL) (Beall et al. 2011). This cannot be determined with certainty, however, using the in-clinic assay and further testing using the quantitative reference method is recommended.

A recent validation study showed that there is a 90 to 100% agreement between the SNAP cPL and the reference Spec cPL (Beall et al. 2011). A recent multi-institutional study reported that SNAP cPL has a sensitivity between 91 and 94% and a specificity between 71 and 78% for pancreatitis (McCord et al. 2012). However, the main use of this diagnostic tool is to rule-out pancreatitis (i.e. a normal result makes diagnosis of pancreatitis very unlikely) and therefore, the sensitivity of this test is more important than its specificity. Abnormal results could be seen in a dog with a Spec cPL concentration in the gray zone or consistent with the diagnosis of pancreatitis and further testing using the quantitative Spec cPL assay would be necessary in such cases. Diagnosis of pancreatitis cannot be based on the result of the SNAP cPL alone.

Feline PLI: Studies in cats with both experimental and spontaneous pancreatitis have repeatedly shown that serum fPLI concentration is the most sensitive and specific serum marker for feline pancreatitis currently available (Parent et al. 1995, Swift et al. 2000, Gerhardt et al. 2001, Forman et al. 2004, Allen et al. 2006, Zavros et al. 2008, Forman et al. 2009). In a recent clinical study in abstract form that included 182 cats, the sensitivity of serum Spec fPL concentration was reported at 79% (Forman et al. 2009). In another study that included primarily cats with chronic pancreatitis that also had an acute histopathological
component, serum fPLI was found to be 100% sensitive for histopathologically moderate to severe pancreatitis (Forman et al. 2004). In the same study, the sensitivity of fPLI was 54% for histopathologically mild pancreatitis, with an overall sensitivity of 67%. For comparison, the overall sensitivity of fTLI in the same study was only 28%. Similar to dogs, histopathological lesions associated with chronic pancreatitis such as pancreatic fibrosis and atrophy are not expected to be associated with leakage of pancreatic enzymes, and therefore, the sensitivity of fPLI is believed to be lower for chronic pancreatitis (without a concurrent acute pancreatitis) than for acute pancreatitis. Therefore, as in dogs, false negative results cannot be excluded especially in cats with chronic or mild pancreatitis. However, the clinical significance of mild chronic pancreatitis remains to be determined.

Similar to its sensitivity, the specificity of serum fPLI concentration for feline pancreatitis is very high, ranging between 67 and 100% (Forman et al. 2004, 2009). In a large clinical study in abstract form that included 182 cats, the specificity of fPLI was 82% (Forman et al. 2009). In another study also in abstract form, azotaemia as a result of experimentally induced chronic renal failure did not have any clinically significant effect on serum fPLI concentrations (Xenoulis et al. 2009). Similar to dogs, laparoscopic pancreatic biopsy in healthy cats did not have any significant effect on serum fPLI concentrations (Cosford et al. 2010). It is unknown whether pancreatic biopsy of an inflamed pancreas would lead to an increase of serum fPLI concentration. Finally, in a recent study, endoscopic retrograde cholangiopancreatography (ERCP) was found to cause temporary increases in serum fPLI concentrations (Xenoulis et al. 2008). Feline TLI has been evaluated for the diagnosis of spontaneous pancreatitis in cats and several cut-off values have been suggested (Swift et al. 2000, Gerhardt et al. 2001, Allen et al. 2006). When cut-off values allowing adequate specificity of the assay are used (i.e. 100 µg/L), the sensitivity of fTLI for the diagnosis of pancreatitis in cats is suboptimal (28 to 64%). In addition, the specificity of fTLI has been questioned, because mildly increased serum fTLI concentrations have been reported in cats with no demonstrable pancreatic disease (although focal lesions might have been missed on pancreatic biopsy) but had other gastrointestinal disorders (e.g. inflammatory bowel disease (IBD) or gastrointestinal lymphoma) or azotaemia (Swift et al. 2000, Simpson et al. 2001, Allen et al. 2006). Similar to dogs, a clearly increased serum fTLI concentration in a cat that is not azotaemic is indicative of pancreatitis. However, pancreatitis cannot be excluded on the basis of a normal serum fTLI concentration within the reference interval.

In cats with experimentally induced pancreatitis, feline TLI (fTLI) concentration increases sharply after induction of pancreatitis, but returns below the cut-off value within 48 hours (Zavros et al. 2008). Feline TLI has been evaluated for the diagnosis of spontaneous pancreatitis in cats and several cut-off values have been suggested (Swift et al. 2000, Gerhardt et al. 2001, Allen et al. 2006). When cut-off values allowing adequate specificity of the assay are used (i.e. 100 µg/L), the sensitivity of fTLI for the diagnosis of pancreatitis in cats is suboptimal (28 to 64%). In addition, the specificity of fTLI has been questioned, because mildly increased serum fTLI concentrations have been reported in cats with no demonstrable pancreatic disease (although focal lesions might have been missed on pancreatic biopsy) but had other gastrointestinal disorders (e.g. inflammatory bowel disease (IBD) or gastrointestinal lymphoma) or azotaemia (Swift et al. 2000, Simpson et al. 2001, Allen et al. 2006). Similar to dogs, a clearly increased serum fTLI concentration in a cat that is not azotaemic is indicative of pancreatitis. However, pancreatitis cannot be excluded on the basis of a normal serum fTLI concentration.

**Feline SNAP PL**: The SNAP fPL test has recently been released and is based on the same principles as the canine SNAP cPL test (see preceding text). Although studies on the validation and clinical performance characteristics for the diagnosis of pancreatitis of the SNAP fPL have not been reported in the literature yet, the manufacturer indicates that this test has an 82 to 92% agreement with the Spec fPL assay. Therefore, the sensitivity of the SNAP fPL should theoretically be high and similar to the one reported for Spec fPL (see preceding text). Consequently, a normal SNAP fPL result is a good indicator that pancreatitis is unlikely. However, abnormal results could be in the gray zone or consistent with the diagnosis of pancreatitis and further testing using the quantitative Spec fPL assay is necessary. As in dogs, diagnosis of pancreatitis cannot be based on the results of the SNAP fPL alone.

**Trypsin-like immunoreactivity (TLI)**

TLI assays are immunoassays that measure trypsinogen and, to a lesser degree, trypsin concentrations in serum and have been shown to be of limited usefulness for the diagnosis of canine and feline pancreatitis. Serum canine TLI (cTLI) concentrations increase after experimental induction of pancreatitis in dogs, but decrease to concentrations within the reference interval as early as 3 days after induction of pancreatitis in some dogs (Simpson et al. 1989). In addition, cTLI has been shown to increase significantly after ERCP, but this increase in transient and is not associated with clinical evidence of acute pancreatitis (Spillmann et al. 2004). The sensitivity of serum cTLI for the diagnosis of spontaneous pancreatitis is low (36 to 47%), possibly due to the short half-life of trypsinogen in serum (Mansfield & Jones 2000a, Steiner et al. 2001a, 2008). In addition, although there is strong evidence that trypsinogen is exclusively of pancreatic origin (Simpson et al. 1991), it is cleared by glomerular filtration, and serum cTLI concentration can be increased in dogs with renal failure (Simpson et al. 1989, Mansfield & Jones 2000a). This clearly affects the specificity of the test and complicates the interpretation of increased cTLI concentrations in dogs with azotaemia (which is not uncommon in dogs with pancreatitis). A clearly increased serum cTLI concentration in a dog that is not azotaemic is indicative of pancreatitis. However, pancreatitis cannot be excluded on the basis of a normal serum cTLI concentration within the reference interval.

**Serum amylose and lipase activities**

Serum amylose and lipase activities have long been considered markers for pancreatitis in dogs (Strombeck et al. 1981, Jacobs et al. 1985). Although serum activities of these two enzymes increase during experimental canine pancreatitis, several studies have shown that these markers, when measured with the traditional methods, are not useful and should not be used for the diagnosis of spontaneous canine pancreatitis due to their low sensitivity and specificity (Brobst et al. 1970, Mia et al. 1978, Strombeck et al. 1981, Jacobs et al. 1985, Simpson et al. 1989, 1991, Steiner et al. 2008). Many tissues other than the pancreas (e.g. gastric mucosa, hepatic parenchyma and many others) synthesise amylases and lipases (Simpson et al. 1991, Steiner et al. 2006). This leads to the establishment of wide reference intervals for amylose and lipase activity assays that are at least partially associated with the low sensitivity of those assays for pancreatitis. Furthermore, traditional catalytic assays are not able
to differentiate amylases and lipases according to their tissue of origin. Specifically for amylase, it is not even certain that organ-specific isoenzymes exist in dogs and cats (Williams 1996). This leads to a low specificity of serum amylase and lipase activities for pancreatitis (Strombeck et al. 1981, Mansfield & Jones 2000a).

In one study, approximately 50% of dogs with an increased serum activity of either amylase or lipase did not have pancreatitis based on histopathological examination of the pancreas (Strombeck et al. 1981). In another more recent study that investigated the specificity and sensitivity of a new serum lipase activity assay, the specificity was similar (53%) (Graca et al. 2005). The main non-pancreatic conditions associated with increased serum amylase and/or lipase activities include renal, hepatic, intestinal, and neoplastic diseases, as well as corticosteroid administration (only for lipase activity). It has been suggested that only increases of amylase and lipase activities of more than three to five times the upper limit of the reference interval should be considered suggestive of pancreatitis in dogs, in order to increase the specificity of these assays (Williams 1996, Steiner 2003). However, it has been shown that such increases can result from non-pancreatic disorders (Strombeck et al. 1981, Polzin et al. 1983, Williams 1996, Mansfield & Jones 2000a). Therefore, increased serum amylase and/or lipase activities do not confirm the presence of pancreatitis and more specific tests need to be utilised. The sensitivity of serum amylase and lipase activities for spontaneous canine pancreatitis varies but is generally low (32 to 73% for lipase activity and 41 to 69% for amylase activity) and it is even lower when a cut-off value of three or five times the upper limit of the respective reference interval is used (14% for lipase activity and 18% for amylase activity in one study) (Hess et al. 1998, Steiner et al. 2001a, 2008). Thus, many dogs with pancreatitis may have serum activities of these enzymes within the reference interval and, therefore, serum amylase and/or lipase activities within the reference interval cannot rule out pancreatitis (Strombeck et al. 1981, Hess et al. 1998).


Recently, a new lipase activity assay (DGGR) using the substrate 1,2-dilauryl-rac-glycero glutaric acid-(6-methyl resorufin)-ester was validated for use in dogs (Graca et al. 2005). A more recent study has evaluated the use of the DGGR lipase activity assay for the diagnosis of pancreatitis in cats and has found that, when specific cut-offs are used, there is substantial agreement between this assay and the Spec IPL assay (Oppfliger et al. 2013). Specifically, in this study of 250 cats, the best agreement (κ=0.775) was found for a cut-off of DGGR lipase of >34 U/L. A similar study in 142 dogs also found high agreement between the DGGR lipase assay and the Spec cPL assay, with the best agreement (κ=0.80) for a cut-off of DGGR lipase of >216 U/L (Kook et al. 2014). Based on these initial results, the DGGR lipase activity assay shows promise as a test to aid in diagnosis of feline and canine pancreatitis. However, more studies are necessary in different populations of cats and dogs comparing the specificity and sensitivity of the DGGR lipase assay to other tests used for the diagnosis of pancreatitis.

Other diagnostic markers

Several other diagnostic markers for pancreatitis have been developed and studied, but none of those can currently be recommended for the routine diagnosis of canine and feline pancreatitis in clinical practice, either because their diagnostic performance has not been sufficiently evaluated clinically or because they have been shown to have a low specificity and/or sensitivity. In addition, the availability of most of these diagnostic tests is currently limited. Such tests include serum concentrations of pancreatic elastase-1 (Mansfield et al. 2011), phospholipase A2 (Westermarck & Rimaila-Pärnänen 1983), trypsin-α,-anti-trypsin complexes (Suchodolski et al. 2001, Steiner et al. 2008), α₂-macroglobulin (Ruaux et al. 1999), plasma and urine concentrations of trypsinogen activation peptide (TAP) (Mansfield & Jones 2000a,b, Mansfield et al. 2003, Allen et al. 2006) and lipase activity in peritoneal fluid (De Arespacochaga et al. 2006). Of these markers, serum pancreatic elastase-1 and TAP concentrations seem to hold some promise and might prove helpful for the diagnosis or the assessment of severity of pancreatitis in the future.

Abdominal radiography

Abdominal radiography is of no value for the diagnosis of canine and feline pancreatitis because, in the majority of cases, abdominal radiographs are normal or only show non-specific findings (Gibbs et al. 1972, Suter & Lowe 1972, Akol et al. 1993, Hill & Van Winkle 1993, Hess et al. 1998, Gerhardt et al. 2001, Ferretti et al. 2003). In a group of 70 dogs with fatal acute pancreatitis, the sensitivity of abdominal radiography for pancreatitis was only 24% (Hess et al. 1998). In addition, radiographic abnormalities observed in dogs and cats with pancreatitis can be present in other conditions and are therefore non-specific for pancreatitis. Such findings include an increased soft tissue opacity and decreased serosal detail in the cranial right abdomen, displacement of the stomach and/or duodenum from their normal positions, gaseous dilation of bowel loops adjacent to the pancreas and abdominal effusion (Gibbs et al. 1972, Suter & Lowe 1972, Hill & Van Winkle 1993, Hess et al. 1998, Gerhardt et al. 2001, Saunders et al. 2002, Ferretti et al. 2003). When pancreatitis is in the list of differential diagnoses, radiography should always be followed up by more sensitive and specific serum tests and/or imaging methods in order to confidently diagnose or rule out pancreatitis. However, radiography remains a logical initial approach for patients suspected of having pancreatitis because it is relatively inexpensive and useful for the diagnosis and/or to rule out other diseases that cause similar clinical signs.
Abdominal ultrasound

Abdominal ultrasound is considered the imaging method of choice for the diagnosis of pancreatitis in dogs and cats. Furthermore, abdominal ultrasound is helpful for the diagnosis or rule out of other diseases that cause similar clinical sings. There is only a limited number of studies that have systematically evaluated the performance of abdominal ultrasonography for the diagnosis of pancreatitis in dogs and cats, and most of these studies are more than a decade old. Since then, there have been significant advances in both the quality of the equipment and the expertise of the radiologists, and the level of suspicion for canine and feline pancreatitis in small animal medicine has increased. Therefore, the performance of ultrasonography is expected to have improved since the original reports were published. However, although abdominal ultrasound is considered to be both relatively sensitive and specific for the diagnosis of canine and feline pancreatitis, its exact sensitivity and specificity is largely unknown. When interpreting the results of studies investigating the clinical performance of abdominal ultrasound for the diagnosis of pancreatitis, it is important to realise that abdominal ultrasonography is typically evaluated based upon an imperfect gold standard (i.e. histopathology).

It is of utmost significance to underline the fact that the performance of abdominal ultrasonography in the diagnosis of pancreatitis is highly dependent on the expertise of the ultrasonographer and the quality of the equipment used. In most reported studies, abdominal ultrasonography has been performed at teaching hospitals by board certified radiologists, and therefore, the performance of abdominal ultrasound for pancreatitis is expected to be considerably lower when less experienced clinicians are performing the ultrasound examination and the equipment used is of lower quality. In addition, the lack of standardised criteria for the ultrasonographic evaluation of the pancreas in dogs and cats leads to great variation in the interpretation of imaging results even among radiologists and makes the need for specialised ultrasonographers even greater.

The sensitivity of abdominal ultrasound has been reported to be about 68% in dogs with severe acute pancreatitis (Hess et al. 1998) and between 11 and 67% in cats with pancreatitis (Swift et al. 2000, Saunders et al. 2002, Ferreri et al. 2003, Forman et al. 2004). This high range of sensitivities likely reflects differences in the level of suspicion or the skills of the ultrasonographer, the equipment used and the severity of lesions and highlights the lack of standardised diagnostic criteria. The sensitivity of abdominal ultrasound reported in the earlier studies indicates that a normal pancreas on ultrasound examination is not sufficient to rule out pancreatitis in either dogs or cats. This is particularly true in cases of chronic or mild pancreatitis, where pancreatic changes are mild and often not detected during ultrasound examination. In one study in a small number of dogs with chronic pancreatitis, finding any change in the pancreas on ultrasound examination led to a sensitivity of only 56% (Watson et al. 2010).

The specificity of abdominal ultrasound for canine and feline pancreatitis has been traditionally thought to be relatively high, although this has not been systematically investigated in well-designed studies. Other diseases of the pancreas (e.g. neoplasia, hyperplastic nodules, oedema due to portal hypertension or hypoaalbuminaemia) may display similar ultrasonographic findings and cannot be differentiated from pancreatitis in many cases (Lamb et al. 1995, Lamb 1999a, Hecht & Henry 2007, Hecht et al. 2007). In a recent study where ultrasonography was performed in 26 dogs and cats with suspected gastrointestinal disease, 6 (23.1%) of the animals had ultrasonographic evidence consistent with pancreatitis, while histopathology revealed either a normal pancreas or pancreatic hyperplasia (Webb & Trott 2008). In the same study, there was only a 22 and 33% agreement between the ultrasound report and pancreatic histopathology in dogs and cats, respectively. These data raise concerns regarding the accuracy of ultrasonography in evaluating the pancreas and underscore the importance of not overinterpreting ultrasonographic findings. However, the findings of this particular study should be evaluated with caution because pancreatic lesions suggestive of pancreatitis might have been missed on histopathology. In another more recent study, a significant agreement existed between the use of serum fPLI concentration and abdominal ultrasonography for the diagnosis of traumatic pancreatitis in a group of cats with high-rise syndrome (Zimmermann et al. 2013). Finally, another recent study of a group of cats with pancreatitis that used serum fPLI as the standard for diagnosis of pancreatitis showed that pancreatic ultrasonography had a sensitivity of 84% and a specificity of 75% for diagnosing pancreatitis (Williams et al. 2013). Specific ultrasonographic changes (such as peripancreatic fat echogenicity, pancreatic thickness, pancreatic margins) were evaluated in that study and the usefulness of each one of those findings described.

Ultrasonographic findings in dogs and cats with pancreatitis include hypoechoic areas within the pancreas (possibly indicating necrosis or fluid accumulation), increased echogenicity of the surrounding mesentery (due to necrosis of the peripancreatic fat), enlargement and/or irregularity of the pancreas, dilation of the pancreatic or biliary duct and abdominal effusion (Fig 1) (Hess et al. 1998, Lamb 1999b, Swift et al. 2000, Saunders et al. 2002, Ferreri et al. 2003, Hecht & Henry 2007). Specifically in cats, it was suggested that the presence of a thick left limb of the pancreas, severely irregular pancreatic margins and hyperechoic peri-pancreatic fat in cats with appropriate clinical signs and increased serum fPLI concentrations are highly supportive of pancreatitis (Williams et al. 2013). On occasion, hyperechoic areas of the pancreas can be identified, possibly indicating the presence of pancreatic fibrosis. Cavitary lesions, a thickened duodenum, biliary obstruction or mass-like lesions might also be noted (Hecht & Henry 2007). It has been suggested that a dilation of the pancreatic duct is suggestive of pancreatitis in cats, but recent studies have not confirmed this hypothesis (Hecht et al. 2006).

Other imaging modalities

Contrast-enhanced computed tomography (CECT) is an extremely valuable tool for the evaluation of human patients with suspected pancreatitis (Bollen 2012). The computed tomographic anatomy of the canine pancreas has been described (Probst & Kneissl 2001) but, the usefulness of computed tomography for the diagnosis of pancreatitis in dogs has not been thoroughly
Diagnosis of pancreatitis in dogs and cats

The evaluation of severity of pancreatitis have been proposed for both dogs and cats (Newman et al. 2004, De Cock et al. 2007, Watson et al. 2007). However, in contrast to humans, histopathological criteria for the classification of pancreatitis have not been universally standardised in veterinary medicine and substantial confusion exists regarding both classification and terminology of canine and feline pancreatitis. The presence of permanent histopathological changes (namely fibrosis and acinar atrophy) is generally considered suggestive of chronic pancreatitis (Fig 2), while the absence of such changes in an inflamed pancreas indicates acute pancreatitis (Fig 3) (Newman et al. 2004, Watson et al. 2007, Bostrom et al. 2013). The predominant inflammatory cellular infiltrate (neutrophils or lymphocytes) is often used to further divide pancreatitis into suppurative or lymphocytic, and some authors consider a suppurative inflammation compatible with acute disease and lymphocytic infiltration compatible with chronic disease (Hill & Van Winkle 1993,

Histopathology of the pancreas

At present, histopathological examination of the pancreas is considered the gold standard for the diagnosis of pancreatitis, as well as the definitive differentiation between acute and chronic pancreatitis in dogs and cats. Histopathological scoring systems for investigated to date. A report of the use of CECT in two cases of canine pancreatitis (Jaeger et al. 2003) showed some encouraging results. However, a recent study in which the findings of different imaging modalities in dogs with acute abdomen were compared showed that contrast-enhanced multi-detector helical computed tomography (CE-MDCT) had low sensitivity for diagnosing pancreatitis in a small number of cases (n=7) (Shanaman et al. 2013). In cats, computed tomography performed in cases with histologically confirmed pancreatitis showed disappointing results (Forman et al. 2004). Other imaging methods (e.g. ERCP, endoscopic ultrasonography) have been used in healthy dogs and cats as well as in dogs and cats with pancreatitis with varying results (Spillmann et al. 2005a,b, 2013, Schweighauser et al. 2009). Also, a recent study evaluated the usefulness of magnetic resonance imaging (MRI) and magnetic resonance cholangiopancreatography (MRCP) for the diagnosis of pancreatitis in cats and reported promising results (Marolf et al. 2012). However, due to the lack of standardised criteria for the diagnosis of pancreatitis, the complexity of these imaging modalities, the necessity for general anaesthesia, the limited availability and the cost of the equipment, none of the above-mentioned methods can currently be recommended for the routine diagnosis of canine or feline pancreatitis. It is possible that after proper and meticulous evaluation, some of these methods will be used in the future for the diagnosis of pancreatitis in cases where all other diagnostic approaches result in equivocal results.

Histopathology of the pancreas

At present, histopathological examination of the pancreas is considered the gold standard for the diagnosis of pancreatitis, as well as the definitive differentiation between acute and chronic pancreatitis in dogs and cats. Histopathological scoring systems for diagnosed
Ferreri et al. 2003). A significant degree of necrosis is usually used to characterise the pancreatitis as necrotising. It should be noted that the histopathological distinction between acute and chronic pancreatitis is not always clear, and many animals have histopathological evidence of both acute and chronic pancreatitis.

Although still considered the gold standard for the diagnosis of pancreatitis, there is accumulating evidence that pancreatic histopathology is associated with several and important limitations, and therefore, cannot be considered an ideal gold standard. First, determining the clinical significance of histopathological findings is often challenging. In a necropsy study, 64% of 73 dogs that were presented for necropsy for various reasons had microscopic evidence of pancreatitis (Newman et al. 2004). In another study, histopathological lesions of pancreatitis were found in 67% of all cats examined, including 45% of healthy cats (De Cock et al. 2007). Currently, there are no standardised criteria that distinguish microscopic findings leading to clinical disease from those that do not, and it is possible that clinically insignificant pancreatic lesions could lead to a false diagnosis of clinical pancreatitis. On the other hand, exclusion of pancreatitis based on histopathology can be difficult because inflammatory lesions of the pancreas are often highly localised and can easily be missed (Hill & Van Winkle 1993, Saunders et al. 2002, Newman et al. 2004, De Cock et al. 2007, Pratschke et al. 2014). Therefore, multiple sections of the pancreas must be evaluated in order to increase the likelihood of finding microscopic lesions, although this is not always feasible in clinical practice. The absence of histopathological findings of pancreatitis must be evaluated with caution, especially when only one section of the pancreas has been examined (Newman et al. 2004, De Cock et al. 2007). Finally, pancreatic biopsy requires invasive procedures that are expensive and potentially detrimental in patients with pancreatitis that are haemodynamically unstable (Webb & Trott 2008, Corder et al. 2010). Therefore, pancreatic biopsy is rarely performed in clinical practice for the diagnosis of pancreatitis, unless a laparotomy is performed for other reasons. Nevertheless, in contrast to what was believed in the past, a large number of studies have shown that pancreatic biopsy per se is a rather safe procedure and can be used for the diagnosis of pancreatitis in dogs and cats (Westermark et al. 1993, Wiberg et al. 1999, Harmoinen et al. 2002, Webb & Trott 2008, Corder et al. 2010, Cosford et al. 2010).

In a recent retrospective study (Pratschke et al. 2014), the most common complications following surgical biopsy of the pancreas included vomiting, abdominal pain, nausea, anorexia, and lethargy.

Gross lesions of the pancreas (e.g. peripancreatic fat necrosis, pancreatic haemorrhage and congestion, pancreatic oedema, dull granular capsular surface) are present in some dogs and cats with pancreatitis but this finding is neither sensitive nor specific for pancreatitis (Fig 4) (Hill & Van Winkle 1993, Saunders et al. 2002, Steiner et al. 2008). When present, gross lesions of the pancreas are preferred sites for biopsy. However, gross pathological lesions are often absent in dogs and cats with pancreatitis or may be the result of neoplasia or nodular hyperplasia (Hill & Van Winkle 1993, Saunders et al. 2002, Newman et al. 2004).

Because concurrent inflammation of the intestines and/or liver appears to be a common problem in cats (Weiss et al. 1996, Callahan Clark et al. 2011) and may also occur in dogs, intestinal and hepatic biopsies should be collected in patients (especially cats) suspected of having pancreatitis that are undergoing exploratory laparotomy or laparoscopy. Likewise, cats with IBD and/or cholangitis that undergo laparotomy or laparoscopy should also have their pancreas evaluated.

Cytology of the pancreas

FNA of the pancreas and cytological examination of the aspirated material is a minimally invasive technique that is increasingly used for the diagnosis of pancreatitis in dogs and cats (Bjorneby & Kari 2002). To date, there are no studies that have evaluated the sensitivity and specificity of this diagnostic modality for the diagnosis of canine or feline pancreatitis. It is logical to assume...
that the finding of inflammatory cells within the aspirated material from the pancreas should be specific for pancreatitis. Pancreatic acinar cells constitute the majority of the cells found in FNA smears from a normal pancreas (Fig 5) (Bjorneby & Kari 2002). In animals with acute pancreatitis, the cytological picture is mainly characterised by hypercellularity and the presence of entire and degenerate neutrophils and degenerate pancreatic acinar cells (Fig 6). In animals with chronic pancreatitis, small numbers of lymphocytes and neutrophils are usually present, and the specimen is often characterised by low cellularity, possibly due to replacement of the normal pancreatic tissue by fibrotic tissue (Bjorneby & Kari 2002). It should be highlighted that, as for histopathology, highly localised lesions might be missed. Thus, negative FNA cytology results are not sufficient to rule out pancreatitis. FNA of the pancreas is usually performed either under ultrasonicographic guidance or during laparotomy (Bjorneby & Kari 2002). Although considered relatively innocuous, the safety of pancreatic FNA has not been evaluated in dogs and cats with pancreatic diseases. Pancreatic sampling by ultrasound-guided FNA or surgical biopsy did not cause increases in serum cPLI concentrations or clinically detectable pancreatitis in healthy dogs (Cordner et al. 2010). Endoscopic ultrasound-guided FNA of the pancreas has also been described in medium-sized healthy dogs and reported to be feasible and safe (Kook et al. 2012).

**ASSESSMENT AND PREDICTION OF THE SEVERITY OF PANCREATITIS**

Assessment of the severity of human acute pancreatitis is based on the application of standardised severity scores that are frequently modified and updated (Bradley 1993, Papachristou et al. 2007, Pavlidis et al. 2010). Prediction of the severity of pancreatitis constitutes a very important component of the diagnosis of pancreatitis, because it allows prediction of the likelihood of complications and morbidity and helps determine the optimal therapeutic plan before the patient enters a critical stage. It has been hypothesised that the severity of a pancreatitis episode can be determined by events that occur within the first 24 to 48 hours of the episode (Papachristou et al. 2007). These events are reflected through clinical, clinicopathological and imaging findings that can be used to predict the severity of the pancreatitis (Papachristou et al. 2007, Pavlidis et al. 2010).

In veterinary medicine, no well-established and universally accepted severity scores for pancreatitis have been described. Serum PLI and TLI concentrations are believed to lack prognostic significance because they correlate poorly with histopathological severity (Steiner et al. 2008). However, in a recent study, serum pPLI concentrations as well as dyspnoea and hyperkalaemia at the time of admission were found to be significant and independent prognostic indicators for outcome in cats hospitalised because of pancreatitis (Stockhaus et al. 2013). Currently, severity of canine and feline pancreatitis is determined based on the clinician’s clinical judgment, and typically a diagnosis of severe pancreatitis is made after the animal has entered a critical stage. In general, evidence of systemic complications (e.g. oliguria, renal azotaemia, icterus, severely increased hepatic enzyme activities, hypocalcaemia, hypoglycaemia, severe hyperglycaemia, hyperkalaemia, leukocytosis, shock or DIC) are considered indicators of severe disease and a poor prognosis (Ruaux & Atwell 1998, Kimmel et al. 2001, Mansfield et al. 2008). In a recent study (Tvarijonaviciute et al. 2014), serum paraoxonase 1 activity together with triglyceride and C-reactive protein concentrations were suggested to represent potential of disease severity.

However, prediction of the severity of pancreatitis has not been sufficiently studied in dogs and cats. Further studies are needed to establish the use of convenient and valuable clinical severity scores for pancreatitis in these species.

Although not directly related to severity of pancreatitis, results of two recent studies from the UK suggest that some dogs and cats with IBD have increased serum PLI concentrations. In one of those studies, increased serum cPLI concentrations in dogs with IBD were associated with a negative outcome; specifically, increased serum cPLI concentration was identified as the only variable that significantly affected survival in these dogs (Kathrani et al. 2009). In the other study, increased serum pPLI concentrations in cats with IBD were significantly associated with hypoalbuminaemia and hypocobalamininaemia also suggesting more severe clinical disease (Bailey et al. 2010).

**Conclusive remarks**

No single diagnostic modality is 100% reliable for the diagnosis of canine or feline pancreatitis. Maintaining a high level of suspicion for pancreatitis, especially in animals that are presented with mild and non-specific clinical signs, is of utmost importance for a correct diagnosis. In addition, other diseases that cause similar clinical signs should be judiciously excluded. Careful evaluation of the animal’s history, physical examina-
tion and routine clinical pathology findings, as well as the use of highly specific and sensitive tests (serum PLI concentration, abdominal ultrasonography, cytology and/or histopathology), is crucial for an accurate diagnosis of pancreatitis. In clinical practice, a combination of the clinical picture of the patient, serum PLI concentration and abdominal ultrasonography is considered to be the most practical and reliable means for an accurate diagnosis or exclusion of pancreatitis compared with other diagnostic modalities.

References


P. G. Xenoulis

Journal of Small Animal Practice • Vol 56 • January 2015 • © 2015 British Small Animal Veterinary Association
Trivedi, S., Marks, S. L., Kass, R. H., et al. (2011) Sensitivity and specificity of canine pancreatic-specific isozyme (cPLI) and other markers for pancreatitis in 70 dogs with and without histopathological evidence of pancreatitis. Journal of Veterinary Internal Medicine 25, 1077-1082