Acute pancreatitis in dogs and cats:
medical imaging, biopsy, treatment and prognosis

Acute pancreatitis bij honden en katten:
medische beeldvorming, bioptname, behandeling en prognose

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ABSTRACT

Diagnosing acute pancreatitis in dogs and cats is difficult. Abdominal ultrasonography provides specific information about the size, shape and homogeneity of the pancreas, but is very dependent on the experience of the operator and the quality of the echography machine. Abdominal radiography is less useful, while computed tomography is less practicable in veterinary patients because of the anesthesia risks, the need for experienced operators, and the high cost. Furthermore, computed tomography has low diagnostic value in cats. Biopsy of pancreatic tissue remains the gold standard. Treatment consists of fluid therapy and nutritional support, combined with pain medication, anti-emetics and antibiotics. The prognosis in dogs and cats is variable and largely depends on the clinical condition of the patient at admission. It is usually guarded, especially in cats.

SAMENVATTING

Het diagnosticeren van acute pancreatitis bij honden en katten is moeilijk. Abdominale echografie verschaft specifieke informatie over de grootte, vorm en homogeniciteit van de pancreas maar is erg afhankelijk van de ervaring van de uitvoerder en de kwaliteit van het echografietoestel. Radiografieën van het abdomen zijn minder nuttig, terwijl computertomografie minder bruikbaar is bij diergeneeskundige patiënten omwille van het anesthesierisico, de nood aan ervaren uitvoerders en de hoge kostprijs. Bovendien heeft computertomografie een lage diagnostische waarde bij de kat. De biopsie van pancreasweefsel blijft de gouden standaard. De behandeling omvat vloeistoftherapie en nutritionele ondersteuning in combinatie met pijnmedicatie, anti-emetica en antibiotica. De prognose bij de hond en de kat is variabel en afhankelijk van de klinische toestand van de patiënt op het tijdstip dat hij aangeboden wordt, maar ze is meestal gereserveerd, vooral bij katten.

INTRODUCTION

In practice, acute pancreatitis is a common disorder which can be difficult to diagnose. Because of the nonspecific signs and limitations of the currently available laboratory tests, medical imaging plays an important role in diagnosing acute pancreatitis in dogs and cats. Because delayed therapy can lead to a fatal outcome, a rapid recognition of the disease is important. This report is the second one in a series of three, which gives a review of acute pancreatitis in dogs and cats. This article will discuss the indications, as well as the advantages and disadvantages of the various medical imaging techniques and of pancreatic biopsies. In addition, the treatment options and prognosis will be reviewed.

MEDICAL IMAGING

Radiography

Under normal circumstances, the pancreas is not visible on plain radiographs (Simpson and Lamb, 1995; Bischoff, 2003). In dogs with acute pancreatitis, increased opacity and loss of visceral detail can be seen in the right cranial abdomen ('ground glass' appearance) associated with local peritonitis (Hess *et al*., 1998; Bischoff, 2003; Ruaux, 2003) (Figures 1a and 1b). On ventrodorsal projections, the inflamed pancreas can cause a displacement of the pyloric antrum to the left, the descending duodenum to the right and the transverse colon caudally (Simpson and Lamb, 1995; Hess *et al*., 1998; Bischoff, 2003; Ruaux, 2003; Mix and Jones, 2006). In some patients, the proximal duodenum appears dilated and fixed (C-shaped), displaced late-

Figure 1a. Loss of serosal detail in the right cranial abdomen (arrow) on a ventrodorsal radioraphic image of a dog with acute pancreatitis.

rally and dorsally, with a widening of the pyloroduodenal angle (Bunch, 2003; Ruaux, 2003; Watson, 2004). A static gas pattern can be noted in the transverse colon and the descending duodenum, the wall of which can be thickened (Hess *et al.*, 1998; Bischoff, 2003). Gastric distention suggesting gastric outlet obstruction is another possible abnormality (Bunch, 2003). Radiographs of the thorax can show pleural effusion (Bischoff, 2003) or pulmonary disease (edema or pneumonia) (Hess *et al.*, 1998).

Unfortunately, in one study of fatal cases of canine pancreatitis (Hess *et al.*, 1998), these possible abdominal radiographic signs compatible with acute pancreatitis were seen in only 24% of the patients, whereas 68% showed ultrasonographic abnormalities suggestive of pancreatitis. Therefore, abdominal radiography has a low sensitivity in diagnosing pancreatitis. In spite of this disadvantage, radiography offers the assessment of other abdominal organs for ruling out differential diagnoses, such as intestinal foreign body. Furthermore, radiography is a widely and easily available technique, which remains relatively inexpensive. Radiography can be used in conjunction with abdominal ultrasound (Watson, 2004; Mix and Jones, 2006).

In cats with acute pancreatitis, the same radiographic changes can be seen as in dogs (Gerhardt *et al.*, 2001; Ferreri *et al.*, 2003). However, these signs are often subtle and inconsistent (Hill and Van Winkle, 1993; Mansfield and Jones, 2001), and the most reported features are reduced abdominal contrast (28-50%), dilated bowel loops (24-42%) and pleural effusion (20-29%) (Gerhardt *et al.*, 2001; Saunders *et al.*, 2002; Ferreri *et al.*, 2003). In cats, hepatomegaly can be seen in cases of concurrent hepatic lipidosis (Akol *et al.*, 1993).

Abdominal ultrasonography

One of the most reliable and increasingly used diagnostic tools for pancreatitis in dogs and cats is ultrasound (US) of the abdomen. US has the advantage of being non-invasive, safe and relatively low in cost. Information can be obtained immediately and the whole


Figure 1b. Lateral radiographic image of the abdomen of the dog seen in figure 1a.

abdomen can be evaluated at the same time. In addition, it is becoming more available for general practitioners (Watson, 2004). It is however important to underline that the diagnostic value of US is strongly operator and machine dependent. Furthermore, the degree of pancreatic inflammation and edema also plays a role (Simpson and Lamb, 1995; Ruaux, 2003; Watson, 2004; Mix and Jones, 2006). In contrast to radiography, ultrasonography gives more specific information about the size, shape and homogeneity of the pancreas (Simpson and Lamb, 1995; Bunch, 2003; Watson, 2004). However, false negative results are possible (Ruaux, 2003), while not all lesions can be correlated with the clinical status of the patient (Mix and Jones, 2006). Therefore, it cannot be used as an exclusion diagnostic procedure. In cats, more work has been published to evaluate the sensitivity of several US abnormalities of the pancreas. In contrast, the available information in dogs is limited and further investigation is required.

Most typically, there is a focal area of pain when the US probe is placed over the region of the pancreas. Due to edema, pancreatic swelling and peri-pancreatic fat necrosis, the inflamed pancreas is more easy to localize than the normal pancreas (Watson, 2004). Findings suggestive for acute pancreatitis in dogs include a diffusely enlarged pancreas (more than 2 cm in diameter) with hypoechoic parenchyma, hyperechoic surrounding mesentery and generalized or local peritoneal effusion (Simpson and Lamb, 1995; Hess *et al.*, 1998; Ruaux, 2003; Mansfield, 2004; Watson, 2004; Mix and Jones, 2006) (Figure 2). Thickening of
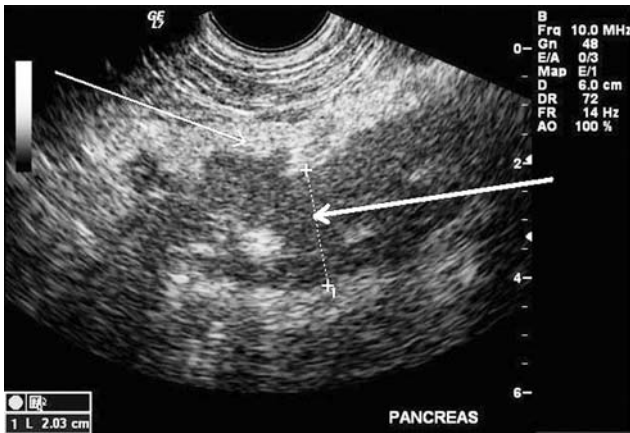
Figure 2. Ultrasonographic image: hypoechoic enlarged pancreas (big arrow) lined by hyperechoic mesentery (small arrow) in a dog with acute pancreatitis.
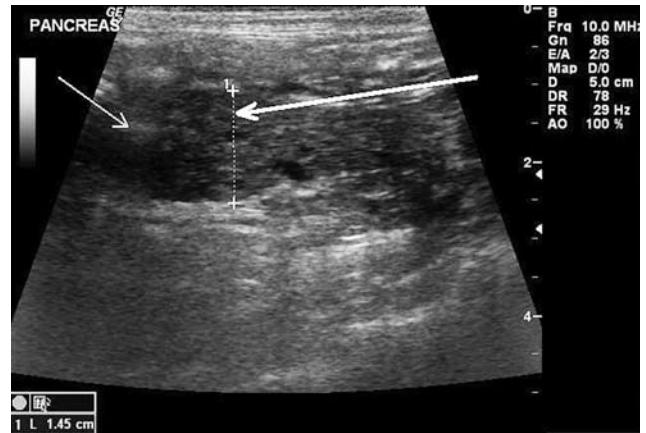
Figure 3. Ultrasonographic image: hypoechoic enlarged pancreas (big arrow) with several, regularly outlined hyperechoic spots (small arrow) in a cat with acute pancreatitis.
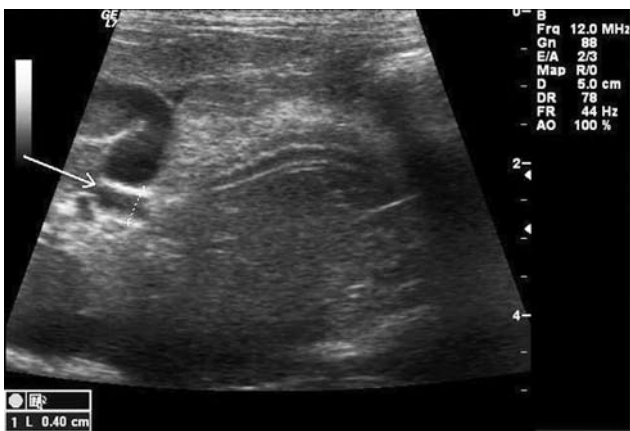
Figure 4. Ultrasonographic image: dilation of the common bile duct (arrow) in a cat with acute pancreatitis.

the stomach or duodenal wall and dilated bile ducts can be present (Simpson and Lamb, 1995; Bunch, 2003; Watson, 2004; Mix and Jones, 2006). In one study, pancreatitis was found to be the most common cause of corrugated small intestine (especially involving the duodenum) in both dogs and cats (Moon *et al*., 2003). Less frequently, dilatation of the pancreatic duct may be detected, which is considered pathognomonic for pancreatitis in human patients, and probably also in companion animals (Simpson and Lamb, 1995; Watson, 2004).

Ultrasonography is a very useful imaging technique in diagnosing acute pancreatitis in cats, especially when it is combined with other tests. However, as a single test, its sensitivity is controversial: depending on the author cited, the sensitivity lies between 11% en 67% (Swift *et al*., 2000; Gerhardt *et al*., 2001; Forman *et al*., 2004). In a study by Saunders *et al*. (2002), ultrasonographic evidence of acute pancreatic necrosis was only present in 7 of 20 cats. This relatively low sensitivity (35%) might be attributable to the inappropriate adaptation of the ultrasonographic diagnostic criteria used in dogs to cats. Indeed, the typical image of a hypoechoic pancreas with hyperechoic mesentery often seen in dogs was only present in 25 to 35% of the cats in this study and in a study by Ferreri *et al*. (2003). However, an enlarged,

irregular or hypoechoic pancreas and hyperechoic peripancreatic mesentery were found by Kimmel *et al*. (2001) in respectively 64% and 43% of the cases involving cats (Figure 3). Beyond this, more subtle and non-pancreatic changes can be diagnostically important as well. Additional ultrasonographic abnormalities in cats include abdominal effusion (31-45%), distention of the gallbladder and common bile duct (17-24%) (Figure 4), and thrombosis of the pancreaticoduodenal vein (5%). A hyperechoic, enlarged liver consistent with hepatic lipidosis was seen in 28-45% of cats with acute pancreatitis (Akol *et al*., 1993; Gerhardt *et al*., 2001; Kimmel *et al*., 2001; Saunders *et al*., 2002; Ferreri *et al*.; 2003). Less frequent findings included small hyperechoic kidneys, mesenteric lymphadenopathy, intestinal abnormalities and small gallbladder with inspissated bile (Saunders *et al*., 2002).

Advanced imaging

Computed tomography

In contrast to human medicine, where computed tomography (CT) is the preferred modality for the diagnosis and assessment of the severity of acute pancreatitis, this technique has limited usefulness in veterinary patients with suspected pancreatitis (Ruaux, 2003; Mix and Jones, 2006). The three main reasons for this are the requirement of anesthesia to avoid movement artifacts, the need for operator experience and technical skills, and the high cost (Ruaux, 2003; Mix and Jones, 2006). However, in large practices and teaching hospitals, where availability and cost are less of an issue, CT can develop into a useful diagnostic step.

In a study using CT as a diagnostic test for pancreatitis in dogs, 64% of the patients had pathologic changes (Spillman *et al*., 2000). In two case reports in dogs, pancreatic necrosis and associated vascular complications such as splenic vein thrombosis and renal infarction were diagnosed by contrast enhanced CT (Jaeger *et al*., 2003).

In cats, CT has a low diagnostic value. In one study by Gerhardt *et al.* (2001), visualization of the pancreas remained difficult after intravenous administration of contrast medium. In contrast to this finding, Forman *et al.* (2004) were able to visualize the pancreas in 95% of the cats (with and without pancreatitis) using contrast-enhanced CT. The sensitivity is low: evidence of pancreatitis was observed in only 2 out of 10 cats with acute pancreatitis (Gerhardt *et al.*, 2001). Furthermore, the measurement of pancreatic size is influenced by the positioning of the patient, which can create discrepancies in patient-to-patient measurements (Forman *et al.*, 2004).

Magnetic resonance imaging

Several studies have been published concerning magnetic resonance imaging (MRI) in diagnosing neuroendocrine pancreatic tumors in dogs. To the authors' knowledge, no information is yet available about the use of this imaging technique in small animals with acute pancreatitis.

Based on the current knowledge, the authors suggest that abdominal US is clearly superior to CT as a first test in dogs, especially small dogs, and in cats suspected of pancreatitis. However, when US is negative and the patient can tolerate anesthesia, CT can be considered in medium and large breed dogs.

PANCREATIC BIOPSY AND FINE NEEDLE ASPIRATION

Biopsy of the pancreas is considered the most reliable test for diagnosing acute pancreatitis in dogs and cats and is often used in publications as the golden standard for evaluating the accuracy (sensitivity, specificity) of a diagnostic test (Watson, 2004; Mix and Jones, 2006; Zoran, 2006, De Cock *et al.*, 2007; Watson, 2007b). In a study by Newman *et al.* (2004), 73 pancreata from dogs presented for post-mortem examination were histologically evaluated: while only 5.5% of them showed gross lesions suggestive of pancreatitis, 64.4% revealed microscopic evidence. So the lack of gross lesions during exploratory celiotomy does not exclude the presence of pancreatitis, and it is this fact that makes clear the importance of pancreatic biopsy. In the same study, acute pancreatitis was found to be present in 48.9%, as defined by the presence of neutrophils and pancreatic necrosis. De Cock *et al.* (2007) found acute pancreatitis in 15.7% of 115 cats presented for necropsy, irrespective of the cause of death. Histologic lesions were characterized by neutrophilic inflammation, surrounded by areas of necrosis.

Biopsy is a specific technique, but not very sensitive (Mix and Jones, 2006; Mansfield, 2004; Zoran, 2006), because the pancreatic lesions can be localized instead of diffuse. Newman *et al.* (2004) and De Cock *et al.* (2007) concluded that pancreatic inflammation occurs in discrete areas within the pancreas rather than diffusely, which might suggest that multiple biopsies are required. Because the lesions are randomly distributed, there is no preferred site for biopsy samples unless gross lesions are present (Newman *et al.*, 2004).

Another limitation is that histologic evidence of pancreatic inflammation is common, even in patients not suspected of pancreatic disease. This forms a dilemma for determining the clinical relevance of inflammatory lesions on surgical biopsy (Newman *et al.*, 2004). Pancreatic biopsies can be obtained by laparoscopy or by celiotomy. The need for anesthesia is an important disadvantage for both, because patients suspected of pancreatitis are often poor anesthetic candidates. Recently, laparoscopy has been evaluated and appears to be safe and useful for the evaluation of pancreatic disease (Webb and Trott, 2008). In addition, this technique is less invasive than celiotomy. However, the latter technique allows a more complete exploration of the abdomen (Mix and Jones, 2006).

Ultrasound-guided fine-needle aspiration does not require anesthesia and may reveal necrosis or inflammation of the pancreas. Because the pancreas is difficult to visualize ultrasonographycally, the experience of the operator plays an important role (Mix and Jones, 2006).

TREATMENT AND PROGNOSIS

Treatment and prognosis of acute pancreatitis in dogs and cats are closely associated with the severity of the disease (Watson, 2004). In general, the goals of treatment include eliminating the underlying cause, restoring fluid and electrolyte balance, decreasing pancreatic secretion, controlling vomiting, relieving pain, providing nutritional support if necessary and, if possible, managing complications such as acute renal failure or diffuse intravascular coagulation (Bunch, 2003; Zoran, 2006). Treatment is mainly supportive. As for other diseases, the treatment options are not always based on scientific evidence and studies, but rely rather on experience in practice and experience in human medicine. Unfortunately, evidence based on properly designed prospective, randomized, placebo controlled studies is currently almost nonexistent for the treatment of pancreatitis in dogs and cats. However, every part of the treatment can be explained by the pathologic changes that take place in acute pancreatitis. Doses and product names of frequently used medications can be found in Table 1.

Fluid and nutritional therapy

Fluid therapy and nutritional support are the cornerstones of treating dogs and cats with acute pancreatitis (Bunch, 2003). Fluids will provide maintenance requirements, reverse dehydration, replace ongoing losses, restore electrolyte imbalances and support adequate tissue perfusion to avoid ischemia (Bunch, 2003; Watson, 2004). Traditionally, complete pancreatic rest by starvation was recommended to avoid enzyme secretion and prevent further autodigestion of the inflamed pancreas and peri-pancreatic tis-

Table 1. Frequently used medication in patients with acute pancreatitis.

Classification	Group	Examples	Product	Dose
Analgetics	Opioid	Fentanyl	Fentanyl®*	1-5 µg/kg IV q 20-30min; 2-5 µg/kg/h CRI; bandage 4 µg/kg/h
	Opioid	Butorphanol	Dolorex®+	0.1-0.5 mg/kg SC, IM or IV
	Dissociative anesthetic	Ketamine	Anesketin®	3-5 µg/kg/min CRI
Anti-emetics	Serotonine-inhibitor	Ondansetron	Zofran®*	0.5 mg/kg IV loading dose, followed by 0.5 mg/kg/h CRI for 6h or 0.5-1 mg/kg PO q 12-24h
	Phenotiazine	Prochlorperazine	Buccastem®*, Prochlorperazine EG®*	0.5-1 mg/kg PO q 8-12h 0.1-0.5 mg/kg SC, IM or IV
	Anti-emetic and prokinetic	Metoclopramide	Primperan®* Metoclopramide EG®*	0.2-0.5 mg/kg PO, SC or IM q 6-8h 1-2 mg/kg IV over 24h as CRI
	Neurokinin-1 receptor-antagonist	Maropitant	Cerenia®+	2 mg/kg PO q 24h 1 mg/kg SC q 24h
Anti-ulcer medication	Histamine-2 blocker	Ranitidine	Zantac®*	2 mg/kg PO, IM or IV q 8-12h
	Gastric mucosal protectant	Sucralfate	Ulcogant®*, Antepsin®*, Carafate®*	0.5 g PO q 6-8h (< 20kg) 1-2 g PO q 6-8h (> 20kg) Cats: 0.25 g PO q 8-12h
	Proton pump inhibitor	Omeprazole	Gastrogard®*, Mepradec®*, Zanprol®* Omeprazole EG	0.5-1.5 mg/kg PO or IV q 24h Cats: 0.75-1 mg/kg PO q 24h Maximum of 8 weeks
Antibiotics	Lincosamide	Clindamycine	Antirobe®, Clindabuc®	5.5 mg/kg PO q 12h 11 mg/kg PO q 24h
	Fluoroquinolone	Enrofloxacin	Baytril®°	2.5 mg/kg PO q 12h 5 mg/kg SC or IV q 24h
	Sulphonamide/ Trimethoprim	Sulphonamide/ Trimethoprim	Tribrissen 80®	15 mg/kg PO q 12h
	Aminoglycosides	Amikacin	Amukin®*	5-10 mg/kg SC, IM or IV q 8h 10-15 mg/kg SC, IM or IV q 24h
	Aminopenicillines	Ampicillin	Albipen-LA®, AMPI-kel®	10-20 mg/kg PO, SC, IM or IV
	Aminopenicillines associated with beta-lactamase inhibitor	Amoxicillin clavulanic acid	Clavubactin® Clavobay®	12.5 mg/kg PO q 12h
Antibacterial and antiprotozoal medication	Nitroimidazole	Metronidazole	Stomorgyl® (with spiramycin)	12.5 mg metronidazole + 23.4 mg spiramycine/kg PO q 24h

CRI: constant rate infusion
*: Not registered for dogs and cats
+: Not registered for cats
°: Not registered for intravenous use in dogs and cats

sues (Qin *et al*., 2002). However, now it is thought that feeding small amounts of food or providing another type of nutritional support is beneficial, because patients with protein-calorie malnutrition have a worse prognosis (Mansfield, 2004; Watson, 2004). Indeed, the uptake of nutrients prevents abnormal enterocyt metabolism, gut atrophy and bacterial translocation (Watson, 2004; Zoran, 2006).

In dogs and cats that are alert and not dehydrated, small amounts of water followed by small amounts of a low-fat, high-carbohydrate diet can be presented at least 24 hours after the last episode of vomiting (Bunch, 2003; Watson, 2004). A diet low in fat (< 25g/1000kcal) and with a moderate protein content (generally greater than 18% or 60g/1000kcal) is the best choice for dogs, because these two ingredients will stimulate pancreatic enzyme secretion (Simpson, 2006). Cats can be offered highly digestible food, which ideally should contain high carbohydrate and low to moderate fat concentrations, except when concurrent diabetes mellitus is present. Because such a diet is often not commercially available, the essential thing is to find a diet that is well tolerated by the gastrointestinal tract (Zoran, 2006). Forced feeding must be avoided (Zoran, 2007). Garbage or low-protein, high-fat diets should be avoided to prevent relapse (Simpson, 2006; Lem *et al*., 2008).

Hospitalization and more aggressive therapy are

needed in more severe cases (Williams, 2000). Patients presented in shock need intravenous crystalloids at shock rate (60-90 ml/kg/h), followed by or combined with synthetic colloids at a rate of 10 to 20 ml/kg/day (Simpson and Lamb, 1995; Watson, 2004). Regular adjustment of fluid therapy is required (Bunch, 2003). It is advised to monitor packed cell volume, total protein concentration and kidney function on a daily basis. Serum electrolytes should be checked daily as long as the animal is vomiting and should be supplemented if needed. Especially hypokalemia should be tightly controlled, as it can delay recovery due to gastrointestinal atony and contribute to mortality (Watson, 2004).

A transfusion of fresh frozen plasma (FFP) (or whole blood) can supply protease inhibitors and albumin, although there is no proof of these beneficial effects either in animals or in humans (Simpson and Lamb, 1995; Holm *et al.*, 2003; Mansfield, 2004; Watson, 2004; Mansfield, 2007). Transfusion of plasma can be combined with the administration of heparin to prevent disseminated intravascular coagulation and to ensure pancreatic perfusion (Simpson and Lamb, 1995: Bunch, 2003; Watson, 2004), but the benefit of this approach has not yet been proven (Bunch, 2003). In our experience, FFP transfusions have always been tolerated in dogs and cats with severe acute pancreatitis.

If anorexia continues or if vomiting persists for 2 or 3 days despite anti-emetic treatment, other nutritional support is warranted (Watson, 2004). This nutritional support in an early stage of the disease is even more important in cats than in dogs, because of the risk of developing hepatic lipidosis (Mansfield and Jones, 2001; Bunch, 2003; Zoran, 2006; Watson, 2007a). During the first days, partial peripheral parenteral nutrition (PPN) can supply about 50% of the daily energy requirements in dogs and cats and can prevent further catabolism by supplying readily available glycerol as an energy source (Watson, 2004; Wortinger, 2006). On a long-term basis (> 5 days), nutritional support can be delivered by total parenteral nutrition (TPN) via a central venous catheter (Simpson and Lamb, 1995; Watson, 2007a). Both forms require working strictly aseptically, because the solutions are ideal media for the growth of bacteria and septicemia is a serious complication (Delaney *et al.*, 2006). Other complications include electrolyte and metabolic disturbances (hyperglycemia, hyperlipidemia), adynamic ileus, thrombophlebitis and the refeeding syndrome, a disorder involving electrolyte shifts associated with glucose transport following the reintroduction of food after prolonged anorexia (Qin *et al.*, 2002; Qin *et al.*, 2003; Mansfield, 2004; Delaney *et al.*, 2006). Although fewer complications were seen with PPN than with TPN, survival is probably more related to the underlying disease than to the type of nutritional support delivered (Chan *et al.*, 2002). Villous atrophy and increased intestinal permeability, disadvantages associated with PPN and TPN, are less of a problem with total enteral nutrition (TEN). A study by Qin *et al.* (2002) proved that early intrajejunal

nutrition (EIN) via a jejunostomy tube improves the integrity and function of the intestinal mucosa and reduces bacterial and endotoxin translocation. Furthermore, it is the most natural route for administering nutrients and it reduces nosocomial infection, multiple organ failure and length of hospitalization (Qin *et al.*, 2002; Qin *et al.*, 2003; Wortinger, 2006). TEN also moderates the acute phase response and improves disease severity and clinical outcome (Qin *et al.*, 2002). While not evaluating exclusively patients with pancreatitis, Chan *et al.* (2002) documented that significantly more animals receiving supplemental enteral nutrition survived compared to those receiving PPN alone. This fact could prove the benefits of enteral nutrition, although animals that tolerate enteral nutrition could simply be less ill. The complications of TEN include problems associated with surgery, obstruction of the tube, aspiration pneumonia, overfeeding and refeeding syndrome (Delaney *et al.*, 2006). It is important that TEN be delivered into the distal jejunum, because the enteral hormone secretion (such as cholecystokinin, secretin and gastrin) that causes pancreatic stimulation is mostly located more proximally in the gastrointestinal tract (gastric antrum, duodenum and proximal jejunum). Indeed, two studies (Qin *et al.*, 2003; Qin *et al.,* 2007) showed that early intrajejunal nutrition (in the form of an elemental diet) does not significantly increase pancreatic juice secretion or enzyme-protein synthesis and release. Simpson (2006) shares the opinion that enteral nutrition is superior to parenteral nutrition, but questions whether jejunal delivery of nutrients is necessary, because evidence exists that pancreatic enzyme synthesis is down regulated in dogs with acute pancreatitis. If this is indeed the case, then the benefit of enteral nutrition would be due rather to reductions in the systemic inflammatory response and the translocation of enteric bacteria than to the reduction of pancreatic stimulation (Simpson, 2006). Furthermore, possible complications of EIN include surrounding peritonitis, reduced gastrointestinal motility, osmotic diarrhea and vomiting, the risks of anesthesia and the difficulty of placing a tube surgically (Mansfield, 2004; Watson, 2004; Wortinger, 2006; Zoran, 2006). A feasible alternative is the laparoscopic-assisted placement of jejunostomy feeding tubes. This technique allows direct visualization of the abdominal contents and the jejunostomy site. It requires smaller incisions and results in decreased postoperative pain, while the associated complications are mild and comparable to those seen with surgical placement (Hewitt *et al.*, 2004). If vomiting is under control in anorectic animals, parenteral nutrition or EIN can be replaced by naso-esophageal, esophagostomy or gastrostomy tube feeding, which can be used for, respectively, short-, medium- or long-term nutritional support (Watson, 2004). Naso-esophageal tubes are the easiest to place and anesthesia is not required, in contrast to the two other types (Delaney *et al.*, 2006; Wortinger, 2006).

In conclusion, despite its possible disadvantages, EIN should still be preferred over TPN, which must be restricted to patients who do not tolerate enteral feeding (Simpson, 2006; Zoran, 2006; Watson, 2007a).

Analgetics and anti-inflammatory agents

The benefit of analgesia in pancreatitis cases should not be underestimated, because most patients suffer from abdominal pain. Pain relief can be achieved using opioids, both partial and full agonists, which have the advantage of causing few changes in pancreatic ducts or secretions (Simpson and Lamb, 1995; Bunch, 2003; Mansfield, 2004; Watson, 2004). An exception to this rule is morphine, which causes spasms of the pancreatic duct (Zoran, 2006) and increased bile duct pressure (Mansfield, 2004). A worthy alternative that should be considered is a constant rate infusion of a low dose of ketamine (dissociative anesthetic), because of its minimal effects on gastrointestinal motility (Watson, 2004). During exploratory celiotomy, intra-abdominal bupivacaine or lidocaine (local anesthetics) can be used (Mansfield, 2004).

Nonsteroidal anti-inflammatory drugs (NSAIDS) are absolutely contra-indicated due to their significant side effects: gastrointestinal ulceration and prolonged bleeding times (Watson, 2004). Furthermore, they have the potential to evoke renal failure in animals with hypotension and/or shock. Just like NSAIDS, corticosteroids increase the risk for gastroduodenal ulcers. Because there is no clinical evidence that corticosteroids reduce pancreatic inflammation in small animals and because they impair the removal of α macroglobuline-proteases complexes from the plasma by the reticulo-endothelial system, their use should be avoided (Bunch, 2003; Watson, 2004; Watson, 2007b). The only exception to this rule is their use in cats with acute pancreatitis and concurrent inflammatory bowel disease or lymphocytic/plasmacytic cholangiohepatitis (Zoran, 2006).

It has been suggested that supplementation with pancreatic enzymes could help in relieving postprandial pain, probably due to a negative feedback mechanism, but evidence in animals is still missing (Mansfield, 2004; Watson, 2004; Watson, 2007b).

Anti-emetics and anti-ulcer medication

Preventing oral intake is a first step in tempering acute vomiting, but administering anti-emetics is often necessary. Central-acting drugs, such as phenothiazines (e.g. chlorpromazine, prochlorperazine) and serotonine-inhibitors (e.g. ondansetron, dolastron), are preferred in dogs and cats (Bunch, 2003; Watson, 2004; Zoran, 2006), although the first group can cause sedation (Watson, 2004). Metoclopramide is an antagonist of the dopamine (D2) receptors at the chemoreceptor trigger zone. It owes its anti-emetic action to the fact that it produces increased tonus of the lower esophageal sphincter, accelerated emptying of the stomach and increased activity of the upper intestinal tract. This could cause extra pancreatic stimulation, which can better be avoided (de la Puente-Redondo et al., 2007; Mansfield, 2007). However, in patients with ileus and gastric hypomotility, which can contribute to refractory vomiting, this prokinetic effect can be beneficial (Zoran, 2006). Maropitant has recently been registered for dogs, in contrast to the phenothiazines, serotonine-inhibitors and metoclopramide, which all require off-label use. This highly specific neurokinin-1 receptor-antagonist is a strong anti-emetic that inhibits both central and peripheral causes of vomiting. Compared with metoclopramide, maropitant showed a higher efficacy in the treatment of ongoing emesis caused by a wide range of underlying clinical etiologies, including pancreatitis. Therefore, the duration of anti-emetic treatment was also shorter with maropitant. It is well tolerated and clinically safe, and once-daily administration is appropriate (de la Puente-Redondo et al., 2007).

Compromised gastric mucosal viability and gastrointestinal ulceration are side effects of pancreatitis. If gastrointestinal ulceration or compromised gastric mucosal viability are suspected or diagnosed, a therapy with mucosal protectants (e.g. sucralfate) and histamine-2 (H2) blockers (e.g. ranitidine, cimetidine) should be started (Watson, 2004). Proton pump inhibitors, such as omeprazole, are good acid inhibitors (Watson, 2004). Omeprazole only requires once daily administration, but is not registered for use in dogs or cats (Ramsey, 2008).

Antibiotics

Since bacteria do not play a role in the pathogenesis of acute pancreatitis in dogs and cats, and septic complications are rather rare, the benefit of routine antibiotic therapy has been called into doubt (Mansfield, 2007). In opposition to this consideration, however, necrotizing pancreatitis is known to be an ideal environment for bacterial colonization, and antibiotic treatment has indeed led to a better outcome in human patients and experimental canine cases (Watson, 2004; Zoran, 2006). In most cases, and especially if patients have fever or sepsis, parenteral broad-spectrum antibiotic treatment is started (Washabau, 2001; Bunch, 2003; Watson, 2004; Zoran, 2006). Holm et al. (2003) restrict the use of antibiotics to patients with documented pancreatic infection and to protracted cases of acute pancreatitis failing to respond to supportive therapy. In human patients, pancreatic infections are most commonly caused by Gram-negative enteric pathogens (Holm et al., 2003).

Antibiotics frequently used in patients with acute pancreatitis include trimethoprim-sulphonamides (TMS), aminoglycosides (e.g. amikacin) and fluoroquinolones (e.g. enrofloxacin) (Bunch, 2003; Watson, 2004). The fluoroquinolones penetrate well in several tissues, including the pancreas, because they are highly lipophilic drugs, while TMS is less effective in the presence of necrotic tissue (Ramsey, 2008). All previous types of antibiotics have a bactericidal effect

against Gram-negative bacteria, while TMS and fluoroquinolones are also effective against some Gram-positive micro-organisms (Ramsey, 2008). Since anaerobe bacteria are not sensitive to these types of antibiotics, it is advisable to combine them with lincosamides (e.g. clindamycine) or nitro-imidazoles (e.g. metronidazole) (Holm *et al.*, 2003; Mansfield, 2007). Another option is the use of ampicillin, which is an aminopenicillin. Its spectrum includes many Gram-positive and Gram-negative aerobic organisms and obligate anaerobes, but it is inactivated by organisms that produce beta-lactamases (Bunch, 2003; Ramsey, 2008). To avoid this disadvantage, aminopenicillin can be combined with a betalactamase-inhibitor. Several products are registered for companion animals and have few side effects.

Surgical treatment

Surgical intervention is warranted in cases of pancreatitis that are persistent or recurrent despite medical management to confirm the diagnosis and to detect neoplasia or complicating factors such as an infection (Simpson and Lamb, 1995; Simpson, 2006). Other cases, such as permanent bile duct obstruction and infected pancreatic necrosis, require surgical intervention (Simpson and Lamb, 1995; Bunch, 2003). If pancreatitis is localized to a focal area, this lobe can be surgically removed. If surgery is performed, cultures and biopsies are indicated (Williams, 2000). In a recent study in human patients with acute pancreatitis, peritoneal lavage helped in removing cytokines and enzymes (Caronna *et al.*, 2009). Since there are no controlled clinical studies in dogs, this technique, if used at all, should be used very cautiously (Holm *et al.*, 2003).

Prognosis

The prognosis of acute pancreatitis is variable because of the unpredictable nature and the wide spectrum of severity of the disease. Dogs with only one episode of mild pancreatitis usually have a good prognosis (Bunch, 2003). In patients with severe pancreatitis, the prognosis depends on the number of complications (Bunch, 2003; Holm *et al.*, 2003), but is mostly guarded to poor (Watson, 2004). Increase in trypsinogen activation peptide and certain abnormalities in the blood analysis (such as hypoglycemia, azotemia, elevated d-dimers) are considered worse prognostic indicators (Simpson and Lamb, 1995). In contrast to humans, the presence of necrosis alone cannot be used as an indicator of poor prognosis, because it is rather the systemic complications induced by the necrosis that cause death (Mansfield *et al.*, 2003). Several severity scoring systems have been described in canine patients with acute pancreatitis. One system, based on human criteria, classified pancreatitis as severe if two or more of the following parameters were present: necrosis of pancreatic tissue, systemic complications, severe clinical symptoms causing profound obtundation and de-

velopment of abdominal complications (Mansfield *et al.*, 2003). It is reliable, but has the disadvantage that biopsy of pancreatic tissue to assess for necrosis is seldom performed ante-mortem in companion animals. Another approach is the use of a scheme based on clinicopathologic abnormalities due to the compromise or failure of extra-pancreatic organs. In 68 cases of spontaneous canine acute pancreatitis, this classification correlated with outcome (Ruaux and Atwell, 1998). However, the scoring system devised did not assess definitively confirmed cases of pancreatitis and non-clinicopathologic findings were not used. Recently, a clinical severity index for dogs with acute pancreatitis has been developed, based on abnormalities of the cardiac and respiratory system, intestinal integrity and vascular forces (changes in albumin concentration and systolic arterial blood pressure). Intestinal health is of especially great importance in dogs with acute pancreatitis, in particular during the period in which enteral nutrition is lacking. This index showed a good correlation between outcome and interval from hospital admission until discharge or death. The overall mortality rate among all dogs was 23%, while 53% of the dogs with the worst clinical severity index score died (Mansfield *et al.*, 2008).

Because of the usually severe forms and the difficult ante-mortem diagnosis, the prognosis in cats is guarded (Bunch, 2003). Hypocalcemia (plasma ionized calcium just below reference range), leucopenia, hypoalbuminemia, severe dehydration, tachycardia, tachypnea and pyrexia are known as poor prognostic signs (Hill and Van Winkle, 1993; Kimmel *et al.,* 2001; Bunch, 2003; Zoran, 2006).

CONCLUSION

As the clinical signs and laboratory findings in acute pancreatitis are non-specific, medical imaging is usually needed to confirm the diagnosis and to assess for concurrent diseases or complications. Currently, abdominal ultrasonography is the preferred test, but it requires an experienced sonographer. Further work needs to be done to evaluate more advanced imaging techniques such as MRI. Although pancreatic biopsy and histologic evaluation are very sensitive tests if multiple biopsies are taken, this is seldom used in general practice because of the expense and the need for anesthesia. Most patients need intensive therapy and extensive monitoring to improve the chances for survival and to prevent or address complications rapidly. For the most severe cases, referral to an intensive care facility needs to be considered. There is an obvious need for well designed prospective studies that evaluate the different aspects of the management of pancreatitis. Hopefully, this will lead to a better prognosis in the future.

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Mededeling