Triaditis in the cat, an enigmatic and challenging condition

Practical clinical advice on its diagnosis and management

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Introduction

The term 'triaditis' is used to describe a condition of three concurrent inflammatory diseases that involve the liver, pancreas and small intestine (Weiss and others 1996, Fragkou and others 2012, Mansfield 2014), although occasionally only two of these organs may be involved (Fragkou and others 2012). The presenting clinical signs of depression, anorexia or polyphagia, vomiting, diarrhoea and/or weight loss can prove to be challenging for the clinician to make a definitive diagnosis as these signs are non-specific and in some cases they can be very subtle. Forming a diagnosis can be further compounded by the need to take histopathological biopsy samples for final confirmation (Cattin 2013). And, the management of three comorbidities will inevitably bring its own set of challenges from both a medical and nutritional standpoint.

Our guest author once again is Dr Penny Watson, a Senior Lecturer in Small Animal Medicine at the Queen's Veterinary School Hospital, Cambridge, UK. Dr Watson's research focuses on liver and pancreas disease in the dog and cat, particularly chronic disease and fibrosis. Dr Watson has given practical clinical advice in these proceedings on feline triaditis, its aetiology, how to make a definitive diagnosis as well as the long-term medical management of this enigmatic disease.

In the second half of these proceedings we explore the best practical advice on what to feed cats with triaditis. Veterinary literature has been reviewed in order to provide practical recommendations on what type of dietary matrix can be fed as part of a medical protocol for successful patient management.

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- Cattin I (2013). Feline triaditis. Veterinary Focus; 23 (2): 2-8
- Fragkou F, Adamama-Moraitou KK, Poutahidis T, et al (2012). Feline 'triaditis': A prospective study of 47 cases. ECVIM-CA Congress, Maastricht, The Netherlands, 2012; 1525 [abstract]
- Mansfield C. Triaditis in cats-does it exist? (2014). In: Proceeding WSAVA, Cape Town, South Africa, September: 111-113
- Weiss DJ, Gagne JM, Armstrong PJ (1996). Relationship between inflammatory hepatic disease and inflammatory bowel disease, pancreatitis, and nephritis in cat. JAVMA; 209 (6): 1114-1116

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Authors' biography

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Dr Penny Watson is a Senior Lecturer in Small Animal Medicine at the Queen's Veterinary School Hospital, Cambridge, UK. She holds the Royal College of Veterinary Surgeons (RCVS) Certificate in Veterinary Radiology and Diploma in Small Animal Medicine, is a Diplomate of the European College of Veterinary Internal Medicine and a former head examiner of their Internal Medicine Diploma exam (DipECVIM). Penny Watson's research focuses on liver and pancreas disease in dogs and cats, particularly chronic disease and fibrosis. Her research has defined the prevalence of pancreatic lesions at post-mortem and breed-related differences in pancreatic pathology which suggest differences in aetiology between breeds. Dr Watson also runs a busy internal medicine teaching and referral clinic at the veterinary school and is Honorary Secretary of the British Small Animal Veterinary Association.

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David Morgan graduated from Cambridge University Veterinary School (UK) in 1986. He has worked in both large animal and companion animal practice. In 1990 he gained the post-graduate Certificate in Veterinary Radiology. In 1993 he joined P&G Pet Care and since 2000 has been based in Geneva and is a Scientific Communication Manager. One of his main interests is how nutrition can help provide support for normal healthy animals as well as how it can be part of a successful management protocol for those with clinical disease.

Triaditis in the cat

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Part 1: Feline triaditis: does it exist and what is the cause?

What is triaditis?

'Triaditis' is the term coined many years ago in a lecture by David Twedt in the USA to denote concurrent chronic cholangitis, chronic pancreatitis and inflammatory bowel disease in cats. It is a frustrating term because in fact, a literature search will show you there are NO publications on 'triaditis' in cats. There *are* publications on 'triaditis' in humans but they mean something very different – inflammation of the portal triad - i.e. confined to the liver. The term as used for cats could therefore lead to confusion, particularly in comparative studies – but it has gained widespread acceptance as a short-hand way of reminding us that these three conditions can occur together in cats.

There is continuing debate about whether these three conditions are really related in cats. The first published report was Weiss and others in 1996 (Weiss and others 1996) who reported an increased prevalence of inflammatory bowel disease (IBD) and pancreatitis in cats with cholangiohepatitis. More recent studies of cholangiohepatitis seem to support this: for example, in a study of MRI in cats with cholangitis or pancreatitis, 8 out of 10 cats had both histologically confirmed pancreatitis and cholangiohepatitis on laparoscopic biopsies (Marolf and others 2013). In another study of ultrasound in 26 cats with cholangitis, 17 had concurrent ultrasonographic abnormalities in the gut wall and 7 had concurrent pancreatic abnormalities (Marolf and others 2012).

The evidence does suggest, therefore, that a sub-set of cats has concurrent gut, liver and pancreas disease. There are also cats which suffer from one or the other but not all three. These lectures will explore potential aetiologies, diagnosis and treatments of chronic pancreatitis; chronic cholangitis and inflammatory bowel disease in cats, both together and individually.

Why does 'triaditis' occur in cats?

The short answer is nobody knows. There are a number of possible reasons but more research will be needed to identify which of these are important. Broadly speaking, chronic pancreatitis, chronic cholangitis and IBD could occur because of an infectious process; an autoimmune process or something physical (such as duct obstruction). An autoimmune disease could also involve food allergy (particularly in the gut) and an infectious cause could also encompass an unusual host reaction to their own microflora. In reality, particularly for chronic pancreatitis and chronic cholangitis, it is likely that cats suffer from several different diseases and not just one disease and that the aetiologies vary. It will be very difficult to define effective treatments until we know the causes and can separate out cats into their different groups.

Many authors simplistically suggest that cholangitis and pancreatitis occur because the pancreatic and bile ducts join before they enter the duodenum. Cats are like humans in this respect, whereas in most dogs the ducts don't join and enter the duodenum separately. Having a single outflow through the sphincter of Oddi would certainly pre-dispose to pancreatitis and cholangitis (although not explain the concurrent IBD) if both ducts were blocked concurrently. This is unusual in cats – in humans, the commonest reason for this to occur would be gall stones blocking the ducts near the sphincter of Oddi. This is very rare in cats. Cats do sometimes suffer from poorly defined sphincter dysfunction which may cause this syndrome: 'sphincter of Oddi dysfunction' has been described in both humans and cats (Furneaux 2010) and describes a spasm of the sphincter which can block both pancreatic and bile ducts. It produces a dynamic obstruction which can be very difficult to diagnose without dynamic imaging with stimuli for gall bladder emptying. However, it is diagnosed more often in humans with IBD and it is proposed that inflammation in the intestinal wall around the sphincter predisposes to it.

Too few cases have been reported in cats for us to know if there is any association with IBD – but it is likely to be a condition which is under-diagnosed in cats because it will not be found unless you are looking for it.

Some cats may get ascending infection from the gut into both ducts, which potentially could be predisposed by vomiting or overgrowth of bacteria secondary to IBD, but it is not clear how often this happens. Bacteria could also pass across the mucosal barrier and into the portal blood circulation and then enter the liver (Twedt and others 2014). A second possible reason could be close proximity of the pancreas, bile duct and small intestine, such that inflammation of infection in one organ has a 'local' effect spreading to the others. This could be particularly true with pancreatitis as the bile duct passes through the pancreas so could be blocked during an episode of pancreatic inflammation and the neighbouring small intestinal wall might also be involved. David Twedt and Kenny Simpson have performed fluorescent in situ hybridization (FISH) on liver and pancreas from cats with cholangitis and pancreatitis and shown bacteria within the organs: but it is not clear whether these are a primary cause or secondary phenomenon (Twedt and others 2014, Simpson and others 2011).

The third possible reason, which seems very plausible in a number of cases, is that all three organs are affected by the same disease process, as can occur in humans. The bile duct, pancreatic duct and small intestine might all be concurrently affected by autoimmune disease, similar to IgG4+ cholangitis in humans. It is worth considering human biliary tract disease because it helps to understand how relying entirely on histology in cats may be leading us to put several diseases together. We need to develop better methods of imaging and blood tests to help us understand these feline diseases further.

A summary of human diseases with similar clinical and histological appearances to each other and to chronic cholangitis in cats

There are three diseases of the biliary tract in humans which all have a very similar appearance on histology and yet are clinically very distinct.

- Primary sclerosing cholangitis (PSC)
- Primary biliary cirrhosis (PBC)
- IgG4+ cholangitis

PSC: is a disease of young men (+ paediatrics) in which 60-80% have concurrent IBD in the form of ulcerative colitis. At least 20% also have other autoimmune disease such as type 1 diabetes mellitus (DM); thyroid disorders and psoriasis. It has a slowly progressive course but eventually leads to liver failure, transplant or tumour within 9-12 yrs. PSC greatly increases the risk of cholangiocarcinoma (160x); colonic cancer and hepatocellular carcinoma (HCC). It is defined as a LARGE duct disease which leads to strictures. Diagnosis is made on the basis of IMAGING the biliary tract to show strictures and ruling out other causes. Many autoantibodies can be measured in the blood but none are diagnostic. The histology overlaps other conditions: it has been estimated that liver biopsy in patients with known PSC (assured by endoscopic retrograde cholangiography) added new information and affected clinical management in only 1.3% Moreover, serial liver biopsies demonstrated a high degree of sampling variability so are not recommended. PSC is proposed to be autoimmune but does not respond to immunosuppressives. Steroids are not usually used because they increase the risk of biliary tract infection. Treatment revolves around ursodeoxycholic acid and eventually liver transplant.

PBC: is commonest in older women particularly 50-60 years old with a 9:1 to 20:1 Female: Male ratio and is never described in children. It has a variable course – some cases are slowly progressive. It is a SMALL duct disease which is proposed to be autoimmune involving an interaction between genes / environment / immunosenescence. Other concurrent autoimmune diseases may be present including hypothyroidism and Sjogren's syndrome (dry eye and dry mouth). PBC predisposes to hepatocellular carcinoma (+ cholangiocarcinoma). Diagnosis is made on the basis of blood tests which show cholestasis and positive anti-mitochondrial anti-bodies which is a very specific test. Histology is not necessary and it can look very similar to PSC and IgG4+ disease.

IgG4+ disease: Recently recognised: this is what we think English Cocker spaniels may have (please see my notes in the proceedings 'Chronic pancreatitis in the dog; the rediscovery of a forgotten disease' highlighted in the addendum page 38). This is a relatively newly recognised disease in humans so it is too early to know if it predisposes to cancer. It is a multi-systemic disease which also causes autoimmune pancreatitis; nephritis; Sjogren's syndrome and others. It is diagnosed predominantly in older men and is diagnosed on the basis of serum (+ tissue) IgG4+. Again, histology doesn't help differentiate from the other causes of biliary tract disease unless immunohistochemistry is performed against IgG4. This disease differs from PSC and PBC in being very responsive to steroids.

Cat Study

In a recent, multi-centre, unfinished (!) project, we looked at 39 cases of chronic cholangitis in cats to ask the questions: what type of pathology is present? Are any similar to primary sclerosing cholangitis in humans?

Based on the human classification systems, a human pathologist, grading the cats 'blind', categorised nine cases as secondary biliary cirrhosis – suspected chronic extra-hepatic obstruction; seven cases as PSC-like changes; five cases as vanishing bile duct syndrome; one case as PBC-like changes and the rest non-specific 'cholangiopathy'. Whatever is going on in these cats with chronic cholangitis, we undoubtedly have several diseases present and we are undoubtedly missing the diagnosis of extra-hepatic biliary tract disease in many cases.

For references and further reading please see pages 13-14.

Part 2: Diagnosis of pancreatitis, cholangitis and IBD

Diagnosis of pancreatitis, cholangitis and IBD is challenging. All three conditions produce similar clinical signs, whether they present together or individually. Definitive diagnosis of 'triaditis' would require biopsies of all three organs at laparoscopy or laparotomy. This is rarely achieved and often the diagnosis is made on the basis of blood and imaging findings and the assumption that triaditis is present. This may not change the treatment of affected cats significantly but it must be remembered that definitive diagnosis cannot be made without histology: there is an over-lap in the clinical signs of acute and chronic cholangitis and without culture of the bile, it is impossible to rule out biliary tract infection completely. The clinician must also keep an open mind to the possibility of biliary tract obstruction and consider investigations for this if the cat is not responding to conservative management as well as expected.

Diagnosis of chronic cholangitis in cats relies on hepatic histopathology, although ultrasonographic and clinco-pathologic findings (Callahan Clark and others 2011) can support a presumptive clinical diagnosis. Because of the elevation in liver enzymes and classical changes on imaging, cholangitis will probably be presumptively diagnosed in cats more often than pancreatitis or IBD. In lymphocytic cholangitis the liver enzymes are mildly to moderately increased, and tend to be less marked than in cats with neutrophilic cholangitis (Callahan Clark and others 2011), although there is an overlap of results. Peripheral blood neutrophilia is less common in lymphocytic cholangitis than in cats with the acute neutrophilic disease, but it may be present. Most cats with lymphocytic cholangitis show an increase in gamma-globulin concentration, which may cause confusion with Feline Infectious Peritonitis (FIP). And, there may be hepatomegaly on X-rays (which is often due to enlargement of the larger bile ducts) and in some cases, ascites. Ultrasonography reveals dilation of the biliary tract in some but by no means all cases. The common bile duct typically appears dilated and there may be dilation of the gallbladder and 'sludge' within it. The main differential diagnosis is extra-hepatic biliary obstruction which should be ruled out by carefully imaging the surrounding pancreas, small intestine, and mesentery. Unfortunately, recent publications indicate that ultrasonography of the biliary tract can look normal in cats with biliary tract disease: even with extra-hepatic biliary obstruction. This makes diagnosis difficult without a laparotomy and checking the patency of the biliary tract.

It is very important to check clotting function prior to performing a liver biopsy in cats in view of how commonly coagulation times are prolonged in cats with liver disease. Vitamin K should be given prior to biopsy. It is wise to submit the liver biopsy to culture as well as histopathology, given the theory that some of these cats have chronic persistent bacterial infection. Carefully taking a sample of bile from the gall bladder for culture is even more helpful.

Histological definitions of chronic cholangitis remain rather controversial. The World Small Animal Veterinary Association (WSAVA) liver standardisation group (Rothuizen and others 2006) recommends that feline chronic cholangitis is split in to three groups histologically:

a) Neutrophilic cholangitis:
   - This can be purely neutrophilic, which is equivalent to the old definition of 'suppurative' cholangitis and is an assumed ascending bacterial infection

- or it can be a mixed neutrophilic and lymphocytic inflammation termed 'chronic neutrophilic' which is assumed to be a persistent bacterial infection. This is equivalent to many of the cases we used to call 'chronic cholangitis' and I think it is too simplistic to say all cases with some neutrophils are definitely bacterial in origin. It is also a contradiction in pathological terms to call something 'chronic neutrophilic'

b) Lymphocytic cholangitis: this is purely peri-portal lymphocytes and some cases may be difficult to distinguish from a small cell lymphoma
c) Chronic cholangitis associated with liver fluke – not recognised in the UK

The older papers put the line between acute and chronic somewhere different:

- Acute (suppurative) cholangitis: neutrophils only and high association with ascending infections
- Chronic (non-suppurative): includes those with mixed inflammatory infiltrates (classed as chronic neutrophilic cholangitis by the World Small Animal Veterinary Association) and lymphocytic cholangitis

However, the truth may be somewhat different from both of these. To quote Warren and others 2011: '...there remains uncertainty in the relationship between chronic neutrophilic cholangitis and lymphocytic cholangitis. We propose that *non-suppurative cholangitis-cholangiohepatitis* better reflects pathologic processes characterized for this syndrome...'

The diagnosis of chronic pancreatitis in cats is challenging (Armstrong and Williams 2012, Bazelle and Watson 2014). The only pancreas serum marker of any help is feline pancreatic lipase immunoreactivity (fPLI:) but the sensitivity and specificity for a diagnosis in every cat, with acute or chronic pancreatitis, is unclear. Ultrasound has a low sensitivity but high specificity (i.e. if a lesion is seen, it is there, but very often the pancreas looks normal even with severe disease). Traditional amylase and lipase are of no clinical use in cats because elevations bear no relationship to presence or absence of pancreatitis, although the new DGGR-lipase catalytic assay (1,2-o-dilauryl-rac-glycero-3-glutaric acid-[6'-methylresorufin] ester) is reported to work in cats (Oppliger and others 2013). However, there are very few studies as yet reporting the sensitivity and specificity of this new test. Feline trypsin-like immunoreactivity (fTLI:) is very useful to diagnose exocrine pancreatic insufficiency (EPI) in cats (when it is low) but is of low sensitivity and specificity in the diagnosis of pancreatitis (when fTLI *should* be elevated) (Swift and others 2005; Forman and others 2004).

Preliminary results from studies evaluating the fPLI test show it has the highest sensitivity and specificity of any test for the diagnosis of pancreatitis in cats. It has high sensitivity (100%) and specificity for moderate to severe pancreatitis in cats, but in milder cases its sensitivity drops to 54%, with an overall sensitivity of 67% (Forman and others 2004).

Ultrasound also has a low sensitivity for diagnosis of pancreatitis in cats, with studies reporting a sensitivity of between 24% (Gerhardt and others 2001) and 67%. One study (Ferreri and others 2003) showed that there were no specific clinical, clinicopathological, radiographic or ultrasound changes which would differentiate acute pancreatitis (AP: 30 cats) from chronic pancreatitis (CP: 33 cats). And, cats with CP were more likely to have concurrent disease than were cats with AP (100% vs. 83%, respectively) and had significantly higher serum alanine aminotransferase (ALT) and alkaline phosphatase (ALP), but these were the only differences identified. Recognised negative prognostic indicators specifically in cats with pancreatitis include low ionised calcium and leukopenia (Kimmel and others 2001).

Cats with pancreatitis are thus a diagnostic challenge and cats with severe necrotising fatal pancreatitis may still have mild clinical signs.

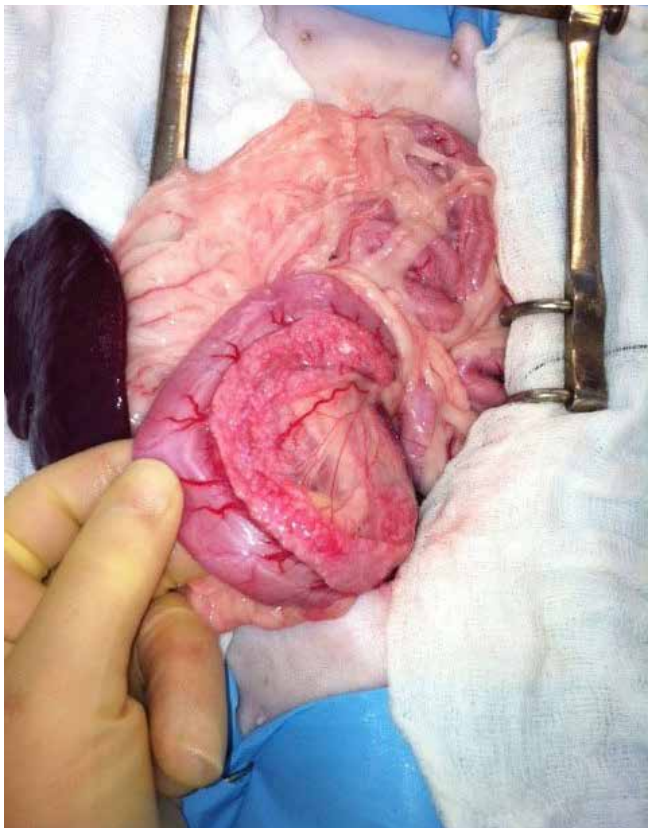

Figure 1. Pancreas of a cat at laparotomy (right limb) with an inflamed appearance. A biopsy was taken carefully from this (see fig 2, page 11).

Establishing a definitive diagnosis relies on obtaining a pancreatic biopsy (De Cock and others 2007). However, this will not be indicated in most cases until there are effective treatments, because a biopsy is relatively invasive procedure and its results do not alter treatment or outcome. Cytology of ultrasonography-guided transcutaneous fine needle aspirates of the pancreas may help differentiate neoplasia or dysplasia for inflammation, but veterinary experience in this area is very limited. If the clinician is performing a laparotomy to obtain other biopsies, it makes perfect sense to obtain a pancreatic biopsy at that time too (fig 1). Pancreatitis is not a risk, provided the pancreas is handled gently and the blood supply is not disrupted. However, the biopsy should be small and from the tip of a lobe, so this may miss the disease which is usually patchy, particularly early on, and can also be centred on large ducts, so even biopsy has its limitations. Careful consideration should be given to taking other biopsies at the same time: particularly liver and small intestine.

Chronic pancreatitis is recognized is the most common form of pancreatitis in cats (Armstrong and Williams 2012, Bazelle and Watson 2014). A postmortem prevalence of feline CP of 60% has been reported (De Cock and others 2007). It must be noted that postmortem studies tend to overestimate the prevalence of chronic diseases, which leave permanent architectural changes in the organ, whereas the prevalence of acute, totally reversible diseases will be underestimated, unless the animal dies during the episode. Nevertheless, it is clear that there are many more cases of CP in cats than currently recognized.

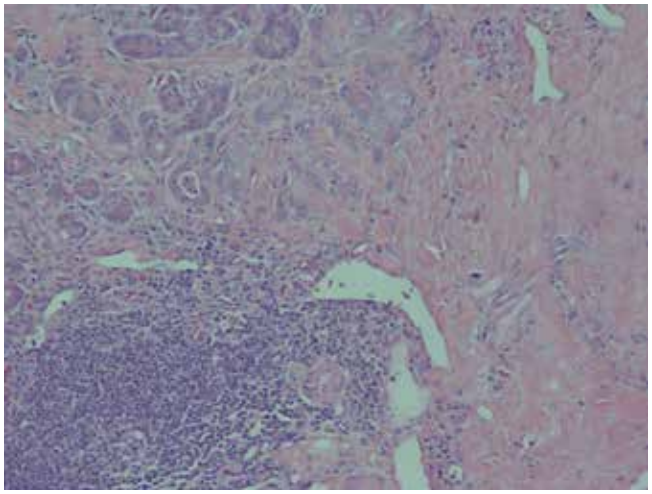

Figure 2: Histology of pancreas of cat shown in figure 1 showing chronic pancreatitis. Note dense lymphocytic inflammatory infiltrate (small purple cells) and fibrosis (pink material) surrounding remaining acinar cells. Photo courtesy of Pathology Department; Queen's Veterinary School Hospital, University of Cambridge.

Chronic pancreatitis is defined as: 'a continuing inflammatory disease characterized by the destruction of pancreatic parenchyma leading to progressive or permanent impairment of exocrine or endocrine function or both' (fig 2).

Diagnosis of IBD relies on both response to treatment and biopsies, as in dogs, although gut biopsies are often difficult to justify because they often do not change prognosis or treatment. The biggest reason to biopsy the cat's small intestine is to rule out lymphoma. IBD is less well investigated in cats than in dogs, but as in dogs, it is believed to represent an abnormal response to gastrointestinal antigens (both bacterial and food) in a genetically susceptible individual. In addition, gut wall inflammation will occur secondary to other diseases such as giardia and viral infections (Jergens 2012). IBD is by definition 'idiopathic' so ideally dietary intolerance, antibiotic responsive diarrhoea and parasites should be ruled out first before the gut is biopsied. The WSAVA recommends endoscopic biopsies because they carry a lower morbidity than full thickness biopsies at laparotomy or laparoscopy. The obvious problem in a cat with suspected 'triaditis' is that endoscopy will not allow visualization and biopsy of the liver and pancreas.

For references and further reading please see pages 13-14.

Part 3: Treating cats with triaditis

Treatment of chronic cholangitis: There is no universal agreement about ideal treatment of these cats, likely reflecting our uncertainty about the aetiology. Immunosuppressive doses of corticosteroids are usually recommended - these tend to ameliorate the acute flare-ups of the disease but they do not lead to long term resolution of signs, and the condition invariably recurs. Antibiotic therapy is wise, at least early in the treatment, until an infectious aetiology has been ruled out. There is good logical reason to use ursodeoxycholic acid for it choleretic and anti-inflammatory effect, as well as its effect on modulating the bile acid pool and reducing toxic bile acids. Use of anti-oxidants such as S-adenosylmethionine and vitamin E is also logical because bile is a potent oxidizing toxin in the liver. However, there is little evidence base for any of these suggestions. A recent study retrospectively compared the use of prednisolone alone (n = 10) with ursodeoxycholic acid alone (n = 13) in cats with lymphocytic cholangitis (Otte and others 2012). In that study, cats treated with prednisolone alone lived significantly longer than those treated with ursodeoxycholic acid alone – but of course this was a small group biased in a number of ways: for example, there was a strong male bias and many cats were Norwegian Forest cats. This does not answer the question of what happens if you use both prednisolone and ursodeoxycholic acid and if, as suspected, chronic cholangitis is caused by a number of syndromes, then a different population of cats might respond differently. Cats with more acute signs, particularly associated with concurrent intestinal and/or pancreatic disease may require hospitalization and IV fluid therapy.

The prognosis for cure in chronic cholangitis appears to be poor (as it is in PSC in humans), as the disease appears to wax and wane chronically in spite of treatment. However, few cats with lymphocytic cholangitis die from their disease and most cats die for another reason. This is likely because, unlike in dogs, the disease does not generally progress to end stage cirrhosis.

Treatment of chronic pancreatitis

The current state-of-the-art is symptomatic treatment and is similar to dogs. The three 'pillars' of therapy in acute flare-ups of disease are:

- Early aggressive fluid therapy – and in cats, with particular attention to potassium concentrations
- Analgesia
- Feeding

Analgesia should always be considered: cats are renowned for hiding their pain so the clinician should be alert to subtle signs. In mild to moderate cases, injectable or transmucosal buprenorphine may be adequate: absorption is good by this route in cats (Robertson and others 2003). Non-steroidals should be avoided. Maropitant is usually the most effective anti-emetic and may also provide some analgesia as part of a multi-modal approach because substance P has been implicated in the pain of pancreatitis. Particular care should be taken to feed cats early even with acute pancreatitis because of their high risk of hepatic lipidosis. Serum B_{12} concentration should be measured regularly and cobalamin should be supplemented parenterally as necessary. The correct diet for cats with pancreatitis has not been investigated. There is a paucity of low fat feline diets available and some authors have suggested that the amount of dietary fat does not matter in cats with pancreatitis: but we have anecdotally noted that feline pancreatitis cases appear painful when fed high fat diabetic diets, so would prefer to use intestinal type diets in these cases. These seem logical given the high prevalence of concurrent IBD.

Oxidative stress is increasingly recognised as important in humans in pancreatitis, so the use of anti-oxidants such as SAMe in cats with pancreatitis would be logical, although as with so many other treatments, there is no evidence currently to show whether they are beneficial.

In cats with end-stage disease, exocrine and/or endocrine deficiency may develop. Cats with EPI and/or DM are managed with enzymes and insulin as necessary in the usual way and most do surprisingly well long-term.

EPI in cats is almost exclusively due to end stage chronic pancreatitis, because pancreatic acinar atrophy is extremely rare in cats.

Treatment for inflammatory bowel disease should start with a careful single protein source novel diet and a course of metronidazole. If this doesn't resolve the clinical signs, prednisolone should be added in to the treatment. In cats with more severe inflammation or where small cell lymphoma is suspected, chlorambucil is often used in addition to prednisolone (Jergens 2012).

In all three diseases (cholangitis; pancreatitis and IBD) it is important to ensure that affected cats eat in order to avoid the development of concurrent hepatic lipidosis. David Morgan will be discussing diet in much more detail in these

proceedings (pages 15-28). A highly digestible, high-quality diet without protein restriction is often indicated. A diet formulated for feline intestinal disease might be the most appropriate (fig 3) because of the relatively high prevalence of concurrent inflammatory bowel disease. Cats may need a feeding tube placed and this should certainly be considered if the cat is having a general anaesthetic for biopsies.

Figure 3. Eukanuba Veterinary Diets Intestinal for Cats. It has a moderate fat content, beet pulp for the mucosal barrier and omega-3 fatty acids. Dry and canned versions can be mixed to maximize patient compliance.

References and further reading

- Armstrong PJ, Williams DA (2012). Pancreatitis in cats. *Topics in Companion Animal Medicine*; 27: 140-147
- Bazelle J, Watson P (2014). Pancreatitis in cats. Is it acute, is it chronic, is it significant? *Journal of Feline Medicine and Surgery*; 16: 395-406
- Callahan Clark JE, Haddad JL, et al (2011). Feline cholangitis: a necropsy study of 44 cats (1986-2008). *Journal of Feline Medicine and Surgery*; 13(8): 570-576
- De Cock HE, Forman MA, et al (2007). Prevalence and histopathologic characteristics of pancreatitis in cats, *Vet Pathol*; 44: 39-49
- Ferreri JA, Hardam E, et al (2003). Clinical differentiation of acute necrotizing from chronic nonsuppurative pancreatitis in cats: 63 cases (1996-2001). *Journal of the American Veterinary Medical Association*; 223(4): 469–474
- Forman MA, Marks SL, et al (2004). Evaluation of serum feline pancreatic lipase immunoreactivity and helical computed tomography versus conventional testing for the diagnosis of feline pancreatitis. *Journal of Veterinary Internal Medicine*; 18(6): 807–815
- Furneaux RW (2010). A series of six cases of sphincter of Oddi pathology in the cat (2008–2009). *Journal of Feline Medicine and Surgery*; 12(10): 794-801
- Gerhardt A, Steiner J M, et al (2001). Comparison of the sensitivity of different diagnostic tests for pancreatitis in cats. *Journal of Veterinary Internal Medicine*; 15: 329-333
- Kimmel SE, Washabau RJ, Drobatz KJ (2001). Incidence and prognostic value of low plasma ionised calcium concentration in cats with acute pancreatitis: 46 cases (1996-1998). *Journal of the American Veterinary Medical Association*; 219: 1105-1109
- Jergens AE (2012). Feline Idiopathic Inflammatory Bowel Disease: What we know and what remains to be unraveled. *Journal of Feline Medicine and Surgery*; 14(7): 445–458
- Marolf AJ, Leach L, et al (2012). Ultrasonographic Findings of Feline Cholangitis. *Journal of the American Animal Hospital Association*; 48(1): 36–42
- Marolf AJ, Kraft SL, et al (2013). Magnetic resonance (MR) imaging and MR cholangiopancreatography findings in cats with cholangitis and pancreatitis. *Journal of Feline Medicine and Surgery*; 15(4): 285-294

- Oppliger S, Hartnack S, et al (2013). Agreement of the Serum Spec fPL™ and 1,2-o-Dilauryl-Rac-Glycero-3-Glutaric Acid-(6'-Methylresorufin) Ester Lipase Assay for the Determination of Serum Lipase in Cats with Suspicion of Pancreatitis. Journal of Veterinary Internal Medicine; 27(5): 1077–1082

- Otte CMA, Penning LC, et al (2012). Retrospective comparison of prednisolone and ursodeoxycholic acid for the treatment of feline lymphocytic cholangitis. *The Veterinary Journal*: 195(2); 205-209

- Robertson SA, Taylor PM, Sear JW (2003). Systemic uptake of buprenorphine by cats after oral mucosal administration. *Veterinary Record*; 152(22): 675–678

- Rothuizen J, Bunch SE, et al (2006). WSAVA Standards for clinical and histological diagnosis of canine and feline liver disease. Philadelphia: Saunders Elsevier

- Simpson KW, Twedt DC, et al (2011). Culture-independent detection of bacteria in feline pancreatitis. Proceedings of the Forum of the American College of Veterinary Internal Medicine, June 15th to 18th

- Swift NC, Marks SL, et al (2005). Evaluation of serum feline trypsin-like immunoreactivity for the diagnosis of pancreatitis in cats. *Journal of the American Veterinary Medical Association*; 217(1): 37–42

- Twedt DC, Cullen J, et al (2014). Evaluation of fluorescence in situ hybridization for the detection of bacteria in feline inflammatory liver disease. *Journal of Feline Medicine and Surgery*; 16(2): 109-117

- Warren A, Center S, et al (2011). Histopathologic Features, Immunophenotyping, Clonality, and Eubacterial Fluorescence In Situ Hybridization in Cats With Lymphocytic Cholangitis/Cholangiohepatitis. *Veterinary Pathology*; 48(3): 627–641

- Weiss DJ, Gagne JM, Armstrong PJ (1996). Relationship between inflammatory hepatic disease and inflammatory bowel disease, pancreatitis, and nephritis in cats. *Journal of the American Veterinary Medical Association*; 209(6): 1114–1116

The nutritional management of triaditis

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Introduction

The domestic cat (*Felis catus*) provides many idiosyncratic diagnostic and treatment challenges for veterinarians across many disciplines of veterinary medicine. Some of these challenges are due to its unique physiology and metabolism that sets it aside from the domestic dog (*Canis lupus familiaris*). And, other challenges have as their basis some key anatomical differences between the two companion animal species. With feline triaditis we find some of these differences meeting head on to provide the clinician with an enigmatic disease that can be demanding from both a diagnostic and management perspective (fig 1). Firstly, to try and understand how triaditis could occur, it is important to remind ourselves of the cat's close anatomical relationship of its liver, small intestine and pancreas.

Figure 1. Cats with triaditis provide a diagnostic challenge for the clinician to make a definitive diagnosis as the presenting signs are often non-specific and in some cases they can be very subtle. Image courtesy of Dr Sarah Caney, www.vetprofessionals.com

Anatomical communication of the liver, pancreas and small intestine

The cat's gallbladder nestles in the cystic fossa between the quadrate and right medial lobes of the liver (Sebastiani and Fishbeck 2005). In the liver many small hepatic ducts converge to form two or more quite prominent hepatic ducts leading from the left lobes and right lateral lobe of the liver to join the cystic duct, which in turn is draining the gallbladder (fig 2). Together they now form the common bile duct that extends parallel with the hepatic portal vein. One key anatomical idiosyncrasy of the cat is in the arrangement of the common bile duct and main pancreatic ducts (one per pancreatic lobe) and that they all join together before exiting into the duodenum at the hepatopancreatic ampulla (fig 2). Therefore, in most cats (>80%) the pancreatic and biliary ducts unite (Zawie and Garvey 1984), a situation also seen in humans. And, in approximately 10-20% of cats an accessory pancreatic duct is also present, leading from the gastrosplenic portion of the pancreas and opens a short distance distal to the hepatopancreatic ampulla. When present, the accessory pancreatic duct does not communicate with the common bile duct.

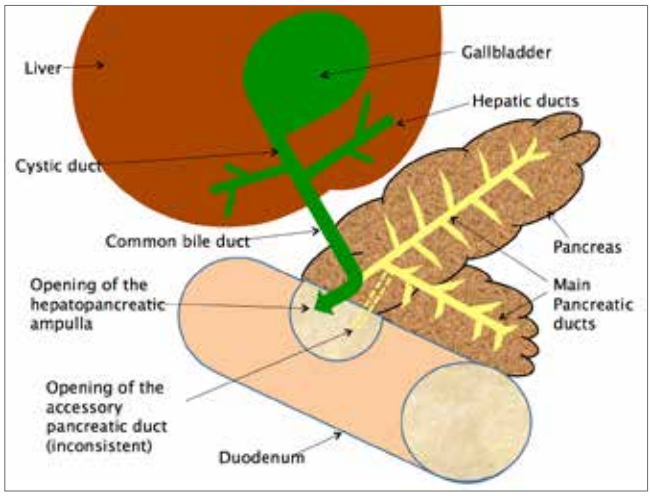


Figure 2. Anatomy of the pancreatic and biliary system in the cat.

The pancreas in the dog nearly always has two excretory ducts (Evans 1993, Mansfield 2012). The largest excretory duct is the accessory pancreatic duct which opens into the duodenum as the minor duodenal papilla. The pancreatic duct in the dog is the second and smaller duct, however it may occasionally be absent. The pancreatic duct's opening is adjacent to the opening of the common bile duct and usually enters the duodenum on the major duodenal papilla alongside the common bile duct. But, unlike the cat there is *no communication between these two ducts* before they enter the duodenum. The associated sheath of muscle fibres that make up the sphincter of Oddi (Evans 1993) helps

prevent duodenal contents from entering the pancreatic duct at the choledochoduodenal junction (Steiner 2008).

Triaditis

The close anatomical communication, through the combined bile and pancreatic ducts, and of the liver, pancreas and duodenum, is just one factor thought to predispose cats to concurrent inflammation in these three organs (see the text by Dr Penny Watson in these proceedings for more details on the proposed aetiology). An additional factor is that there is a very high bacterial colonization of the feline duodenum. It is reported that the feline duodenum has one hundred times more total bacteria (median, $>10^5$ cfu/ml: Johnston and others 2001) than that of the canine. Therefore, a single episode of vomiting due to one organ being affected can cause a reflux of duodenal secretions, including bacteria, to enter the liver and pancreas simultaneously. In one very recent study 33% of cats with inflammatory liver disease had intrahepatic bacteria detected by fluorescence in situ hybridization (FISH) and the predominant bacteria identified were common enteric forms such as *E coli* and *Enterococcus* species (Twedt and others 2014). In this study the frequent concurrent pancreatic and intestinal disease, alongside the intrahepatic distribution of enteric bacteria, actually suggested a possible translocation across the intestinal tract as a likely route of infection. And in another similar study, 35% of cats with acute, or chronic pancreatitis, when evaluated by FISH, had bacteria in their periductal areas or glandular parenchyma (Simpson and others 2011).

Nutritional management of triaditis

As there are important differences in the aetiology, pathogenesis and medical management of the three different conditions described under triaditis, then this section on the nutritional approach to its management will be subdivided with each disease being discussed separately. Advice will be given at the end of this section on how to manage the three diseases when they come together as triaditis.

1. Feline Inflammatory Liver Disease

Previously we have seen the terms *cholangitis/cholangiohepatitis complex* being described in the literature. The World Small Animal Veterinary Association (WSAVA) has helped to reconcile the terminology by using as the basis the type of cellular infiltrate which broadly classifies the cholangitis into three distinct forms: lymphocytic cholangitis, neutrophilic cholangitis and cholangitis with liver fluke (Van den Ingh and others 2006). They suggested that the term *cholangitis* rather than *cholangiohepatitis* be used as inflammation of the hepatic parenchyma is not a consistent feature and, if present, is usually an extension of a primary cholangitis. The neutrophilic form (previously termed *suppurative* or *exudative cholangitis/cholangiohepatitis*) is currently split by the WSAVA into two forms: neutrophilic and chronic neutrophilic cholangitis. The latter describes a mixed inflammation with lymphocytes and neutrophils and over-laps with previous reports of cholangiohepatitis or chronic cholangitis. This is the form of cholangitis usually considered to be part of the triaditis complex (Weiss and others 1996, Harvey and Gruffydd-Jones 2010, Cattin 2013). Inflammatory bowel disease (IBD) has been recognized as a coexisting feature in cholangitis and was diagnosed in 83% of cats with cholangitis in a retrospective pathologic study (Weiss and others 1996). And in the same study, coexisting pancreatitis was found in 50% of 18 cases with cholangitis, although a more recent publication has challenged such a strong association between cholangitis (hepatic involvement) and pancreatitis (Armstrong and Williams 2012). The close association of these entities may indicate a common underlying disease process in some cases. Neutrophilic cholangitis is understood to result from an ascending infection of the biliary tract from the intestine. However, chronic neutrophilic cholangitis could have other causes, as detailed in Dr Penny Watson's notes. It is possible that the presence of IBD may predispose to ascending infection. As already mentioned, intrahepatic bacteria have been observed in 33% of cats with inflammatory liver disease alongside a strong suggestion their source was due to translocation across the intestinal tract (Twedt and others 2014). Even more intriguing was that in this study all the 13 cats with intrahepatic bacteria had concurrent non-hepatic disease, predominantly pancreatic and intestinal.

Cats that are diagnosed with acute neutrophilic cholangitis will typically present with acute illness: anorexia, lethargy and pyrexia. There can be evidence of abdominal pain as

Figure 3. A cat showing ptyalism. Note the saliva staining on the nurse's tunic, around the cat's mouth and on its whiskers. Image courtesy of Dr David Miller, Johannesburg Veterinary Specialist Centre, South Africa.

well as vomiting and ptyalism (fig 3). The chronic form of neutrophilic cholangitis can result in milder and less specific clinical signs or waxing and waning signs that could be missed. Because cats with cholangitis can present with anorexia then our nutritional focus is on addressing this potentially serious problem.

Nutritional intervention: cholangitis

a) Cats with a history of anorexia (partial or complete)

Any cat with intractable anorexia, or even hyporexia (reduction of appetite) requires careful evaluation for primary or secondary hepatic lipidosis (HL) (Armstrong and Blanchard 2009). Proactive nutritional intervention is recommended in these cats when weight loss is above 10% (even in overweight cats), or when there has been partial (<85% daily intake of calculated energy requirements) or complete anorexia for more than 3 days. Anorexic cats, especially those overweight that then start to experience rapid weight-loss, have a high risk of developing HL. Under these conditions lipolysis of peripheral fat stores induces a dramatic increase of the concentration of free fatty acids in the blood. The free fatty acids enter the liver and can either be metabolized by beta-oxidation for energy, or esterified into triglycerides (TG) and stored in lipid vacuoles in the hepatocytes. Normally some of the TG would be incorporated into very low-density lipoproteins (VLDL) and secreted in the blood. Even though hepatic secretion of VLDL is actually increased in cats with HL, this is not sufficient to prevent TG overload of hepatocytes. In fact any systemically ill cat will generally develop some degree of hepatocelluar fatty vacuolation (Scherk and Center 2010). However, while hepatic TG accumulation is not always an issue, it does become problematic when the degree of vacuolation becomes severe. The TG content in the liver of cats with lipidosis averages 43% compared to 1% in healthy cats. Clinical experience indicates that the clinical syndrome can develop rapidly in overweight cats that undergo excessive calorie restriction, in approximately one week, or cats may only have been anorexic for as little as 2 to 7 days (Armstrong and Blanchard 2009). Cats of any age can be affected by HL and the clinical signs (inappetence, vomiting, lethargy and weakness) may now compound those of the underlying triaditis. HL has also been frequently associated with chronic pancreatitis (see page 22) which is not surprising given that anorexia and weight loss are typically seen in pancreatitis due to its chronic progression. The prevalence of pancreatitis lesions in cats with HL varies according to the study, from 5 to 38%. In one study a greater prevalence was seen with chronic pancreatitis (30%) than acute pancreatitis (10%) (Ferreri and others 2003). A very comprehensive review of feline hepatic lipidosis is Armstrong and Blanchard 2009.

One key aspect of an effective treatment regimen is client education and their participation in supportive care. HL can carry a poor prognosis, however, HL rarely reoccurs and therefore the client can be encouraged that their support will be invaluable in achieving successful recovery of their cat. A recovery rate of 80 to 88% can be seen if the primary disease is identified and treated successfully and the patient survives the first 72 hours of critical care support.

The cornerstone of HL therapy is enteral nutritional support centering on meeting protein and calorie requirements. A nasoesophageal tube should be inserted on the day of admission to help stabilize the patient and then an esophagostomy or gastrostomy tube can be placed a few days later when it is safe to anesthetise the cat (table 1). Enteral tube feeding is continued until voluntary intake resumes. A balanced diet is used that's rich in protein, moderate in lipids, which will deliver the required nutrients and the resting

Tube	Size	Use/remarks
Nasoesophageal	8 Fr with radiopaque marker (5 Fr for very small cats and brachycephalic breeds)	Available for immediate placement in any anorectic cat even while diagnostic tests are pending. Does not require sedation or anesthesia for placement. Verify correct positioning radiographically. Duration of use usually <2 weeks.
Esophagostomy	14 Fr	Requires short anesthesia for placement. Place after enteral support given for several days. Suitable for longer duration use (weeks to a few months).
Percutaneous gastrostomy	18 Fr	Requires short anesthesia for placement. Place after enteral support given for several days. Suitable for very long duration use (months).

Table 1. Enteral feeding tube choices: from Armstrong and Blanchard 2009

Diet	Calories (kcal/100g DM)	Protein (% DM)	Fat (% DM)	Carbohydrate (% DM)	Comments
Eukanuba Veterinary Diets High Calorie Canine & Feline	535	44	42	8	1.9 kcal/ml for tube feeding (undiluted). Warm diet to help make more liquid. Can be diluted with water and blended.
Royal Canin Convalescence Support Feline *Instant Diet*	478	42	25	19	1.1 kcal/ml (when reconstituted to 200ml = 1x 50g sachet + 150ml water).
Royal Canin Recovery Feline *Canned Diet*	421	51	22	9	1.1 kcal/ml 'as fed'.
Hill's™ Prescription Diet™ a/d™ Feline Critical Care	469	44	30	16	1.1 kcal/ml (undiluted). Warm diet to help make more liquid. Can be diluted with water and blended.
Abbott Animal Health CliniCare Canine/ Feline Liquid Diet	442	36	22	29	1.0 kcal/ml. Liquid form, suited for nasoesophageal tube feeding (5 or 8 Fr).
DM = Dry Matter					

Table 2. Examples of commercially available convalescence veterinary diets that can be used with a feeding tube (adapted from Bazelle and Watson 2014, and data taken from web sites [November 2014] or current product compendiums [January and October 2014]).

energy requirements (RER) (Scherk and Center 2010). The RER (the number of calories required for homeostasis while the animal rests quietly in a postabsorptive state) should be the *initial* caloric goal for the patient.

Calculating the RER for a cat uses a simple linear equation: kcal/day = (30 x body weight in kg) + 70 (Marks 2010b, Boysen and Freeman 2014) or an allometric equation: kcal/day = 70 x (body weight in kg)$^{0.75}$ (Marks 2010b) using either the current body weight (for cats with an ideal body weight) or if overweight then use the estimated ideal weight (Armstrong and Blanchard 2009). More recently there has been less emphasis on multiplying the RER by various 'illness factors' and present recommendations are to use a more conservative approach to energy requirements to avoid overfeeding (Marks 2010b, Chan 2013). Therefore, nutritional support should *initially* deliver sufficient calories and protein to meet the cat's RER at its current weight, adjusted for body condition (Marks 2010b). The final aim is to get the cat back up to its maintenance energy requirements (MER). A selection of diets suitable for enteral feeding is shown in Table 2.

Many cats with HL are initially volume sensitive. Two important aspects need to be considered: the amount of food per day and per meal and the interval between consecutive meals. The stomach volume of a cat with HL may be dramatically reduced to as little as 10% of its original volume. For prolonged anorexia then a good approach is to ultimately reach daily MER over an extended period (table 3). If the cat has experienced a relatively short period of anorexia then you can reach the *full RER* more rapidly: feed 1/3rd of the RER on day 1, 2/3^{rds} on day 2 and the full amount on day 3 (see page 30 in the addendum for an example calculation of RER and feeding regimen). Care has to be taken (no matter which choice of providing energy is chosen, over an extended period or over 3 days) because if feeding is instituted too rapidly then there is a potential risk of the *refeeding syndrome* (Brenner and others 2011). The refeeding syndrome is associated with caloric repletion (enteral or parenteral) of the starved patient and is characterized by the development of severe hypophosphataemia. It can also variably include hypokalaemia, hypomagnesaemia, vitamin deficiencies, fluid intolerance and glucose intolerance: with the return to feeding, anabolism is stimulated and insulin released, this leads to the cellular uptake of phosphorus

Days of refeeding	D1	D2	D3	D4	D5	D6 to D9	Until appetite is recovered
% of MER to cover	10-20	20-30	30-40	40-50	50-60	60-100	100
Kcal ME/kg optimal body weight	5-12	10-18	15-24	20-30	25-36	30-60	50 to 60
Number of meals (at least 3hr between meals)	4-5	4-5	4	4	4	4	4 to 3
ME = metabolizable energy, MER = maintenance energy requirement; 50 kcal ME/kg for neutered cats at optimal body weight							

Table 3. Suggested extended refeeding plan for cats with hepatic lipidosis (Armstrong and Blanchard 2009)

and inorganic phosphates, leading to hypophosphataemia. Carbohydrates and amino acids promote anabolism, and glycosis, leading to intracellular translocation of phosphorus, potassium and magnesium. It has been suggested that to avoid the refeeding syndrome in high risk cases that the human patient approach is made: use the patient's basal energy requirement rather than the RER and increase the caloric intake over 4-10 days rather than 3 days (Brenner and others 2011). However, *in any identified high risk feline patient* the electrolyte values (potassium, phosphorus and magnesium), and packed cell volume, should all be monitored daily until total RER is achieved.

TIP: Food boluses must be infused slowly, over approximately 1 minute, to allow for gastric expansion. Or continuous rate infusion (CRI) can be done. Feeding should be stopped at the first sign of gulping, retching, or salivating. The meals size should then be reduced by 50% for 12 hours and then increased gradually. After each meal the tube needs to be water-flushed to clear any food residue. When the patient is volume sensitive it is important to know the minimum volume required to flush the tube. On page 30 in the addendum there is a worksheet to help calculate the amount of energy and feeding volumes for a semi-liquid high calorie/convalescent diet. A useful reference for tube placement can be found in Marks 2010a.

Fig 4. Eukanuba Veterinary Diets High Calorie for Dogs & Cats. It has a high energy density (1.9 kcal/ml) making it ideal for tube feeding, contains beet pulp for mucosal barrier health and omega-3 fatty acids. For more product information go to pages 32-33.

Supplementation with other nutrients has been suggested but their use is still poorly scientifically documented in the cat. The most studied supplement is L-carnitine and some authors recommend it is provided at 250 to 500mg/day (based on obese healthy cats undergoing weight loss and its action in promoting fatty acid oxidation and retention of lean body mass), but evidence is lacking that it provides any benefit in recovery from HL. High calorie recovery diets, based on animal protein ingredients, will supply L-carnitine and therefore supplementation is not critical (fig 4).

In some cats a high protein diet will worsen signs of encephalopathy during the first few days of feeding. Attempts should be made to ameliorate this by feeding smaller amounts more frequently, rather than by reducing the protein content of the diet (Watson and Bunch 2009a). Long-term protein restriction is reserved only for patients with irrefutable signs of hepatic encephalopathy (Scherk and Center 2010).

2. Inflammatory Bowel Disease (IBD)

The World Small Animal Veterinary Association's Gastrointestinal Standardization group has defined idiopathic IBD as 'gastrointestinal signs of greater than 3 weeks in duration, incomplete response to dietary trials and anthelminthics, histologic lesions of mucosal inflammation on biopsy, and clinical response to immunomodulatory therapies' (WSAVA 2005, Trepanier 2009). The underlying pathogenesis is thought to be a disturbance in the mucosal

barrier, dysregulation of mucosal immunity, or disturbances in the microbiome (Hall and German 2010). Although the precise immunologic events of feline (and canine) IBD remain to be determined, a prevailing hypothesis for the development of IBD is the loss of immunologic tolerance to the normal microbiome (bacterial flora) or dietary antigens (suggested because of the clinical benefit of dietary therapy in some cases of IBD), leading to abnormal T cell immune reactivity in the gut microenvironment: IBD has been defined immunologically by the innate and adaptive response of the mucosa to gastrointestinal antigens. Therapy for IBD has therefore been aimed at reducing antigenic stimulation to the gut and modulating the local gut immune response. IBD can be extremely debilitating for the patient (fig 5).

Figure 5. Weight and muscle loss in a cat with IBD. Image courtesy of Dr David Miller, Johannesburg Veterinary Specialist Centre, South Africa.

Nutritional intervention: IBD

One critical first step in the management of IBD in cats is dietary manipulation. Even though idiopathic IBD is defined in part by an incomplete response to dietary trials, it's an important first step to take as part of a staged approach to IBD (Cave 2006, Trepanier 2009, Hall and German 2010). Indeed, some cats with even more severe inflammatory changes on their gastrointestinal (GI) histology (mild lymphocytic-plasmacytic enteritis, moderately severe lymphocytic-plasmacytic enteritis and severe eosinophilic enteritis), due to idiopathic GI problems, may respond to dietary manipulation alone (Guilford and others 2001). In this study almost 50% of the cats responded well to an

Fig 6. Eukanuba Veterinary Diets Lamb & Barley for Cats. It has a novel protein and carbohydrate combination, beet pulp for mucosal barrier health and omega-3 fatty acids. For more product information go to pages 34-35.

elimination diet. Novel protein (elimination) diets (fig 6) are designed to avoid exposure to proteins to which the cat's gut mucosal system may have been previously sensitized. They should always be considered for first line therapy of chronic GI disease in cats since they are associated with high response rates (Cave 2006, Trepanier 2009). Clients may need to be committed to a 4-6 week dietary trial, although a shorter period for response, 2-3 days, was seen in the cats shown to have food sensitivity (Guilford and others 2001). It has therefore been suggested that those cats with GI disease may only need up to 4 days for an elimination trial (Guilford and others 2001), although most times a longer period is recommended especially if there are concurrent dermatological signs. The problem that cat owners face when trying to implement any food trial is that there is easy access to other foodstuffs (particularly protein) if their cat goes outside, or if they have another cat in the household fed a different type of food. These scenarios could result in an apparent failure of any food trial, even if it is just due to licking clean another cat's bowl. Separating cats when they are fed is one option as is feeding all the cats the elimination diet.

An alternative to elimination/novel protein diets are the hydrolysed protein diets. Hydrolysis is undertaken to minimise the antigenicity of the intact protein sources which tend to be a common dietary protein. Hydrolysed protein diets have the advantage over an intact novel protein diet in the management of IBD because there is less concern about sensitization to the new diet during the initial treatment phase. The concern over a newly acquired dietary hypersensitivity has led to the concept of using ''sacrificial proteins'' when treating intestinal disorders due to the loss of oral tolerance. Theoretically, hydrolysed protein diets might lead to a more rapid improvement if inappropriate immune responses, directed against novel dietary antigens previously fed, are contributing to the ongoing enteritis (Cave 2006).

	Eukanuba Veterinary Diets	Royal Canin		Hill's™ Prescription Diet™	
	Lamb & Barley (can)	Hypoallergenic (dry)	Sensitivity Control (pouch) Chicken & Rice	z/d™ Low Allergen (dry)	d/d™ (can) Venison
Protein	Lamb liver, lamb lung, lamb	Hydrolysed soya protein isolate, hydrolysed poultry liver	Chicken liver, chicken meat	Rice protein concentrate, chicken liver hydrolysate, dried chicken liver hydrolysate	Venison, pea protein concentrate
Carbohydrate	Barley	Rice	Rice	Brewers' rice	Green pea flour
Fibre source	Beet pulp	Vegetable fibre, beet pulp	Vegetable fibre	Cellulose	Cellulose
Protein % DM	45	27	36	39	37
Fat % DM	30.4	21.1	25	15.6	30.4
DM = Dry Matter					

Table 4. Comparison of a selection of available feline veterinary diets indicated for IBD (data taken from web sites [November 2014] or current product compendiums [January and October 2014]).

However, the initial selection of a commercial hydrolysed protein diet for the cat should probably be based on the *actual* protein source unless the available commercial diet is sufficiently hydrolyzed to guarantee 100% the complete absence of all allergens (Cave 2006, Cave 2014). Therefore, it is prudent to select a diet that does not contain a protein source that the patient is known or suspected to be sensitized to (Cave 2006, Cave 2014). It should also be noted that there are other potentially intact proteins found in the carbohydrate and fat sources. These may not be subjected to the same degree of hydrolysis as the core protein used, therefore the whole diet also needs careful consideration (Cave 2014). Indeed, it has been seen in dogs that a significant proportion, 21%, prior sensitized to the intact compounds of soy and corn, still reacted adversely to a diet containing hydrolysed soy protein and cornstarch (Jackson and others 2003). And again in dogs, reactions were seen on a soy hydrolysate and rice based commercial diet but not to a soy-based homemade diet (Biourge and others 2004). Such reactions could be due to the creation of a new antigenic site (neoantigen) in the hydrolysed protein source during manufacturing, lack of destruction of the original epitope, an allergen within the carbohydrate complex or a hapten effect (Cave 2006, Cave 2014). Diarrhoea or lack of palatability can be a problem in some cats (Trepanier 2009), however, these hydrolysed diets do offer the clinician and patient another alternative for the sole therapy in the dietary management of IBD (Trepanier 2009). A good review on hydrolysed protein diets in dogs and cats is by Cave 2006. A selection of diets suitable for IBD is shown in Table 4.

Adjunct nutritional support: IBD

The use of both probiotics (*beneficial live microorganisms*) and prebiotics (*promotes the growth of beneficial micro-organisms*) to help modulate the enteric flora can be considered in IBD (Hall and German 2010); both have helped reduced intestinal inflammation in mouse models of IBD. There is some evidence supporting the efficacy of probiotics in humans with IBD, although effects are strain- and dose-specific. In one study using the prebiotics fructooligosaccharide (FOS) in cats there was no overall changes in the duodenal bacterial flora (Sparkes and others 1998a). However, there were beneficial changes to the colonic microflora (Sparkes and others 1998b). A secondary effect of prebiotics is the production of beneficial short chain fatty acids (SCFAs) through selective fermentation by beneficial microorganisms. In particular one SCFA, butyrate, is a key source of energy for the colonocytes lining the large bowel and is a key SCFA produced through fermentation of FOS. Mucosal disruption is seen in IBD and therefore any dietary component that promotes mucosal integrity should be considered. The most important stimulus for mucosal

cell proliferation is the direct presence of nutrients in the intestinal lumen (Marks 2010b). Short chain fatty acids can help promote mucosal integrity which is important to reduce the risk of bacterial translocation into the systemic circulation (Frossard and others 2008, Marks 2010b). This would be a prudent step given the current thinking on the translocation across the mucosal barrier of enteric bacteria as the source of intrahepatic bacteria in cases of feline inflammatory liver disease (Twedt and others 2014). Another option is to use a moderately fermentable fibre source such as beet pulp. Extensive studies have shown that in the cat beet pulp produces a favourable mix of short chain fatty acids, including butyrate, that will 'feed the gut' and help to promote mucosal health (Sunvold and others 1995a, 1995b). Poorly fermented fibres, such as cellulose, are generally considered not to provide the gut with energetic substrates.

Glutamine, a five carbon amino acid that plays a key role in the citric acid cycle, is the preferred fuel of the small intestinal mucosa and therefore its dietary presence is important to help maintain mucosal integrity. Supplementation into a diet mixture pre-manufacturing is difficult as it is very labile during the cooking process. However, diets with a good animal based protein supply will provide good levels of glutamine.

Omega-3 polyunsaturated fatty acids (PUFAs) also offer adjunctive therapy for IBD. This class of PUFAs decrease the formation of pro-inflammatory eicosanoids, such as leukotriene B4 (LTB4), which is also a potent neutrophil chemotactant. And, *in vitro* studies have shown that the twenty carbon omega-3 eicosapentaenoic acid (EPA), and twenty-two carbon docosahexaenoic acid (DHA) can change the lipid environment in membrane microdomains of tight junction and can prevent cytokine-induced intestinal permeability defects (Li and others 2008).

A final important consideration in cats with chronic GI disease is to assess cobalamin (vitamin B_{12}). Low cobalamin impairs normal enterocyte function through inhibiting nucleic acid synthesis and can contribute to ongoing malabsorption and clinical signs in affected cats. Studies indicate that cats have a very rapid turnover of cobalamin compared to humans (Simpson and others 2001). In cats with hepatic lipidosis 40% had subnormal values. And, low serum cobalamin appears to be common in cats with GI disease, especially those with a low body condition score (Reed and others 2007). It can be caused by ileal malabsorption (the site of exclusive cobalamin uptake), or dysfunction (either pancreatitis or exocrine pancreatic insufficiency). Pancreatic conditions are associated with impaired release of pancreatic intrinsic factor (in the dog intrinsic factor is produced by the stomach and pancreas, and in the cat it is exclusively from the pancreas), which is needed for cobalamin absorption, and impaired secretion of bicarbonate into the duodenum, which is necessary for cobalamin binding to intrinsic factor. The degree of hypocobalaminaemia in IBD correlates with the degree of histologic damage and a poorer prognosis, at least in dogs, and it would be logical to assume the same might be true in cats (Hall and German 2010). Parenteral supplementation of cobalamin is associated with improvement of clinical indices such as body weight and owner-reported signs of gastrointestinal disease (e.g. vomiting or diarrhoea) in some cats presented with gastrointestinal disease and hypocobalaminaemia (Ruaux and others 2005). Even with normal pancreatic function it has been reported that up to 30-40% of cats older than 12 years of age have problems absorbing cobalamin (Williams and Czarnecki-Maudlin 2014). It was shown that oral cobalamin supplementation in these geriatric cats (>12 years) with idiopathic chronic enteropathy, can effectively increase serum cobalamin, but following cessation of the supplementation the serum concentration decreases rapidly and can become subnormal again within as little as 4 weeks. If blood sampling reveals low cobalamin, then it should be supplemented parenterally.

3. Pancreatitis

Not too long ago we thought cats did not get pancreatitis until two case series came along in 1989 (Macy 1989) and 1993 (Hill and Van Winkle 1993), although feline pancreatitis had been recognized since the mid 1970's (Owens and others 1975, Duffell 1975). Acute, chronic active and chronic cases were described in the 1989 series and acute cases in the 1993 series. Then, slightly later, studies on cats with triaditis described that the pancreatitis associated with cholangiohepatitis tended to be *mild* (Weiss and others 1996). In this study mild periductular inflammation was the only pancreatic lesion observed in tissue sections from several cats. Intralobular acinar degeneration, when found, was focal or multifocal and involvement of pancreatic tissue was always less than ten percent. Diffuse inflammation, necrosis or haemorrhage was not observed. More recently the most common histologic form described in triaditis cases was chronic non-suppurative pancreatitis (Mansfield 2014). A mononuclear (often lymphocytic) inflammation occurs, along with disruption of the pancreatic architecture due to concurrent fibrosis: the amount of inflammation may be minimal and recurrent at the time of biopsy. As an aside, histologically *acute* pancreatitis is characterized by a neutrophilic inflammation and varying amounts of pancreatic acinar cell and peripancreatic fat necrosis without fibrosis or exocrine atrophy (Bazelle and Watson 2014). However, chronic disease is suspected to be more common

Figure 7.
A nasoesophageal tube can allow for immediate enteral nutrition and trickle feeding before a large diameter tube can be inserted.

Image courtesy of Dr Sarah Caney, www.vetprofessionals.com

than acute disease in cats (Armstrong and Williams 2012, Bazelle and Watson 2014).

In the 1996 study by Weiss and others, of the 18 cats with cholangiohepatitis, 83% had concurrent IBD and 50% had concurrent pancreatitis. In 39% of the cats, cholangiohepatitis, IBD and pancreatitis all occurred together: this is what is referred to as triaditis. It has been proposed that pancreatitis could result from inflammation or blockage of the distal portion of the common bile duct, which may induce ascending infection or reflux of pancreatic secretions (Weiss and others 1996). And, there are a number of other major hypotheses as to why there could be a relationship between IBD and pancreatitis (Mansfield 2014): (1) inflammation in the gut may cause distant inflammation in the pancreas through up-regulation of inflammatory mediators or their receptors, (2) there may be inflammation in response due to enteric bacteria that have traveled from the intestine to the pancreas. Indeed enteric bacteria have been identified in 35% of pancreases of some cats affected by acute or chronic pancreatitis (Simpson and others 2011). Interestingly, in humans it was Claude Bernard in 1856 who suggested that bile reflux into the common pancreatic duct could trigger acute pancreatitis (Bernard 1856). In humans, as in cats, the pancreatic duct joins the common bile duct before exiting into the duodenum. It is therefore also proposed that in vomiting cats, commonly seen with IBD or cholangitis, the intraluminal pressure may be raised and further increase the risk of pancreaticobiliary reflux (Washabau 2013). Finally, it is also possible that all three organs are affected by a similar immune-mediated process as is seen in humans.

Nutritional intervention: pancreatitis

It should be stated that most of the recommendations for the treatment of feline pancreatitis have been mainly derived by extrapolating human studies. However, it is important to recognize that nutrition remains one of the key cornerstones of treatment, alongside controlling emesis, correction of fluid and electrolyte imbalances, and analgesia. The long-held belief that food should be withheld for 24-48 hours in cases of pancreatitis (acute, acute on chronic or chronic) has been challenged in both human and companion animal patients. Bowel rest is associated with intestinal mucosal atrophy and increased infectious complications due to bacterial translocation from the gut (Frossard and others 2008), therefore you need to 'feed the gut' as soon as possible. Nutrients such as glutamine, and short chain fatty acids, are important respectively for the small and large intestine's mucosal integrity. This may require initial placement of a nasoesophageal tube (fig 7) for a few days allowing for small amount of nutrients to enter the gastrointestinal system (trickle feeding). Cats are often presented with a history of anorexia of several days' duration and commonly show evidence of accompanying hepatic lipidosis. The risk of developing lipidosis is increased by pancreatitis. Therefore, to overcome the associated risk of hepatic lipidosis, and given that starvation is detrimental

to the feline patient, then it is now accepted that feeding should be started as soon as the patient can accept calories (as soon as vomiting is controlled) (Armstrong and Williams 2012, Washabau 2013, Bazelle and Watson 2014).

Proactive nutritional intervention is recommended in cats if, (1) voluntary food intake is not restored rapidly: when there has been partial (<85% daily intake of calculated resting energy requirements) or (2) complete anorexia for more than 3 days. In these pancreatitis patients (acute, acute on chronic, chronic) then the placement of feeding tubes is required once any intractable vomiting is brought under control: nasoesophageal (fig 7, see previous page), oesophagostomy and gastrostomy (fig 8) tubes are commonly used. Ultimately, there is a need to 'feed the gut' and maintain enterocyte integrity and reduce the risk of bacterial translocation. Studies in human patients indicate that enteral nutrition (by nasogastric or nasojejunal feeding) can attenuate the systemic inflammatory response syndrome and may decrease complications (Frossard and others 2008). If the patient is too unstable for anaesthesia then a nasoesophageal tube can be placed for a few days to help stabilize the patient before placement of a larger bore and more secure tube. A useful reference for further reading on tube placement is Marks 2010a. Because of the smaller bore of nasoesophageal tubes (e.g. 5Fr [for very small cats or brachycephalic breeds] to 8Fr) then a liquid convalescence veterinary diet needs to be used (fig 9). With the larger oesophagostomy (e.g. 14 to 15Fr polyvinyl feeding tube) and gastrostomy tubes (e.g. 18Fr) then a semi-liquid convalescence/high calorie veterinary diet can be fed (table 2). These diets are energy dense and have a high protein and fat content (fig 4) and are appropriate for the initial enteral feeding of the pancreatitis patient, despite their high fat content. It is beneficial to have a diet with a high energy density (calories/ml) to help meet the cat's RER through the feeding of small volumes. To avoid the risk of the refeeding syndrome then a gradual introduction of the recovery diet is recommended. A fermentable fibre such as beet pulp can, through fermentation in the gut, aids in providing energy for the cells of the mucosal barrier to help maintain gut wall barrier function. Incorporation of omega-3 fatty acids also has potential benefits (see sections on fibre and fatty acids on pages 21-22). As the voluntary appetite returns, small amounts of food can be offered frequently with an intestinal diet that can be fed long-term (fig 10). The size of the meals should be slowly increased and the frequency of feeding decreased if vomiting does not reoccur. Table 5 shows the protein and fat content of some typical cat veterinary diets available for long-term feeding of the pancreatitis patient.

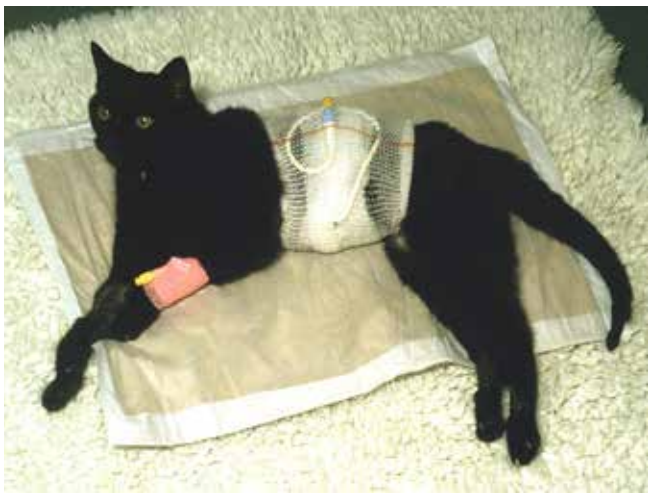


Figure 8. A gastrostomy tube can allow for semi-liquid recovery/ high calorie convalescent diets to be fed. Image courtesy of Dr Sarah Caney, www.vetprofessionals.com

Figure 9. Because of the smaller tube diameter of a nasoesophageal tube, then a liquid recovery diet is required in this cat with pancreatitis. Image courtesy of Dr Sarah Caney, www.vetprofessionals.com

If the cat voluntarily accepts food and its caloric intake is being met effectively (>85% daily intake of calculated resting energy requirements [RER]) then feeding a moderate fat intestinal diet (fig 10) can be undertaken and the patient can be maintained long-term on the diet. Feeding little and often may help with any reduced appetite and avoid feeding canned food that has just been refrigerated as it will be too cold for the cat, let it warm to room temperature. To maximize the success of nutrition it is important to recognize and treat any nausea seen in the patient as this can severely reduce food intake (Bazelle and Watson 2014). Cats can demonstrate overt signs such as vomiting or hypersalivation (fig 3, see page 16), but there can also be more subtle and non-specific signs such as anorexia.

	Eukanuba Veterinary Diets		Royal Canin		Hill's™ Prescription Diet™		Typical Diet *
	Intestinal (dry)	Intestinal (can)	Gastrointestinal Moderate Calorie (dry)	Gastrointestinal Moderate Calorie (pouch)	i/d™ (dry) Original	i/d™ (can) Minced with chicken	Adult cat life-stage
Protein % DM	35.9	43.5	37.6	40	40.5	37.5	38
Fat % DM	14.1	17.4	13.7	15.4	20	24.2	23.9
DM = Dry Matter							

*Table 5. Comparison of available moderate fat feline intestinal veterinary diets indicated for pancreatitis (data taken from web sites [November 2014] or current product compendiums [January and October 2014]). * A typical cat diet is given for comparison of protein and fat levels.*

The reality is that the number of calories and type of nutrient mixtures have yet to be established in cats with pancreatitis and clinical experience suggest that a (very) low fat food does not seem to be necessary (Armstrong and Williams 2012, Bazelle and Watson 2014). The general recommendation is to feed a low carbohydrate, high protein and *moderate* fat diet (fig 10) to help avoid malnutrition and hepatic lipidosis. ***The simple advice is to avoid a high fat diet long-term.***

Note: in pancreatitis patients, with concurrent HL, the dietary recommendation of feeding a high fat recovery diet for the attendant HL does not change in the initial management stage of the anorexic pancreatitis cat. Convalescence/high calorie diets are energy dense and have a high protein content, this makes them suitable for hospitalised patients in this initial stage (table 2, see page 18). The recommendation is to provide enteral nutrition as soon as possible once any intractable vomiting is controlled (Watson and Bunch 2009a). Once the cat has sufficient voluntary intake of calories then it can be moved to a moderate fat diet for maintenance.

Fig 10. Eukanuba Veterinary Diets Intestinal for Cats. It has a moderate fat content, beet pulp for the mucosal barrier and omega-3 fatty acids. Dry and canned versions can be mixed to maximize patient compliance. For more product information go to pages 36-37.

Parenteral nutrition

If the cat has severe malnutrition and persistent anorexia, then parenteral nutrition (PN) can be considered. However, all attempts should be made to provide *some* enteral nutrition to help maintain the gut wall barrier function (Frossard and others 2008). A useful reference on PN is Chan 2010.

Adjunct nutritional support of pancreatitis

From reports in human medicine there is compelling experimental and clinical evidence for the important role oxidative stress plays in the pathophysiology of chronic pancreatitis. Increased oxidative stress has been implicated as a potential mechanism in the aetiopathogenesis of chronic pancreatitis. A number of studies have demonstrated that patients with chronic pancreatitis have compromised antioxidant status, which may be a contributing factor to the enhanced oxidative state associated with the disease (Grigsby and others 2012). Supplementation with antioxidants leads to reduction in oxidative stress and can be associated with a reduction in abdominal pain (Tandon and Garg 2011).

For cats an antioxidant commonly used is S-adenosyl-methionine (SAMe), an important hepatocellular metabolite and glutathione donor with hepatic and systemic antioxidant

Figure 11. A cat with EPI. Note the weight loss, poor coat condition and greasy fur around the perianal region and back legs that indicates poor fat digestion.

Image courtesy of Dr Sarah Caney, www.vetprofessionals.com

effects. Oral administration of SAMe in healthy cats increases plasma SAMe and liver glutathione. The commonly used dosage of SAMe is 35 to 60 mg/kg PO q24 hours. Medical grade SAMe (Denosyl, Nutramax Laboratories, Inc., Edgewood, MD, USA) is recommended. For optimal absorption, SAMe must be given as an intact tablet on an empty stomach (ideally 1 hour before feeding). Finally, based on data from human patients with pancreatitis, consideration may need to be given to using a combination of antioxidants in cats, such as SAMe, vitamin C, vitamin E, and/or selenium.

Nutrition of Exocrine pancreatic insufficiency (EPI) and diabetes mellitus (DM)

EPI: the loss of acinar tissue, due to end stage chronic pancreatitis, is believed to be the main cause of exocrine pancreatic insufficiency (EPI) in the cat (Bazelle and Watson 2014). Diagnostic screening for EPI (fig 11) would be prudent in a cat suspected to have triaditis. Cats with EPI are often best managed on a novel protein intestinal type diet because of the high incidence of concurrent IBD. Eukanuba Veterinary Diets Dermatosis LB (fig 6) is one recommendation from the literature (Watson and Bunch 2009b). If the cat also has DM then the recommendation is not clear as to what type of diet to feed, an intestinal diet or a propriety feline diabetes diet? (Watson and Bunch 2009b). One important consideration in cases of DM would be to make sure there was both dietary consistency and an established feeding routine.

Practical Advice: what to feed cats with triaditis?

The final, and key question, is what's the *best* diet to feed the cat that *actually* does have cholangitis, IBD and pancreatitis? In cats with multiple diseases, as seen in triaditis, it can be difficult to identify which disorder is most clinically relevant (Armstrong and Williams 2012). All may need attention so as to treat and manage the patient most effectively. We have been aided by greater diagnostic capabilities for pancreatitis, and a greater understanding of the pathogenesis of IBD, but the cat still needs to be managed optimally, both medically and nutritionally.

If the cat is not meeting its nutritional intake of calories, or has lost weight (>10%), and is at risk of hepatic lipidosis, or has already developed hepatic lipidosis, then the cat needs pro-active nutritional support in the form of enteral (tube) feeding. This will inevitably mean a high protein, high fat, low carbohydrate convalescent diet such as High Calorie (fig 4, see page 19). Such high protein, high fat diets are not believed to be contraindicated if the cat has pancreatitis and *needs* initial enteral tube feeding or is inappetent due to cholangitis, but they are not the limited antigen/novel protein diets, or hydrolysed protein diets, as recommended for IBD. However, any cat that has reduced calorie intake/anorexia/weight loss is a risk and therefore the implementation of tube feeding *has* to be undertaken. Once the cat is stable, taking in adequate calories voluntarily then the patient can be slowly transitioned onto a long-term maintenance

veterinary diet. But which diet? The recommendation is to use a moderate fat intestinal diet (fig 10, see page 25) to help manage the pancreatitis as our first choice. It does appear that if cats are fed a high fat diet *they do seem to show post-prandial pain*, they are just less 'vocal' about this pain than dogs which may give a clinical impression that high fat diets are fine. If the IBD flares-up then the novel/limited protein diets, as well as hydrolysed diets, can provide support for IBD cases during these periods of recrudescence, however they are generally high(er) in fat (table 4, see page 21) than the intestinal type diets (table 5, see page 25) and all attempts should be made to move the cat back onto the low(er) fat intestinal diet.

References and further reading

- Armstrong PJ, Blanchard G (2009). Hepatic Lipidosis in Cats. *Vet Clin N Am Small Anim Pract*; 39: 599-616
- Armstrong PJ, Williams DA (2012). Pancreatitis in cats. *Topics Comp Anim Med*; 27 (3): 140-147
- Bazelle J, Watson PJ (2014). Pancreatitis in cats. Is it acute, is it chronic, is it significant? *JFMS*; 16: 395-406
- Bernard C (1856). Leçons de physiologie experimentale. Paris. Bailliere; 2: 278. *Cited in*: Frossard JL, Steer ML, Pastor CM (2008). Acute pancreatitis. *Lancet*; 371: 143-152
- Biourge VC, Fontaine J, Vromm MW (2004). Diagnosis of adverse reactions to food in dogs: efficacy of a soy-isolate hydrolyzate-based diet. *J Nutr*; 134: 2062S–2064S
- Boysen S, Freeman LM (2014). Medical and nutritional management of critical care patient structure. In: Proceeding WSAVA, Cape Town, South Africa, 16th – 19th September: 466-468
- Brenner K, KuKanich KS, Smee NM (2011). Refeeding syndrome in a cat with hepatic lipidosis. *JFMS*; 13: 614-617
- Cattin I (2013). Feline triaditis. *Veterinary Focus*; 23(2): 2-8
- Cave NJ (2006). Hydrolzed protein diets for dogs and cats. *Vet Clin N Am Small Anim Prac*; 36: 1251-1268
- Cave NJ (2014). Hydrolysed Diets. Royal Canin Webinar, UK, 27th August
- Chan DL (2010). Parenteral nutritional support. In: Textbook of Veterinary Internal Medicine. Eds. Ettinger SJ & Feldman EC, Saunders Elsevier, St Louis, Missouri, USA: 7th Edition; Chapter 179: 701-707
- Chan DL (2013). Making a difference – nutritional support in critically ill patients. *Veterinary Focus*; 23 (1): 8-13
- Duffell SJ (1975). Some aspects of pancreatic disease in the cat. *JSAP*; 16: 365-374
- Evans HE (1993). The pancreas. In: Miller's Anatomy of the dog. Ed. Evans HE. Saunders, Philadelphia, USA, 3rd Edition: 458-462
- Ferreri JA, Hardam E, et al (2003). Clinical differentiation of acute necrotizing from chronic nonsuppurative pancreatitis in cats: 63 cases (1996–2001). JAVMA; 223: 469-474
- Frossard JL, Steer ML, Pastor CM (2008). Acute pancreatitis. *Lancet*; 371: 143-152
- Grigsby B, Rodriguez-Rilo H, Khan K (2012). Antioxidants and chronic pancreatitis: theory of oxidative stress and trials of antioxidant therapy. *Dig Dis Sci*; 57(4): 835-841
- Guilford WG, Jones BR, et al (2001). Food sensitivity in cats with chronic idiopathic gastrointestinal problems. *JVIM*; 15: 7-13
- Hall EJ, German AJ (2010). Diseases of the small intestine. In: Textbook of Veterinary Internal Medicine. Eds. Ettinger SJ & Feldman EC, Saunders Elsevier, St Louis, Missouri, USA: 7th Edition; Chapter 270: 1527-1572
- Harvey AM, Gruffydd-Jones TJ (2010). Feline inflammatory liver disease. In: Textbook of Veterinary Internal Medicine. Eds. Ettinger SJ & Feldman EC, Saunders Elsevier, St Louis, Missouri, USA: 7th Edition, Chapter 278: 1643-1648

- Hill RC, Van Winkle TJ (1993). Acute necrotizing and acute suppurative pancreatitis in the cat: a retrospective study. *JVIM*; 7: 25-33
- Jackson HA, Jackson MW, et al (2003). Evaluation of the clinical and allergen specific serum immunoglobulin E responses to oral challenge with cornstarch, corn, soy and a soy hydrolysate diet in dogs with spontaneous food allergy. *Vet Dermatol*; 14 (4): 181–187
- Johnston KL, Swift NC, et al (2001). Comparison of the bacterial flora of the duodenum in healthy cats and cats with signs of gastrointestinal tract disease. *JAVMA*; 218:45-51
- Li Q, Zhang Q, et al (2008). n-3 polyunsaturated fatty acids prevent disruption of epithelial barrier function induced by proinflammatory cytokines. *Mol Immunol*; 45 (5): 1356-1365
- Macy DW (1989). Feline pancreatitis: In: Current Veterinary Therapy X. Eds. Kirk RW & Bonagura JD, WB Saunders, Philadelphia, PA, USA: 893-896
- Mansfield CS (2012). Acute pancreatitis in dogs: advances in understanding, diagnostics, and treatment. *Top Companion Anim Med* 27:123-132
- Mansfield CS (2014). Triaditis in cats – does it exist? In: Proceeding WSAVA, Cape Town, South Africa, 16th - 19th September: 111-113
- Marks SL (2010a). Nasoesophageal, esophagostomy, gastrostomy, and jejunal tube placement techniques. In: Textbook of Veterinary Internal Medicine. Eds. Ettinger SJ & Feldman EC, Saunders Elsevier, St Louis, Missouri, USA: 7th Edition, Chapter 85: 333-340
- Marks SL (2010b). The principles and implementation of enteral nutrition. In: Textbook of Veterinary Internal Medicine. Eds. Ettinger SJ & Feldman EC, Saunders Elsevier, St Louis, Missouri, USA: 7th Edition, Chapter 182: 715-717
- Ownes JM, Drazner FH, Gilbertson SR (1975). Pancreatic disease in the cat. *JAAHA*; 11: 83-89
- Reed N, Gunn-Moore D, Simpson K (2007). Cobalamin, folate and inorganic phosphate abnormalities in ill cats. *JFMS*; 9: 278-288
- Ruaux CG, Steiner JM, Wiliams DA (2005). Early biochemical and clinical responses to cobalamin supplementation in cats with signs of gastrointestinal disease and severe hypocobalaminemia. *JVIM*; 19: 155-160
- Sebastiani AM & Fishbeck DW (2005). Accessory Digestive Organs. In: Mammalian Anatomy: The Cat. Eds Sebastiani AM & Fishbeck DW. Morton Publishing Company, Colorado, USA, 2005. Chapter 4: 90-102
- Scherk MA, Center SA (2010). Toxic, Metabolic, Infectious, and Neoplastic Liver Diseases. In: Textbook of Veterinary Internal Medicine. Eds. Ettinger SJ & Feldman EC, Saunders Elsevier, St Louis, Missouri, USA: 7th Edition; Chapter 280: 1672-1689
- Simpson KW, Fyfe J, et al (2001). Subnormal concentrations of cobalamin (vitamin B_{12}) in cats with gastrointestinal disease. *JVIM*; 15: 26-32
- Simpson KW, Twedt DC, et al (2011). Culture-independent detection of bacteria in feline pancreatitis. In: 21st ACVIM Forum, Denver, Colorado, USA, June 15-18
- Sparkes AH, Papasouliotis K, (1998a). Bacterial flora in the duodenum of healthy cats, and effect of dietary supplementation with fructo-oligosaccharides. *AJVR*; 59: 431-435
- Sparkes AH, Papasouliotis K, (1998b). Effect of dietary supplementation with fructo-oligosaccharides on fecal flora of health cats. *AJVR*; 59: 436-440
- Steiner (2008). Exocrine pancreas. In: Small Animal Gastroenterology. Ed. Steiner JM. Schlutersche Verlagsgeselleschaft mbH & Co.KG, Hannover. Chapter 8: 283-307
- Sunvold GD, Fahey GC, (1995a). In vitro fermentation of selected fibrous substrates by dog and cat fecal inoculum: Influence of diet composition on substrate organic matter disappearance and short-chain fatty acid production, *Journal of Animal Science*; 73: 1110-1122
- Sunvold GD, Fahey GC, (1995b). Dietary fiber for cats: In vitro fermentation of selected fiber sources by cat fecal inoculum and in vivo utilization of diets containing selected fiber sources and their blends, *Journal of Animal Science*; 73: 2329-2339
- Tandon RK, Garg PK (2011). Oxidative stress in chronic pancreatitis: pathophysiological relevance and management. *Antioxid Redox Signal*; 15(10): 2757-2766
- Trepanier L (2009). Idiopathic inflammatory bowel disease in cats. *JFMS*; 11: 32-38
- Twedt DC, Cullen J, et al (2014). Evaluation of fluorescence in situ hybridization for the detection of bacteria in feline inflammatory liver disease. *JFMS*; 16(2): 109-117
- Van den Ingh TSGAM, Cullen JM, et al (2006). Morphological classification of biliary disorders of the canine and feline liver. In: WSAVA Liver Standardization Group; Standards for Clinical and Histological Diagnosis of Canine and Feline Liver Diseases. Saunders; 61-76
- Washabau RJ (2013). Necrosis and inflammation: feline. In: Washaubau RJ and Day MJ (eds). Canine and Feline gastroenterology. 1st ed. St Louis: Saunders Elsevier: 821-848
- Watson PJ and Bunch SE (2009a). Hepatobiliary disease in the cat. In: Small Animal Internal Medicine. Eds: Nelson RW & Couto CG, Elsevier, St Louis, Missouri, USA. 4th Edition; Chapter 37: 521-540
- Watson PJ and Bunch SE (2009b). The exocrine pancreas. In: Small Animal Internal Medicine. Eds: Nelson RW & Couto CG, Elsevier, St Louis, Missouri, USA. 4th Edition; Chapter 40; 579-606
- Weiss DJ, Gagne JM, Armstrong PJ (1996). Relationship between inflammatory hepatic disease and inflammatory bowel disease, pancreatitis, and nephritis in cat. *JAVMA*; 209 (6): 1114-1116
- Williams DA, Czarnecki-Maudlin G (2014). Cobalamin concentration in geriatric cats with idiopathic malabsorption, but concentrations decrease rapidly following cessation of supplementation. ECVIM-CA Congress, Mainz, Germany, September 4th to 6th [abstract]
- WSAVA (2005). http://www.wsava.org/educational/gastrointestinal-standardization-project
- Zawie DA, Garvey MS (1984). Feline hepatic disease. *Vet Clinic N Am Small Anim Pract*; 2: 1201-1230

Addendum

Practical feeding examples for High Calorie recovery diets

Worksheet to calculate energy requirements and feeding amounts

Step 1. Calculate the cat's resting energy requirements (RER)

(30 x current BWKg) + 70 =

(30 x_____) + 70 =_____ Kcal/day

Step 2. Calculate milliliters of the feeding formula required/day

MER (Kcal/day)/Feeding formula (Kcal/ml) = ml formula/day

_____ /_____=_____ml/day

Step 3. Administration schedule based on gradual refeeding

1/3 of total requirement on day 1 =_____ml/day

2/3 of total requirement on day 2 =_____ml/day

Total requirement on day 3 =_____ml/day

Step 4. Calculate milliliters per feeding on days 1, 2 and 3

(Milliliters/day)/(Desired number feedings day) = Milliliters/per feed

_____ /_____=_____ml/per feed

Example

4.5kg cat and Eukanuba Veterinary Diet High Calorie (1.9Kcal/ml), to be fed 4 times a day

Step 1

RER: (30 x 4.5) + 70 = 205 Kcal/day

Step 2

ml/day: 205/1.9 = 107 ml/day

Step 3; total milliliters per day:

day 1 is 107 X 0.33 = 35 ml

day 2 is 107 X 0.66 = 70 ml

day 3 is 107 X 1 = 107 ml

Step 4: milliliters per feeding

day 1 is 35 / 4 = 9ml

day 2 is 70 / 4 = 18ml

day 3 is 107 / 4 = 27ml

TOP TIPS:
our recommendations for tube feeding Eukanuba Veterinary Diet High Calorie

- **Warm undiluted food to body temperature (37.7-38.8°C). This can easily be done by placing the can in a container or a sink of hot (54-60°C) tap water for five minutes. Warming is physiologically better for the patient and prepares the food to pass through the tube with minimal resistance.**
- **High Calorie is 1.9kcal/ml undiluted. Can be used with a 12 French gauge tube. If it's needed, to make passing of the diet easier, add 25ml of warm water and then liquidize the mixture for 5 minutes giving a final concentration of ≈1.7kcal/ml**
- **Liquidise (5 min) 1 tin of High Calorie with 50ml – 75ml warm water for tube feeding through 10 French gauge or bigger tubes: this gives a final concentration of ≈1.5 to 1.3 kcal/ml respectively.**
- **Liquidise (5 min) 1 tin of High Calorie with 75ml – 100ml warm water for tube feeding through 8 French gauge tubes: this gives a final concentration of ≈1.3 to 1.2 kcal/ml respectively.**
- **Flush tubes with 5ml lukewarm water before and after tube feeding. Care in cats with hepatic lipidosis that are volume sensitive.**
- **Administer the total daily feeding over *at least* 3 meals.**

High Calorie for Cats

Nutritional management of stress and recovery conditions

PRODUCT AVAILABILITY AND PACKAGING

170g

INDICATIONS

- Routine/Major Surgery
- Hyperthyroidism
- Hepatic Lipidosis
- Trauma
- Lactation
- Convalescence
- Show/Performance
- Anorexia/Cachexia/ Malnutrition
- Cancer
- Anaemia
- Sepsis
- Severe burn/injury
- Patients requiring tube feeding
- Patients unable to tolerate a dry formula
- Puppies and Kittens

MAY ALSO BE PRESCRIBED TO NUTRITIONALLY MANAGE:

- Underweight Diabetics
- Conditions that may benefit from moderate sodium restriction
  - – Cardiovascular Disease
  - – Congestive Heart Failure

CONTRAINDICATIONS

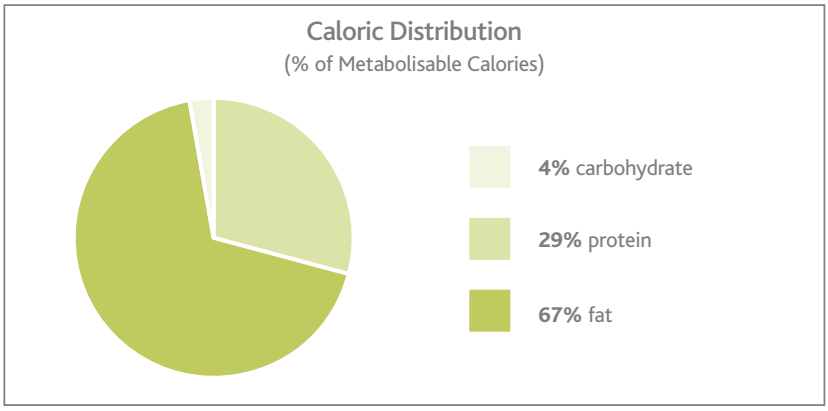
- Chronic renal failure

NUTRITIONAL PROFILE

- **Our most nutrient and calorie dense therapeutic canned diet** - important for recovery and weight gain
- **High quality, animal-based protein** - helps maintain and build muscle mass, promotes wound healing, helps repair muscle and replaces red blood cells, thereby aiding in recovery and repair
- **Targeted omega-6:omega-3 fatty acid ratio** - helps nutritionally manage inflammation at the cellular level and supports a healthy immune system response

NUTRIENTS TO HELP MANAGE OVERALL HEALTH AND WELL-BEING

- **Vitamin E** - an antioxidant to help maintain a strong immune system
- **Beet pulp** - a moderately fermentable fibre that produces butyrate, a short chain fatty acid (SCFA), which is a preferential energy source for the enterocytes and promotes intestinal health



COMPOSITION

Chicken, animal fat, rice, dried beet pulp, fish oil, potassium chloride.

ANALYTICAL CONSTITUENTS

Nutrient/Ingredient		Nutrient/Ingredient	
Protein:	16.0%	Phosphorus:	0.20%
Fat content:	15.0%	Sodium:	0.065%
Omega-6 fatty acids:	1.35%	Vitamin A:	2500IU/kg
Omega-3 fatty acids:	0.27%	Vitamin D_3:	325IU/kg
Crude Ash:	1.60%	Vitamin E (α-tocopherol):	27mg/kg
Crude Fibres:	0.50%	kcals/kg: *	1928
Moisture:	64.00%	MJ/kg: *	8.0
Calcium:	0.25%		

*Metabolizable Energy (Atwater)

FEEDING GUIDELINES

Weight	Feeding for Weight Maintenance (cans per day)	Feeding for Weight Gain (cans per day)
4kg	⅔ - ¾	1 - 1¼
8kg	1¼ - 1⅔	2 - 2⅓

TUBE FEEDING

- Warm undiluted food to body temperature (37.7-38.8°C). This can be done easily by placing the can in a container or a sink basin of hot (54-60°C) tap water for five minutes. Warming is physiologically better for the patient and prepares the food to easily pass through the tube.
- High Calorie will pass through a 2.7mm, 8 French gauge tube.
- Administer the total daily feeding in at least 4 meals.

TRANSITION PRODUCTS

Eukanuba Cat Adult or Senior products

Iams Cat Adult or Senior products

EUKANUBA VETERINARY DIETS

Dermatosis LB for Cats

Nutritional Management of inflammatory skin conditions

PRODUCT AVAILABILITY AND PACKAGING

Canned Formula

170g

PRIMARY INDICATIONS

- Inflammatory Skin and Coat Conditions
- Pruritic Dermatitis (atopic, flea-bite, contact)
- Food Allergy/Intolerance
  - Chronic Otitis Externa
- Eosinophilic Granuloma Complex
- Miliary Dermatitis

MAY ALSO BE PRESCRIBED TO NUTRITIONALLY MANAGE:

- Gastrointestinal disorders associated with food allergy or intolerance:
  - Inflammatory Bowel Disease
  - Colitis
  - Chronic Gastroenteritis
  - Intestinal Pathogen Overgrowth
  - Vomiting
  - Malabsorption/Maldigestiony

CONTRAINDICATIONS

- Allergy to Lamb
- Allergy to barley

NUTRITIONAL PROFILE

- **Novel protein and carbohydrate sources** - lamb/barley to reduce food allergy and intolerance
- **Targeted omega-6:omega-3 fatty acid ratio** - helps nutritionally manage atopy and inflammation at the cellular level
- **Beet pulp** - a moderately fermentable fibre that produces butyrate, a short-chain fatty acid (SCFA), which is a preferential energy source for the enteroycytes and promotes intestinal health. Helps optimal stool consistency.

NUTRIENTS TO HELP MANAGE OVERALL HEALTH AND WELL-BEING

- **Vitamin E** - an antioxidant to help maintain a strong immune system
- **High quality animal-based protein** - vital for skin & coat health

COMPOSITION

Lamb liver, lamb lung, lamb, barley, maize oil, dried beet pulp, dicalcium phosphate, calcium carbonate, potassium chloride, sodium chloride.

ANALYTICAL CONSTITUENTS

Nutrient/Ingredient		Nutrient/Ingredient	
Protein:	10.5%	Phosphorus:	0.20%
Fat content:	7.0%	Magnesium:	0.02%
Omega-6 fatty acids:	1.30%	Vitamin A:	10000IU/kg
Omega-3 fatty acids:	0.26%	Vitamin D_3:	125IU/kg
Crude Ash:	1.90%	Vitamin E (α-tocopherol):	25mg/kg
Crude Fibres:	0.50%	Beet pulp:	0.9%
Moisture:	77.00%	kcals/kg: *	1156
Calcium:	0.25%	MJ/kg: *	4.8

*Metabolizable Energy (Atwater)

FEEDING GUIDELINES

Weight	Feeding (cans per day)
2kg	½ - ¾
4kg	1 - 1½
6kg	1⅔ - 2¼
8kg	2¼ - 3
10kg	2⅔ - 3¾

TRANSITION PRODUCTS

Dermatosis LB for cats is complete and balanced for long term feeding under veterinary supervision.

EUKANUBA VETERINARY DIETS

Intestinal for Cats

Nutritional management of intestinal disorders

PRODUCT AVAILABILITY AND PACKAGING

Dry Formula
1.5kg

Canned Formula
170g

INDICATIONS

- Acute and Chronic Gastroenteritis
- Small and Large Bowel Diarrhea
- Colitis
- Inflammatory Bowel Disease
- Constipation
- Dietary Indiscretion
- Megacolon
- Exocrine Pancreatic Insufficiency
- Malabsorption/Maldigestion
- Pancreatitis
- Antibiotic Responsive Diarrhea (ARD)
- Short Bowel Syndrome

MAY ALSO BE PRESCRIBED TO NUTRITIONALLY MANAGE:

- Recovery Conditions
  - – Intestinal Surgery
  - – Severe Parasitism
  - – Cancer

CONTRAINDICATIONS

- Growth
- Reproduction
- Lactation

NUTRITIONAL PROFILE

- **MOS (mannanoligosaccharides)** - binds potentially pathogenic bacteria preventing them from adhering to the intestinal wall and excreting them safely with the faeces*
- **Beet pulp** - a moderately fermentable fibre that produces butyrate, a short chain fatty acid (SCFA), which is a preferential energy source for the enterocytes and promotes intestinal health. Helps regain optimal stool consistency.
- **FOS (fructooligosaccharides)** - prebiotics which aid in GI health and have been shown in a clinical study to help maintain the balance between beneficial and potentially pathogenic bacteria
- **Low fat levels** - decrease the workload of the pancreas and help digestive function that can be compromised by GI issues. Help minimise steatorrhea.
- **Targeted omega-6: omega-3 fatty acid ratio** - helps nutritionally manage inflammation at the cellular level

*Demonstrated in vivo with species other than dog and cat.

NUTRIENTS TO HELP MANAGE OVERALL HEALTH AND WELL-BEING

- **Vitamin E** - an antioxidant to help maintain a strong immune system
- **High quality animal-based protein** - aids in recovery and overall health and well-being

COMPOSITION

Dry: Dried Chicken and Turkey, maize, maize grits, animal fat, dried beet pulp, dried whole egg, chicken digest, brewer's dried yeast, fructooligosaccharides, potassium chloride, calcium carbonate, fish oil, mannanoligosaccharides, sodium chloride.

Canned: Chicken, chicken liver, beef by-products, rice, white fish, maize grits, fish meal, dried whole egg, dried beet pulp, potassium chloride, fructooligosaccharides, calcium carbonate, brewer's dried yeast, monosodium phosphate, mannanoligosaccharides.

ANALYTICAL CONSTITUENTS

Nutrient/Ingredient	Dry	Canned	Nutrient/Ingredient	Dry	Canned
Protein:	33.0%	10.0%	Sodium:	0.40%	0.10%
Fat content:	13.0%	4.0%	Vitamin A:	12000IU/kg	5250IU/kg
Omega-6 fatty acids:	2.25%	0.50%	Vitamin D_3:	900IU/kg	100IU/kg
Omega-3 fatty acids:	0.30%	0.10%	Vitamin E (α-tocopherol):	140mg/kg	14mg/kg
Crude Ash:	6.70%	1.60%	Magnesium:	0.085%	
Crude Fibres:	1.90%	0.50%	Beet pulp:	4.4%	0.85%
Moisture:	8.00%	77.00%	FOS:	0.73%	0.2%
Calcium:	1.20%	0.25%	MOS:	0.15%	0.05%
Phosphorus:	0.95%	0.20%	kcals/kg: *	3585	1011
Potassium:	0.85%	0.25%	MJ/kg: *	15.0	4.2

*Metabolizable Energy (Atwater)

FEEDING GUIDELINES

Weight	Dry Feeding (grams per day)	Canned Feeding (cans per day)
2kg	30-40g	⅔ - ¾
3kg	40-60g	
4kg	55-80g	1¼ - 1⅔
5kg	70-100g	
6kg	85-115g	1¾ - 2½
8kg	110-155g	2⅓ - 3⅓
10kg	140-195g	3 - 4¼

TRANSITION PRODUCTS

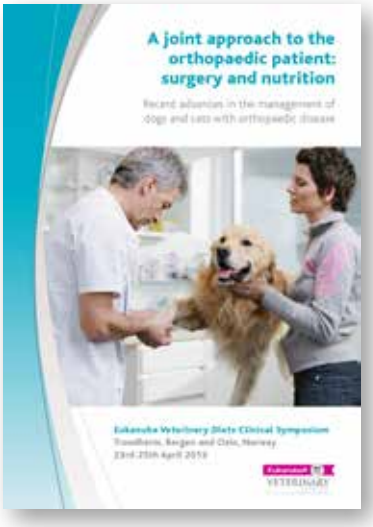
Eukanuba Cat Adult or Senior Products.

Iams Cat Adult or Senior products Dry & Wet

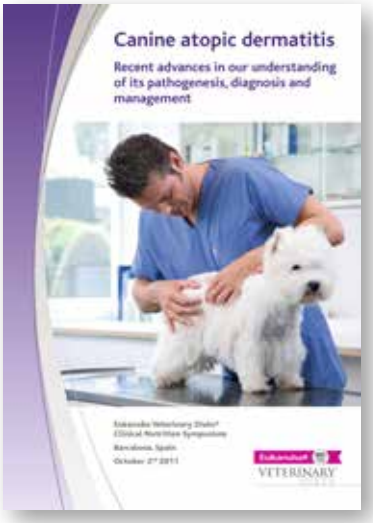
EUKANUBA VETERINARY DIETS

Symposia Proceedings

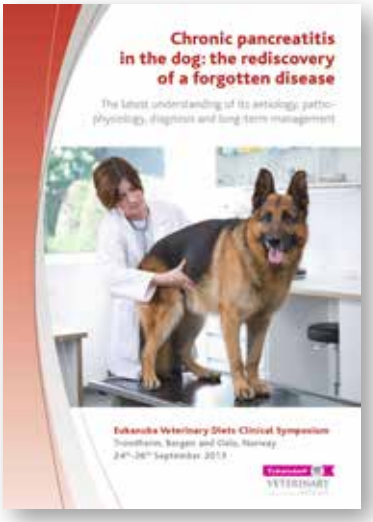
Other symposia proceedings from a selection of European experts are available and cover a range of subjects.
To download a PDF copy of each proceeding please go to: **http://petproducts.no/no/forhandlernett/**



A joint approach to the orthopaedic patient: surgery and nutrition



Canine atopic dermatitis



Chronic pancreatitis in the dog; the rediscovery of a forgotten disease

Veterinary dentistry

Managing renal disease for improved patient outcome

Triaditis in the cat, an enigmatic and challenging condition

Practical clinical advice on its diagnosis and management

P&G Pet Care

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