

**Chronic Diarrhoea in Cats**; including Triaditis,  
Feline Inflammatory Bowel Disease and Associated Diseases

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**INTRODUCTION**

**Causes of diarrhoea.**

- Diarrhoea is a common clinical sign in cats. It can be associated with a large number of different disorders, including primary gastrointestinal tract (GIT) diseases and extra-intestinal diseases (such as hyperthyroidism). There are many differentials for both acute and chronic diarrhoea (**Table 1**). However, cases are not always straightforward, and some differentials can cause both acute and chronic clinical signs.

**Diagnosis.**

- A good **clinical history** is essential in gaining information to tailor the diagnostic and therapeutic approach. Careful questioning will help to indicate the likelihood of extra-intestinal disease, or highlight potential causes for the diarrhoea such as dietary change, environmental factors, infectious agents, drugs or toxins. In multi-cat households, the presence of clinical signs in multiple cats usually indicates an infectious or environmental aetiology. Unfortunately, the duration and frequency of clinical signs can be difficult to determine in cats that have access to the outdoors as can the differentiation between acute and chronic diarrhoea, and small and large intestinal diarrhoea. **Table 2** details some of the clinical signs that can help to distinguish between diarrhoea of small intestinal and large intestinal origin. However, in cats, these differences are usually less marked than in dogs, and many of cats with diarrhoea have features of both. Interestingly, some cats with colonic inflammation present with constipation rather than diarrhoea.
- **Physical examination** should help to determine the presence of extra-intestinal disease (e.g palpable thyroid nodule), or the need for more aggressive investigations or treatment (e.g. dehydration, tachycardia/bradycardia, weak peripheral pulses, abdominal discomfort, palpable abnormalities suggestive of a foreign body, mass or intussusception).
- **Where the investigation goes next is usually dependant on whether or not there is evidence of systemic disease or obvious findings on clinical examination** (e.g. a gut mass requiring surgery).
- **If there is no evidence of systemic disease or obvious findings on clinical examination:**
  - In cases of acute diarrhoea affecting only one cat, with no other associated clinical signs and no detectable abnormalities on physical examination, it is acceptable to instigate non-specific symptomatic therapy (i.e. 12 hour period of starvation followed small frequent meals of a bland diet e.g cooked chicken, Hills i/d, Waltham/Royal Canin Sensitivity Control, or similar) without further investigations. It is also advisable to administer broad-spectrum worming treatments (e.g Drontal Cat® {praziquantel and pyrantel embonate} Bayer; Milbemax® {milbemycin oxime and praziquantel} Novartis) particularly if recent worming history is poor.
  - If the diarrhoea has become chronic or if more than one animal in the household is affected, then full faecal analysis is the next diagnostic step.

- **Faecal parasitology** - It is important to examine fresh faeces (ideally <2 hours old) as with time any eggs, oocysts or larvae may not stay in a diagnostic state. In order to see the motile trophozoites of *T. foetus* faeces needs to be <1 hour old, ideally <10 minutes. It is also important to check with your laboratory to ascertain which infectious agents are being looked for and by which methodology. For example, sedimentation techniques are preferable for recovery of larvae that may be present in only small numbers, but this can result in more faecal debris, making it difficult to find very small organisms such as coccidia oocysts and Giardia cysts, which can be more readily detected using a floatation technique.
  - **Methods for detecting faecal parasites include:**
  - **Direct smears** - These are used to recover trophozoite stages of parasites (e.g. *T. foetus* and Giardia spp). The smear should be made with saline as water can rupture the trophozoites. Negative smears are not uncommon if parasite levels are low. Smears can also be stained to look for bacteria.
  - **Faecal flotation** - This method is used to recover nematode ova, coccidia oocysts and Giardia cysts. A centrifugation flotation technique will markedly increase the sensitivity of detecting organisms. Fragile cysts can sometimes become too distorted to identify.
  - The ability to float depends on the organism having a lower specific gravity than the flotation medium. The use of zinc sulphate as the flotation medium will improve detection of Giardia cysts. The method employed for flotation is very important and preparations need to be examined as soon as possible since any delay will distort delicate oocysts so that they are missed or incorrectly identified.
  - **Antigen detection tests** are available for a number of different organisms (see individual sections).
- **Faecal cultures** are often performed in cats presenting with diarrhoea, however they are usually of limited diagnostic value since potentially enteropathogenic bacteria are frequently isolated from healthy animals, making it difficult to interpret the clinical significance of any positive results. If an infectious aetiology is suspected, which is often based on the history or presence of acute onset haemorrhagic diarrhoea or concurrent evidence of sepsis, then faeces should be cultured for specific pathogens including Salmonella, Campylobacter and *Clostridium perfringens* and *C. difficile*.
- **Where there is evidence of systemic disease or obvious findings on clinical examination** or there is persistence or recurrence of chronic diarrhoea despite dietary trial and exclusion of gastro-intestinal infectious agents:
  - Further investigations should include a **complete blood count** and **serum biochemistry** to investigate the possibility of underlying systemic diseases, and to look for potential consequences of intestinal disease such as anaemia from enteric blood loss, and hypoproteinaemia resulting from severe infiltrative diseases (e.g intestinal lymphoma, severe IBD). In elderly cats serum thyroxine should also be measured to exclude hyperthyroidism. Serological screening for FeLV and FIV should also be performed. Serum should be sent for assessment of **serum folate and cobalamin (B<sub>12</sub>)** levels and **feline trypsin-like immunoreactivity (FTLI)** and **feline pancreatic lipase immunoreactivity (fPLI)** activity (see sections on Inflammatory Bowel Disease [IBD] and pancreatitis).
  - Survey **abdominal radiographs** are of limited benefit in the majority of cats with diarrhoea but are important to perform if a foreign body, intussusception or mass is suspected.
  - **Abdominal ultrasonography** is useful for detecting masses, intestinal wall thickening and/or loss of layering, intussusceptions, mesenteric lymphadenopathy, liver disease and pancreatic involvement.
  - Occasionally, the use of **contrast radiography**, for example administration of barium impregnated polyspheres (BIPS) may be useful for demonstrating partial obstructions or motility disorders.
  - If no diagnosis has been made at this point (and the animal is not extremely ill) an acceptable approach is to **perform a dietary trial**. A large number (30-50%) of cats with chronic diarrhoea will respond well to an exclusion diet, eg boiled chicken and water only for 2-3 weeks.
  - If a diagnosis has not yet been reached following the above investigations, then **gastrointestinal biopsies** may be indicated. If the decision for gastrointestinal biopsies has been made, the next decision to make is whether endoscopic or full thickness biopsies are to be taken. Endoscopic biopsies are generally most appropriate initially, although full thickness biopsies may be needed at

a later stage if a diagnosis is not reached and there is poor response to symptomatic therapy. If ultrasonographic abnormalities have been detected (e.g mesenteric lymphadenopathy, focal intestinal thickenings, abnormalities of the submucosa/muscularis) then full thickness biopsies are more appropriate. When endoscopy is performed, both upper and lower endoscopy should ideally be performed, since small intestinal disease will often be present even if clinical signs are more suggestive of diarrhoea of large intestinal origin. Unfortunately, endoscopy misses disease located in the distal small intestine, which is a common site for inflammatory bowel disease and intestinal lymphoma.

### Treatment.

- The first decision to make regarding treatment is whether or not the cat requires hospitalisation and more intensive treatment and monitoring. If diarrhoea is acute in onset and significant abnormalities are detected on physical examination, then hospitalisation may be required. In addition, very young animals, particularly those with profuse watery diarrhoea can very quickly become severely dehydrated, so it is preferable to hospitalise and administer intravenous fluid therapy early in the course of disease.
- A **12 hour period of starvation**, followed by the introduction of small frequent meals of bland food (eg cooked chicken) is the commonest treatment option for simple acute diarrhoea where the cat is otherwise well. Oral water intake should be maintained and oral electrolyte/glutamine supplementation may also be beneficial.
- **Probiotics** are used to try to repopulate the intestine with beneficial bacteria e.g. *Bifidobacter*, *Lactobacilli* and *Enterococcus faecium*. **Prebiotics** (eg fructo-oligosaccharides [FOS] and inulin) are used to try to change the substrate of the intestinal flora and promote the growth of more beneficial populations. Several of these types of products are now commercially available for use in dogs and cats. Whilst there is some data available to support their use, more studies are needed to investigate their use. They may be particularly useful when diarrhoea is caused by diet change (eg associated with rehoming, hunting, or introduction of a prescription diet), or when diarrhoea results from drug administration (eg antibiotics, chemotherapy).
- In critically ill or anorexic patients **microenteral nutrition** may be beneficial. This delivers small amounts of water, electrolytes and readily absorbable nutrients (glucose, amino acids and small peptides) to the intestinal tract to help preserve the integrity of the intestinal mucosal barrier and hence help to prevent bacterial translocation. Solutions containing glutamine are particularly useful for this purpose (eg Glutalyte® Norbrook Companion Animal Range), since this is the preferred energy source for the intestinal epithelium.
- **Antibiotics** are not indicated unless a specific bacterial agent had been identified or if there is evidence of intestinal ulceration (ie haemorrhage), in which case antibiotics should be initiated in order to reduce the risk of septicemia as a result of bacterial translocation through the damaged mucosal barrier.
- **Corticosteroids** are contraindicated, and in many cases (eg infectious diseases, pre-existing mucosal damage) will prove detrimental. They are generally only indicated where IBD is very strongly suspected and preferably when it has been confirmed on histopathology. Even then, many cats with mild to moderate IBD can be controlled with dietary therapy alone or, possibly, with the addition of metronidazole or tylosin (see section on IBD).
- **Sulphasalazine** is a 5-aminosalicylic acid derivative that is frequently used as a treatment for acute colitis in dogs. Sulphasalazine is a prodrug that in dogs is cleaved by colonic bacteria, releasing the active drug which acts locally in high concentrations in the colon as an anti-inflammatory agent. However, in cats salicylates are readily absorbed (particularly if there is any small intestinal disease) and can induce toxicity so they should only be used with great caution.
- **Adsorbents** are frequently administered in acute diarrhoea to bind bacteria and toxins, to protect the intestinal mucosa, and potentially for an antisecretory effect. Commercially marketed adsorbents include kaolin, pectin and montmorillonite. In most products the adsorbent is combined with other agents e.g. Promax ® (montmorillonate, probiotics and glutamine), Diarsanyl® (montmorillonate, electrolytes), Kaobiotic® (kaolin and neomycin).
- **Motility modifiers** - anticholinergics (e.g. hyoscyne) are not recommended as they can promote or exacerbate ileus. Opiates (e.g. diphenoxylate, loperamide) predominantly reduce intestinal secretions and promote absorption, in addition to stimulating segmental intestinal contractions, and so can on occasion be

useful in the short-term management of acute diarrhoea. However, their use is not advisable in young kittens and they should not be used if an obstructive or infectious aetiology has not been excluded.

- **Treating and controlling infectious causes of diarrhoea** (general guidelines, but using Giardia as an example):
  - Treat all affected and in-contact animals
  - Use the least toxic drug options first. e.g. the most commonly used treatments for Giardia are fendendazole and/or metronidazole. Fenbendazole is recommended as a first line treatment, and if treatment fails with this alone, metronidazole can be added in.
  - Healthy uninfected cats should be separated from symptomatic cats and from infected but asymptomatic cats
  - Any new animals should also be kept separately
  - Faecal debris should be removed from any animals with diarrhoea
  - Litter trays should be cleaned and disinfected daily with quaternary ammonium compounds to kill cysts, or bleach (diluted 1:32).
  - Where possible, housing should also be treated with quaternary ammonium compounds
  - If there is a vaccine available, consider using it.

## INTESTINAL INFECTIONS

### Pathogenesis and clinical signs.

- In most cases, for an infectious agent to cause diarrhoea the '**Epidemiological Triad**' involving **infectious agent** (number of organisms, presence of virulence factors, etc.), **host animal** (age, immune status, state of its GIT, stress, etc.) and **environmental pressure** (housing conditions, stocking density, diet changes, antibiotics, recent surgery, etc.) all come into play.
- **Asymptomatic carriage is common and disease is seen most frequently in young animals (<6 months)**, especially if they are **group housed, stressed** (e.g. rescue or stray populations), **and/or fed raw food**. Infectious diarrhoea is therefore seen most commonly in young or immuno-compromised animals, or those housed in large numbers of unhygienic conditions. The prevalence of infections may also vary with geographic location, whether or not the cat is an indoor or outdoor animal, and whether or not it hunts and eats its prey. Episodes of disease may be seen in kittens or cats of similar ages, and may be preceded by a stressful event such as an environment change, diet change, addition of new cats, or weaning, etc.
- Clinical signs vary but typically include **diarrhoea and vomiting**, and in some cases **anorexia** may also be present.
- **Asymptomatic carriage means potentially harmful organisms** can be found in many apparently healthy animals. For example, depending on the population investigated **Cryptosporidium can be found in up to 12% of healthy cats, Giardia in up to 14%, Salmonella in up to 18% and Campylobacter in up to 45%**.
- **For infection to arise a number of steps have to occur:**
  - Faecal contamination of environment, food, or water
  - Ingestion by host
  - Ability to overcome host defences, such as secretions (gastric acid, digestive enzymes), GI motility, mechanical barriers (mucus, enterocytes, tight junctions), immunoglobulins (IgA), competition with resident flora, and immune responses
  - Reach preferred site and attach to or invade cells
- **A number of different situations can lead to compromise of the host defences and therefore predispose to the development of infection, these include:**
  - Reduced digestive secretions, and/or reduced ability to digest and/or absorb nutrients e.g. with IBD or exocrine pancreatic insufficiency (EPI)
  - Motility disorders e.g. ileus
  - Presence of enterotoxins
  - Increased gut permeability or damage to enterocyte tight junctions

- Reduced levels of immunoglobulins, especially IgA
  - Administration of antibiotics (which leads to alterations in resident microflora populations)
  - Immuno-suppression, can result from chemotherapy, corticosteroids, FeLV, FIV, uraemia, malnutrition, etc.
  - Presence of foreign body, obstruction, or abrasions
- Many infectious causes of diarrhoea are **potentially zoonotic** so when any animal presents with diarrhoea owners should be given appropriate advice regarding hygiene and told to preventing contact between the affected animal and any immuno-compromised individuals.
- Intestinal infections that can affect cats and may cause clinical signs such as weight loss and chronic diarrhoea and/or vomiting include **viruses** (parvovirus, enteric coronavirus, intestinal FIP, FIV, FeLV, Toravirus, Astrovirus, Rotavirus), **bacteria** (Campylobacter, Salmonella, Clostridium, *E. coli*, Yersinia, Mycobacteria), **protozoans** (coccidians *Isoospora felis*, *I. Rivolta*, *Cryptosporidium parvum* and *Cryptosporidium felis* and flagellates *Giardia lamblia* and *Tritrichomonas foetus*), **nematodes** (large ascarid roundworms *Toxocara cati* and *Toxascaris leonina*, and hookworms *Ancylostoma braziliense*, *A. tubaeforme* and *Uncinaria stenocephala*), and **cestodes** (tapeworms *Dipylidium caninum* and *Taenia taeninaeformis*). **Parvovirus, T. cati and Isoospora spp. are the most common infections of kittens. Campylobacter, Salmonella, G. lamblia, D. caninum and T. taeninaeformis are the most common infections of adult cats.**
- **Feline panleukopenia** (FPV) is a highly contagious parvovirus infection of cats that can cause severe acute diarrhoea and death. It is very similar to canine parvovirus in terms of its pathogenicity and gastro-intestinal signs. Mortality in young kittens is very high, however it rarely causes chronic disease, and the wide spread use of vaccination has reduced the prevalence of FPV-associated diarrhoea. (*For more extensive notes on this infection please contact the author*).
  - **Feline enteric coronavirus** is a ubiquitous virus which may cause self-limiting diarrhoea in infected kittens, and occasionally causes chronic disease in susceptible individuals. It is believed that mutation of enteric coronavirus can result in the development of feline infectious peritonitis (FIP). Although diarrhoea is not usually a feature of FIP, isolated intestinal granulomas resulting in diarrhoea have been reported. (*For more extensive notes on this infection please contact the author*).
  - **FIV** is often associated with chronic diarrhoea, but immuno-suppression following infection also increases susceptibility to other infectious agents that may result in acute diarrhoea. **FeLV** has been associated with a fatal peracute enterocolitis and lymphocytic ileitis. (*For more extensive notes on these infections please contact the author*).
  - **Toravirus** has been linked with ‘third eye-lid prolapse and diarrhoea syndrome’ where the diarrhoea is usually self limiting but can persist for weeks to months.
- Gastrointestinal infections with **potentially pathogenic bacteria** usually result in acute diarrhoea. However, they are also often isolated from animals with chronic diarrhoea, and in these situations the significance of infection is unclear, as they may also be isolated from clinically healthy animals (see above).
  - Most **Campylobacter** (*C. jejuni* and *C. upsaliensis*) infections are asymptomatic, with the organism being isolated in up to 45% of healthy cats and dogs. Clinical disease is usually restricted to young, parasitized, or immuno-compromised animals. More severe disease may be encountered if there is concurrent infection with other bacterial, viral or parasitic enterotides.
  - Most **Salmonella** infections are asymptomatic, with up to 18% of healthy cats carrying the bacteria. Bacterial translocation from the intestinal tract may occur resulting in septicaemia and endotoxaemia. Infected cats may show vague mild signs without any evidence of gastrointestinal disease, but development of an acute febrile illness with or without diarrhoea has also been reported.
  - Enterotoxin-producing **Clostridium perfringens** have been associated with both acute and chronic diarrhoea, however enterotoxin has also been detected in faeces of healthy animals so its role in causing

- diarrhoea is controversial. The clinical significance of *C. difficile* is also unknown but it has been incriminated as a cause of chronic diarrhoea in some cases.
- Many strains of *E.coli* are normal intestinal commensals, however some strains may result in acute diarrhoea, whilst other strains may cause chronic diarrhoea. Enterotoxigenic strains of *E.coli* have been associated with acute diarrhoea, but the identification of pathogenic strains requires specialised assays, so the significance of positive isolation alone is debatable.
  - *Yersinia pseudotuberculosis* infection may occur in cats following ingestion of infected rodents or birds. Severe diarrhoea, weight loss, jaundice and mesenteric lymphadenopathy follows and the disease is often fatal. *Y. enterocolitica* can be a commensal of the GIT but is rarely a cause of acute colitis.
  - *Mycobacterium* spp. infection, especially *M. avium*, may occasionally involve the gastrointestinal tract (GIT) resulting in diarrhoea, vomiting, mesenteric lymphadenopathy and weight loss. (*For more extensive notes on this infection please contact the author*).
  - Adult *T. cati* and *T. leonina* live in the **small intestine** of cats. Eggs are passed into the environment with the faeces to be ingested by other cats. With *T. cati* these **migrate via the liver and lungs** to the small intestine. With *T. leonina* they **mature in the wall of the small intestine**.
    - While *T. cati* larvae can be **transmitted lactationally** to kittens, prenatal infection does not occur with either parasite.
    - Rodents can act as transport hosts.
    - *T. cati* (but not *T. leonina*) can cause **visceral larva migrans in humans**.
    - Clinical signs are uncommon and in adult cats infections are usually subclinical. Young kittens with very heavy burdens can develop small bowel diarrhoea, vomiting, abdominal discomfort, a pot bellied appearance, poor coat condition, a failure to thrive and, rarely, intestinal obstruction/intussusception.
  - The prevalence of **hookworms** varies. *Ancylostoma* spp. prefer **warm, humid climates**, while *U. stenocephala* can live in **colder climates**. Severe hookworm infections are usually seen in warm, moist climates.
    - Adult hookworms live in the **small intestine** of cats. Eggs are passed into the environment with the faeces and then hatch. They can be ingested by other cats or infect them by **skin penetration**.
    - Lactational and prenatal infections do not occur.
    - Rodents can act as transport hosts.
    - Infection can cause **cutaneous larva migrans in humans**.
    - Infections cause less disease in cats than dogs, and most disease is seen in young adult cats that live in poorly-cleaned, crowded conditions. A heavy infection can cause weight loss, poor coat condition and melaena.
  - Adult **tapeworms** live in the **small intestine** and both *D. caninum* and *T. taeninaeformis* require an **intermediate host** to complete their life cycle. Gravid proglottids containing many eggs are released from the adult worms. They may rupture within the intestines, or remain intact and pass out in the faeces and be seen around the cat's anus.
    - **Dog and cat fleas** and lice are the **intermediate hosts** for *D. caninum*.
    - Rodents are the intermediate hosts for *T. taeninaeformis*.
    - Infections are usually subclinical, but heavy infections can occasionally cause anal pruritus, vomiting, diarrhoea, weight loss and, occasionally, intestinal obstruction.
  - *Isospora* spp. are the commonest coccidial agents of cats (*I. neorivolta*, *I. felis*, *I. rivolta*). Up to 2% of feline faecal samples are infected. Infection occurs following ingestion of oocysts or paratenic hosts. They live in **intestine** of cats and shed oocysts into the environment via the faeces. Sporulated oocysts can be directly ingested by other cats.
    - Rodents harbouring cyst stages can act as transport hosts.
    - Infection and clinical disease (diarrhoea) is seen most commonly in kittens kept in large unhygienic groups.

- Infection rarely causes clinical disease in adult cats unless they are stressed or immuno-compromised. In kittens, infections can range from subclinical through to severe haemorrhagic diarrhoea.
- *C. parvum* and *C. felis* live in the **small intestine** and sheds oocysts that can either break open to release sporozoites into the intestine resulting in chronic infection or be passed out into the environment where they can remain viable for many months.
  - In cats *C. felis* is the species seen most commonly.
  - Infection can cause severe disease in immuno-deficient animals and occasionally humans.
  - Infections are usually subclinical, but can also cause acute or chronic small bowel diarrhoea, or result in lymphocytic-plasmacytic duodenitis. This infection can be found in 4-8% of cat faecal samples, and 1.5-2% of canine samples.
- In cats, *G. lamblia* lives in the **jejunum and ileum**. Environmentally resistant cysts are shed in faeces, contaminate drinking water or food, and are then ingested by other cats.
  - Infection and clinical disease is seen most commonly in **cats kept in large unhygienic groups, and in cats that are <4 years old**.
  - The majority of infections are subclinical, but clinical signs can vary from acute to chronic small or large intestinal diarrhoea. The severity of disease is often determined by the presence of other intestinal pathogens or other concurrent intestinal disease. This infection can be found in up to 14% of feline faecal samples, and up to 39% of canine samples.
  - *Giardia spp.* show a degree of host-specificity. In cats the most commonly seen Assamblages are AI and F, with B, D and E being seen less commonly; AI is a common cause of disease in humans.
  - Infections can be subclinical, or cause acute, chronic or episodic small bowel diarrhoea, where intestinal malabsorption may result in mucoid, soft, foul-smelling faeces.
  - *Giardia spp.* cysts are most often found in the faeces of cats that a history of chronic diarrhoea (>2 weeks), and that are also found to have concurrent *Cryptosporidium spp.* oocysts and/or coccidial oocysts.
- In cats, *T. foetus* lives in the **colon** and sheds flagellated protozoa into the faeces.
  - Infection and clinical disease is seen most commonly in **cats kept in large unhygienic groups**. Although cats of all ages can be affected with diarrhoea, it is most commonly seen in young cats and kittens, the majority being under 12 months of age. Most of the affected cats have come from rescue shelters and pedigree breeding colonies.
  - Infection is presumably spread between cats by close and direct contact. There has been no evidence of spread from other species, or spread via food or water. Studies have shown that 31% of cats at a cat show in the USA were infected with this organism, compared to 14-31% in the UK; suggesting that this may be an important, common, and previously unrecognised cause of diarrhoea in cats.
  - Infections can be subclinical, or result in chronic large bowel diarrhoea, with increased frequency of defecation, semi-formed to liquid faeces, and sometimes fresh blood or mucus in the faeces. With severe diarrhoea the anus may become inflamed and painful, and in some cases the cats may develop faecal incontinence. Although the diarrhoea may be persistent and severe, most affected cats are otherwise well, and do not show significant weight loss. (*For more extensive notes on this infection please contact the author*).

#### Diagnosis.

- Intestinal infection should be **suspected** in any cat with diarrhoea, but especially those coming from a **poorly cleaned multi-animal environment in a geographic region with a high prevalence of infection**.
- Unfortunately, it can be very difficult to prove that diarrhoea in a particular cat is due to a specific organism. This is because **infectious agents can be present in normal animals, parasite eggs, protozoa, and bacteria are often excreted intermittently, some bacteria are difficult to culture, many tests are not validated in cats, and clinical signs of disease may spontaneously resolve before the test results come back**.

- Diagnosis is usually on the basis of faecal analysis and/or culture as these generally non-systemic infections rarely cause systemic changes. However, haematology may reveal an eosinophilia and, in severe cases, low serum proteins may be found on serum biochemistry.
- For more about faecal examination and culture see the sections in the Introduction. With the exception of tapeworm segments, most intestinal parasites are not noticed by owners in their cat's faeces.
- Faecal floatation techniques are used to diagnose most intestinal parasites (round worms, hook worms and *Isospora spp.*).
- **Special techniques may be necessary for some parasites:**
  - Few have been validated for cats, and they have variable sensitivity and specificity. While some PCR-based tests are now available, which are reliable, specific and sensitive, they are often expensive.
  - Faecal Parvovirus antigen ELISA is available for canine parvovirus and also detects feline parvovirus as they are antigenically very similar. Vaccination status should be considered when interpreting these tests as animals will shed virus particles following vaccination with live vaccine and so can lead to result in false positive results. A faecal Parvovirus PCR is available at a limited number of specialist centres.
  - Faecal Clostridium enterotoxin ELISA assays are available.
  - *C. parvum* and *C. felis* – special stains may be needed and faecal antigen tests are available e.g. Immunofluorescent antibody assay (IFA).
  - Giardia cysts are only excreted intermittently so it may be necessary to examination of up five fresh samples in order to detect them using direct saline faecal smears. Faecal antigen tests, including ELISA and IFA, have recently become available and are more sensitive and do not have to rely on the expertise of a technician in identifying the cysts.
  - *T. foetus*. – can be diagnosed by direct saline faecal smears, the 'In Pouch' culture system, or PCR.
- In some cases, rather than confirming the presence of an infection with faecal tests, a **therapeutic trial** with a suitable drug may be considered.
- Since some parasites can be transmitted lactationally (*T. cati*), and infections are frequently more severe in young cats, **all young cats should be evaluated for intestinal parasites or treated against the common parasites of the region.**

#### Differential diagnoses.

- Differential diagnoses include most of the other causes of weight loss with a good appetite. **Inadequate nutrition** becomes the most likely differential when there are no signs other than weight loss. However, the variable presence of **gastrointestinal signs is more suggestive of some of the malassimilation syndromes such as IBD, EPI, or early alimentary lymphoma.**

#### Treatment.

- The treatment of choice for **Campylobacter** is **erythromycin** (10-20 mg/kg q 8-12 hours PO), but vomiting is a common side effect which precludes its use in some cases. **Marbofloxacin** (2 mg/kg q 24 hours PO), or other fluoroquinolones, are appropriate alternatives in these cases.
- **Metronidazole** can be used in cases where **Clostridium** has been isolated (8-10 mg/kg q 12 hours PO).
- Antibiotics are contraindicated in cats where **Salmonella** has been isolated and the cat is asymptomatic or has diarrhoea without evidence of bacteraemia. This is because treatment can promote bacterial resistance and a carrier state. If severe haemorrhagic diarrhoea or evidence of bacteraemia is present then parenteral antibiotics such as fluoroquinolones, should be initiated.
- **Roundworms and hookworms** may be treated with **pyrantel pamoate** (20 mg/kg/day - 2 doses need to be given 2-3 weeks apart) or **fenbendazole** (20-50 mg/kg/day usually given for 3-5 days, then repeated 2-3 weeks later) which are both safe and effective in cats.
- **Tapeworms** may be treated with **praziquantel** (3.5-7.5 mg/kg SC, PO) or **epsiprantel** (2.75 mg/kg PO). One dose is effective against *D. caninum* and *T. taeninaeformis*.
- **Isospora spp.** may be treated with **trimethoprim/sulphonamide** (15 mg/kg q 12 hours PO for 10-14 days), plus improved sanitation.

- *C. parvum* can be difficult to treat, but **tylosin** (10-15 mg/kg q 12 hours PO for 28 days, but may need higher doses), **azithromycin** (7-15 mg/kg q 12 hours PO for 5-7 days) may be effective, **paromycin** (125-165 mg/kg q 12 hours PO for 5 days) – but this should not be used in cats with bloody faeces as absorption can result in acute kidney failure and deafness, or nitazoxanide (25mg/kg q12h PO for 7-28d) is used in humans and is being investigated in cats; but it may cause vomiting.
- **Giardia spp.** may be treated with **fenbendazole** (20-50 mg/kg/day PO for 5 days) – safe except for rare cases of idiopathic hypersensitivity, but effective perhaps only 50% of the time, or **metronidazole** (10-25 mg/kg q12-24 hours PO for 5-7 days). Repeated treatment may be needed.
- **T. foetus** may be treated with **ronidazole** (10-30 mg/kg q 24 hours PO for 14 days). (*More information about T. foetus infection in cats is available on the FAB website [www.fabcats.org](http://www.fabcats.org); the PCR test are available in the UK from Capital Diagnostics in Edinburgh (0131 535 3145) and in the USA from North Caroline State University, USA, [www.cvm.ncsu.edu/mbs/gookin\\_jody.htm](http://www.cvm.ncsu.edu/mbs/gookin_jody.htm); and information on the use of ronidazole for the treatment of this infection in cats in the UK is available from [Danielle.Gunn-Moore@ed.ac.uk](mailto:Danielle.Gunn-Moore@ed.ac.uk)).*

#### Prevention.

- Severe infections can usually be prevented by having a good preventative worming policy, giving prompt and effective treatment to any animals found to be infected or carrying these organisms, improving sanitation, and reducing stocking densities.

#### Prognosis.

- If given the correct treatment, the prognosis for full recovery is usually good.
- Severe infections can occasionally result in permanent intestinal damage and chronic clinical signs.
- Resistant *C. parvum*, *Giardia spp.* and/or *T. foetus* infections can occasionally result in chronic disease.

## INFLAMMATORY BOWEL DISEASE

#### Pathogenesis.

- **Inflammatory bowel disease (IBD)** is a group of chronic idiopathic gastrointestinal tract disorders that are characterised by **infiltration with inflammatory cells**. The infiltration may consist of lymphocytes, plasma cells, neutrophils, eosinophils, and/or macrophages, and the inflammation may involve the stomach, small intestine and/or colon.
- **The aetiology is probably multifactorial** and appears to involve host hypersensitivity responses to antigens within the bowel lumen or mucosa. Suspected antigens include food, bacteria, parasites, or self-antigens.
  - The hypersensitivity may result from a primary, possible genetic, disorder, or arise secondary to mucosal injury incurred by a number of different disorders including bacterial, viral, protozoal or fungal infections, bacterial overgrowth, food hypersensitivity, drug administration, metabolic disease, neoplasia, pancreatitis, or cholangitis.
  - Regardless of the initial cause of the hypersensitivity, it results in **increased mucosal permeability** that allows **luminal antigens to cross the mucosa**, leading to inflammation and further mucosal damage.

#### Clinical signs.

- **IBD can occur in any age, sex or breed of cat.** While it is most commonly seen in middle-aged to older cats, a third of cases occur in cats of less than 2 years of age. Some purebred cats may be predisposed.
- **Clinical signs include any combination of progressive weight loss, and/or vomiting, and/or diarrhoea.**
- Weight loss may result from malabsorption and/or inappetence (which usually occurs late in the disease). Not all cases show significant enteric signs, so some cats present with only weight loss and a variable appetite.

- **Vomiting is often intermittent** and may occur every few days to weeks, often accompanied by anorexia and lethargy. Vomiting is rarely associated with feeding. It may contain froth, bile-stained fluid, and food or, occasionally, blood.
- **Diarrhoea can vary in consistency** from almost well formed to liquid. Some cats may show evidence of large bowel involvement with mucus and/or blood and increased frequency.
- **Clinical signs may wax and wane**, and tend to vary with the type and severity of inflammation.
- **Physical examination is often unremarkable**, but may reveal a thin cat, palpably thickened intestines, enlarged mesenteric lymph nodes, and/or abdominal discomfort.
- **Concurrent pancreatitis and/or cholangitis** may result in jaundice, a palpably enlarged liver and/or anterior abdominal discomfort. When concurrent disease of this nature is present the condition is termed 'triaditis'.
- When lymphangectasia is present, which is rare in cats, severe hypoproteinaemia may lead to subcutaneous oedema and/or ascites.

#### Diagnosis.

- **Before a diagnosis of IBD can be made, all other causes of enteropathy must be ruled out.** These include bacterial enteritis (*Helicobacter* spp., *Salmonella* spp., *Campylobacter* spp., *Clostridium perfringens*, *E. coli*), intestinal parasites (helminths, cestodes, protozoans [*Giardia* spp., *Tritrichomonas foetus*, *Cryptosporidium* spp.]), fungal enteritis, GI neoplasia (lymphoma, adenocarcinoma), and viral enteritis (feline leukaemia virus, feline immunodeficiency virus, feline coronavirus, feline panleukopenia virus). **IBD is diagnosed by documenting histopathological evidence of GI inflammation and excluding all of other causes of it.**
- **Baseline laboratory tests include** haematology, serum biochemistry (including total T4 concentration in older cats), FeLV and FIV tests, urinalysis, faecal culture for pathogenic bacteria, and a full examination for faecal parasites.
  - Performing all of these investigations can be expensive so the investigation should, where possible, be tailored to the patient, and many clinicians start with a dietary trial (see below).
  - Since the investigations are being performed to rule out other causes of enteropathy they are frequently unremarkable. However, IBD may be associated with a number of non-specific findings:
    - **Haematology** may reveal an inflammatory response; neutrophilia, eosinophilia, lymphopenia or monocytosis. Microcytic anaemia may result from chronic blood loss associated with severe IBD. Macrocytosis may result from prolonged and profound hypocobalaminaemia (reduced B<sub>12</sub>: which is usually caused by severe IBD affecting the terminal ileum, and/or severe chronic pancreatitis).
    - **Hyperglobulinaemia** may result from chronic inflammation. **Panhypoproteinaemia** may be seen with severe protein-losing enteropathies.
    - **Hypophosphataemia** is commonly seen with chronic GI disease.
    - **Increases in liver enzymes** may result from associated hepatic and/or biliary tract inflammation.
- **Non-invasive screening tests may provide additional information.** These include abdominal radiography, ultrasound examination, assessment of serum folate and cobalamin (B<sub>12</sub>) levels, serum TLI and PLI levels, examination of faecal smears for the presence of undigested fats or starch, fat absorption tests, breath hydrogen analysis and sugar permeability studies (where available).
  - **Survey radiographs** tend to be unrewarding, but may reveal gas or fluid-filled loops of intestines. **Barium studies** may reveal flocculation or persistent adherence of the barium to the mucosa, irregular mucosal surfaces, or delayed transit times.
  - **Ultrasound examination** may reveal intestinal wall irregularity or echogenicity. It may also be used to examine the mesenteric lymph nodes and other intra-abdominal structures.
  - **Serum folate and cobalamin** levels may be reduced because of malabsorption and, in the case of cobalamin, severe and/or chronic pancreatic inflammation.

- **Serum feline trypsin-like immunoreactivity (fTLI) and feline pancreatic lipase immunoreactivity (fPLI)** may be helpful in the diagnosis of exocrine pancreatic insufficiency (EPI) and pancreatic inflammation, respectively.
- **Breath hydrogen analysis and sugar permeability studies** may be used to try to demonstrate malabsorption and/or small intestinal bacterial overgrowth (SIBO)/antibiotic-responsive diarrhoea – but are only available in some referral centres.
- **A dietary trial** should be performed in all except very ill patients prior to more invasive investigation.
  - Feed a single highly digestible source of protein (eg boiled chicken and water, for other suggestions see the section on diet below) for 1-4 weeks and see if the clinical signs resolve. Approximately 30-50% of cats will respond favourably to this, often after as little as a few days. Since few cases then recur on re-introducing more complex diets it is unlikely that true food allergy is involved in many cases. It appears that simply by reducing the antigenic challenge to the GIT it can often repair itself.
- **It is inadvisable to carry out treatment trials with antibiotics or corticosteroids prior to making a definitive diagnosis**
  - This delays making the correct diagnosis, and may cause complicating intestinal bacterial overgrowth (antibiotics) or exacerbate secondary infections (corticosteroids).
- **Definitive diagnosis requires the collection of intestinal biopsies.**
  - **Mucosal biopsies** may be collected by endoscopy. Unfortunately, it is not always possible to make a definitive diagnosis from these biopsies, so in some cases, full-thickness biopsies must be collected via laparotomy or laparoscopy.
  - IBD often causes no gross mucosal changes, but changes that may be seen include increased granularity and friability, the presence of erythaema, ulcerations, and/or mass lesions, and poor distensibility.
  - **Multiple biopsies should be taken** since the inflammatory infiltrates may not be spread diffusely throughout the GI tract.
  - When performing laparotomy or laparoscopy it is advisable to **collect biopsies of the mesenteric lymph nodes, liver** and, if possible, **pancreas**, as well as from **multiple intestinal sites**.
  - Collection of **duodenal aspirates for quantitative culture** may help to determine the bacterial load of the small intestine. Bile can also be aspirated and sent for culture.
  - **Gastric biopsies** should always be assessed for the **presence of *Helicobacter* spp.**
  - **Histopathology reveals inflammatory cells infiltrating the lamina propria**, plus variable degrees of epithelial abnormality and glandular distortion.
    - **Lymphocytic-plasmacytic IBD** is the most common form of IBD in the cat. It may occasionally progress to intestinal lymphoma (typically small cell or lymphocytic lymphoma).
    - **Granulomatous enterocolitis** is less common, and often presents as GI obstruction.
    - **Eosinophilic IBD** is rare. It may be associated with eosinophilia and/or hypereosinophilic syndrome where tissues other than the GI tract are also affected.
    - **Suppurative IBD** is usually associated with an infectious aetiology.
    - Other forms also exist and many cats have mixed populations of inflammatory cells.
  - Unfortunately, when lymphangectasia is present, severe hypoproteinaemia may render these patients a poor anaesthetic and surgical risk. It may therefore be necessary to make a presumptive diagnosis based on the presence of diarrhoea, panhypoproteinaemia, and lymphopenia in the absence of finding other diseases on haematology, serum biochemistry, faecal evaluation, abdominal ultrasound examination, ± mucosal biopsies.

#### **Differential diagnosis.**

- These include most of the other causes of weight loss with a good or variable appetite. However, since cats with IBD usually develop vomiting and/or diarrhoea, **other causes of enteropathy, cholangitis, pancreatitis, hyperthyroidism and the other malabsorption syndromes** (including alimentary lymphoma) should be considered as important differentials.

## Treatment.

- The basic aims of treatment are to remove the source of antigenic stimulation and to suppress the inflammatory response within the GI tract.
  - **Treatment typically involves dietary management, ± a corticosteroid e.g. prednisolone, and possibly metronidazole or tylosin.**
  - Treatment should be tailored to each patient.
  - Relapses warrant critical reassessment of the case, and often require repeated intensification of treatment, and/or the addition of more potent immunosuppressive drugs.
- **The diet should contain a single highly digestible source of protein**, ideally that the cat has not eaten before.
  - Feeding an exclusion diet of some form typically results in resolution of clinical signs in up to 50% of cats with IBD.
  - The diet should preferably contain few food additives, be gluten-free, lactose-free, low residue, not too high in fat, and adequately supplemented with vitamins and minerals, especially B vitamins and potassium.
  - Carbohydrates are not needed in exclusion diets for cats.
  - High fibre diets may help when the large bowel is affected.
  - No other foods should be fed concurrently.
  - During the **initial phase of treatment**, when the bowel is recovering, it may be preferable to **feed either a home-cooked diet, a ‘sacrificial protein’** which the cat will then not be fed again, or **protein hydrolysate** which has reduced molecular weight protein and is supposed to be less antigenic. This should be fed for ~1 month. However, cats often respond favourable after only a few days. After the clinical signs have resolved and the GIT has had time to recover the cat can then be fed a commercial ‘hypoallergenic’ diet, or further protein sources can be gradually reintroduced. If feeding homemade diets long-term, great care should be taken to ensure that they are balanced.
- **Immunosuppressive agents:**
  - **Immunosuppressive doses of corticosteroids** are usually required. Administer prednisolone at 2-4 mg/kg q 12-24 hours PO, then taper over 1-3 months and maintain on every other day doses, if needed. Budesonide (1mg/cat PO q8-24h) may be used where systemic effects of corticosteroids need to be limited, but its effects can be unpredictable.
  - Other immunosuppressive agents may be considered. While they all have potential side effects and warrant regular monitoring **chlorambucil** (2-5 mg/m<sup>2</sup> PO up to once every 48h or 2-4mg PO q1-3 weeks) is often very well tolerated. Other potential options include **cyclophosphamide** (50 mg/m<sup>2</sup> PO up to 4 times a week), **cyclosporine** (0.5-8.5 mg/kg every 12-24 hours, indefinitely) or, in the cases of **colonic disease**, **sulfasalazine** (10-20 mg/kg/day PO for 7-10 days).
- **Metronidazole** - Its effect against **anaerobic bacteria** helps to reduce secondary bacterial overgrowth. It is also effective against **protozoa** (e.g. *Giardia* spp.), has positive effects on **brush border enzymes levels**, and is believed to **alter the immune function** of the GI tract, perhaps by altering neutrophil chemotaxis and inhibiting cell-mediated immunity. Administer 7.5-15 mg/kg PO q 8-12 hours for 2-4 weeks. However, some authors suggest that it is inadvisable to give prolonged courses because of cumulative neurotoxicity and possible carcinogenic side effects.
- **Tylosin** may be effective for its antibiotic actions as well as other, as yet undefined, effects (5-20 mg/kg every 6-12 hours PO). This may be a better choice than metronidazole.
- **Supportive therapies are often recommended.** However, few have been assessed using controlled studies in cats.
  - **Motility modifiers** may give short term palliative relief in cases of very watery diarrhoea (**loperamide** 0.04-0.2 mg/kg every 8-12 hours PO).
  - **Metoclopramide** may be useful for its anti-emetic and prokinetic effects (0.2-0.5 mg/kg PO up to 4 times a day, being given just prior to feeding, or as a constant IV infusion of 1-2mg/kg over 24h). Maropitant is also an anti-emetic (0.5-1 mg/kg q24h PO).
  - **Cisapride** is a good prokinetic, but it is now more difficult to obtain (0.3-1.0 mg/kg every 8-12

hours PO).

- **Cobalamin and folate** may be needed as they are often reduced by malabsorption (cobalamin 125-250 ug/week SC or IM for 6-8 weeks [50-100 ug/cat/day PO]; folate 0.5-1.0 mg/cat/day PO for 1 month: the simplest way to supplement for this is to give folic acid solution, sold as Lexpec, by Rosemont Laboratories 2.5mg/5ml, at 0.1-1.0ml PO q24h).
- **Probiotics** are used to try to repopulate the intestine with beneficial bacteria e.g. *Enterococcus faecium*, *Bifidobacter* and possibly *Lactobacilli*. **Prebiotics** (eg fructo-oligosaccharides [FOS] and inulin) are used to try to change the substrate of the intestinal flora and promote the growth of more beneficial populations.
- **Vitamin K1** is often required because fat malabsorption results in poor absorption of fat soluble vitamins like vitamin K, and this can result in abnormal haemostasis (0.5 mg/kg/day SC for 3-4 days, then once weekly).
- **Glutamine** may be given as an energy source for the GI mucosal cells (250-5000 mg/cat/day PO, indefinitely).
- Various nutritional supplements may be given for their potential anti-inflammatory properties. These include **vitamin E** (50-200 IU/ cat/day PO), **vitamin A** (1000-5000 IU/ cat/day PO), **vitamin C** (50-80 mg/kg/day PO), **zinc** (7.5 mg/ cat/day PO), and **N-acetyl glucosamine** (125-1500 mg/cat/day PO).

#### Prognosis.

- The prognosis depends on the nature and severity of the GI infiltration, and the presence of concurrent and/or associated disease, such as pancreatitis, cholangitis. In general, the prognosis for control is reasonably good, but the condition cannot be cured, and many cats will need treatment for the rest of their life.

#### Prevention.

- Since it is not known what triggers IBD to develop, it is not currently possible to prevent its onset.

## ALIMENTARY LYMPHOMA

#### Pathogenesis.

- **Lymphoma is the most common GI neoplasia of cats.**
- Alimentary lymphoma can occur isolated to the intestine, or as part of multicentric disease.
- It can occur as a **focal lesion or diffuse intestinal thickening**. It can arise in the stomach, small intestines and/or colon, and involvement of the **ileocolic junction** is common.
  - Concurrent involvement of mesenteric lymph nodes, liver and/or spleen is not uncommon.
- The cells may be lymphocytic, lymphoblastic, of B or T cell origin or, occasionally, large granular lymphocytes or globular leukocytes.
- Lymphoblastic lymphoma is more likely than lymphocytic lymphoma to present as an abdominal mass.
- **Alimentary lymphoma may arise secondary to chronic lymphocytic-plasmacytic IBD.**

#### Clinical signs.

- Typically seen in older cats of any sex or breed.
- **History usually includes anorexia and weight loss, but early in the disease the appetite may be good or even increased. Vomiting and/or diarrhoea may or may not be present.** Occasional cases present with clinical signs of acute intestinal obstruction; e.g. severe vomiting and collapse.
- Some cats develop fever, ascites or jaundice, and at this stage they usually have a poor appetite.
- **Physical examination typically reveals a thin cat with a palpable abdominal mass (es) and/or thickened intestines.**

#### Diagnosis.

- **Haematology** may reveal non-specific changes including neutrophilia and lymphopenia. Lymphoblasts may occasionally be seen in the circulation. Macrocytosis may result from prolonged and profound hypcobalaminaemia.
- **Serum biochemistry** may reveal panhypoproteinaemia and/or hyperbilirubinaemia, and/or hypophosphataemia; serum cobalamine (B<sub>12</sub>) is often low.
- Most cats test negative for FeLV and FIV infections.
- **Survey radiographs** may reveal gas or fluid-filled loops of intestines. Barium studies may reveal flocculation or persistent adherence of the barium to the mucosa, irregular mucosal surfaces, luminal narrowing or intramural thickening.
- **Ultrasound examination** may reveal intestinal wall irregularity, thickening, or altered echogenicity, and/or enlarged mesenteric lymph nodes, liver or spleen.
- **Diagnosis** is made by examination of a **GI tract fine needle aspirate or biopsy**, with or without biopsies from mesenteric lymph nodes and/or other abdominal organs.
- Differentiating lymphocytic alimentary lymphoma from lymphocytic-plasmacytic IBD can be very difficult.
- Determining which types of cells are involved can aid in treatment and prognosis (see below).

#### Differential diagnosis.

- Initially, these include most of the other causes of weight loss with a good appetite. However, since cats with alimentary lymphoma usually develop vomiting and/or diarrhoea, **other causes of enteropathy, IBD, cholangitis, pancreatitis, hyperthyroidism** and the **other malassimilation syndromes** should be considered as important differentials. Later (more severe or extensive) cases are generally inappetent, so while the differential diagnoses may still include those listed above, other severe systemic diseases should also be considered, including hepatic lipidosis (although cats with this disease are more likely to be fat than those with intestinal lymphoma), end stage renal failure, severe pancreatitis, and systemic neoplasia.

#### Treatment.

- **Localised alimentary lymphoma** may respond to **surgical resection** and adjunct chemotherapy.
  - Large masses involving the entire thickness of the bowel wall should not be treated with chemotherapy alone as this may result in **gut perforation**.
- **Diffuse lymphoma are best treated with combination chemotherapy.**
  - **Lymphoblastic lymphoma** and lymphoma affecting more than just the GI tract are best treated with combinations of cyclophosphamide, vincristine and prednisolone, ± doxorubicin, ± l-asparaginase.
  - **Lymphocytic lymphoma** may respond more favourably to a combination of only prednisolone (10 mg/cat/day PO) and chlorambucil (2-5 mg/m<sup>2</sup> PO up to once every 48h or 15 mg/m<sup>2</sup>/day for 4 days PO, every 3 weeks or 2-4mg PO q1-3 weeks).

#### Prognosis.

- **The prognosis is guarded.** The best prognostic indicators are response to therapy and the duration of the first remission.
- Response rates to chemotherapy range from 30-70%, with median remissions of 4-23 months.
- Being **FeLV positive or having lymphoblastic lymphoma are negative indicators**, while having lymphocytic lymphoma is a positive indicator.
  - **Lymphoblastic lymphoma** has a complete remission rate of 18%, and median survival time of 2.7 months.
  - **Lymphocytic lymphoma** has a complete remission rate 69%, median survival time 22.8 months.

#### Prevention.

- Since it is not known what triggers lymphoma to develop, it is not currently possible to prevent its onset. However, since lymphocytic IBD has been seen to progress to lymphoma, it would appear sensible to try to control lymphocytic IBD as well as possible, to try to prevent its progression.

## PANCREATITIS / EXOCRINE PANCREATIC INSUFFICIENCY

### Pathogenesis.

- **Pancreatitis** develops when there is **activation of digestive enzymes** within the pancreas which results in some degree of auto-digestion. While there are many possible causes of pancreatitis in cats, over 90% are idiopathic.
- In cats, the **most common forms** of pancreatic disease are **chronic non-suppurative** (lymphocytic/plasmacytic or, occasionally, eosinophilic) pancreatitis and **suppurative** (neutrophilic) pancreatitis, while acute septicaemic pancreatitis and exocrine pancreatic insufficiency (EPI) are seen less frequently.
- **It is the presence of EPI that results in weight loss with a good, often ravenous, appetite.**
  - **Primary EPI is uncommon in cats. However, EPI secondary to chronic, often episodic, pancreatitis is being recognised more frequently.**
  - In EPI the lack of pancreatic digestive enzymes leads to maldigestion and malabsorption.
- **In cats, pancreatitis is often seen in association with idiopathic inflammatory bowel disease (IBD), cholangitis complex, or both (termed 'TRIADITIS').**
  - This association is believed to occur because, in cats, the **pancreatic duct enters the common bile duct** before it opens into the duodenum. (The accessory pancreatic duct is always small and only present in ~20% of cats).
  - Cats have naturally high bacterial numbers in their proximal duodenum, so this, coupled with concurrent IBD, vomiting and their unusual feline pancreatiticobiliary anatomy predispose to reflux of bacteria (typically *E.coli* or other intestinal bacteria) and intestinal contents into the pancreatic and biliary system.
  - When disease occurs in the small bowel it may therefore ascend the common bile duct and from there affect the pancreas and the rest of the biliary tree. For the same reason, disease of the biliary tree or pancreas may affect the other two regions.
  - Regardless of which organ is affected first, the other 2 organs tend to become involved as inflammatory mediators, infectious agents, bile and/or pancreatic secretions pass from one area to another.

### Clinical signs.

- **Acute pancreatitis** can occur in **any sex or breed of cat**, the **history and clinical signs of may be very acute or very variable and non-specific** if the cat is experiencing an acute exacerbation of chronic pancreatitis. They usually include **anorexia, depression and lethargy**, with or without vomiting and/or diarrhoea, and/or possible abdominal pain. Some will show **dyspnoea associated with pleural fluid and/or pulmonary oedema** (resulting from pleural and/or pulmonary inflammation secondary to circulating inflammatory mediators).
- **Chronic pancreatitis** can occur in **any sex or breed of cat**, and is typically seen in middle-aged or older cats.
- **History and clinical signs** of chronic pancreatitis tend to be **very variable and non-specific**.
- They usually include **episodes of anorexia or variable appetite, with or without vomiting and/or diarrhoea, weight loss and/or possible abdominal pain**.
- **Once EPI develops** the cat may be **thin, have a greasy coat** and produce large quantities of voluminous, fatty, foul-smelling faeces, or have severe diarrhoea.
- Cats with chronic pancreatitis **may also develop episodic or persistent diabetes mellitus (DM)**, which is seen as polyuria and polydipsia.
- When both EPI and DM occur concurrently the **polyphagia** can be profound.
- Physical examination is often unremarkable, but may reveal anterior abdominal discomfort, a palpably irregular and enlarged pancreas, or hepatomegally associated with cholangitis complex.

### Diagnosis.

- **Pancreatitis is very difficult to diagnose.**
- Haematology and serum biochemistry may reveal non-specific changes.
  - **Haematology** may show neutrophilia, neutropenia (associated with sequestration during acute exacerbation), monocytosis, and/or a mild non-regenerative anaemia.
  - **Serum biochemistry** may show hyperglobulinaemia, bilirubinaemia and raised liver enzymes (depending on the degree of associated cholangitis complex), and/or hypercholesterolemia, hypertriglyceridaemia, and hyperglycaemia (often associated with concurrent diabetes). Hypocalcaemia may be present in severe pancreatitis due to peri-pancreatic fat saponification.
  - **Serum amylase and lipase tests are rarely useful** in the diagnosis of pancreatitis in cats, although a raised lipase level may be seen occasionally.
- **With chronic pancreatitis serum cobalamin and folate levels are often decreased.**
- A number of older tests are very unreliable and are now rarely used. These include staining faecal smears to demonstrate undigested fat (Sudan III or IV stain) and starch (iodine stain), and fat absorption tests.
- Abdominal radiographs are usually unremarkable.
- **Ultrasound examination** may reveal pancreatic enlargement, irregularity, or heterogeneity, evidence of peri-pancreatic fat necrosis, enlargement of mesenteric lymph nodes, and/or evidence of post-hepatic biliary obstruction (enlarged gall bladder, thickened bile, or tortuous common bile duct), or the presence of ascites.
- Evaluation of serum **Trypsin-Like Immunoreactivity (TLI)** may be helpful.
  - The species-specific assay must be performed on a fasted serum sample.
  - Serum TLI may be increase with pancreatitis and decrease with EPI.
  - While it consistently diagnoses EPI, it often fails to confirm pancreatitis, possibly because chronic inflammation has reduced the overall ability of the pancreas to produce TLI.
- Evaluation of serum **Pancreatic Lipase Immunoreactivity (PLI)** may be helpful.
  - The species-specific assay must be performed on a fasted serum sample.
  - Serum PLI may be increase with pancreatitis and appears to be more sensitive than TLI.
- **A therapeutic trial with replacement pancreatic enzymes may be considered** (see under treatment).
  - Providing that any associated IBD and/or cholangitis complex has been addressed, the response to treatment may be dramatic. However, a positive response is not diagnostic of chronic pancreatitis and/or EPI.
- **Pancreatic biopsy is required to confirm a diagnosis of pancreatitis.**
  - Because triaditis is common, it is advisable to collect liver and intestinal biopsies at the same time, and send part of the liver biopsy and a sample of bile for culture.

#### Differential diagnosis.

- With acute pancreatitis these include any cause of acute abdominal crisis and/or collapse, so this list is extensive e.g. hepatic lipidosis, systemic intoxication, sepsis, end stage renal failure, congestive heart failure, and systemic neoplasia.
- With chronic pancreatitis these include most of the other causes of weight loss with a good appetite. However, since cats with chronic pancreatitis and EPI usually develop diarrhoea and/or vomiting, other **causes of enteropathy, IBD, cholangitis, alimentary lymphoma, hyperthyroidism and the other malassimilation syndromes** should be considered as important differentials.

#### Treatment for acute pancreatitis.

- **Typically consists of iv fluids and systemic analgesia** (e.g. buprenorphine 10-30 mg/kg iv q8h). Other potentially beneficial interventions include the administration of H<sub>2</sub> blockers (e.g. ranitidine), anti emetics (e.g. metoclopramide, maropitant), systemic antibiotics, hepatic and coagulatory support (SAMe, vitamins E and K), and tube feeding.
- **Close monitoring is essential**, particularly of red cell numbers (because of increased fragility leading to haemolytic anaemia), white cell count (a left shift may indicate bacterial infection and a degenerative left shift may indicate sepsis), electrolytes and serum biochemistry (particularly potassium, magnesium, phosphate and albumen which are all prone to fall, and so may need to be replaced, and liver and kidney

parameters which may rise if inflammation and/or metabolic changes start to involve other body systems).

#### **Treatment for chronic pancreatitis.**

- **Replace pancreatic enzymes** by adding pancreatic enzyme replacement to food (~ half a teaspoonful of powder per meal, or to effect, ideally incubating it with the food for 30 minutes before feeding to reduce the risk of lip irritation), or add fresh-frozen then defrosted pig pancreas (~20-40g per meal, or to effect).
- **Immunosuppression:** In the non-suppurative form of pancreatitis, immunosuppressive doses of **corticosteroids** may be needed to reduce ongoing inflammation (prednisolone 2-4 mg/kg q 12-24 hours PO, then taper over 1-3 months and maintain on every other day doses if needed). Alternately, **chlorambucil** could be considered (2-5 mg/m<sup>2</sup> PO up to once every 48h or 2-4mg PO q1-3 weeks).
- **Supportive therapies:**
  - **Feed a highly digestible, ‘bland enteric diet’**, which is low in fat. Feed small meals frequently.
  - **Cobalamin** is often reduced by lack of pancreatic intrinsic factor and malabsorption and should be supplemented (125-250 ug/week SC or IM for 6-8 weeks then SC q3 weeks long-term; or possibly 50-100 ug/cat/day PO).
  - **Vitamin K1** is often required because fat malabsorption results in poor absorption of fat soluble vitamins like vitamin K, and this can result in abnormal haemostasis (0.5 mg/kg/day SC for 3-4 days, then once weekly).
  - **Vitamin E** may be given for its anti-oxidative properties (50-200 IU/cat/day PO).
  - **Antacids** may help to reduce post-prandial pain (e.g. ranitidine 3.5 mg/kg PO q12h, or famotidine 0.5-1.0 mg/kg PO q12-24h)
- **Surgical intervention may be required** if complete biliary obstruction occurs (cholecystotomy or cholecystoduodenostomy), or if a focal pancreatic mass is detected (partial pancreatectomy to remove a pancreatic pseudocyst, abscess, fibrotic mass, or tumour).
- DM that develops secondary to chronic pancreatitis can be very difficult to stabilize. Insulin requirements may vary widely because of the ongoing pancreatic pathology, and treatment is complicated further when corticosteroids also need to be given.
- It is essential to diagnose and treat any concurrent disease (e.g. IBD and/or cholangitis complex).

#### **Prognosis.**

- Prognosis depends on the severity of damage. Successful treatment of acute pancreatitis can be very difficult, and it is not possible to determine whether the episode of pancreatic inflammation will be a ‘one-off’ event which is unlikely to recur, or whether it may lead on to chronic often waxing and waning disease. If affected cats survive the initial episode chronic cases may live with low-grade smouldering pancreatitis for many years. Once EPI and/or DM has developed the prognosis is worse.
- In rare cases of congenital EPI, the prognosis is good as long as the cat receives pancreatic supplementation.

#### **Prevention.**

- Since it is not known what triggers pancreatitis to develop, it is not currently possible to prevent its onset. However, since chronic pancreatitis can progress to EPI, it would appear sensible to try to control it as well as possible to try to prevent its progression.

## **CHOLANGITIS COMPLEX**

#### **Pathogenesis.**

- The **Cholangitis Complex** (WSAVA Update Liver Standardization Group on Feline Hepatobiliary Disease 2006) comprises **lymphocytic cholangitis**, **neutrophilic cholangitis** (which can be acute neutrophilic [suppurative] or chronic), and chronic cholangitis associated with liver fluke (not present in the UK). (Chronic neutrophilic cholangitis has previously been referred to as non-suppurative or lymphocytic-plasmacytic cholangitis/cholangiohepatitis).

- In cats, the term cholangitis (inflammation of the biliary tract) is used rather than cholangiohepatitis (inflammation of the peribiliary hepatocytes as well as the biliary tract) because the inflammation is almost always centred on the biliary ducts, with any hepatic involvement occurring as a secondary process.
- **Mild lymphocytic portal hepatitis** should not be over-interpreted as it is believed to be a non-specific reactive change possibly reflecting extra-hepatic disease or resolving hepatitis: ~80% of cats >10 years of age have these mild changes).
- **The pathogenesis and interaction of lymphocytic and neutrophilic cholangitis is poorly understood.** It is highly probably that each of these conditions incorporates a number of different diseases, and acute neutrophilic change can progress to become chronic.
- That said, the pathogenesis of **lymphocytic cholangitis is probably immune-mediated**, although it may also be associated with progression of the neutrophilic cholangitis.
- **Both neutrophilic and lymphocytic forms of cholangitis are often associated with IBD and/or pancreatitis, and when all 3 areas show inflammatory change this is termed “triaditis”** (for the pathogenesis of this see the section on pathogenesis of pancreatitis).
- In cats any cause of anorexia or hepatopathy can result in delayed emptying of the gall bladder. The bile then becomes dehydrated and forms ‘bile sludge’. In cats, while bile sludge occurs commonly, gall stones are seen only very rarely.
- Obstruction to bile flow can lead to periductal fibrosis, if it remains for >6 weeks it can lead to biliary cirrhosis.

#### **Clinical signs of neutrophilic cholangitis.**

- **Cats of any age** may be affected, but acute disease is seen most typically in young to middle aged cats while chronic disease is seen most typically in middle aged to older cats.
- With acute disease clinical signs are typically severe, and can occasionally be preceded by milder signs for a variable period. Chronic disease typically has a waxing and waning time course of months to years.
- **Acute disease** typically presents with **fever, anorexia, vomiting and lethargy.**
- **Chronic disease** typically includes periods of **anorexia, vomiting and weight loss.**
- **Vomiting is frequent in all types of biliary disease**, possibly because inflammation of the bile ducts stimulates their rich autonomic nerve supply and triggers the emetic centre of the brain.
- **Cats with acute disease** may be **jaundiced, and may have abdominal pain. Cats with chronic disease** may be **jaundiced, and may have hepatomegally; ascites is rare.**
- Acute disease may progress to chronic disease and/or secondary hepatic lipidosis, with hepatic encephalopathy, ascites, and bleeding tendencies.
- Systemic signs may be associated with secondary infections, typically of the liver and/or pancreas and triaditis is common: ~80% of cases also have concurrent IBD while ~50% have pancreatitis.

#### **Clinical signs of lymphocytic cholangitis.**

- **Cats of any age** may be affected, but disease is seen most typically in **young to middle aged cats. Persian cats** may have an increased risk.
- **Clinical signs are usually very chronic and insidious in nature.**
- Affected cats are **typically jaundiced, but appear to be clinically well, and are often polyphagic. Weight loss and anorexia can also be seen, as can vomiting and/or diarrhoea.**
- Cats may have a **palpably enlarged liver, and mild generalized lymphadenopathy** may also be present.
- Cats may show **intermittent signs of systemic illness**, with **fever, anorexia, weight loss, and vomiting.** Systemic signs are sometimes associated with secondary infections, typically of the liver and/or pancreas.
- The disease may progress to causing chronic biliary cirrhosis with ascites, hepatic encephalopathy, and bleeding tendencies.
- May be associated with triaditis (concurrent IBD and pancreatitis)
- Ascites may be present – in acute cases due to a hepatic exudates (which can make this condition difficult to differentiate from wet FIP), and in chronic cases from portal hypertension resulting from periportal fibrosis and cirrhosis)

- Mixed forms also exist
- It is difficult to determine whether these two groups are two different diseases or two ends of a spectrum.

#### Diagnosis of neutrophilic cholangitis.

- **Serum biochemistry:** initially, with acute disease, when the inflammation is limited to the larger bile ducts and gall bladder, there may be little or no changes in the total bilirubin and even the liver enzymes. More typically, there are mild to moderate increases in ALP, GGT and bilirubin, and as the inflammation extends into the hepatic parenchyma there will also be increases in ALT, AST, and bile acids. Most chronic cases have raised liver enzymes (with GGT typically being proportionately higher than ALP); ~50% of cases have raised bilirubin levels or hypergammaglobulinaemia.
- Cats with concurrent chronic pancreatitis may have increased PLI levels and/or hypcobalaminaemia ( $\downarrow B_{12}$ ).
- **Haematology** may reveal a mild to moderate leukocytosis. Chronic or severe disease may result in mild anaemia, lymphopenia or lymphocytosis, monocytosis, and/or thrombocytopenia. **Blood clotting times are frequently prolonged.**
- **Radiographs** are often unhelpful. **Ultrasound** examination may or may not show hepatic changes in acute disease, but with chronicity the liver generally develops periportal hyperechogenicity. Acute disease may cause the bile ducts to become dilated with or without signs of obstruction, while with chronic disease the intrahepatic and extrahepatic bile ducts tend to become tortuous and dilated. Bile 'sludge' may be present at any stage of the disease, and with chronicity the gallbladder wall may become thickened, suggesting chronic cholecystitis, and cholelithiasis (gall stones) may occasionally develop. Associated findings may include enlarged mesenteric lymph nodes, pancreatic irregularity, and/or thickening of the duodenal walls.
- **A fine needle aspirate** of the liver may reveal suppurative inflammation as may an ultrasound guided aspirate of bile from the gall bladder (taken through the right medial liver lobe where the gallbladder is attached to the liver to reduce the risk of intraperitoneal leakage of bile). Aspirates from both the liver and bile should be sent for cytological assessment and bacterial culture (preferably aerobic and anaerobic culture).
- For histopathology see below.

#### Diagnosis of lymphocytic cholangitis.

- **Serum biochemistry** often reveals mild to moderately (occasionally severely) increased liver enzymes, increased bile acids, hyperbilirubinaemia, hyperglobulinaemia, and hypoalbuminaemia.
- **Haematology** may reveal mild anaemia, lymphopenia or lymphocytosis, monocytosis, and/or thrombocytopenia. **Blood clotting times are frequently prolonged.**
- **Ascitic fluid**, if present, is typically high in protein.
- **Ultrasound** examination may show blotchy hepatic hyperechogenicity, biliary tree distension and irregularity, 'sludging' of bile, a thickened gall bladder wall (which is most typically associated with the presence of a secondary infection), and/or evidence of common bile duct obstruction. Associated findings may include enlarged mesenteric lymph nodes, pancreatic irregularity, and/or thickening of the duodenal walls.
- For histopathology see below.

#### A definitive diagnosis is made by **histopathological examination of a liver biopsy.**

- A fine needle aspirate is rarely diagnostic, so a **percutaneous needle biopsy or surgical wedge biopsy** is required. Blood clotting times and/or a PIVKA test (protein induced by vitamin K absence or antagonism) should be assessed first, and a platelet count should be performed.
- Typical gross findings include a **very friable or firm often irregular liver**, and a thickened and distended gallbladder and common bile duct, which often contain inspissated bile. Enlarged mesenteric lymph nodes, pancreatic irregularity, and/or thickening of the duodenal walls may also be present.
- If performing an exploratory laparotomy, it is sensible to check the patency of the biliary outflow, and then collect biopsies from the mesenteric lymph nodes, small intestines and pancreas as well as liver. Send bile and part of the liver biopsy for culture.

- Histopathology of **acute neutrophilic cholangitis** reveals neutrophils within the walls and lumen of the intrahepatic ducts and surrounding portal area, bile duct epithelial degeneration and necrosis, and the inflammation may extend through the limiting plate to involve the periportal hepatic parenchyma; intrahepatic bile ducts may be dilated but there is usually minimal biliary hyperplasia or periportal fibrosis.
- Histopathology of **chronic neutrophilic cholangitis** reveals mild to severe infiltration of the portal areas by plasma cells, lymphocytes and neutrophils, with biliary epithelial degeneration and necrosis. There may be lymphoid aggregates in the portal areas. Inflammation is usually centred within the walls and lumen of the intrahepatic ducts and may extend through the limiting plate to involve the periportal hepatic parenchyma. Biliary hyperplasia, periductal (sclerosing) fibrosis and bridging fibrosis may also be present.
- Histopathology of **lymphocytic cholangitis** reveals moderate to marked infiltration of small lymphocytes restricted to the portal areas, often associated with variable portal fibrosis and biliary proliferation. Lymphoid aggregates may be present, as may obliteration of the bile ducts, biliary hyperplasia and fibrosis, or bridging portal fibrosis. There may be a few portal plasma cells and/or eosinophils. Chronic cases may develop biliary cirrhosis. It can be difficult to differentiate between lymphocytic cholangitis and well-differentiated lymphocytic lymphoma.
- **Mild lymphocytic portal hepatitis** it is characterized by the presence of small numbers of neutrophils, lymphocytes or plasma cells in the portal areas without evidence of cholangitis or disruption of the limiting plate or periportal necrosis).

#### Differential diagnosis.

- With acute cholangitis these include any cause of acute abdominal crisis and/or collapse, so this list is extensive e.g. hepatic lipidosis, ruptured viscera/septic peritonitis, systemic intoxication, end stage renal failure, congestive heart failure, systemic neoplasia, etc.
- With chronic cases these include most of the other causes of weight loss with a good appetite. However, since affected cats often develop vomiting and/or diarrhoea enteropathies (including IBD), **pancreatitis, and the other malabsorption syndromes** should be considered as important differentials. In cases of lymphocytic cholangitis that develop ascites, the **wet form of feline infectious peritonitis (FIP)** should also be considered. This is because both conditions produce a protein-rich ascitic fluid and have similar biochemical and haematological changes. However, the presence of polyphagia usually differentiates the two conditions as cats with FIP are usually anorexic.

#### Treatment.

- Treatment is largely empirical. However, it is important to remember that **there are NO specific treatments for liver disease.**
- **First do no harm!** This is very important with cats - remember that they have a deficiency of glucuronyl transferase, etc
  - First decide - What is the pathogenesis?
  - Then decide - Is there enough liver left to survive?
 At best all we can usually try to do is:
  - Eliminate the cause
  - Slow down progression and try to aid recovery
  - Treat secondary complications
  - Always remember that the liver has great regenerative ability
- **Immediately post-operatively following liver biopsy.**
  - Depends to some extent on whether or not pancreatitis is also present
  - **Analgesics** – Buprenorphine (10-30 µg/kg IV, SQ, PO q8h)
  - **IV fluids** – add potassium (extra K<sup>+</sup> is almost always needed)
  - **Feeding** – nasogastric tube, oesophagostomy tube, gastrotomy tube, jejunostomy (J)-tube, partial

- parenteral nutrition (PPN), total parenteral nutrition (TPN)
  - **Antiemetics** – especially if pancreatitis is also present (see below)
  - **Antibiotics**
- **Antibiotics, if needed (with neutrophilic cholangitis):**
  - Ideally as directed by culture and sensitivity of bile and/or liver samples.
  - Ampicillin (10-40 mg/kg q 8 hours PO), amoxicillin/clavulinate (11-22 mg/kg q 8-12 hours PO), or cephalexin (10-35 mg/kg q 8-12 hours PO), marbofloxacin (2 mg/kg PO q24h – the author does not like to use enrofloxacin because of the risk of irreversible blindness in cats) or other quinolones - all are well concentrated in bile
  - Add **metronidazole** for its effect against anaerobes and its immune-modulating effects (7.5-10 mg/kg every 12 hours PO). Do not use higher doses, as these can be hepatotoxic, neurotoxic and potentially teratogenic.
  - In very severe cases give according to ‘4 quadrant cover’ IV (ie to cover Gram positive and negative, anaerobes and aerobes – eg ampicillin clavulinate + fluroquinolone + clindamycin or MZL)
  - May need to be given for 1-3 months
- **Immunosuppressive agents (with chronic neutrophilic cholangitis and lymphocytic cholangitis):**
  - Immunosuppressive doses of **corticosteroids** (prednisolone 1-4 mg/kg q12-24 hours PO, then taper over 6-12 weeks to 1.0 mg/kg PO q48h) and maintain on every other day doses if needed.
  - Other immunosuppressive agents may be considered e.g. **methotrexate** (0.13 mg/cat every 12 hours x 3 doses PO or a total of 0.4 mg PO ÷ into 3 over 24h; given q7-10d), **chlorambucil** (2-5 mg/m<sup>2</sup> PO up to once every 48h or 2-4mg PO q1-3 weeks), or **cyclosporin A** (measure serum levels, start at 2 mg/kg PO q12h). Do not give **azathioprine** – it is a slow poison to cats. Care – these drugs are all potentially hepatotoxic
- **Supportive therapies (all forms of cholangitis):**
  - **Ursodeoxycholic acid** (UDCA, Destolit): Synthetic hydrophilic bile acids that aid bile flow. It has anti-inflammatory, immuno-modulatory, and anti-fibrotic activities, and is cytoprotective to hepatocytes. Where complete biliary obstruction is present it should be removed before starting treatment (10-15 mg/kg PO q24h)
  - **S-Adenosylmethionine** (SAME): Nucleotide synthesized by all cells (from methionine + ATP). It is essential for major hepatic biochemical pathways; especially transmethylation (for gene expression and for maintaining stable cell membranes), aminopropylation (for cell replication and liver regeneration and repair), and transsulphuration (for the generation of the major hepatic anti-oxidant glutathione [GSH] and [in dogs] for taurine production)
    - GSH (+ taurine)** = hepatic anti-oxidants + essential for detoxification
    - GSH is significantly reduced in liver disease; in >50% of dogs and >75% of cats**
    - Giving oral SAME repletes GSH in the liver and the red blood cells (The latter is very important in cats as cat red blood cells are extremely sensitive to oxidative damage)
    - In vitro and in vivo studies in humans, dogs and cats have shown that SAME has anti-oxidant, detoxification, cytoprotective, analgesic and anti-inflammatory actions
    - SAME is recommended for all forms of acute + chronic liver disease**
    - It is also recommended to counter potential hepatotoxicity associated with drug administration (eg steroids, chemotherapy), and to reduce red cell fragility** (18-40 mg/kg PO q24h)
  - **Milk thistle** (common name for *Silybum marianum*): the most biological active component of which is silibinin (sylibin / silymarin) may be useful for treatment of chronic and acute liver disease, including exposure to hepatotoxins (e.g. *Amanita phalloide*; "Death Cap Mushrooms"), and cirrhosis (optimal dosage unknown, range from 20-50 mg/kg per day)
  - **Maropitant** (anti-emetic: 0.5-1.0 mg/kg PO, SC, q24)
  - **Ondansetron** (anti-emetic: 0.5 mg/kg/h CRI; 0.1-0.2 mg/kg slow IV q6-12h; 0.5-1.0 mg/kg PO

- q12-24h)
- **Metoclopramide** (anti-emetic + pro-kinetic: 0.2-1.0 mg/kg PO, SC, q8h, ½ h before food, or 1-2 mg/kg q24h as constant rate infusion)
- **Ranitidine** (antacid: 2 mg/kg PO, slow IV, q12h) or **famotidine** (antacid: 0.5-1.0 mg/kg PO q24-48h)
- **Vitamin K1** (see below – altered haemostasis)
- **Vitamin E** - an anti-oxidant and free radical scavenger with significant hepatoprotective properties (20-100 mg/cat PO, IM q24h)
- **Colchicine** – an anti-fibrotic which may be used where significant fibrosis is occurring (0.01-0.03 mg/kg PO q24h)
- **B12** (cobalamin - 125-250 µg/cat SQ q7-28 days)
- **B1** (100 mg/cat SQ, PO q12-24h)
- **B-Complex** (1-2 ml/l of fluids – keep out of light)
- **Vit C** (30 mg/kg PO q24h)
- **L-carnitine** (250-500 mg/cat PO q24h)
- **Taurine** (250-500 mg/cat PO q24h)
- **Zn** (7-10 mg/kg elemental Zn PO q24h)
- Some authors suggest feeding either hypoallergenic or high fiber diets.
- **Cisapride** (0.1-0.5 mg/kg PO q8-12h) – if significant GI stasis is present
- **Altered haemostasis:**
  - Abnormal clotting times are seen in >80% of cats and >90% of dogs with various forms of liver disease. This results from reduced synthesis and increased consumption of clotting factors.
  - Vit K is required for the normal function of factors II, VII, IX + X. It comes from the diet and is made by small intestinal microflora. However, because it is fat soluble it needs bile salts for absorption. **Vit K levels are low in 50% of cats with liver disease.** This is due to inappetence (causing reduced intake), concurrent small intestinal disease (causing reduced production) and cholestasis (resulting in reduced absorption)
  - **Acute treatment:**  
**Vit K1** (0.5-1.5 mg/kg SQ, IM, q12h for 1-2 days before biopsy or surgery)  
 N.B. Vit K cannot help in very severe liver disease when ~ all clotting factors may be lost  
**Fresh whole blood or plasma** (6-10 ml/kg IV, as needed)  
**Heparin** (50-100 iu/kg SQ q8-12h, with plasma, for disseminated intravascular coagulation)
  - **Chronic treatment:**  
**Vit K1** (0.5-1.5 mg/kg PO, SQ, q7-21days (Care, excess can cause Heinz body anaemia)  
**Correct cholestasis and treat small intestinal disease**
- **Surgery** will be required where **complete biliary obstruction** occurs (cholecystotomy or cholecystoduodenostomy).
- It is important to address any associated or underlying conditions, such as IBD, pancreatitis, extrahepatic bile duct obstruction, or cholecystitis.

#### Prognosis.

- For all forms of cholangitis the prognosis is **very variable and often unpredictable**. Some cases respond well and only need temporary treatment, others require continued therapy to maintain remission, while others progress relatively rapidly and require euthanasia. Once severe fibrosis, cirrhosis or ascites has developed the prognosis is usually guarded.

#### Prevention.

- Since it is not known what triggers the development of cholangitis complex, it is currently not possible to prevent its onset.

## **HYPERTHYROIDISM**

### **Pathogenesis.**

- **99% of cases of hyperthyroidism result from benign nodular hyperplasia/adenoma.**
  - Disease results from autonomous secretion of thyroxine (T4) and triiodothyroxine (T3). Negative feedback on the pituitary suppresses release of thyroid-stimulating hormone (TSH) and normal thyroid tissue atrophies.
  - **Cause is unknown** but may involve diet (iodine content, frequent changes, food additives), environmental causes (in cat litter, toxins, pollution, exposure to allergens), genetic mutation, abnormal immune and/or hormonal responses.
  - **70% of the cats have both thyroid glands affected.**
- **1% of cases result from mild to moderately malignant thyroid carcinoma.**
- GIT signs may result from polyphagia, malabsorption, or intestinal hypermotility.
- Polyuria/polydipsia may result from diuretic effects of T4, increased renal blood flow, associated renal insufficiency, or compulsive polydipsia.
- Cardiac effects result from a high output state, induced, in part, by a demand for increased tissue perfusion to meet the needs of increased tissue metabolism. Cardiovascular changes include left ventricular hypertrophy, left atrial and ventricular dilation, increased myocardial contractility, and decreased peripheral vascular resistance. Other contributors are the direct effect of thyroid hormones on cardiac muscle and the nervous system.
- Associated cardiac hypertrophy may cause congestive heart failure with tachycardia, a gallop rhythm, systolic murmurs, dyspnea, apathy, hindlimb weakness due to aortic thromboemboli, or collapse.
- Associated hypertension may be seen as ocular haemorrhage, or may cause clinical signs associated with cerebrovascular accidents, dementia, and/or renal failure.

### **Clinical signs.**

- **Hyperthyroidism is the most common endocrinopathy of cats.**
- **It is seen mainly in older cats** (>8 years of age); it is occasionally seen in cats as young as 4 years, and has even been documented in an 8-month old kitten.
- There is no sex or breed predisposition, but Siamese cats appear to be under-represented.
- **Most cats have a history of weight loss and polyphagia.**
- Weight loss usually occurs over several months.
- 10-20% of cats will present with signs of inappetence with weight loss.
- Cats may have a history of **restlessness, aggression, and a lack of grooming.**
- Cats may also show **tachycardia ± a gallop rhythm, vomiting and/or diarrhoea** (faeces may become bulky), **and/or polyuria/polydipsia.**
- GIT signs may result from polyphagia, malabsorption, or intestinal hypermotility.
- Polyuria/polydipsia may result from diuretic effects of T4, increased renal blood flow, associated renal insufficiency, or compulsive polydipsia.
- Associated cardiac hypertrophy may cause congestive heart failure with tachycardia, a gallop rhythm, systolic murmurs, dyspnea, apathy, hindlimb weakness due to aortic thromboemboli, or collapse.
- Associated hypertension increases the chance of finding a heart murmur, and may be seen as ocular hemorrhage, or may cause clinical signs associated with cerebrovascular accidents, dementia, and/or renal failure.
  - Up to 85% of cats with hyperthyroidism may develop systemic hypertension, either initially, or even some time after apparently successful treatment.
- Many hyperthyroid cats are presented for their routine vaccination with no owner complaints.

### Diagnosis.

- Hyperthyroidism should be suspected when any older cat presents with weight loss, and especially when the weight loss is associated with a good appetite. However, inappetence should not rule out hyperthyroidism.
- Physical examination usually reveals a thyroid nodule on either or both sides of the trachea in the ventral cervical region (80-90%).
- Tachycardia and/or a gallop rhythm are usually present.
- Liver enzymes (ALT and/or SAP) are often raised. Hepatopathy may be secondary to a direct toxic effect of thyroid hormones, hepatic lipidosis, malnutrition, or hepatic hypoxia resulting from cardiac failure.
- **Definitive diagnosis is based on detecting elevated serum concentrations of total T4 (and/or T3).**
- **Some cats with hyperthyroidism have a T4 concentration that is within the normal range.** This may be due to:
  - Early or mild hyperthyroidism.
  - T4 concentrations varying during the day.
  - Severe systemic illness causing a reduction in T4 (euthyroid sick syndrome).
- If hyperthyroidism is suspected despite a high normal T4 concentration:
  - **Retest the cat** – either immediately, or in a few weeks time.
  - **Check free T4** – by equilibrium dialysis.
  - **T3 suppression test** – Collect blood sample, give 7 x 25mg doses of T3 PO every 8h, then collect blood 2-4h after the 7<sup>th</sup> dose (i.e. on day 3). An increase in T3 concentration confirms successful medication. Suppression of T4 concentration (below 50% of baseline, <20 nmol/l [1.5 ug/dl]) does not usually occur in hyperthyroid cats.
  - **Thyrotropin-releasing hormone (TRH) stimulation test** – Collect blood give 0.1 mg/kg TRH IV, then collect second blood sample 4 hours later. Assess both samples for serum T4 concentration. Stimulation to > 50% does not occur in hyperthyroid cats. Side effects of TRH include transient salivation, vomiting, tachypnoea, and defecation.
  - **Thyroid-stimulating hormone (TSH) response test** – The usefulness of this test has been questioned and TSH is very difficult to obtain.
  - **Nuclear isotope scanning** detects hyperactive thyroid tissue. Procedure is relatively safe and simple to perform, but requires access to a licensed facility, which is not always available.
  - **Trial course of anti-thyroid therapy** (see below) of approximately 30 days is not without risk of toxic side effects.
  - Cats with hyperthyroidism that develop significant diarrhoea may have significant reductions in **serum folate and/or cobalamin levels**. It is necessary to identify and correct these deficiencies before the intestines can recover because successful treatment of the hyperthyroidism is not sufficient to resolve the diarrhoea.

### Differential diagnosis.

- These include most other causes of weight loss with a good appetite. However, hyperthyroidism typically occurs in older cats and presents with polyuria, polydipsia, vomiting and/or diarrhoea. So diabetes, renal disease, malabsorption syndromes (including IBD, pancreatitis/ exocrine pancreatic insufficiency, and early intestinal lymphoma), acromegaly, and hyperadrenocorticism are perhaps the most important differentials.

### Treatment.

- Hyperthyroidism can be treated medically, surgically, or with radioiodine ( $I^{131}$ ).
- **Prior to deciding which treatment to use the cat should be assessed for concurrent disease, especially renal disease, systemic hypertension and heart disease**, all of which occur commonly in association with hyperthyroidism.
  - The interplay between systemic blood pressure and renal function is complex. While **systemic hypertension is detrimental to kidney function**, a sudden fall in blood pressure or a reduction in

glomerular filtration rate (e.g. associated with a sudden fall in T4) can exacerbate renal dysfunction by causing a sudden fall in renal blood flow. **Changes in T4 need to be made gradually** so there are no sudden changes in renal blood pressure.

- By maintaining renal blood pressure, hyperthyroidism can mask low-grade renal insufficiency. It is essential to check serum urea and creatinine concentrations and urine specific gravity prior to inducing irreversible reduction of T4 (i.e. by thyroidectomy or I<sup>131</sup> treatment). A short course of medical therapy may reveal the presence of masked renal insufficiency.
- **Medical therapy** tends to be given to stabilize the cat prior to surgical treatment, to check for masked renal disease prior to thyroidectomy or I<sup>131</sup> treatment, or when neither I<sup>131</sup> nor surgery are possible.
- **Methimazole and carbimazole** block T3 and T4 synthesis. It takes 1-3 weeks before a significant decrease in T4 concentrations occur after beginning treatment.
  - Carbimazole is broken down to methimazole in vivo. Bioavailability and volume of distribution of methimazole is highly variable between cats.
  - Dose for both is 1.25-5.0 mg PO every 8-24 hours initially, reducing to every 12-24 hours. If the cat has concurrent renal insufficiency, start with a low dose and monitor renal values as dose is gradually increased. Preliminary studies with topical transdermal applications show promise.
  - When cat and owner compliance is good, the successful response rate is approximately 85% with medical treatment.
  - **Poor compliance results** from:
    - The need for **frequent medication**.
    - The need for **frequent blood samples** to look for possible side effects. Blood dyscrasias occur in 2-10% of cats and include eosinophilia, lymphocytosis, leukopenia, thrombocytopenia, and/or agranulocytosis, hepatopathy, and rarely, immune-mediated hemolytic anaemia (IMHA).
    - **Frequent side effects**. Up to approximately 20% of cats develop anorexia, vomiting, lethargy, hepatopathy ± jaundice, cutaneous reactions (typically pruritus of the head and neck), bleeding tendencies or, very occasionally, myasthenia gravis, or IMHA.
    - Mild side effects may resolve despite continued treatment.
- **Other medical therapies include:**
  - **Propranolol** (β-adrenoceptor blocking agent) may be added to reduce tachycardia, arrhythmias, and hypertension (2.5-5.0 mg/cat PO every 8-12 hours).
  - **Stable iodine** helps to decrease T3 and T4 synthesis and reduce thyroid gland vascularity, but the effect can be transient and inconsistent. Give potassium iodide 30-100mg/cat/day PO for 10-14 days prior to surgery using 100g potassium iodide/100ml solution, or potassium iodate ~20mg/cat every 12 hours PO.
  - **Calcium or sodium ipodate** is a radiopaque iodine agent that reduces T3 concentrations. Its effect can be transient, and it may be difficult to obtain (15 mg/kg PO every 12 hours).
- **Surgical thyroidectomy**. The success depends on the stability of the patient, the expertise of the surgeon (a bilateral thyroidectomy is usually performed), and the expertise of the anesthetist (e.g. do not give atropine).
  - Successful response rate is > 95%. Ectopic overactive thyroid tissue is a cause of failure, as it is usually missed at surgery.
  - Reduce the risks of surgery by making the cat euthyroid prior to surgery (see *medical therapy* above).
  - Surgical risks include anesthetic risks in older patients (often with concurrent renal ± cardiac disease), iatrogenic damage to parathyroid tissue leading to transient or permanent hypocalcemia, or to the local nerves leading to laryngeal paralysis or Horner's syndrome.
- **Radioiodine (I<sup>131</sup>)** is taken up by and destroys the overactive thyroid tissue, but spares the normal tissue.
  - Successful response rate is > 95%, but it may take a few weeks, or occasionally months, for the normal tissue to recover function.
  - Availability of facilities and length of stay in hospital varies from 2 days to 4 weeks depending on country and state, as it often depends on the interpretation of radiation safety laws.

- Side effects are few and include transient dysphagia or dysphonia, or permanent hypothyroidism (~2%).

**Prognosis.**

- Without treatment, cats with hyperthyroidism will usually die of concurrent renal disease, heart disease, liver disease, or systemic hypertension.
- With **treatment, prognosis varies from very good to guarded**, dependent on the presence of heart disease, renal disease, and systemic hypertension, whether or not any damage has become permanent prior to treatment of the hyperthyroidism, and which treatment options are available.

**Prevention.**

- Since it is not known what triggers the development of hyperthyroidism, it is currently not possible to prevent its onset.

**Table 1: Causes of diarrhoea in cats**

**Intestinal Diseases:**

- Dietary related (sudden change in diet, dietary indiscretion, intolerance, hypersensitivity)
- Infectious diseases
  - Viruses* – parvovirus, enteric coronavirus, intestinal FIP, FIV, FeLV, Toravirus ('third eye-lid prolapse and diarrhoea syndrome'), Astrovirus, Rotavirus
  - Bacteria* – Campylobacter, Salmonella, Clostridium, *E.coli*, Yersinia, Mycobacteria
  - Protozoa* – coccidia (Isospora, Cryptosporidia), Giardia, *Tritrichomonas foetus*
  - Helminths* – roundworm (Toxocara), tapeworm (Dipylidium), whipworm (Trichuris)
- Inflammatory bowel disease e.g. plasmacytic-lymphocytic, eosinophilic, suppurative, etc.
- Neoplasia e.g. lymphoma, adenocarcinoma
- Intussusception
- Partial intestinal obstruction
- Short bowel syndrome (usually post surgical)
- Adynamic ileus and intestinal pseudo-obstruction

**Extra-intestinal diseases:**

- Polysystemic infection – bacteraemia, septicaemia, FeLV, FIP, FIV
- Liver disease
- Pancreatic disease
- Endocrine disease eg hyperthyroidism
- Renal disease
- Miscellaneous, such as toxaeemias (eg peritonitis) or various toxins and drugs

**Table 2: Features that can help differentiate large and small intestinal diarrhoea**

	<b>Small Intestinal disease</b>	<b>Large Intestinal disease</b>
<b>Faecal volume</b>	Increases	Normal or decreased
<b>Presence of mucus</b>	Rarely present	Common
<b>Melaena</b>	Maybe present	Absent
<b>Haematochezia</b>	Absent except in acute haemorrhagic enteropathy	Can be present
<b>Steatorrhoea</b>	Present with malabsorption	Absent
<b>Urgency in defaecating</b>	Absent unless in acute	Usually but not invariably
<b>Tenesmus</b>	Absent	Frequent
<b>Frequency of defaecation</b>	2-3 times normal	>3 times normal
<b>Dyschezia</b>	Absent	Present in distal colon or rectal disease
<b>Flatulence/ Borborygmi</b>	May occur	Absent
<b>Vomiting</b>	Common in acute infectious disorders or as part of triaditis	May occur in 30-35% of acute colitis
<b>Appetite</b>	Usually normal but can be reduced	Usually remains normal
<b>Weight loss</b>	Usually only occurs as disease becomes chronic	Unusual
<b>Faecal incontinence</b>	Rare only associated with severe enteritis and large amounts of watery diarrhoea	May be present
<b>Perianal Irritation</b>	Absent	Occasionally present