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FORT DODGE

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What's new in Feline Inflammatory Hepatobiliary Disease

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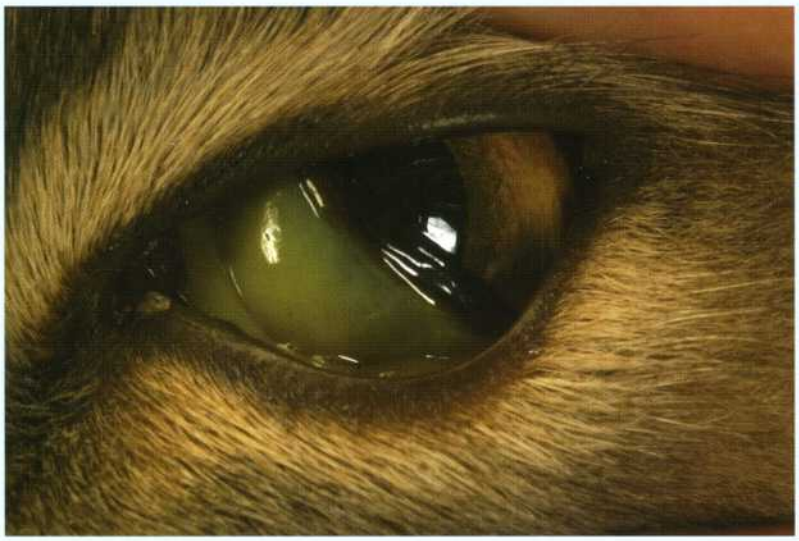

Fig. 1: Jaundice is a common clinical sign in cats with inflammatory liver disease .

Introduction

The most common feline liver disorder in the USA is hepatic lipidosis. Although this is being recognised increasingly frequently in the UK, the most common form of liver disorder in cats seen here is inflammatory hepatobiliary disease. This term encompasses the different forms of the feline cholangitis and cholangiohepatitis complex.

Feline inflammatory liver disease has long been regarded as a controversial area. Some cases are recognised as clearly suppurative in nature whilst others involve a predominantly lymphocytic infiltrate, but not all cases fit into these categories. Some cases are more difficult to characterise and in other cases there may be overlap in the features, with both a lymphocytic and neutrophilic infiltrate. The crucial question for the clinician is what relevance this has as to how a case should be treated and managed. Antibiotics would generally be the mainstay of treatment for the suppurative form and corticosteroids would be used for lymphocytic cholangitis. But how should the less clear cut cases be managed?

Signalment, clinical signs, blood test results and imaging of the liver can help the clinician in establishing a presumptive diagnosis. Since the different form of feline inflammatory liver disease are classified by their characteristic histopathological lesions, definitive diagnosis is dependent on histology interpretation which requires liver biopsy. However one of the problems in the past has been the controversy regarding the classification and differentiation of inflammatory liver diseases in cats. Certain diseases have been given more than one name and it has also been observed that different hepatic disorders have been given the same name. Additionally there has been marked inter-observer variation in the interpretation of tissue samples potentially leading to different diagnoses for the same case depending on the evaluating pathologist. Following the example set by the World Small Animal Veterinary Association (WSAVA) for inflammatory bowel disease (IBD), which is another area of controversy regarding criteria for diagnosis, the WSAVA established a Liver Standardization Group which suggested standards for clinical and histological diagnosis of canine and feline liver disease in 2006. The aim of this international expert group was to establish world-wide acceptable standards and criteria for the diagnosis of all known liver diseases of dogs and cats.

CONTENTS

This article will briefly summarise the classifications for feline inflammatory liver disease proposed by the WSAVA and discuss the relevance the clinical features, diagnosis and treatment.

Classification

The WSAVA Liver Standardization Group has described three distinct forms of feline cholangitis:

1. **Neutrophilic cholangitis: *a. acute b. chronic***
2. **Lymphocytic cholangitis**
3. **Chronic cholangitis secondary to liver fluke infestation**

Since inflammatory lesions are centred on intrahepatic bile ducts and do not always involve hepatic parenchyma the WSAVA Liver Standardization Group uses the term cholangitis rather than cholangiohepatitis. In the cases where disruption of the limiting plate occurs and inflammation involves hepatic parenchyma it is regarded as a consequence of a primary cholangitis.

Neutrophilic cholangitis

Neutrophilic cholangitis has been divided into two separate forms - acute and chronic - which are hypothesised to be different stages of the same condition.

Acute neutrophilic cholangitis

This form of cholangitis is characterised by a primarily neutrophilic infiltrate in the portal areas and the walls and lumen of intrahepatic bile ducts. Degeneration of the bile duct epithelium and necrosis can be seen in association with this. Commonly the inflammation also involves the liver parenchyma. This form of cholangitis is believed to result from an ascending bacterial infection of the biliary tract and commonly isolated bacteria from the bile of affected cats indicate an enteric origin. Some authors consider anatomic abnormalities of the gall bladder to be a predisposing factor. In some cases of neutrophilic cholangitis where a bacterial aetiology is suspected bile culture results are negative. Possible reasons for this are prior antibiotic treatment, the difficulty to culture certain bacteria in vitro and inappropriate sample handling particularly for anaerobic culture.

Chronic neutrophilic cholangitis

The chronic form of neutrophilic cholangitis is characterised by infiltration of portal areas and/or bile ducts with plasma cells, lymphocytes and fewer neutrophils and occasionally macrophages. Bile duct degeneration and necrosis may be seen and the inflammation may extend beyond the limiting plate. Bile duct hyperplasia is a common finding and depending on the duration of the process various degrees of fibrosis might be present.

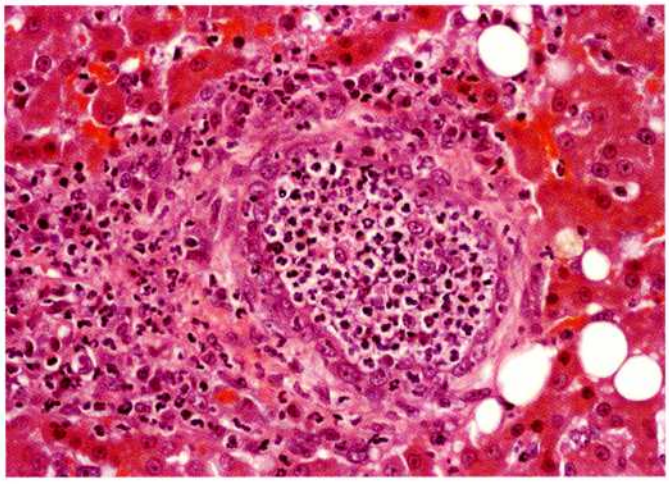

Fig. 2: Histopathology of liver showing neutrophilic cholangitis: The bile duct is dilated and contains many neutrophils. Neutrophils extend into the surrounding portal area and hepatic parenchyma.

Chronic cholangitis may represent a tissue response to chronic injury which may not be related to bacterial infection and it has also been suggested that it may be a progression from the acute form of the disease. However there are no reports of any cats in which chronic disease has been diagnosed subsequent to an acute episode. The chronic neutrophilic cholangitis group probably represents the cases previously described as unclassified with mixed inflammatory infiltrates.

Neutrophilic cholangitis is frequently associated with other disease entities such as pancreatitis and inflammatory bowel disease (IBD). The term triaditis describes a syndrome where all three entities occur concurrently and potentially are a result of a related underlying disease process. As for the aetiology of neutrophilic cholangitis ascending bacterial infection is also believed to play an important role in the development of pancreatitis. In the cat the pancreatic and bile ducts enter the duodenum together which might predispose cats to the concurrent development of cholangitis and pancreatitis. Some authors suggest that IBD might predispose to ascending infections. The predominant clinical signs in cats with triaditis usually result from the cholangitis. Pancreatitis and IBD are usually identified as complicating factors.

Lymphocytic cholangitis

This condition is characterised by a moderate to marked infiltrate of portal areas with small lymphocytes. Fewer numbers of other inflammatory cells, especially neutrophils, may also be present. In some cases the inflammation breaks through the limiting plate and extends into the periportal liver parenchyma.

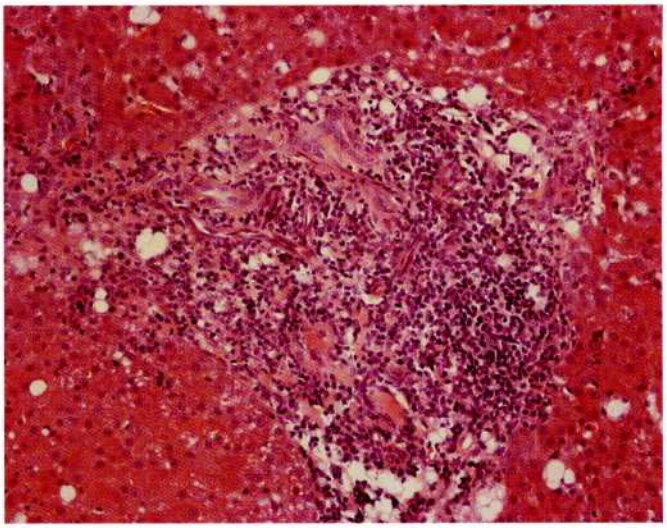

Fig. 3: Histopathology of liver showing lymphocytic cholangitis: The portal area contains a dense lymphocytic infiltrate.

In more chronic stages there tend to be less lymphocytes and various degrees of fibrosis such as portal to bridging lobular fibrosis or periductular fibrosis can be seen. This may lead to disruption of the vasculature with prominent small blood vessels on the liver surface. Lymphocytes within the bile duct walls is another finding which is more common in chronic disease. Concurrent pancreatitis has been reported but there does not seem to be a striking association. The aetiology of this condition is uncertain. An immune-mediated pathogenesis has been suggested and there has been a suggestion recently that *Helicobacter pylori* may play a role in the development of this condition. In the past a connection between the neutrophilic and lymphocytic form of cholangitis had been suspected suggesting that lymphocytic cholangitis was a progression of the neutrophilic form. This is however generally now believed not to be the case and the two conditions are distinct, separate diseases.

Lymphocytic portal hepatitis has been described as a form of inflammatory liver disease. Its characteristics are lymphoplasmacytic infiltrates confined to the portal areas without involvement of the hepatic parenchyma and bile ducts. It has been shown that small amounts of lymphocytes and plasma cells can be found in portal areas of healthy young cats and a more prominent lymphoplasmacytic portal infiltrate can commonly be seen in cats over 10 years of age. This finding is often linked to extrahepatobiliary problems. It is not entirely clear whether this condition is a distinct disease or merely a histologic lesion frequently found in older cats and it is therefore not included in the WSAVA classification scheme.

Chronic cholangitis secondary to liver fluke infestation

This form of inflammatory liver disease is caused by infestation with liver flukes belonging primarily to the family *Opisthorchiidae*. Cats which are one of the possible final hosts acquire infection by ingestion of metacercariae present in the second intermediate host (reptile, amphibian and a wide variety of fish) in the fluke life cycle.

This infection is commonly seen in endemic areas (e.g. Central and South America, many countries in Asia, Southern Europe) and depending on the parasite burden cats may or may not show signs of liver disease. This form of cholangitis is of little relevance to the UK.

Clinical Features, Diagnosis, Treatment

Acute Neutrophilic cholangitis

This form of cholangitis is most often seen in young cats (median age 3.3 years) and a predisposition in male cats has been noted. These animals are usually acutely ill with a history of anorexia, lethargy, vomiting and potentially diarrhoea. They usually are jaundiced and may show fever, dehydration, abdominal pain and less frequently hepatomegaly and hypothermia.

On routine laboratory evaluation raised ALT and bilirubin are the most consistent findings. ALP, γGT and serum bile acid concentrations are usually also increased. Haematology frequently reveals a moderate leukocytosis with neutrophilia and left shift. Although spontaneous haemostatic complications are rare prolonged clotting times may be seen.

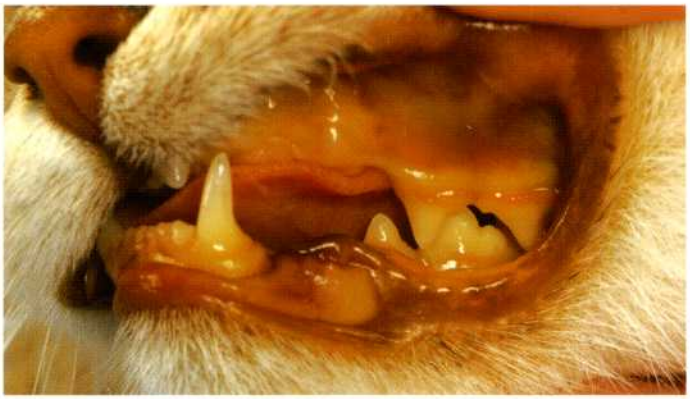

Fig. 4: Note the severely jaundiced oral mucous membranes.

There are generally no specific changes on abdominal radiographs that would indicate acute neutrophilic cholangitis, but certain features may be seen such as distension of the gall bladder or the presence of choleliths. Ultrasonography is more reliable in identifying distension of the gall bladder and bile duct. Thickening of the gall bladder wall, biliary sludge, and occasionally cholelithiasis may also be identified. A liver biopsy is necessary in all cases to confirm the diagnosis. Fine needle aspirates (FNA) are not recommended due to their inherent severe limitations. These tissue samples will not show the characteristic alterations in liver architecture, nor the location of the infiltrate or pattern of fibrosis. However they are less invasive than other sampling techniques and may help to identify a neutrophilic process. Laparotomy allows for a wedge biopsy sample, for aspiration of bile and also for direct visualisation of the liver, biliary tree, pancreas and intestines. With a liver biopsy needle percutaneously collected tissue samples are also appropriate for histopathology. Liver tissue and bile samples should also be submitted for bacteriological culture. Generally it might be safer in cats with signs of liver disease to postpone liver biopsy, especially if general anaesthesia is necessary, until 2 to 3 days of supportive treatment and other specific therapy have been given *(see below)*.

Chronic Neutrophilic cholangitis

In these cats the clinical signs are usually present for more than 2 weeks and are often intermittent, waxing and waning over months. Common findings consist of vomiting, icterus and hepatomegaly. In these cases leukocytosis is not commonly seen on haematological examination however most of them will show increased ALT, γGT, ALP and bilirubin measurements. In severe end stage liver disease coagulopathies and hepatic encephalopathy might be seen. Like for all inflammatory liver conditions diagnosis has to be made through histological evaluation of a liver tissue sample.

The mainstay of treatment for both acute and chronic neutrophilic cholangitis is antibiotic therapy. Whenever possible the antibiotic should be chosen based upon the results of bile or hepatic tissue culture and sensitivity testing. Initially however until these test results become available empirical treatment should consist of a broad spectrum, bactericidal antibiotic which is excreted in bile in its active form and does not require hepatic metabolism for activation or excretion. Popular initial choices are ampicillin, amoxicillin or amoxicillin clavulanic acid, cephalosporins or fluoroquinolones often in combination with metronidazole for additional cover of anaerobes. It is recommended that for these cases treatment is maintained for 4 to 6 weeks to minimise the risk of recurrence.

In cases of complete biliary obstruction due to inspissated bile or choleliths surgical intervention may become necessary. The aim is, whenever possible, to preserve the normal anatomy of the biliary tract and avoid any by-pass procedures. The postoperative prognosis for cats requiring surgery is guarded.

In some cases of acute neutrophilic cholangitis the judicious short term use of corticosteroids at anti-inflammatory doses might be helpful by facilitating bile flow through reducing inflammation of the biliary tree. In addition choleretics are used to promote bile flow in cases where extrahepatic biliary obstruction can be ruled out. Ursodeoxycholic acid is given orally at a dose of 10 to 15 mg once daily. It reduces the amount of hydrophobic bile acids and therefore limits their toxic effect on hepatocyte membranes. There are no controlled studies available proving its beneficial effects in cats, it has however been shown to improve the quality of life in human liver patients. It appears to be safe in cats and adverse reactions are usually limited to mild diarrhoea and are rare. In those cases where hepatic disease has led to haemostatic dysfunction supplementation with vitamin K is indicated at 5 mg (0.5 mg/kg s.c. q 12 h for 2 doses) orally or subcutaneously. The use of nutraceuticals in the treatment of feline liver disease has increased in recent years. S-adenosyl-L-methionine (SAMe) is used frequently. It is believed to reduce oxidative damage to the liver by restoring glutathione levels which are reduced in liver disease and by increasing levels of cysteine and taurine which have cytoprotective effects and are needed for bile acid conjugation. The vitamins E and C and phosphatidylcholine, a phospholipid, can also be used. Recently there has been interest in the herb milk thistle which might also have beneficial effects.

Another important component in the treatment of acute neutrophilic cholangitis is pain relief, as abdominal pain might be present and is not always easy to detect. Nonsteriodal anti-inflammatory drugs are best avoided because the gastrointestinal tract may already be compromised.

In general supportive care consisting of fluid therapy, the correction of any electrolyte imbalances and nutritional support is necessary for all patients with liver disease. It is important to meet the caloric and protein requirements of the cat in order to treat any concurrent hepatic lipidosis, prevent the development of fatty changes and to aid in recovery. Only in cases of hepatic encephalopathy should protein be restricted.

Cats suffering form the chronic form of neutrophilic cholangitis show a mixed inflammatory liver infiltrate and therefore the dilemma for the clinician is whether to treat with corticosteroids or antibiotics. Frequently both are used in combination or corticosteroids are added if no response is seen within 2 weeks of antibiotic treatment. A commonly used regime for prednisolone is as follows: 1 mg/kg twice daily for 2 weeks, followed by 1 mg/kg once daily for 2 weeks, 0.5 mg/kg once daily for 2 weeks, 0.5 mg/kg every other day for 4 weeks. The clinical response and biochemical parameters should be satisfactory before each reduction of the prednisolone dose. Budesonide is another possible choice for cases where prednisolone should be avoided.

Only limited information is available on the prognosis for cats with neutrophilic cholangitis. One study of 15 cats showed that about half of the cats survived more than 1 year and the median survival time was 29 months.

Lymphocytic cholangitis

In the UK this type of liver disease is seen more frequently compared to other countries especially the USA. In one study of 21 cats with lymphocytic cholangitis 14 cats were under 4 years of age. Persian cats appear to have a predisposition. Icterus and/or progressive ascites are the main presenting signs in lymphocytic cholangitis and in contrast to cases of neutrophilic cholangitis many of these cats do not appear ill. Anorexia and weight loss are not a consistent finding, some cats show polyphagia. Pyrexia is not commonly seen. Generalised mild lymphadenopathy is frequently present and abdominal palpation may reveal hepatomegaly which in some cases can be severe. Hepatic encephalopathy may develop in advanced stages of this disease due to cirrhosis and portal hypertension. This finding is however very rare. Common clinicopathologic features are increases in ALT, ALP, γGT and bile acids which can be severe. Bilirubin levels may often be elevated severely enough to cause jaundice. Serum globulins are frequently increased. On haematology the most consistent finding is lymphopenia. Mild anaemia and neutrophilia may also be present. Examination of ascites will generally reveal a clear to yellow tinged thick fluid with a low cellular and a high protein content consisting mainly of globulins. Abdominal radiography is unrewarding in cases where ascites is present. Severe hepatomegaly can be seen in some cases which is suggestive of this type of cholangitis. Ultrasonography may reveal a heterogenous appearance of the liver parenchyma and in advanced cases with extensive cirrhosis it may be hyperechoic. The limitations of FNA have been discussed above however they may reveal a lymphocytic infiltrate. Prominent blood vessels might be present on the liver surface in chronic stages of this condition and the possible depletion of liver-dependent clotting factors due to severe liver disease can add to the risk of post-biopsy haemorrhage. Therefore

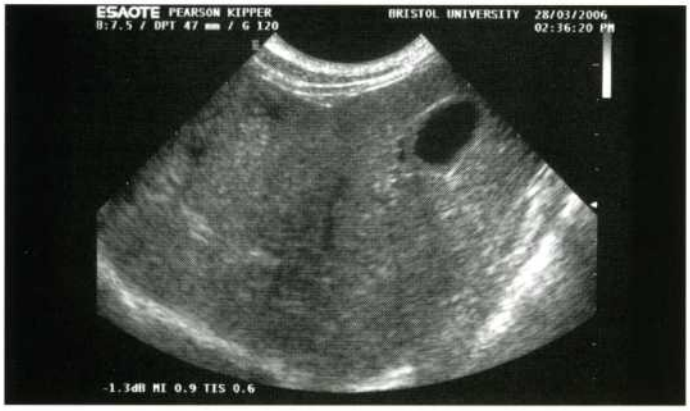

Fig. 5: Ultrasound image of the liver of a cat diagnosed with lymphocytic cholangitis. Note the heterogenous appearance of the liver parenchyma.

sample collection during laparotomy might be preferable to percutaneous biopsy techniques since it allows the surgeon to visualise the biopsy site and to provide adequate haemostatic control if necessary. Other liver diseases, lymphosarcoma and especially FIP are important differential diagnoses for lymphocytic cholangitis. Cats suffering from FIP can have very similar clinical signs and laboratory findings and it can be difficult to distinguish the two diseases. If features such as uveitis, neurologic signs and pleural effusion can be identified in addition, FIP is more likely, but reliable differentiation may depend on histopathologic examination.

Treatment for lymphocytic cholangitis cases primarily consists of immunosuppressive agents in order to counteract immune-mediated damage to the liver. Prednisolone is a frequent choice and is given orally at immunosuppressive doses of 1 to 2 mg/kg twice daily. Depending on the progress of the case this dose is then gradually reduced over a period of 6 to 12 weeks. Clinical experience demonstrates its usefulness whereas there is little information available on other immunosuppressive agents. Colchicine has been used to counteract fibrosis although there are no controlled studies available proving a beneficial effect. Like for the treatment of the neutrophilic form of cholangitis choleretics, SAMe and nutritional support may be helpful. Severe abdominal distention due to ascites might have to be relieved by abdominocentesis. In cases of mild ascites loop diuretics such as furosemide at 1 to 2 mg/kg twice daily and dietary salt restriction might be useful. Alternatively potassium-sparing diuretics and angiotensin-converting enzyme inhibitors can be tried. Cats may respond well to treatment, but there may be recurrence and further progression of the liver disease. As with neutrophilic cholangitis, monitoring of liver parameters may be useful. Re-biopsy may be helpful but is often not feasible. Cats with jaundice generally respond better than those with ascites. Repeated courses of prednisolone or long term low dose treatment might be necessary for some cases.

WHAT'S NEW IN FIHD 4 *Feline Update Online*

References are available on request.

A FLEA TING GLIMPSE OF NEWLY RECOGNISED VECTOR BORNE DISEASES IN CATS

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Fleas are effective vectors for numerous microbial pathogens of medical and veterinary importance. There is increasing interest in the role of the cat flea, *Ctenocephalides felis (Bouché, 1835)*, in the epidemiology of zoonotic flea-transmitted diseases including cat scratch disease (bartonella species) and the spotted fever rickettsial species *(Rickettsia felis)*.

Although best adapted to parasitize domesticated cats and dogs, *C. felis* can feed on a wide range of hosts including wildlife species that live close to urban areas. Under optimal conditions, large flea burdens can build up inside houses and *C. felis* will bite humans in this situation, particularly in the absence of a more suitable cat or dog host.

There is some evidence that *C.felis* may under certain circumstances transfer from its preferred host, the cat or dog, to other hosts and therefore transmit pathogens. *C. felis* has a variety of roles in the ecology of the pathogens it transmits.

It is a biological vector for *R. felis,* which can be naturally maintained within a flea population by transovarial transmission. The mechanisms involved in maintenance or amplification of *Bartonella henselae* within *C. felis* are still to be elucidated by micro-evaluation of attachment to and invasion of the flea gut. The different organisms that infect fleas are processed in different ways which may alter the pathogenesis to the mammalian host on which the fleas feed.

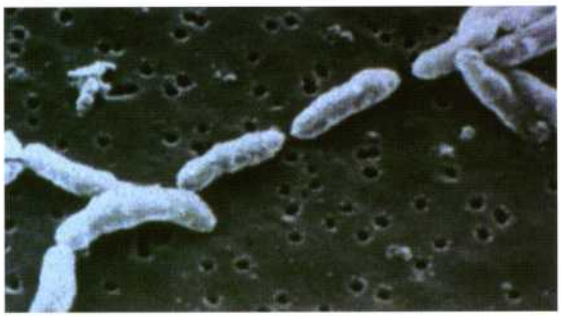

Fig 1: Electron microscopy image of *Bartonella henselae.*

Flea adapted Rickettsia species are transmitted directly by flea bites, whereas *B. henselae* is transferred indirectly by inoculation of infected flea faeces through skin abrasions.

Although these newly recognised infectious agents appear to cause only limited clinical disease in cats in Europe, they are of zoonotic importance. Veterinary surgeons need to be aware of the potential for human disease and be ready to advise on prevention through appropriate flea control

BARTONELLOSIS

Bartonellosis is caused by Gram-negative, intraerythrocytic, arthropod-transmitted bacteria of the genus, Bartonella. Several species are pathogenic in cats *(Bartonella henselae, B. koehlerae, B. clarridgeiae).* Asymptomatic infection with *B. henselae* (or *B. clarridgeiae)* is common in cats, and cats are a major reservoir for human infection. In humans, *B. henselae* (and potentially *B. clarridgeiae*) is the cause of cat scratch disease (CSD), and can cause endocarditis, prolonged bacteraemia and various ocular disorders including Perinaud oculoglandular syndrome, neuroretinitis and chorioretinitis. In immunosuppressed humans, *B. henselae* has been associated with the vasculo-proliferative disorders, bacillary angiomatosis and peliosis hepatis. Genotypic and phenotypic variations in *B. henselae* strains have been demonstrated in domestic and wild cats and those from different geographical locations.

The zoonotic potential of *B. henselae* is significant. For example, in the UK, 4.5 million households (or more than 1in 4) house over 7.5 million cats, of which about 10% are *B.*

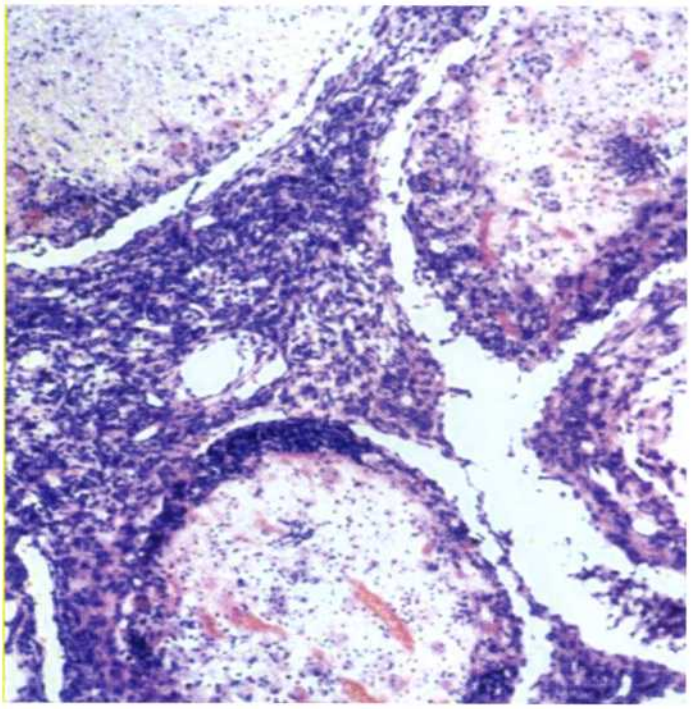

Fig 2: Lymph node biopsy: severe diffuse necrotising lymphadenitis.

henselae bacteraemic. The potential threat of this reservoir is reflected in the frequency with which humans acquire *B. henselae* infections, most commonly manifesting as cat scratch disease (CSD). In the USA about 24,000 cases of CSD are reported each year, of which about 2,000 require hospitalisation. Fortunately, this syndrome is usually benign and self-limiting, manifesting as a regional lymphadenopathy and affecting mainly children and young adults. However, systemic complications may arise leading to more serious disease. Accurate diagnosis of CSD is important as it requires differentiation from other potentially more serious causes of lymphadenitis such as abscesses, lymphoma, mycobacterial infections, toxoplasmosis and Kawasaki disease.

When first characterised in the late 1980s, *B. henselae* was recognised as a potential opportunistic infection in AIDS patients. The advent of more effective prophylactic therapy for these patients has seen the incidence of these complications decline in the USA and Europe, although they are likely to remain a significant health issue in Africa and other developing parts of the world where therapies are not currently affordable. Medical interest in zoonotic bartonellae, however, continues today as an increasing spectrum of syndromes among immuno-competent individuals is encountered. Perhaps of most relevance currently is the emergence of *B. henselae* in the aetiologies of ocular syndromes such as uveitis and neuro-retinitis.

Cat fleas are considered the main vector of *B. henselae* in cats and recent work has shown transmission by skin inoculation of infected flea faeces. However, the role of the cat flea in the transmission of *B. henselae* from cats to humans has not been proven.

Prevalence

Asymptomatic infection with *Bartonella henselae* is common in cats; 40-70% with seropositivity and 9-90% with bacteraemia (prevalence of *B. clarridgeiae* far lower). Prevalence variability may be related to small survey sizes, differences in cat population characteristics (cattery, stray, feral and captive wild cats) and seasonal variation as well as true differences in geographic prevalence. Flea populations and exposure to *B. henselae*, are favoured by warm temperatures with high humidity but the relatively high prevalence of *B. henselae* in temperate climates reflects the maintenance of the flea life cycle in heated domestic environments the effect of climate change. *B. henselae* is more common in young to middle-aged cats but there is no breed or gender predisposition. Genotypic and phenotypic variations in *B. henselae* strains have been demonstrated in domestic and wild cats and those from different geographical locations.

Pathogenicity and clinical signs

Disease association with naturally occurring feline Bartonella infection is difficult to determine. Although clinical disease (fever, lethargy, transient anaemia, lymphadenomegaly, neurological dysfunction or reproductive failure) has been reported following experimental infections with *B. henselae* and *B. clarridgeiae*, naturally occurring disease associated with infection is more difficult to define because of its high prevalence in apparently asymptomatic cats. Although Bartonella infection has been associated with several clinical syndromes based on positive blood culture, the association is difficult to evaluate unless the presence of organisms in lesions is confirmed.

Fig 3: Two one-year old littermates, one of which has a febrile syndrome with pyogranulomatous lymphadenitis. Blood from the cat was PCR positive for *B. henselae*.
"From Shaw & Day: Arthropod-borne Infectious Diseases of the Dog and Cat, ISBN 978-1-84076-057-6, price £35.00, published by Manson Publishing Ltd."

Diagnosis

Difficulties in interpreting the significance of positive blood cultures and serology necessitates the use of multiple diagnostic methods. Diagnosis of bartonella-induced disease is best confirmed by demonstration of organisms in infected tissues using histological immuno- histological or molecular histological methods. See table 1 on next page.

Therapy

Doxycycline, amoxicillin, amoxicillin/clavulanate used at higher than recommended dose rates have

Culture:

Blood culture of *B. henselae* and *B. clarridgeiae* from antibiotic-free cats is relatively simple microbiologically but requires prolonged incubation which limits its practicality for routine diagnosis.

Serology:

Different serological methods have been used to detect circulating antibodies to Bartonella. There is persistence of Bartonella IgG which limits the diagnostic usefulness of elevated antibody levels. The estimated positive predictive value of seropositivity as an indicator of bacteraemia is less than 50%. In addition, interpretation is compromised by cross-reactivity between Bartonella species and non-Bartonella a-subgroup Proteobacteria.

Histopathology and Warthin-Starry (WS) silver stain:

These are essential to demonstrate the presence of organisms within compatible lesions.

Molecular diagnosis:

PCR-based methods have been described targeting a range of DNA fragments of the 16S rRNA-encoding gene, the 16S-23S intergenic spacer region, and the citrate synthase-encoding gene (gltA). Real time PCR techniques are rapid and specific. However, the same issues regarding distinguishing infection from disease

Table 1: Methods of diagnosis of bartonellosis.

been reported to be successful in suppressing bacteraemia in experimental infections. However, more detailed study suggested that although enrofloxacin was more efficacious than doxycycline for the treatment of *B. henselae* or *B. clarridgeiae*, neither drug eliminated the infection in all animals, even when administered for 4 weeks. Data relating to the treatment of naturally infected cats are scant. However, because of the difficulty in eliminating bacteraemia, antibiotic therapy is only recommended for those cats that have confirmed bartonella-associated disease or those in contact with immunosuppressed owners.

Prevention and control

No vaccination is currently available. Lack of cross protection between strains is a problem and suggests that any vaccine would require incorporation of multiple Bartonella epitopes.

The prevalence of Bartonella bacteraemia in cats and the risk of Bartonella-associated disease in pet owners, should be decreased by a vigorous integrated flea control programme. When uninfected cats are housed with *B. henselae* bacteraemic SPF cats in an ectoparasite-free environment, there is no evidence of Bartonella transmission between cats. However, despite the availability of effective flea adulticide treatments, bartonella infections remain common, even in the domestic cat populations of industrialised, affluent countries of Europe and North America. As yet no studies have been carried out examining the efficacy of different ectoparasiticides in the prevention of B. henselae transmission.

RICKETTSIAL INFECTIONS

Rickettsia felis, has been identified in cats, dogs and in cat fleas *(Ctenocephalides felis)* with a world wide distribution. It has been found in peri-urban wildlife (opossums) in the USA but not as yet in other wildlife species in other continents. The reservoir potential of cats and dogs has not been determined but it is likely that *C. felis* itself is the major reservoir. Experimental infection of cats with *R. felis* has been demonstrated. Cats infected with *R. felis* by repeat exposure to feeding fleas, develop a subclinical illness with an incubation period of 2-4 months. However, the pathogenic potential of natural infection with *R. felis* species in dogs and cats is unknown. What is in no doubt, is that cats and dogs will transport *C. felis* into domestic surroundings and as transovarial and trans-stadial transmission of *R. felis* has been shown, a domestic focus of infection for humans could be established.

Fig 4: A female cat flea, *C. felis*, recently engorged on a blood meal.

Diagnosis

Diagnosis has until recently depended on identification of serological methods including micro-immunofluorescence for IgM or rising IgG titres at 2 to 3 week interval. However, cross reactivity may occur between different Rickettsia species. PCR methods have been used to identify rickettsial DNA in blood or tissue specimens. Rickettsial culture can only be done in high bio-containment facilities.

Treatment and prevention

Tetracyclines including doxycycline (5-10mg/kg) are the antibiotics of choice and treatment should be continued for 3-4 weeks. Flea prevention using residual insecticides appropriate for the cat is essential.

YERSINIOSIS (PLAGUE)

Plague is caused by the non-spore-forming bacterium, *Yersinia pestis*. Localised foci of disease occur in temperate, semi-arid areas throughout the world and infection is maintained in reservoir rodent populations via transmission by rodent fleas (such as Xenopsylla species). The cat flea *C. felis*, is a relatively ineffective vector for plague transmission. Epizootic outbreaks of disease occur when Y. pestis infection spills over into more highly susceptible small mammal populations. With semi-urban development now extending into endemic areas of plague, there is increasing risk of domestic cats, being infected by bites from rodent fleas acquired during hunting and ingestion of infected small mammals.

Bacteraemic cats are a source for human infection either directly through aerosol spread, bites or scratches or indirectly by transporting infected fleas into the domestic environment. Infection if recognised early can be treated effectively with antibiotics, but untreated cases may be fatal. Vaccines have been developed but are not commercially available.

Pathogenesis and clinical signs

Following a bite by an infected flea, organisms are phagocytosed by macrophages which transfer infection to local and regional lymph nodes. A capsular envelope ensures their survival. Lymphadenitis develops, and this is followed by dissemination of infection and bacteraemia within 2-6 days. In contrast, after ingestion or inhalation of organisms and entry through a mucous membrane, dissemination and the onset of bacteraemia is more rapid (1-3 days).

Most experimentally infected cats develop mild to moderately severe clinical disease with subsequent recovery. In naturally infected cats, both bubonic and primary pneumonic syndromes (rare) are reported. Bubonic plague is associated with fever, dehydration, weight loss and lymphadenopathy with abscessation and draining tracts affecting the cervical, tonsillar, retropharyngeal and submandibular lymph nodes. Recovery may occur following this stage or there is haematogenous spread with progression to a septicaemic syndrome. Multiple organ involvement, endotoxic shock, oedema and disseminated intravascular coagulation (DIC) with marked leucocytosis are characteristic. Pneumonic involvement during this stage is common and dissemination by aerosol may occur to in-contact humans.

Diagnosis

Notification of government veterinary health services may be required in some countries when plague is suspected. Confirmation of diagnosis is made by cytological or histopathological demonstration of bacteria in affected tonsillar tissue or lymph node aspirates with appropriate Gram and Giemsa staining characteristics, followed by culture. Stringent bio-safety procedures are required in collection, transport and culture of specimens. Demonstration of a rising serum IFA titre provides diagnostic support. PCR is also available in Yersinia reference laboratories.

Treatment and control

The decision to treat cats with plague should always take into consideration the potential for aerosol spread from pulmonary lesions and this should be evaluated by thoracic radiology. Appropriate bio-security procedures are essential. *Yersinia pestis* is sensitive to routine disinfectants and a variety of antibiotics including doxycycline, aminoglycosides, chloramphenicol and fluoroquinolones. Therapy should be continued for a minimum of 21 days. Doxycycline is most commonly used in the bubonic syndrome and can be used for prophylaxis in exposed, subclinical cats.

Flea control in all in-contact cats and dogs is essential. Safe, effective, residual insecticides combined with insect development inhibitors are available which if used regularly will provide excellent vector control. Minimising access of dogs and cats to infected mammal carcasses is also important.

VIRAL INFECTIONS

The major route of transmission for feline leukaemia virus (FeLV) is direct transmission through close contact between cats over a prolonged period of time, but there has been the speculation that *C. felis* may play a role as a vector (mechanical or biological). Specific FeLV RNA can be detected by PCR in fleas and their faeces after artificial feeding on blood from infected cats. RNA was detected from fleas for 30 hours post-feeding and for up to 2 weeks in faeces. The pathogenesis of infection (if present) in the flea vector requires further study.

Further reading

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FELINE UPDATE CONTINUING EDUCATION DAYS

run by the Feline Centre and the Langford
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www.vetschool.bris.ac.uk/newsandevents/

An Insight into Feline Shelter Medicine

– What you need to know for dealing with those feral and rescue cats in your practice!

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- **Early neutering of kittens**
- **"Ten is never enough" - Understanding the causes and consequences of animal hoarding**
- **The "ins and outs" of FIV/FeLV testing and vaccination**
- **Coronavirus and FIP - Do we have to worry about it?**

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Jim Toy *MA vet MB MRCVS*
David Yates *BVSc MRCVS*
Vicky Halls *VN, Member of the Association of Pet Behaviour Counsellors*
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Dr Charlotte Dye *BVM&S CertSAM PhD MRCVS*

Registration fee: £ 80 per person
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For further details and registration please contact:
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The New Fort Dodge Feline Fellow

Gabi graduated from the University of Veterinary Medicine in Vienna, Austria in 2003. She then undertook a doctoral thesis investigating the effectiveness of acupuncture at the Peninsula Medical School, Universities of Exeter and Plymouth. Since December 2003, Gabi has developed a strong interest in feline medicine whilst working in a small animal practice in Devon. She also spent some time working at Paignton Zoo during this period. In October 2007, she was appointed the new Fort Dodge Feline Fellow at the Feline Centre, University of Bristol, Langford. Gabi is very much looking forward to her job at the Feline Centre.

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THE CHANGED FACE OF FELINE LYMPHOMA

Mark Goodfellow
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DSAM Dip ECVIM-CA
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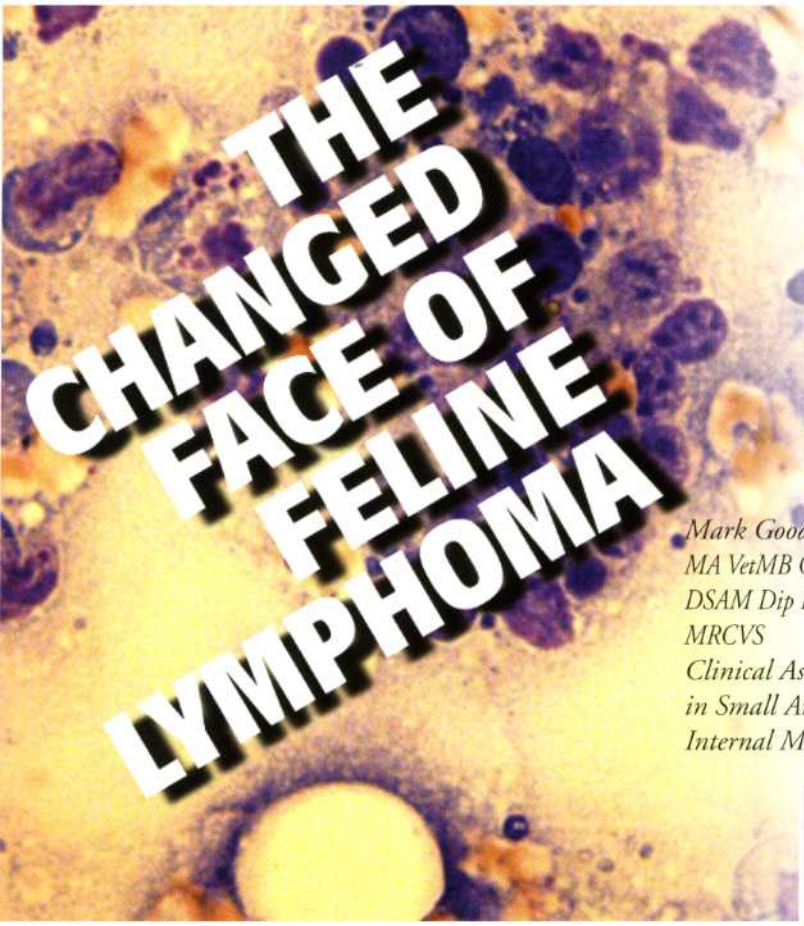

Fig 1: A group of large lymphoid cells with prominent nucleoli in large cell lymphoma

Lymphoma is the most common tumour of the cat, and this disease comprises a heterogenous group of neoplasms that arise from the lymphoreticular cells of the lymph nodes, spleen, bone marrow and elsewhere in the body. In the past lymphoma was often regarded as a disease of the young feline leukaemia virus (FeLV) positive cat. However there have been recent changes in the signalment, presentation and aetiopathogenesis of lymphoma in cats which, together with a reduced prevalence of FeLV infection, have resulted in changes in our understanding of this important disease.

Before the 1980s, FeLV was associated with up to 70% of feline lymphoma cases. At this time cats diagnosed with lymphoma tended to be young and the most common presentation was the mediastinal and/or multicentric form of the disease. The association between FeLV infection and the development of lymphoma is very strong; indeed FeLV-infected cats are 62 times more likely to develop lymphoma than their FeLV-negative counterparts. Overall a quarter of FeLV positive cats are expected to develop lymphoma during their lifetime.

Development of lymphoma was often as a direct consequence of FeLV infection. After initial FeLV infection, if not cleared by the cat's immune system, virus spreads to the bone marrow to infect haematopoetic stem cells. Viral DNA (provirus) is randomly inserted into the host DNA of thesecells. Insertion of viral DNA adjacent to a host gene (most commonly myc) which codes for cellular proliferation (a so-called oncogene), may cause over expression of that gene resulting in cellular proliferation and ultimately neoplasia.

Over the past 20 years a marked change in the FeLV status, signalment, and anatomical forms of disease have been noted in cats diagnosed with lymphoma. This change appears to have temporally coincided with a reduction in the prevalence of FeLV which is likely to have resulted from the widespread use of FeLV diagnostic assays, the introduction of FeLV vaccines and other preventative regimes (e.g. test and elimination schemes). The reduced prevalence of FeLV in the feline population has been mirrored by a decline in prevalence of FeLV-associated lymphoma. Indeed recent data have found that currently the median age of cats diagnosed with lymphoma is 11 years and

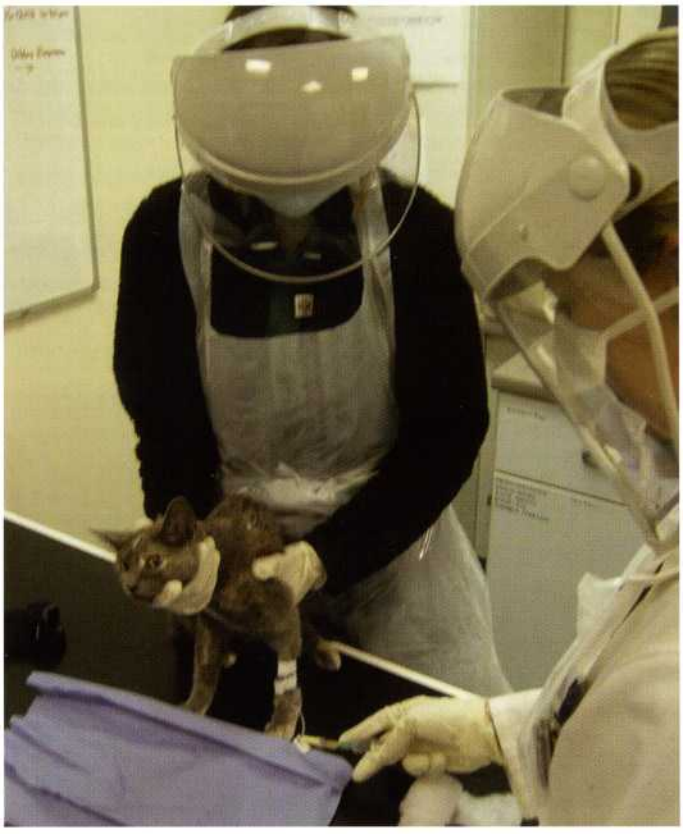

Fig 2: Take adequate safety precautions when administering cytotoxic drugs to a patient. *Photo courtesy of Andrea Harvey.*

only a minority (8-14%) of these older cats are FeLV infected. Overall, however, the prevalence of feline lymphoma actually appears to be increasing, possibly due to improved diagnostics and our ability to identify affected cats and/or an increased frequency of certain types of lymphoma such as abdominal forms.

In the present day, lymphoma cases fall broadly into either a distinct group of young FeLV-infected cats or an older non-FeLV associated group. However diagnostic methods of FeLV detection have also advanced recently, making the demarcation between FeLV-infected and non-infected cats complicated to

define. PCR-based methods to detect FeLV provirus in cats are very sensitive and that it is now possible to identify cats with residual FeLV DNA (provirus) within their genome but which are not FeLV viraemic. Indeed most, if not all, cats that have been infected with FeLV during their lifetime will have proviral DNA incorporated into their genome. This is in contrast to the previous hypothesis in which we believed that the majority of cats could clear the FeLV completely. Thus we are now able to identify older cats with lymphoma (e.g. alimentary lymphoma) which are FeLV negative on ELISA (i.e. they are not antigenaemic) but positive for FeLV provirus on PCR. Whether the development of lymphoma is as a result of the integrated provirus is unclear, but it is possible that the virus is playing an important, if hidden, role in the pathogenesis of feline lymphoma.

Factors other than FeLV status also influence the pathogenesis of feline lymphoma. Feline immunodeficiency virus infection is associated with a five-fold increased incidence of lymphoma, probably via indirect immunosuppressive effects rather than a direct role in tumorigenesis. Cats infected with both FIV and FeLV have a 77-fold greater risk of developing lymphoma compared to uninfected individuals.

Fig 3: Siamese and Oriental cats have a familial form of mediastinal lymphoma.

Non-infectious predisposing factors have also been described. Genetic factors play a role as evidenced by the increased incidence of mediastinal lymphoma in young FeLV non-infected Siamese and Oriental cats. Here inherited forms of tumour suppressor genes (such as p53) prone to mutation may be involved. Additionally lymphoma may be associated with, or result from, chronic inflammation. Serial histological documentation of worsening inflammatory bowel disease in cases which subsequently develop intestinal lymphoma supports this hypothesis as does the identification of similar lymphocyte cell lineages in both IBD and intestinal lymphoma cases. The same may be true of nasal lymphoma in cats with a history of chronic rhinitis.

The role of environmental factors is also emerging. Exposure to cigarette smoke is a risk factor for developing lymphoma in humans and the same appears to be true in cats. Cats exposed to environmental tobacco smoke are 2.4 times more likely to develop lymphoma than their smoke-free counterparts. If they have been exposed to tobacco smoke for more than five years, the risk increases. Tobacco exposed cats are also more likely

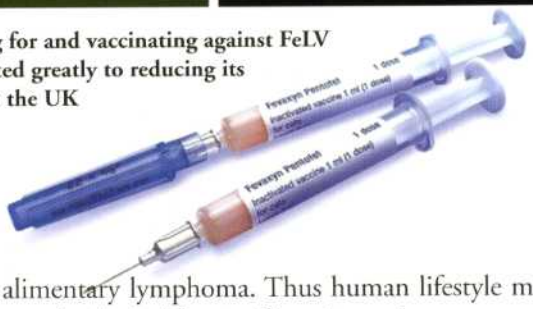

Fig 4: Testing for and vaccinating against FeLV has contributed greatly to reducing its prevalence in the UK

to develop alimentary lymphoma. Thus human lifestyle may influence not only the incidence of lymphoma in our pet cats but also the pattern of lymphoma seen.

Given that alimentary lymphoma appears to be increasing in prevalence and that its treatment is tailored specifically to the histological grade, the remainder of this article will deal with alimentary lymphoma. However the majority of points regarding investigation and treatment remain valid irrespective of the site of the lymphoma.

Alimentary Lymphoma

In the post "FeLV era" of lymphoma, gastrointestinal lymphoma has become the most common anatomic presentation and occurs most frequently in older (median age 11 years) FeLV-negative cats. The disease usually arises in the small intestine, resulting in segmental or generalised thickening, with the stomach, caecum and colon only rarely affected. However lymphoma is still the most common gastric tumour of cats. In most cats with intestinal lymphoma, the mesenteric lymph nodes are also involved. No breed predilection has been identified. As discussed above, cats with intestinal lymphoma have a low incidence of FeLV infection as detected by antigenaemia or viraemia, but a role for prior FeLV infection has been suggested by a significant proportion of affected cases being PCR positive for FeLV provirus.

Cats with alimentary lymphoma usually present with a chronic (often several months) history of anorexia and weight loss. Vomiting and diarrhoea are present in less than half of cases and other uncommon clinical signs include lethargy, weakness, polydipsia, polyuria, pica, and abdominal swelling. Abdominal palpation may reveal thickened bowel loops or an abdominal mass, but is normal in many cats with alimentary lymphoma.

The most common clincopathological finding is hypo-albuminaemia, which occurs in approximately half of patients. Other noteworthy abnormalities include anaemia (non-regenerative or regenerative), raised liver enzymes and hypocobalaminaemia. Elevations in liver enzymes are suggestive of neoplastic lymphoid infiltration into the hepatic parenchyma but normal liver enzyme concentrations do not exclude this possibility. Hypocobalaminaemia can result from distal small intestine involvement. As in all forms of feline lymphoma, in contrast to canine lymphoma, hypercalcaemia is rare.

Abdominal radiography often yields normal or non-specific findings such as a reduction in intra-abdominal contrast, dilation of small intestinal lumen or the presence of an ill defined soft tissue opacity which may be consistent with a mass. Abdominal ultrasonography, however, is very useful and may identify mesenteric lymphadenopathy, thickened intestinal wall, disruption of intestinal wall architecture and/or bowel hypomotility or ileus. These ultrasonographic features are not unique to alimentary lymphoma but may offer help to distinguish lymphoma from inflammatory bowel disease, in which intestinal wall layering is usually preserved, or intestinal adenocarcinoma, in which focal eccentric intestinal luminal narrowing usually occurs without associated lymphadenopathy. Unfortunately normal ultrasonographic findings do not rule out a diagnosis of alimentary lymphoma.

Whilst cytological examination of ultrasound-guided fine needle aspirates, collected from mesenteric lymph nodes or thickened intestinal walls, can be sufficient to allow a diagnosis, the treatment choices and prognosis for cats with alimentary lymphoma are dependent on the tumour grade. Grading of the tumour is achieved by histopathological examination of a biopsy which also allows for more confidence in the diagnosis as compared to that achieved with cytology. Biopsies may be procured by endoscopy or laparotomy. Endoscopy has obvious advantages in being non-invasive and requiring little post-procedure convalescence, but samples obtained are superficial and there is a risk of missing submucosal disease (which is often high grade). Furthermore most endoscopes are unable to reach the jejunum and ileum, where most lymphoma lesions are located. Laparotomy has the advantage of allowing full-thickness intestinal biopsies to be collected and allows biopsy specimens of the liver, mesenteric lymph nodes, and pancreas to be obtained as well, even in the absence of gross lesions. However laparotomy has the disadvantages of requiring significant post-operative healing, which may be problematic in the face of hypoalbuminaemia, and of delaying initiation of chemotherapy for 10-14 days after surgery to prevent complications in wound healing or dehiscence. Additionally it is of note that attempted resection of apparently focal alimentary lymphoma has neither been correlated with increased nor decreased survival times.

Unlike with canine lymphoma, lymphoma stage, according to the World Health Organization's Clinical Staging for Tumors of Domestic Animals, does not appear to be predictive of outcome in cats and thus the cost and invasiveness of complete staging should be weighed against the benefit of the additional information gained. However it should be remembered that older patients may have co-morbidities which can influence prognosis and treatment choices. Thus it is recommended that all cats diagnosed with lymphoma have a complete haematology, serum biochemistry and urinalysis profile performed, as well as retroviral status determined, as a minimum, before undertaking lymphoma treatment.

Feline alimentary lymphoma is categorised histologically into one of three grades; low grade (lymphocytic or small cell), intermediate, or high grade (lymphoblastic, immunoblastic or large cell lymphoma). This classification guides treatment choices and is indicative of prognosis. As discussed above inflammatory bowel disease may be a precursor to intestinal lymphoma and on occasion immunohistochemical stains are required to differentiate between the two. This distinction is very important clinically and prognostically since cats with inflammatory bowel disease may have a significantly better prognosis than those with alimentary lymphoma with appropriate treatment.

SELECTED CHEMOTHERAPY PROTOCOLS FOR CATS WITH ALIMENTARY LYMPHOMA USED BY THE AUTHOR

COP Protocol

- Cyclophosphamide 300mg/m2, IV/PO, q21 days *
- Vincristine (Oncovin) 0.75mg/m2, IV, q 7 days for 4 weeks then every 3rd week
- Prednisone 2 mg/kg, PO, sid for 1 week; then 5mg, PO, eod until relapse or adverse steroid effects in which case taper dose and discontinue

CHOP Protocol

- Cyclophosphamide 200 mg/m2, IV/PO, weeks 2, 7, 13, 21*
- Vincristine (Oncovin) 0.7mg/m2, IV, weeks 1, 3, 6, 8, 11, 15, 19, 23
- Prednisone 2 mg/kg, PO, sid for 28 days; then 1mg/kg, PO, eod until relapse or adverse steroid effects in which case taper dose and discontinue
- Doxorubicin (H) 25mg/m2, IV, weeks 4, 9, 17, 23

Chlorambucil & Prednisolone Protocol

(For lymphocytic alimentary lymphoma only)

- Chlorambucil 15mg/m2 tablet, PO, for 4 consecutive days every third week
- Prednisone 10 mg/cat/day, PO, sid until relapse or adverse steroid effects in which case taper dose and discontinue

**25mg cyclophosphamide tablets available overseas and can be imported via an STC. Seek advice from the VMD (http://www.vmd.gov.uk).*

There are various COP & CHOP style protocols and the reader is advised to always seek advice from a veterinary oncologist prior to undertaking treatment with an unfamiliar protocol.

Doxorubicin and vincristine are vesicants and must be delivered through an intravenous cannula placed cleanly on the first attempt.

Treatment protocols are distinct for the different forms of feline alimentary lymphoma. High grade is treated with conventional CHOP or COP based protocols. The COP protocol (cyclophosphamide, vincristine & prednisolone) is often associated with adverse gastrointestinal effects

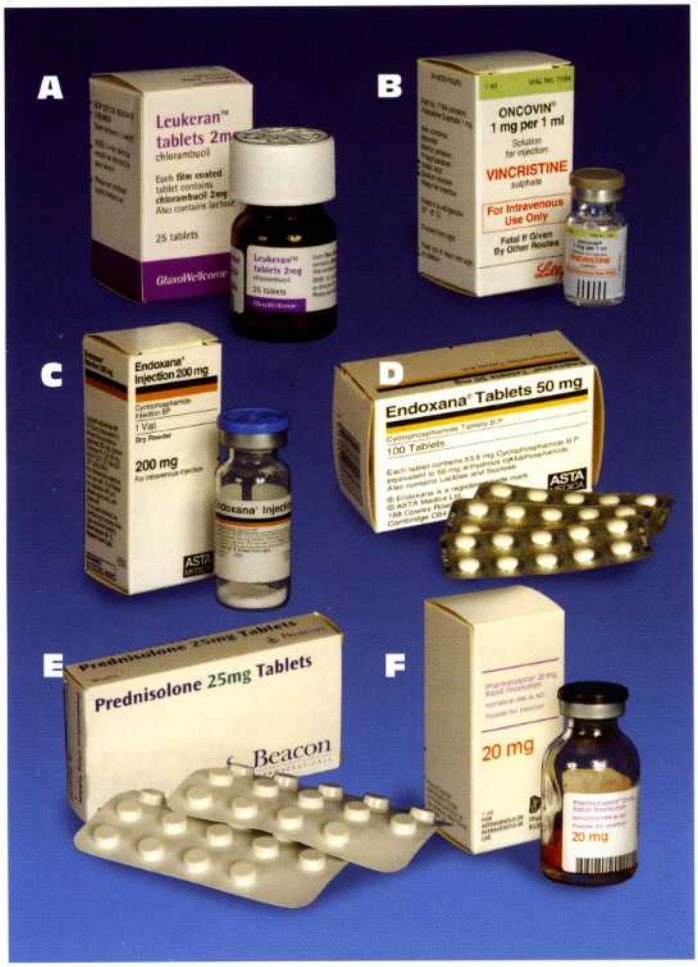

Fig 5: Drugs used in alimentary lymphoma chemotherapy protocols: ***(pack sizes not shown to scale)*** **A. Chlorambucil tablets. B. Vincristine injectable. C. Cyclophosphamide injectable. D. Cyclophosphamide tablets. E. Predinisolone tablets. F. Epirubicin injectable.**

(vomiting, diarrhoea, anorexia) but these symptoms are usually manageable with prompt, appropriate supportive treatment. Both vincristine and cyclophosphamide are myelosuppressive, so haematology must be performed weekly initially and treatment withheld if neutropenia develops. Thankfully cyclophosphamide rarely causes sterile hemorrhagic cystitis in cats as it does more commonly in dogs. Addition of doxorubicin to create a CHOP protocol is of questionable benefit in the case of high grade alimentary lymphoma. Based on a small number of studies, remission rates are no better than using a COP protocol, but those cats who do respond appear to survive longer. Doxorubicin, whilst not cardiotoxic to cats, is profoundly nephrotoxic, in addition to causing adverse gastrointestinal effects and profound myelosupression, and thus its use necessitates frequent monitoring of renal function. At present we are unable to identify those cats which will benefit from the addition of doxorubicin to their cytotoxic regime and the decision of whether to use doxorubicin is made on a case-by-case basis. Overall only 20-30% of patients with high grade alimentary lymphoma achieve full remission, irrespective of the protocol utilised, and median survival times are two to three months only.

In contrast patients with low grade, lymphocytic alimentary lymphoma have a good prognosis with 70% achieving complete remission and a median survival time of 17 months reported. This disease is more slowly progressive so a more tempered cytotoxic protocol is recommended using chlorambucil, an alkylating agent, and prednisolone. Adverse reactions to chlorambucil are rare but can include gastrointestinal toxicity, myelosuppression and hepatotoxicity. Haematology and serum biochemistry should be performed weekly for the first month of treatment and every 3 months thereafter.

Those cats with intermediate grade intestinal lymphoma are treated with a COP or CHOP type protocol. It is thought that the addition of doxorubicin is likely to be of most benefit in these patients, however the use of this drug is based uponthe factors described above together with consideration for its expense, toxicity and the clinician's experience.

Unfortunately, apart from the histological grade of the alimentary lymphoma, there are few other prognostic indicators to guide treatment choice. Initial positive response to treatment is correlated with overall survival, so it can be argued that all cats deserve initial trial therapy for their alimentary lymphoma. Supportive care plays a vital role in the maintenance of quality of life when treating alimentary lymphoma. Oral appetite stimulants, such as cyproheptadine, can be useful in increasing voluntary food intake in addition to standard encouragement techniques such as warming or addition of gravy. If hypocobalaminaemia is present, patients may benefit from cobalamin supplementation as deficiency results in anorexia. Metoclopramide or other anti-emetics may aid in the control of nausea and vomiting, which may result from the disease itself or as a consequence of therapy, and which should be treated aggressively to minimise its deleterious effects on quality of life.

In summary, the pattern of lymphoma in cats has changed over the past three decades with the majority of patients now presenting in older age with previously less common anatomical forms which are unrelated to FeLV antigenaemia. One such form, alimentary lymphoma is now the commonest presenting form of lymphoma and its histological grade is strongly predictive of response to treatment and prognosis.

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ABSTRACTS

Efficacy of a topically applied spot-on formulation of metaflumizone on cats against the adult cat flea, Ctenocephalides felis, flea egg hatch and flea emergence.

Michale W. Dryden, Patricia A. Payne, Vicki Smith, D. Rugg. Proceedings American Association of Veterinary Parasitologists 52nd annual meeting, July 14-17, 2007

A spot-on metaflumizone formulation was evaluated to determine its adulticidal efficacy, effect upon egg production and activity against flea eggs when applied to flea infested cats. Eight male and eight female adult domestic shorthair cats were assigned to two treatment groups. Cats in Group 1 served as non-treated controls. Cats in Group 2 were treated with a minimum of 40 mg/kg metaflumizone as a single spot-on dose on Day 0. Two days prior to treatment and at a weekly interval thereafter up to Day 56 each cats was infested with about 100 unfed cat fleas, *C. felis*. At various time points throughout the study flea eggs were collected and counted and the cats were combed to remove and count live fleas. Egg viability was determined using Petri dishes containing growth media and which were held in a growth chamber. After 5 days hatched eggs were examined and adult emergence was determined 28 days after egg collection. Metaflumizone provided ≥ 99.6% efficacy against adult fleas from Day 3 to Day 45 following a single application. Treatment resulted in reduction of egg production by 51.6% and 99.2% within 24 and 48 hours, respectively. Following subsequent weekly flea infestations egg production from treated cats was negligible out to Day 38, with ≥ 99.5% reduction relative to nontreated cats. Metaflumizone treatment did not appear to have any apparent effect on the hatching of eggs or on the development and emergence of adult fleas from the eggs produced by fleas from treated cats.

Evaluation of Client-Specific Outcome Measure and Activity Monitoring to Measure Pain Relief in Cats with Osteoarthritis

B.D.X. Lascelles, B.D. Hansen, S. Roe, V. DePuy, A. Thomson, C.C. Pierce, E.S. Smith, E. Rowinski

Osteoarthritis (OA) is presumed to be the most common form of degenerative joint disease in cats, however little is known about the incidence of this condition. To date, only retrospective studies are available which are based upon the evaluation of radiographs. These studies have found lesions consistent with appendicular limb OA in 17 to 64% of cats. It has been suggested that in cats OA is not associated with any pain, however most clinicians feel that this condition can be painful and can be associated with impaired mobility. The aim of the present study was to evaluate the effects of a nonsteroidal anti-inflammatory drug (NSAID) administered to cats with naturally occurring OA using a collar-mounted accelerometer-based activity monitor (AM) and a client-based assessment system (client-specific outcome measures, CSOM) to assess the ability of their cats to perform specific spontaneous activities in their home environment. Cats that were considered for this study were cats whose owners described them to have slowed down or have impaired mobility. These cats were screened with physical examination, orthopaedic and neurologic evaluation, CBC, blood chemistry, urine analysis and orthogonal radiographs of every appendicular joint and the entire axial skeleton. Cats with no detectable clinical disease, with an indoor-only life style, that were currently not receiving any anti-inflammatory drugs, and had owner identified mobility impairment and at least one painful joint showing radiographic changes consistent with OA were included in this study. Thirteen suitable cats completed this 3 week long, randomised, masked, cross-over study. Assessments were made at days 0, 7, 14, and 21. The first week (baseline) was regarded as an acclimatisation period and in weeks 2 and 3 each cat received both a 5-day course of the NSAID meloxicam (0.1 mg/kg on day 1, followed by 0.05 mg/kg daily for 4 days) and a 5-day course of placebo in a randomised order. At the end of each week data were collected and blood samples were drawn for CBC and blood chemistry. At the screening visit owners were questioned on the activity of their cat and at day 0 of the study the discussion about the cat's activity was reviewed. Owners were asked to describe 5 time- and place-specific activities of their cat that they considered were altered. At the end of each course of treatment this unique set of activities was reassessed and the owners were also asked to complete a simple global assessment form to evaluate the change in their cat's quality of life as a result of treatment. The mean age of the cats was 14 years (range, 10-19 years), mean weight at day 0 was 5.0 kg (range, 2.9-8.25 kg), and median body score was 2/5 (range 1/5-4/5). Seven were spayed females and 6 were castrated males. A median of 4 appendicular joints in each cat had radiographic changes consistent with OA. The total number of joints assessed was 208. Fifty-five joints were painful upon manipulation; 18 joints had both pain upon manipulation and radiographic signs of OA; and 37 joints had radiographic signs of OA with no evidence of pain. Across all cats 52 regions of the axial skeleton were examined, 25 of which showed radiographic pathology. Seven regions had both radiographic abnormalities and evidence of pain and 18 regions that showed no radiographic pathology produced behavioural signs of pain upon manipulation. There was no significant effect of group or treatment with meloxicam or the placebo on the blood parameters evaluated, however these statistical tests had low power.

CSOM data were collected on all 13 cats however AM data were available from 9 cats only. The CSOM data showed that there was a significant improvement in mobility when cats were given meloxicam compared with the placebo. A significant improvement over baseline was also observed when the cats were administered a placebo. However, the largest improvement from baseline was noted when meloxicam was given. The difference between treatment and baseline was bigger than the placebo effect. The greatest improvement in overall quality of life was observed after administration of meloxicam. Activity counts measured by the AM were significantly greater during NSAID treatment compared to baseline (week 1) but not significantly greater than during placebo treatment. There was no difference between counts during the baseline period and placebo treatment. The average percentage increase in activity counts with treatment

over baseline was 9.3% and the average change in activity counts with placebo with respect to baseline was -1.6%.

The results reported in this study indicate that owners of cats with OA are able to distinguish altered behaviour associated with pain relieve when their cats are administered an analgesic compared with a placebo. Similar findings were shown for dog owners in studies on canine OA. The authors conclude however that much work is needed to refine the subjective assessment system. This study also demonstrates that objective data generated by accelerometer-based AMs can be used to fully validate such objective assessment systems.

Effect of Control of Systolic Blood Pressure on Survival in Cats with Systemic Hypertension

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Systolic hypertension is a common clinical problem in cats which occurs most frequently in association with either renal disease or hyperthyroidism. Hypertension can lead to the damage of many organs such as kidneys, heart, and central nervous system. The most common manifestation however is hypertensive retinopathy or choroidopathy which can be seen in 60% of hypertensive cats. For humans and dogs an association among hypertension, proteinuria, and progression of renal disease has been established. Such a causal link has not been proven for cats. The calcium cannel blocker amlodipine is currently the treatment of choice for the control of hypertension in cats and is an effective and safe treatment when given at a dose of 0.625-1.25 mg PO once daily. Two previous small scale studies that evaluated survival in hypertensive cats did not detect a significant difference in survival of cats that had a "good" response to treatment and those that had a "poor" response to treatment.

The aim of this study was to determine the survival time in a large population of cats with systolic hypertension and whether the degree of blood pressure control over time influences survival. One hundred and forty-one cats were included in the study. These cats were not on any antihypertensive treatment. At each visit a history was taken and complete physical and fundic examinations were performed. In addition to this a systolic blood pressure (SPB) measurement was taken and for entry in the study it was required that all cats had at least one SBP measurement while receiving treatment.

Hypertension was defined as SBP >170 mm Hg on 2 or more occasions or SBP >170 mm Hg on 1 occasion in association with clinical manifestations of hypertension. Blood and urine samples were collected before initiating antihypertensive treatment. A full biochemistry analysis was performed and total thyroxine concentration was measured in all nonazotaemic cats and also in cats where the history and clinical examination finding suggested hyperthyroidism. Urine samples were submitted for urinalysis and also urine culture when where deemed necessary. Urine protein to creatinine ratios (UP:C) were evaluated retrospectively using stored samples from the time of diagnosis of hypertension and after stabilisation of blood pressure with antihypertensive therapy. For most cats treatment with amlodipine besylate was initiated at a dose of 0.625 mg/cat once daily. Cats were re-examined after 7-21 days and if SBP remained higher than 160 mm Hg the dose was increased to 1.25 mg/cat once daily. This became necessary in 50% of cats. The stabilisation period was relatively short for all cats (median, 20 days) with 95.7% of cast requiring only 1-2 visits. The cats' age at diagnosis of hypertension was 15.0 (13.0, 16.0) years. The most common physical examination findings were a palpable goiter in 33%, a systolic heat murmur in 31.2%, and dental diseases in 17%. The ophthalmologic examination identified ocular lesions in 41.4% of cats. Plasma biochemistry results were available for 135 of the 141 cats and urine samples were obtained from 124 cats. Azotaemia was defined as a creatinine concentration >1.9 mg/dL (177 mmol/L) and was found in 58% of cats (78/135) at diagnosis of hypertension. Eighteen cats were classified as nonazotaemic and euthyroid. Fifty-two cats were hyperthyroid at diagnosis of hypertension. A further 12 cats were diagnosed with hyperthyroidism after entry into the study. Paired UP:C measurements were available for 105 cats. The UP:C declined with amlodipine treatment in 69.5% of cats and increased in 30.5% of cats. A significant difference was found in the change in UP:C with amlodipine treatment between cats that were classified as nonproteinuric (UP:C <0.2) and proteinuric (UP:C >0.4) and also between mildly proteinuric (UP:C 0.2-0.4) and proteinuric cats. A significant decline in UP:C was found with amlodipine treatment, most markedly in cats defined as proteinuric.

Fifty-two cats were alive at the endpoint of the study and were therefore censored from the survival analysis. When only evaluating those cats that died or were euthanized a significant difference in survival was identified: nonproteinuric cats (n = 21), 490 days (217-1169 days); mild proteinuria (n = 24), 313 days (124-607 days); proteinuric (n = 33), 162 days (73-406 days). A significant difference was seen between nonproteinuric and proteinuric cats and also between nonproteinuric and mildly proteinuric cats. The median survival time of the cats that died was 260 days (range, 18-1584 days). In this study 86.7% of cats were diagnosed with azotaemia, hyperthyroidism or both conditions coincident with the diagnosis of hypertension and 13.3% (18/135) were nonazotaemic and euthyroid. The presence of renal insufficiency could however not be ruled out completely. The presence or absence of hyperthyroidism was not found to be associated with survival in hypertensive cats.

Overall the prevalence of hypertensive retinopathy/choroidopathy in this study was lower (41.1%) than in previous studies. The authors feel that there is a reduced risk of the development of hypertensive ocular lesions at their target for blood pressure control (<160 mm Hg). The hypertensive retinal lesions/ haemorrhages were documented to have worsened in only 6 of 141 cats after initiation of antihypertensive therapy which substantiates this assumption. The authors state that it is possible that some cats in this study might represent false-positive cases with white-coat hypertension. This study also found that neither SBP at diagnosis nor the level of blood pressure control was significantly associated with survival. It therefore suggests that adequate blood pressure control might not be a primary determinant of survival in hypertensive cats with concurrent renal disease. Amlodipine treatment led to increased survival in cats in which it produced a decrease in proteinuria, but this was independent of its effect on blood pressure.

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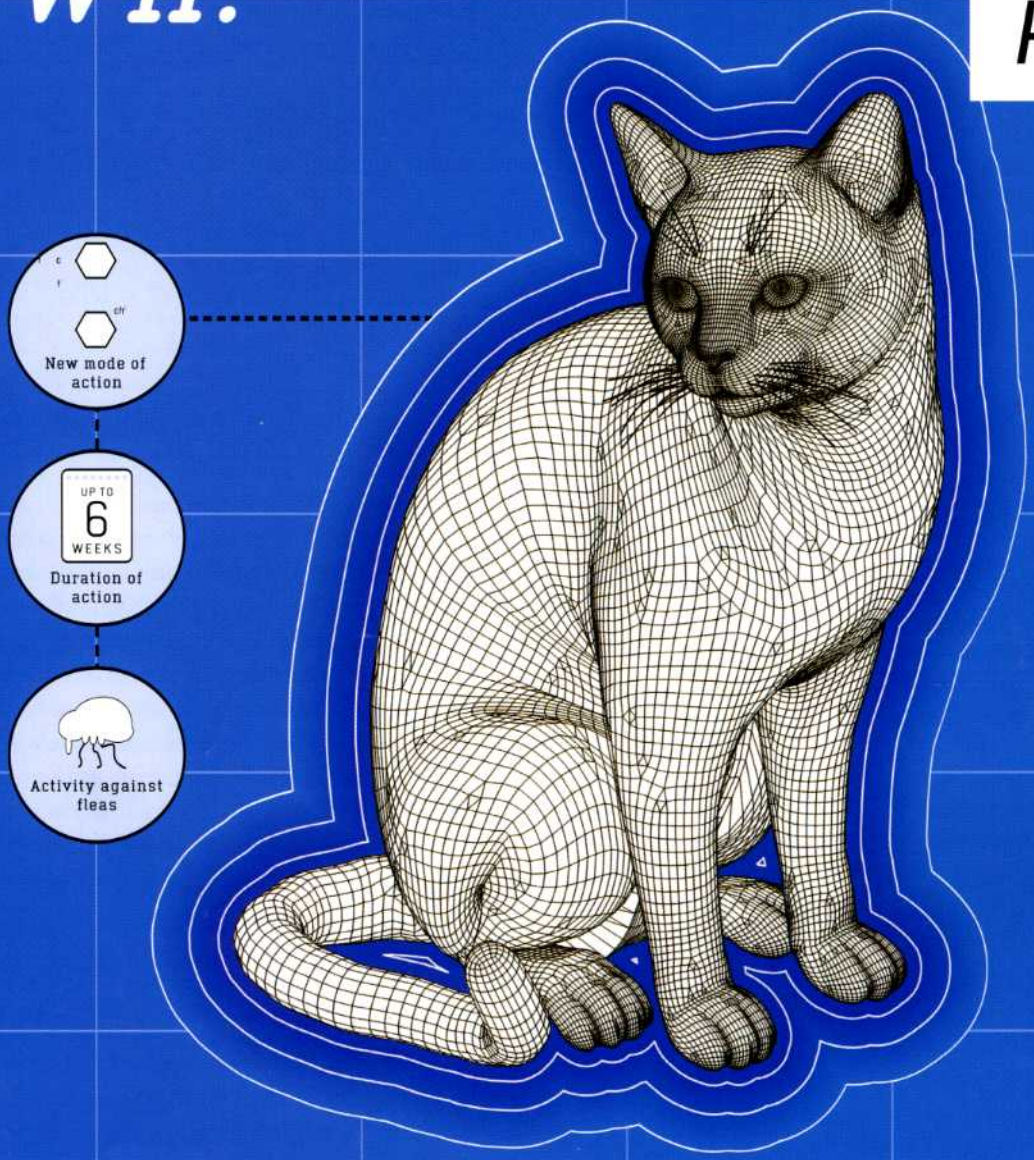

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