FELINE VIRUS INFECTIONS

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VIRUS INFECTIONS OF DOMESTIC CATS

Felid herpesvirus type 1 Feline calicivirus Reovirus	mainly respiratory infections
Feline parvovirus Feline and canine coronavirus Rotavirus, Astrovirus, Torovirus	mainly enteric infections
Feline leukaemia virus Endogenous retroviruses Feline immunodeficiency virus Feline syncytium-forming virus	retroviruses
Cowpox virus Hantavirus Rabies virus Aujeszky's disease virus Canine distemper virus Influenza virus, ?Paramyxoviruses (?Bovine herpesvirus type 4)	miscellaneous and generally not endemic in cats
Venezuelan equine encephalitis virus Flaviviruses, Rift Valley fever virus Tenshaw virus	arthropod-borne viruses not endemic in cats
Spongiform encephalopathy agent(s)	Scrapie-like agent, ?prion

In a brief review, there is no room to cover comprehensively all the viruses which may infect cats, and the following is meant only as a brief introduction to each virus or group of viruses.

RESPIRATORY VIRUSES

Feline herpesvirus type 1 and feline calicivirus

FHV-1 and FCV are, between them, said to be responsible for around 80% of all acute upper respiratory tract disease in cats, or 'cat flu'. FHV-1 generally causes more severe disease than FCV, with heavy nasal and ocular discharges, hypersalivation and sometimes death, especially in young kittens. FHV-1 may also

cause skin lesions. FCV infection is generally associated with milder upper respiratory tract disease, but often causes oral ulceration. FCV may also cause a transient limping syndrome, usually in young, recently weaned kittens. Both viruses cause persistent infections. FHV-1 undergoes latent infection, in which the virus remains dormant, probably in trigeminal ganglia, and is only excreted occasionally, usually after a stress such as weaning or moving living quarters. Latent infection lasts for the cat's whole life, and re-excretion of virus is often not accompanied by clinical signs. FCV causes persistent infection in the cat's oropharynx. Persistent FCV infection is not usually lifelong, but is associated with continuous shedding of virus, often without any clinical disease. Thus it can be appreciated that clinically asymptomatic carriers of FHV-1 and FCV are very important in the epidemiology of the disease. Vaccination against FHV-1 and FCV provides quite effective protection against disease but not against infection and development of the carrier states. In addition, FCV exists as a variety of antigenically different strains, not all of which are covered by the available vaccines, so FCV-related clinical disease is sometimes seen in vaccinated cats.

Feline reovirus

The clinical importance of feline reovirus infection in domestic cats is not known. Reovirus has been isolated from cats with a variety of clinical conditions, but in most cases was probably not the cause of disease. It may be that reoviruses contribute to some cases of upper respiratory tract disease and conjunctivitis in the field.

ENTERIC VIRUSES

Feline panleukopenia virus

Also known as feline infectious enteritis virus or feline parvovirus, this virus is found worldwide in domestic and non-domestic cats, but is largely controlled by vaccination in the UK so the clinical disease is no longer common. Like all parvoviruses, feline panleukopenia virus, including the vaccine strains, can readily survive in the environment for months, can be easily transmitted on fomites or by aerosol, and is resistant to many disinfectants.

Infection is by ingestion, and the virus grows best in rapidly dividing cells, giving rise to the various clinical syndromes. Thus infection of marrow cells and enterocytes in kittens or adults causes leucopenia and enteritis respectively, infection of the fetal or neonatal cerebellum causes cerebellar hypoplasia reflected clinically as ataxia, and infection of the embryo of the early fetus causes resorption or abortion.

Vaccination provides good protection, but in domestic cats it is best to boost every year, and more often if exposed to infection

Live and killed vaccines are available - live vaccines are contraindicated in pregnant queens because they may damage the fetus. Various vaccination protocols have been suggested for non-domestic cats. Because of the severe disease caused by feline parvovirus, and because even vaccine virus may be shed in faeces and infect other cats, it is probably best to avoid live vaccines, especially in smaller cats and cheetahs.

Feline coronavirus infection

Infection with FCoV is associated with several clinical syndromes in the field, although in most cases infection is asymptomatic. Infection with less pathogenic strains (e.g. feline enteric coronavirus; FECV) may cause enteritis which is generally mild and of short duration. It is most common in kittens, particularly just after weaning. More pathogenic strains (e.g. feline infectious peritonitis virus; FIPV) may cause wet or dry feline infectious peritonitis (FIP). Wet FIP is charactersed by the development of ascites and depression, and usually results in death within a few weeks. As well as ascites, pleural and pericardial effusion occurs in about 20% of cases and in these cats dyspnoea is a prominent clinical sign. In dry FIP granulomatous lesions develop in a variety of organs and clinical signs reflect the organs involved. Most frequently affected are organs in the abdominal cavity (particularly the liver and kidney), the CNS and eyes. Dry FIP develops more slowly than wet FIP, and is almost always fatal. As well as the strain and dose of virus, the ability of the cat to mount an effective cell mediated immunity to FCoV is very important in determining the outcome of infection. Thus some cats are able to shrug off infection with even a highly pathogenic strain of virus whereas some other cats may be more susceptible to low pathogenicity strains. The apparently high susceptibility of cheetahs to clinical FIP may be associated with their genetic uniformity, particularly at the major histocompatibility complex.

The main source of infection within a colony is probably the occasional carrier queen who infects her offspring which in turn pass on infection to other kittens. In coronavirus-free colonies the main source of infection is the introduction of carrier cats, which may result in horizontal spread amongst adults. However, canine coronavirus (CCV) can also infect cats, and cats housed in the presence of dog faeces containing CCV can become infected and produce antibody. The role of CCV in clinical FIP in the field is not known. In the absence of a vaccine, as yet, control therefore relies on an understanding of the epidemiology of FCoV infection. In a coronavirus-free colony all cats should be tested for antibody before they enter the colony, and seropositive cats refused as they may be carriers. In a colony with FCoV infection queens and kittens should be isolated from the rest of the colony for twelve weeks, and then the kittens tested before being allowed to enter the colony. Early weaning and removal of kittens from the queen may also help.

Dogs as a possible source of virus should not be forgotten.

Feline rotavirus and astrovirus

There are very few reports of rotavirus infection in cats and in general it is probably not a common cause of disease. Subclinical infection is probably most common, and diarrhoea is only mild and transient. Nevertheless, it is possible that more severe disease might develop if other enteric pathogens are also present. Little has been published on the epidemiology or clinical significance of feline astrovirus infection - one report suggests that less than 10% of cats in the UK have antibody. Most astrovirus isolations have been made from cats with diarrhoea described as persistent (4-14 days), green and watery, and sometimes accompanied by vomiting, pyrexia and depression.

Feline torovirus

Recently, torovirus-like particles and antibody have been detected in cats. Although not reproduced experimentally, there is some evidence to link this virus in cats to a clinical syndrome involving persistent diarrhoea and protrusion of the nictitating membrane.

RETROVIRUS INFECTIONS

Feline immunodeficiency virus

This is a recently discovered lentivirus of cats, related structurally, biochemically and by nucleotide sequence to human immunodeficiency virus (HIV), the cause of AIDS in man. There is no evidence of human infection with FIV.

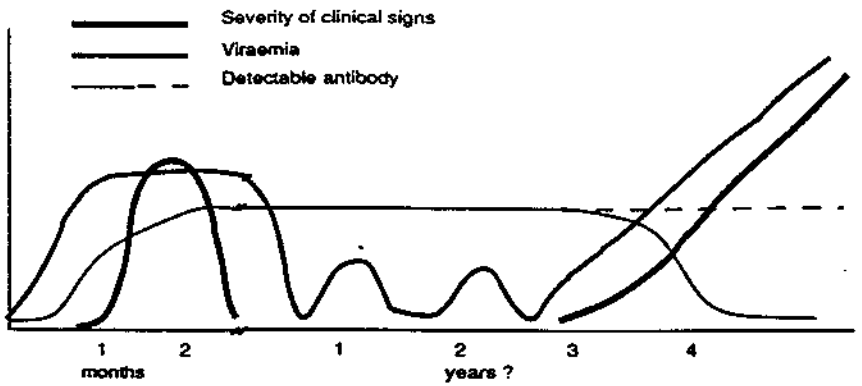
FIV has been detected in cats worldwide. Antibody has been found in domestic cats, Scottish wild cats and big cats in zoos and in the wild. However, while virus is readily isolated from domestic cats, FIV has only been isolated from a few other species. The prevalence of infection in domestic cats varies with the lifestyle and age of cats; generally about 20% random 'sick cats' have antibody to FIV compared with less than 5% healthy cats. Males are more frequently infected than females, and most infected cats are five or more years old. FIV infection is also more common in free-roaming cats, feral cats, and colony cats (but not usually breeding or pedigree colony cats). The main route of transmission is probably through biting - virus can be isolated from the saliva of infected cats.

FIV infection is associated with a variety of clinical syndromes, particularly chronic stomatitis and gingivitis, chronic respiratory disease, intermittent pyrexia, depression, lymphadenopathy, emaciation and sometimes chronic diarrhoea, chronic skin disease and neurological signs. Many cats also show haematological changes, especially anaemia, leucopenia and marked lymphopenia. Many clinically ill cats are hyper-gamma-globulinaemic.

Diagnosis of infection is usually by detection of FIV antibody.

For this commercially available ELISA and CITE kits can be used, but care must be taken in interpreting the result. Occasional 'false' negative results may occur in severely ill domestic cats which may have low or no antibody - a similar phenomenon is seen in terminal AIDS - and false positive results can also occur. Many research laboratories back up the use of commercial kits with more specific, but expensive, tests such as Western blotting or radioimmune precipitation assays. It is important to note that the presence of antibody does not necessarily mean that FIV is involved in any disease seen. Indeed, at the time of writing there have been no published reports of immunodeficiency associated with FIV infection in non-domestic cats.

The pathogenesis of FIV infection is, as yet, poorly understood. Primary infection causes seroconversion by 3-4 weeks (although some cats don't seroconvert for up to 14 months). Cats may develop lymphadenopathy at 6 weeks, and also some haematological changes, especially lymphocytosis. This stage appears to be essentially self-limiting, lasting a few months at most. Cats may have intermittent pyrexia and secondary infections, e.g. bacterial skin infections, and decreased effectiveness of vaccines. After a few months the lymphadenopathy subsides and virus becomes increasingly difficult to isolate with time. End-stage disease usually does not develop for several years. The mechanism of final immune suppression is not known. Like HIV, FIV infects T-lymphocytes, especially T4 lymphocytes (probably using CD4 antigen for entry), macrophages and CNS cells, and a gradual decrease in T4:T8 ratios and lymphoproliferation responses can be detected by about 10 months post-infection.



Probable pathogenesis of FIV infection in domestic cats

Feline leukaemia virus

FeLV is often cited as the most common infectious cause of death in young adult domestic cats. Although FeLV has been reported in non-domestic cats, it does not appear to be common. Infection is mainly by ingestion (virus is excreted in saliva, urine, faeces and milk), with close contact and licking the usual means of spread. Virus replicates in oropharynx and then spreads to various lymphoid tissues, especially bone marrow. Many cats mount an immune response which eliminates the virus at this stage, although latent infection of the bone marrow may still occur. However, more extensive virus replication in the bone marrow can give rise to viraemia and widespread infection, expecially in lymphoid tissues, and epithelial cells of the oropharynx, salivary glands and upper respiratory tract - with consequent virus excretion and transmission to other cats. At this stage cats may still mount an effective immune response and eliminate active infection (giving rise to a transient viraemia lasting 2 days to 8 weeks), but some will develop persistent infection and it is these cats which will go on to develop clinical disease.

The clinical syndromes associated with FeLV infection are mainly associated with infection of the haemopoietic system although the precise mechanisms of pathogenesis are often not known. Infection of the bone marrow can have severe effects on the development of both lymphoid and myeloid cells giving rise to depression (immunodeficiency or anaemia) or proliferation (neoplasia). Aneamia is relatively common in cats compared to other species, and FeLV infection is probably the most important cause. The pathogenic mechanism behind FeLV-induced immunosuppression is complex and not at all well understood - the strain of virus appears to be important. Immunosuppressed cats are susceptible to various secondary infections. Lymphosarcoma is the most common haemopoietic malignancy in the cat and associated with FeLV infection. In addition, FeLV virus is often associated with reproductive failure.

Several companies make and market ELISA or CITE kits for testing blood for FeLV antigen. Glasgow Veterinary School also offers a virus isolation service. It is probably best to confirm positive ELISA results by virus isolation, and cats should be re-tested after 12 weeks in case a cat was only transiently viraemic. Control is generally based on testing all cats, and separating FeLV infected from non-infected. Cats ought to be re-tested every 6-12 months, and all new introductions to a colony isolated from other cats for at least 12 weeks and tested.

A vaccine has been recently launched in the UK which appears to be safe and offer some protection to domestic cats. There is no data available on its use in non-domestic cats.

Feline syncytium-forming virus

FeSFV is frequently isolated from domestic cats, but has not been convincingly associated with any disease.

RODENT VIRUSES

Feline cowpox

Cowpox virus is only found in Eurasia and, despite its name, is rare in cattle. The virus is now thought to be endemic in small wild mammal reservoir hosts, and antibody has been detected in wild wood mice, field voles and bank voles in the UK. However, cats are the most commonly recognised host of cowpox virus. They are thought to become infected when hunting. Most affected cats are adult and come from rural environments; almost all are known by their owners to hunt small mammals. Most cases occur in the autumn because small mammal populations are at maximum size at that time of year, and because individuals are most active and therefore most prone to capture. Cat-to-cat transmission can occur, but generally causes only sub-clinical infection in the recipient cat. Cat-to-human transmission can also occur, and about half of all recent cases in man have been traced to contact with infected cats.

Cowpox virus has also been isolated from cheetahs, a lynx and a serval in British zoos (cheetahs develop a severe pneumonia and often die) and in mainland Europe from several species of big cats as well as okapi, elephants, rhinoceroses and anteaters. In one of these outbreaks, at Moscow Zoo, the source of infection was traced to infected white rats used to feed the big cats.

Most domestic cats present with widespread skin lesions, but many have a history of a recent, single skin lesion on the head, neck or a forelimb. The primary lesions vary in character from large abscesses or areas of cellulitis to small, scabbed papules. Many owners describe the primary lesion as having developed from a small, bite-like wound. Secondary skin lesions develop a few days to weeks after the primary lesion is first noticed. Secondary lesions first appear as small, randomly distributed dermal nodules, which over 3-5 days develop into ulcerated papules up to 1cm in diameter. These quickly become scabbed, and scabs dry and separate after a further 2-3 weeks. Lesions may be pruritic, especially if secondarily infected or when healing. New hair soon grows, and most cats are completely recovered in 6-8 weeks.

Most domestic cats exhibit no clinical signs other than skin lesions and a mild pyrexia, but up to 20% may also develop a mild, serous nasal discharge, conjunctivitis or transient diarrhoea, and some cats may be depressed and anorexic. Systemic illness usually occurs only during the viraemic phase, just prior to and during early development of secondary skin lesions,

and may be accompanied by low grade, transient pyrexia. More severe systemic signs or delayed healing in domestic cats may result from heavy secondary bacterial infection or immunodeficiency resulting from corticosteroid treatment, severe concurrent disease (e.g. chronic renal failure) or infection with FeLV or FIV. However, severe disease appears much more common in otherwise healthy non-domestic cats. Severe systemic signs, particularly evidence of pneumonia or in conjunction with underlying immunosuppressive disease, suggest a poor prognosis, and euthanasia might be considered.

With experience, clinical signs alone may enable a diagnosis to be made, but a laboratory diagnosis is necessary for confirmation. Dry, unfixed scab material can be sent through the post without need for a special transport medium for virus isolation or electron microscopy. Serology can be especially useful for retrospective diagnosis.

Hantavirus

Hantaviruses are enzootic worldwide in wild and laboratory rodent populations, and are often zootic. Hantavirus antibody in cats was first detected in laboratory-housed cats in Belgium, and a recent survey in Britain found serum antibody to Hantavirus in around 10% of cats from a variety of disease and environmental backgrounds. The clinical significance of Hantavirus infection in cats is not known, although the same British survey did suggest a possible association between Hantavirus antibody and chronic disease.

SOME OTHER FELINE VIRUS INFECTIONS

Although pigs are the reservoir host for Aujeszsky's disease virus (ADV), other animals, including cattle, sheep, dogs, cats and rats can also be infected. These species are thought to be 'dead end' hosts, however, and are not thought to transmit the disease themselves, although cats may shed virus in their oral and nasal secretions. There are several reports of Aujeszky's disease in cats, all of whom had either close contact with pigs or who had eaten uncooked, infected pig meat. Aujeszky's disease in dogs and cats is almost always fatal, and often rapidly so.

Canine distemper virus (CDV) can infect domestic cats both experimentally and in the field but generally causes no clinical signs. In some big cats, however, CDV infection has been associated with encephalitis. Influenza virus can infect cats following experimental inoculation, and there is some serological evidence of infection in the field. However, there is no evidence that cat to human transmission might occur, the reverse being more likely during human pandemics. Several reports also exist of paramyxovirus infection of the CNS in cats; these infections have been associated with demyelinating encephalitis and with clinical neurological signs. Cats in some parts of the world

may also become infected with several arthropod-borne viruses. Infection is usually asymptomatic but occasionally causes encephalitis.

FELINE SPONGIFORM ENCEPHALOPATHY (FSE)

Spongiform encephalopathy has been seen in over 20 pet cats and at least two big cats in zoos (a puma and cheetah). Clinical signs include ataxia, hypermetria, hypersalivation, muscle tremors and behavioural changes. The source of infection for cats remains unknown. Retrospective surveys of feline brain material suggest that FSE is probably a new disease.

D. Richardson: I read of the possibilty of a test for rabies from a blood sample. Is this correct?

Dr. Bennett: I don't know. I guess that if animals had been infected for quite a while you could look for antibody.

G. Law: Once a cat has calicivirus, you can't get rid of it, as I understand it. But have there been vaccines produced that are virucidal, that will kill the virus?

Dr. Bennett: Feline calicivirus can cause persistent infections. Most cats manage to get rid of that infection at some stage in their lives. The vaccines tend to protect, if they protect at all, against the disease; they won't protect against infection. If the cat's already infected when you vaccinate it, it's very unlikely to get rid of it. Feline herpes virus causes a persistent infection that lasts for life, and there's no way you're ever going to get rid of that; but the difference is that with FCV, all the time the cat's infected it's shedding the virus, whereas with FHV it'll only shed it on certain occasions, usually when the cat's stressed, which can amount to simply rehousing it.

General observations: Dr. Bennett:

The problem is that most of the literature on these infections relates to work done on domestic cats - there isn't that much on non-domestic cats and what there is is very often clinical signs rather than actual virology. To give you an example, feline panleukopenia virus has been isolated from a large number of big cats. Now, is that really feline panleukopenia virus as we know it, as in domestic cat feline panleukopenia virus, or is it their own virus? Until recently people thought panleukopenia was something only cats in zoos had, but a survey in Kruger National Park found that about 80% of the lions there had antibody to it. Was that originally in lions or has that come with man and his domestic animals? So we may be dealing with different viruses in all these different species. The other way of looking at it is that just because something is mild in the domestic cat, if it got into another species you can't assume it's not going to

cause a problem. An example there would be HIV, where the simian immunodeficiency viruses in their own hosts tend not to cause any clinical signs - but do when they enter another host, for example, man.

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