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FELINE IMMUNODEFICIENCY VIRUS: A BRIEF REVIEW

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SUMMARY

Feline immunodeficiency virus (FIV), previously known as feline T-lymphotropic lentivirus (FTLV), was first described by Pedersen *et al.* (1987) who isolated the virus from cats with a variety of clinical signs suggestive of immunodeficiency. Since then FIV has become one of the most studied feline viruses, not least because of its similarity to human immunodeficiency viruses (HIV) which cause acquired immunodeficiency syndrome (AIDS) in man.

PROPERTIES OF THE VIRUS

FIV is a member of the lentivirus subfamily of the family Retroviridae. Other lentiviruses include human, simian and bovine immunodeficiency viruses, visna maedi of sheep, caprine arthritis-encephalitis and equine infectious anaemia viruses. FIV has similar morphology to the other lentiviruses, being approximately 105–125 nm in diameter and enveloped with a bar or cone-shaped core (Pedersen *et al.*, 1987; Yamamoto *et al.*, 1988). Polyacrylamide gel electrophoresis of purified FIV demonstrates structural proteins similar in size and character to those of HIV and other lentiviruses (Pedersen *et al.*, 1987; Yamamoto *et al.*, 1988; Steinman *et al.*, 1990). The envelope contains a major spike glycoprotein (gp120) and a small transmembrane glycoprotein (gp40) (Egberink *et al.*, 1990b; Steinman *et al.*, 1990; Stevens *et al.*, 1991). Steinman *et al.* (1990) reported some reactivity between the gp120 of FIV and sera from horses infected with equine infectious anaemia virus (EIAV), but showed this was dependent on glycosylation. The major core proteins (p24, p15 and p10) appear to be derived from a precursor (p50); the p24 of FIV cross-reacts with high-titre serum raised in rabbits to the corresponding proteins of EIAV, HIV and simian immunodeficiency virus (SIV), and with some field sera from EIAV-infected horses (Egberink *et al.*, 1990b; Steinman *et al.*, 1990), and the p15 may undergo fatty acid acetylation as in other lentiviruses (Steinman *et al.*, 1990). The core of FIV contains the reverse transcriptase enzyme (RNA-dependent DNA polymerase) which is magnesium dependent (Pedersen *et al.*, 1987; North *et al.*, 1990b) and can be inhibited by some of the drugs also inhibitory to HIV (North *et al.*, 1989, 1990a; Egberink *et al.*, 1990a; Koolen & Egberink, 1990; authors' unpublished observations). Associated with the reverse transcriptase is an

RNase H which also has similar properties to the RNase H of HIV (Cronn *et al.*, 1992).

The entire or partial genomic nucleotide sequences are now known for several FIV isolates (Olmsted *et al.*, 1989a, b; Talbott *et al.*, 1989; Phillips *et al.*, 1990; Miyazawa *et al.*, 1991; Siebelink *et al.*, 1992). The integrated provirus consists of approximately 9500 base pairs (bp), and the overall arrangement of the genome is similar to that of other lentiviruses. The long terminal repeats (LTRs) are about 355 bases in length, and contain several promoter-enhancer sites, a promoter signal and polyadenylation signal, and the 5' LTR is followed immediately by a tRNA-Lys binding site.

The GAG gene (1350 bp) encodes a predicted polyprotein of about 49.5 kDa consisting of predicted 15 kDa, 24 kDa and 10 kDa matrix, capsid and nucleocapsid proteins respectively, and consistent with the major capsid proteins described above. The POL gene (3370 bp) overlaps the 3' end of the GAG gene, and is thought to be expressed as a GAG-POL polyprotein by ribosomal frameshifting similar to that of HIV (Jacks *et al.*, 1988; Olmsted *et al.*, 1989b; Talbott *et al.*, 1989b). Egberink *et al.* (1990b) described just such a transient 160 kDa protein, reactive with monoclonal antibodies to core proteins, in FIV-infected cells. The POL gene encodes a protease, the reverse transcriptase, a dUTPase (Elder *et al.*, 1992), and an integrase. The ENV gene encodes both surface and transmembrane proteins, of predicted size 68 kDa and 27 kDa respectively, but containing about 20 glycosylation sites which, when allowed for, result in predicted molecular weights very similar to those observed (Olmsted *et al.*, 1989b). Unlike the primate lentiviruses, but like visna virus, the FIV ENV gene also contains a 5' region capable of encoding a third protein ('L') of unknown function (Talbott *et al.*, 1989; Phillips *et al.*, 1990; Miyazawa *et al.*, 1991).

In addition to the three major open reading frames (ORFs) GAG, POL and ENV, FIV contains several smaller ORFs which, like the small ORFs of HIV, may encode regulatory factors (Olmsted *et al.*, 1989b; Talbott *et al.*, 1989; Phillips *et al.*, 1990), and activity similar to that of *rev* in simian lentiviruses has recently been described (Kiyomasu *et al.*, 1991).

Although each isolate differs in nucleotide sequence, the differences recorded so far have not been as great as between HIV isolates (Benn *et al.*, 1985; Smith *et al.*, 1988). Most of the differences observed are seen in the ENV gene, in which nucleotide substitutions are not randomly distributed but occur in distinct, variable regions separated by conserved regions in a pattern generally similar to that seen in HIV (Talbott *et al.*, 1989; Phillips *et al.*, 1990; Miyazawa *et al.*, 1991). Comparison of the nucleotide and predicted amino acid sequences of FIV with those of other lentiviruses suggests that FIV is most closely related to EIAV, and diverged from the primate lentiviruses at about the same time as other non-primate lentiviruses (Olmsted *et al.*, 1989b; Talbott *et al.*, 1989).

HOST RANGE AND EPIDEMIOLOGY

FIV has been isolated from domestic cats (Pedersen *et al.*, 1987; Harbour *et al.*, 1988; Ishida *et al.*, 1989), and antibody has been detected in Scottish wild cats

(authors' unpublished observations) and big cats in zoos in North America and Europe (Barr *et al.*, 1989; Letcher & O'Connor, 1991; authors' unpublished observations). Whether or not the virus responsible for antibody in big cats is the same as that infecting domestic cats is not known—we have been unable so far to isolate virus from seropositive lions in European zoos.

FIV does not infect dog, mouse, sheep or human lymphocytes in the laboratory (Yamamoto *et al.*, 1988), and several surveys have detected no antibody in people working with cats or the virus (Yamamoto *et al.*, 1989; Childs *et al.*, 1990). Thus it would appear that FIV, like the other lentiviruses, is fairly host-specific and does not pose a zoonotic risk.

The prevalence of antibody in 'healthy' cat populations varies slightly in different parts of the world, and is generally in the range 1–12% (Ishida *et al.*, 1988, 1989; Lutz *et al.*, 1988; Weijer *et al.*, 1988; Bennett *et al.*, 1989; Hosie *et al.*, 1989; Kobl & Schiller, 1989; Moraillon, 1989; Neu, 1989; Persechino *et al.*, 1989; Shelton *et al.*, 1989c; Yamamoto *et al.*, 1989) although a prevalence of 26% has been reported in Australia (Friend *et al.*, 1990). Although only recently discovered, the widespread prevalence of FIV suggests that it has existed in cats for a long time. Repeated surveys have shown antibody to FIV to be more common in adult cats, with most seropositive cats at least 5 years old (Ishida *et al.*, 1988, 1989; Grindem *et al.*, 1989; Hosie *et al.*, 1989; Shelton *et al.*, 1989c; Yamamoto *et al.*, 1989). FIV antibody is about twice as common in males as females, more common in multicat households than in cats kept alone, more common in non-pedigree than pedigree cats, and more common in free roaming and feral cats than in pet cats kept at home (Bennett *et al.*, 1989; Hosie *et al.*, 1989; Ishida *et al.*, 1989; Yamamoto *et al.*, 1989). The mechanisms of transmission are poorly understood, but it is thought that the main route of spread is by biting (Shelton *et al.*, 1989a; Yamamoto *et al.*, 1988, 1989). That saliva might be involved in transmission is supported by experimental studies and a strong correlation in some surveys between FIV infection and feline syncytium-forming virus (FeSFV) infection (Yamamoto *et al.*, 1989).

CLINICAL SIGNS

Experimental inoculation of kittens with FIV often causes lymphadenopathy, sometimes accompanied by mild pyrexia, depression and leucopenia (Pedersen *et al.*, 1987; Lutz *et al.*, 1988; Yamamoto *et al.*, 1988; Dawson *et al.*, 1991). These signs can be less severe in older cats, however, and, although we have seen a few cases of the lymphadenopathy in FIV-infected cats less than 6 months old, are usually missed in naturally infected cats. The lymphadenopathy gradually disappears after a few weeks to months, and cats may remain healthy for years before clinical disease develops (Bennett *et al.*, 1989; Ishida *et al.*, 1989; Pedersen *et al.*, 1989).

Clinical disease associated with FIV infection is seen mainly in middle-aged or old cats (Grindem *et al.*, 1989; Hosie *et al.*, 1989; Ishida *et al.*, 1989, 1990; Shelton *et al.*, 1989c; Yamamoto *et al.*, 1989). Like AIDS in man, clinical signs are often caused not directly by FIV but by secondary infections, often with micro-organisms which in an immunocompetent animal would cause only mild, if any disease. However, primary neurological disease has been described (Harbour *et al.*, 1988;

Pedersen *et al.*, 1989; Dow *et al.*, 1990), and there is some evidence that FIV may be associated with an increased prevalance of neoplasia (Pedersen *et al.*, 1987, 1989; Ishida *et al.*, 1989; Shelton *et al.*, 1989b, 1990a; Yamamoto *et al.*, 1989; Feder & Hurvitz, 1990; Fleming *et al.*, 1991; Hutson *et al.*, 1991). The clinical syndromes most often associated with FIV infection are chronic stomatitis and severe gingivitis, chronic upper respiratory tract disease, wasting, pyrexia, lymphadenopathy, anaemia, chronic skin disease, chronic diarrhoea and neurological signs (Pedersen *et al.*, 1987, 1989; Gruffydd-Jones *et al.*, 1988; Harbour *et al.*, 1988; Ishida *et al.*, 1988, 1989; Brown *et al.*, 1989; Chalmers *et al.*, 1989; Grindem *et al.*, 1989; Hosie *et al.*, 1989; Knowles *et al.*, 1989; Shelton *et al.*, 1989a, c; Witt *et al.*, 1989; Yamamoto *et al.*, 1989; Tenorio *et al.*, 1991). In addition, careful examination may reveal ocular disease in many FIV-infected cats (English *et al.*, 1990).

Many cats with stomatitis excrete feline calicivirus (FCV) in the oropharynx (Knowles *et al.*, 1989; Ternorio *et al.*, 1991), although it is not known whether this reflects a role for FCV in the pathogenesis of the lesions or merely increased FCV excretion by immunosuppressed cats. Experimental inoculation of FCV isolated from cases of chronic stomatitis into cats without FIV or in the early phase of FIV infection does not cause chronic stomatitis, although FIV-infected cats do take longer than uninfected cats to eliminate FCV infection (Dawson *et al.*, 1991; Knowles *et al.*, 1991). Cats with chronic upper respiratory tract disease are also often infected with FCV or feline herpesvirus. In both chronic oral and chronic respiratory disease bacterial infection undoubtedly also plays a role as antibiotic therapy can alleviate, but usually not eradicate, the clinical signs.

Co-infection of FIV and feline leukaemia virus (FeLV) has been found to be uncommon in most surveys (Hosie *et al.*, 1989; Ishida *et al.*, 1989; Shelton *et al.*, 1989c), although Cohen *et al.* (1990) have reported an association between prevalence of antibodies to FeLV and FIV. When co-infection does occur it may be associated with more rapid development of immunodeficiency and clinical disease both in the field (Ishida *et al.*, 1989) and experimentally (Pedersen *et al.*, 1990). There is no obvious association between FIV infection and feline coronavirus infection or feline infectious peritonitis (Ishida *et al.*, 1989; Lutz *et al.*, 1990), but severe, systemic feline herpesvirus (Pedersen *et al.*, 1989) and cowpox virus infections (Brown *et al.*, 1989; Bennett *et al.*, 1990) have been reported in FIV-infected cats.

There is some evidence that active toxoplasmosis is more common in FIV-infected than non-infected cats (Witt *et al.*, 1989; O'Neil *et al.*, 1991), and FIV-induced immunosuppression may be associated with clinical toxoplasmosis in cats (Ishida *et al.*, 1989; O'Neil *et al.*, 1991) as HIV infection is in man (Navia *et al.*, 1986). Chronic skin disease has been associated with parasites, such as *Notoedres*, *Chyletiella* and *Demodex* species, and with fungal and bacterial infections (Chalmers *et al.*, 1989; Pedersen *et al.*, 1989). Other opportunist or secondary pathogens which may be associated with FIV infection include *Haemobartonella*, intestinal coccidia, *Candida, Aspergillus, Cryptococcus, Pseudomonas*, and mycobacteria (Ishida *et al.*, 1989; Pedersen *et al.*, 1989).

FIV-related neurological disease, which may be more common than generally thought, can present as motor or sensory deficits or as behavioural changes (Harbour *et al.*, 1988; Pedersen *et al.*, 1989; Yamamoto *et al.*, 1989). Although

opportunist infections may occur in the CNS of FIV-infected cats, FIV-associated neurological disease often appears to be caused directly by FIV infection of CNS tissue (Pedersen *et al.*, 1989; Dow *et al.*, 1990), like AIDS-related dementia in man (Wigdale & Kunsch, 1990), and the clinical signs presumably reflect the area of CNS most affected. Ocular disease associated with FIV infection may also be more common than is often thought, but is only detected by careful ophthalmic examination and is often not associatd with obvious loss of vision. English *et al.* (1990) described anterior uveitis, glaucoma or pars planitis in nine FIV-infected cats, and speculated that the syndrome of idiopathic uveitis seen in cats over 6 years old might be FIV-related.

PATHOGENESIS

The pathogenesis of FIV is by no means fully understood. Virus can be isolated from blood, lymphoid organs, saliva (particularly from clinically ill cats) and cerebrospinal fluid (Pedersen *et al.*, 1987; Yamamoto *et al.*, 1988, 1989), and grown *in vitro* in lymphocytes, both T4 and T8 (Pedersen *et al.*, 1987, 1990; Brown *et al.*, 1991b), macrophages (Brunner & Pedersen, 1989; Dow *et al.*, 1990) and astrocytes (Dow *et al.*, 1990; Koolen & Egberink, 1990). Replication occurs best in lymphocytes and macrophages which have been activated or are themselves replicating (Brunner & Pedersen, 1989; Pedersen *et al.*, 1990). In addition, some strains of FIV can also grow in other cell types, for example the feline fibroblast cell line Crfk (Pedersen *et al.*, 1987).

Cats can be experimentally infected by subcutaneous, intramuscular, intraperitoneal or intravenous inoculation, and virus can be most readily isolated from blood and saliva. Horizontal spread amongst cats reared together does occur but not very frequently compared to other feline viruses (Pedersen *et al.*, 1987; Yamamoto *et al.*, 1988, 1989), suggesting that casual contact, sharing of feed bowls and litter trays, is not an efficient means of transmission. There is also little evidence for venereal tranmission among cats. Epidemiological evidence suggests that biting may be the main source of infection in older cats (Yamamoto *et al.*, 1988, 1989; Shelton *et al.*, 1989c); and this has been demonstrated experimentally (Yamamoto *et al.*, 1989). Studies so far have found that transmission of virus from queens to their kittens can occur (Callanan *et al.*, 1991), but is apparently not common (Yamamoto *et al.*, 1988, 1989), and we have observed one case of transmission from kittens to their dam, probably during weaning.

Following experimental inoculation of kittens with high doses of FIV, virus can usually be isolated from lymphocytes after about 1–3 weeks, and antibody develops after about 3 weeks (Lutz *et al.*, 1988; Yamamoto *et al.*, 1988; O'Connor *et al.*, 1989; Hosie & Jarrett, 1990; Dawson *et al.*, 1991). However, inoculation of smaller amounts of virus can markedly increase the time to virus and antibody detection. In most experimental studies, lymphadenopathy becomes apparent after about 4–6 weeks, but its severity depends on the dose and strain of virus, and on the age of cats when inoculated. The acute lymphadenopathy may be accompanied by mild pyrexia and leucopenia, including lymphopenia and neutropenia. Histologically, lymph nodes of acutely infected cats undergo follicular hyperplasia

(Yamamoto *et al.*, 1988), and the follicles may assume bizarre asymmetric forms (Yamamoto *et al.*, 1988; Brown *et al.*, 1991a).

The lymphadenopathy usually disappears after 2–3 months. It may recur transiently in some cats, but otherwise experimentally inoculated cats remain healthy for several years, and the severe, chronic disease seen in the field has not been reproduced experimentally. Similarly, FIV-infected cats in the field appear to remain infected but healthy for at least 3–5 years (Bennett *et al.*, 1989; Pedersen *et al.*, 1989; Yamamoto *et al.*, 1989; Ishida *et al.*, 1990); and, as for HIV infection in man, it is not known what triggers the onset of terminal AIDS-like disease in cats, or even the precise mechanism of immunosuppression.

Deficiencies in some immune functions of FIV-infected cats can be detected within a few months of infection. Decreased numbers of circulating T4 cells and ratios of T4:T8 cells, and reduced *in vitro* proliferation responses to some mitogens and *in vivo* responses to some antigens can be detected within the first 10 months after infection, but more profound immune dysfunction gradually develops with time (Ackley *et al.*, 1990; Hara *et al.*, 1990; Ishida *et al.*, 1990; Lin *et al.*, 1990; Novotny *et al.*, 1990; Siebelink *et al.*, 1990; Taniguchi *et al.*, 1990, 1991; Barlough *et al.*, 1991; Dawson *et al.*, 1991; Lehman *et al.*, 1991; Tompkins *et al.*, 1991; Hoffmannfezer *et al.*, 1992). At the cellular level, infection with FIV causes a transient decreased expression of CD4 antigen and syncytium formation in T4 cell cultures, and persistent infection causes a progressive decreased expression of major histocompatibility complex type II antigens (MHCII) (Willett *et al.*, 1991). It may simply be that the chronic AIDS-like disease develops when the number of functional T4 cells falls below a certain level, which might reflect damage caused by infection of both lymphocytes and macrophages. Alternative theories are that the virus is constantly mutating in order to escape the cat's immune response and AIDS occurs when the virus finally manages this; that FIV infection causes autoimmune responses against the cat's own immune system; or it may be that secondary infections cause the descent into clinical AIDS by either causing mild immunosuppression themselves, or by stimulating lymphocyte multiplication and macrophage activation, thereby enhancing FIV replication in these cells. In addition, feline herpesvirus 1 can activate the long terminal repeat promoter of FIV, suggesting an alternative mechanism whereby other pathogens might enhance FIV replication (Kawaguchi *et al.*, 1991).

Neurological disease is thought to be usually caused directly by FIV replication in the CNS. The histopathology associated with FIV infection in the brain of cats is generally milder than that seen with HIV infection in man, usually consisting of areas of diffuse or focal microgliosis and perivascular cuffing (Dow *et al.*, 1990; Brown *et al.*, 1991a).

LABORATORY DIAGNOSIS AND CLINICAL PATHOLOGY

Diagnosis of FIV infection depends upon detection of either virus or antibody to virus. Virus isolation is expensive, and can be very time consuming. Probably the best sample to take for virus isolation is one or more millilitres of blood, collected in heparin. Although virus in such a sample may survive one day or so at room

temperature, better cell survival and virus yields are obtained if the sample is immediately mixed with three volumes of cell culture medium. The precise protocol used to isolate FIV varies with laboratory (Pedersen *et al.*, 1987; Harbour *et al.*, 1988; Yamamoto *et al.*, 1988; Miyazawa *et al.*, 1989), but in most methods lymphocytes are separated and collected by centrifugation, washed, and incubated in culture medium with a mitogen of cat T-cells, concanavalin A (con A), to stimulate the lymphocytes to divide. However, con A also seems to inhibit virus production, so, after 2–3 days, the cells are washed and resuspended in culture medium as before, but without con A, and usually with interleukin 2 added. Fresh, stimulated, uninfected lymphocytes and media are added every 10 days or so, and the culture is tested for FIV production approximately every week for 6 or more weeks by looking for cytopathic effects, by electron microscopy or by assays for reverse transcriptase or virus antigen production. The cytopathic effect (CPE) consists of syncytia formation, ballooning of cells and cell death, but the amount of CPE produced varies with the virus strain, and feline syncytium-forming virus (FeSFV) can cause similar CPE. Electron microscopy enables identification of FIV virions in ultra-thin sections, but obviously requires ready access to an electron microscope. The reverse transcriptase (RT) assay detects an enzyme, almost unique to retroviruses, which catalyses DNA synthesis from an RNA template (Pedersen *et al.*, 1987; North *et al.*, 1989, 1990b). RT activity due to FIV requires magnesium ions and can therefore be distinguished from the RTs of feline leukaemia virus and FeSFV which require manganese. RT assays can be relatively inexpensive when done in large batches, but for smaller numbers of samples many laboratories use either an antigen-capture enzyme linked immunosorbant assay (ELISA), immunoblotting or immunofluorescence to detect virus-specific antigen in the cell cultures (Pedersen *et al.*, 1987; Yamamoto *et al.*, 1988; Tilton *et al.*, 1990).

Antibody detection is usually done by ELISA or using an immunoconcentration assay (CITE™), by immunoblotting or by immunofluorescence. ELISA and CITE assays, in the latter case combined with an FeLV antigen test, are available commercially for use in the practice laboratory (Idexx Corp., High Wycombe, Bucks) (O'Conner *et al.*, 1989). Because many of the ELISA systems give occasional false positive (and false negative) results, some laboratories confirm ELISA results by immunoblotting or immunofluorescence (Hosie & Jarrett, 1990; Barr *et al.*, 1991). Immunoblotting, or Western blotting, is probably the most specific antibody test since it involves detection of antibody to several viral proteins. But even with immunoblotting there can be some difficulty interpreting borderline reactions both in FIV and HIV infections (Lutz *et al.*, 1988; Hosie & Jarrett, 1990). ELISAs which use recombinant proteins of FIV as antigen are currently being developed (Reid *et al.*, 1991) which may have improved specificity.

Clinical interpretation of a laboratory result for either virus or antibody detection should be undertaken with care, and in the context of the reason for testing. In a healthy cat, virus or antibody detection cannot be used to make a reliable prognosis, as, although field surveys suggest that many cats do eventually progress to AIDS, the incubation period to disease may be many years (Bennett *et al.*, 1989; Pedersen *et al.*, 1989; Yamamoto *et al.*, 1989; Ishida *et al.*, 1990), and it may be that some cats never become clinically ill. Similarly, detection of virus or antibody in an ill cat may be irrelevant to the current disease; for example many cats with cowpox

have antibody to FIV but recover normally (Bennett *et al.*, 1989). On the other hand, lack of detectable antibody in a cat does not necessarily preclude FIV infection (Hopper *et al.*, 1988) as some cats may take a year or more to seroconvert following infection (Yamamoto *et al.*, 1988) and the amount of detectable antibody may decline in the terminal stages of disease (Pederson *et al.*, 1989), a phenomenon also seen in human AIDS (Allain *et al.*, 1987).

Other laboratory investigations which might corroborate a diagnosis of FIV-related disease include persistent leucopenia, especially lymphopenia and neutropenia, anaemia (Yamamoto *et al.*, 1989; Shelton *et al.*, 1990b; Fleming *et al.*, 1991), and hypergammaglobulinaemia. Lymph node biopsy may reveal hyperplasia, or atrophy and involution (Yamamoto *et al.*, 1988; Brown *et al.*, 1991a). In the future, measurement of T4 cell numbers and T4:T8 ratios may be more routinely available as diagnostic and prognostic aids.

TREATMENT AND PREVENTION

In cats showing clinical signs of FIV infection, treatment is largely a matter of controlling secondary infections and alleviating clinical signs. Antibiotics are often used to control secondary and opportunist bacterial infections, and, in some cats, surgery may temporarily alleviate chronic stomatitis and gingivitis. Corticosteroids or megoestrol acetate may also help moderate systemic signs, but probably have little long term beneficial effect. Some of the drugs being developed or used to treat HIV infection in man also inhibit FIV in cell culture (North *et al.*, 1989, 1990a; authors' unpublished data; Egberink *et al.*, 1990a; Koolen & Egberink, 1990), and some clinical effect has been claimed for 9-(2-phosphonomethoxyethyl)adenine (PMEA) and 3'-azido-3'deoxythymidine (AZT, zidovudine, Wellcome Foundation) in cats. If given before inoculation, PMEA has been shown to inhibit detectable FIV infection all the time the drug was being given, although viraemia was detected once treatment was stopped, and some preliminary work suggested that PMEA might cause clinical recovery in some field cases (Egberink *et al.*, 1990a; Koolen & Egberink, 1990). We have reported that two FIV-infected cats treated with AZT appeared to undergo clinical recovery (Smyth *et al.*, 1990) as have Egberink *et al.* (1991), but treatment of further cases has, in our experience, produced at best equivocal results. This lack of effectivity may be due to overwhelming infection in clinically ill cats, and treatment earlier in infection might be more beneficial, as is the case in human HIV infection (Editorial, 1990). However, there is some evidence of side effects in cats following AZT treatment (Tavares *et al.*, 1989; Haschek *et al.*, 1990), and long term treatment might also select AZT-resistant mutants of FIV as occurs *in vitro* (Remington *et al.*, 1991).

As with HIV infection in man, there is no FIV vaccine currently available for use in cats, but there is obviously much scientific and commercial interest in developing one (Gardner, 1991; Yamamoto *et al.*, 1991). At present, therefore, attempts to control FIV infection rely on trying to avoid cat-to-cat transmission. In pet cats kept singly or in small groups, the epidemiological data suggest that prevention of roaming and fighting is the best, if not necessarily the easiest, way to

reduce the risk of infection. Interestingly, although male cats are more likely to be infected than females, there is no evidence that neutering reduces the risk of infection in males. New cats should not be introduced into a household if either the new cat or any existing cats are infected with FIV, as the almost inevitable fighting which follows may place all the cats at risk of infection. On the other hand, if a few cats in a stable multicat household in which fighting is rare are infected with FIV, then the risk of transmission may be small. Certainly, because of the long incubation period to disease, there is no humane reason why a cat should be killed simply because it is infected with FIV.

In a breeding colony with no evidence of FIV infection, it is best simply to avoid the introduction of seropositive cats, although one should be wary of over-reliance on antibody testing (see diagnosis above). If the colony contains cats seropositive for FIV, it is probably best to separate or rehouse infected cats, and, although detectable queen-to-kitten transmission is rare, it is inadvisable to breed from infected cats.

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