

# Synopsis of Feline leukemia virus infection and its relationship to feline infectious peritonitis

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**Background-** Feline leukemia virus (FeLV) is a retrovirus related to murine leukemia virus that has existed among feral cats for tens of thousands of years before its discovery in 1964 (Jarrett, et al., 1964). FeLV infection occurs mainly among cats under 3-8 years of age (reviewed Pedersen, 1998, 1991). The main source of infection is cats in the asymptomatic stage of infection. Virus is shed in all body excretions and secretions and spread is by close contact (Pedersen et al., 1977). FeLV infection in nature usually occurs after cats are old enough to socialize and the primary phase of infection is either inapparent or transient and ends with a long-lasting immune response in 95% or greater of cats. Only a small proportion of infections in nature lead to a chronic viremia. FeLV-associated diseases occur predominantly in the small group of cats with persistent infection.

FeLV disease in feral cats raised no alarms prior to its discovery and any associated mortality went unappreciated among the spectrum of maladies befalling feral cats. Therefore, what we know about the pathogenesis of FeLV infection in feral cats initially came from studies done in the 1970's and 1980's on groups of household cats and laboratory infections (reviewed Pedersen, 1998, 1991).

**Epizootiology-** FeLV appears to have entered unknowingly into owned cat populations from nature prior to the 1960's and rapidly increased in incidence. The first inklings that a virus might be involved with this introduction was in 1964 with the identification of intracellular particles resembling murine leukemia virus in a household of cats with multiple cases of lymphosarcoma (Jarrett, et al., 1964). Our understanding of the severity of FeLV infection and its relationship to diseases other than lymphosarcoma began in 1969 in research laboratories (Hardy et al., 1969). The ultimate spectrum of FeLV-related diseases came from the commercial application of an indirect fluorescent antibody (IFA) test for the detection of viremic cats, beginning in 1972 (Hardy, 1973; Hardy and Zuckerman, 1991). This was followed by rapid in-house FeLV tests based on ELISA (Lutz et al., 1979).

FeLV was identified as a major cause of disease in owned cats, retrospectively in the 1960s and prospectively in the 1970's and 1980's. What caused the panzootic of FeLV infection and disease among owned cats? As understood later, human managed multi-cat environments, especially where young kittens were in contact with older infected kittens and cats, proved ideal for cat-to-cat transmission. The severity of these exposures, coupled with young age (Hoover et al., 1976) and other environmental stressors, greatly increased the incidence of persistent rather than transient infections (Pedersen et al., 1977). Whereas only a small

percentage of cats in nature become persistently viremic, a third or more of cats exposed in a controlled laboratory environment developed persistent viremia.

The end of the FeLV panzootic came with the widespread “testing and removal” of viremic cats as documented by Weijer and colleagues (1986). Test and removal were later augmented by effective vaccines. It is noteworthy, that FeLV infection is no longer a major disease problem in managed multi-cat situations and household pets. It once again exists as an infection of nature, where only 1-5% of feral cats test positive. However, a few viremic cats, especially younger ones, continue to appear among cats brought from nature into foster/rescue and shelter environments.

**Pathogenesis-** Primary FeLV infection is largely inapparent in nature and terminated by a strong immune response and lifelong immunity (reviewed Pedersen, 1991). However, if the severity of the exposure is great enough and/or the cat’s immunity is compromised in some manner, a primary and transient disease may occur. This phase can be manifested by fever, generalized lymphadenopathy, low platelet and wbc count, and mild anemia. This stage is frequently followed by a prolonged and largely asymptomatic viremia lasting for months and years. Cats with persistent FeLV infection will ultimately develop several primary and secondary diseases that are usually fatal. The usual estimate of mortality among viremic cats is around 50% per year (Pedersen, 1988), which means only 12.5% will still be alive after three years. Since infection in nature occurs mainly in younger cats, and most die within 3 years, few FeLV infections in nature are seen in cats older than 5-8 years.

Primary FeLV diseases are associated with various mutants of the infecting strain and include aplastic anemia, various myeloproliferative disorders, and lymphoma that is usually generalized, ocular or neurological (reviewed Pedersen 1988, 1991). Secondary FeLV-associated disease are caused by several common infectious agents of cats that are normally not very pathogenic but that are enhanced by the suppression of T-cell immunity associated with FeLV.

**Association of FeLV infection and FIP-** One-third to one-half of cats with FIP during the 1970’s and 1980s’s were found to be FeLV infected (Cotter et al., 1973; Pedersen et al., 1977). The association between the two infections was shown when young laboratory cats with enzootic feline enteric coronavirus (FECV) infection were housed with FeLV carriers (Pedersen et al., 1977). As these young cats became persistently FeLV infected their coronavirus antibody titers began to increase and within several weeks or months clinical signs of FIP appeared. FIP only occurred in the one-third of cats that became FeLV viremic and no cases were seen in the two thirds of cats that became FeLV immune. In a later study, cats chronically infected with a laboratory strain of feline immunodeficiency virus (FIV) were experimentally infected with FECV (Poland et al., 1996). Two of 19 cats in the chronic immunosuppressive stages of FIV infection developed FIP, while none of 20 non-FIV infected littermates became sick. Studies like this with FeLV and FIV immunosuppression were important in concluding that FIP virus (FIPV) was a commonly occurring mutant of FECV and a minimal pathogen in healthy immunocompetent cats.

**What does FeLV infection mean to FIP treatment?** I confess disfavor for treating FIP in FeLV positive cats. We know that FeLV infection induces a type of immunosuppression that is conducive to the development of FIP. I also suspect that successful FIP treatment with antivirals such as GS-441524 relies on the re-establishment of a protective immune response to FIPV. If true, FeLV-induced immunosuppression may interfere with FIPV immunity and decrease the cure rate to GS treatment or interfere with any long-term protective immunity conferred by successful anti-viral drug treatment. Two other problems with treating such cats need to be considered. Keeping FeLV infected cats creates financial and physical hardships in terms of routine veterinary care and quarantine from susceptible cats. It is also known that only 10% of FeLV infected cats will survive longer than three years. These things beg the question of where resources of foster/rescue groups and individuals are best expended – on cats only with FIP, cats with other treatable disease, or on healthy cats waiting for homes?

**Conclusion** - It is unlikely that foster/rescue people will decide not to treat FeLV positive cats for FIP. However, the decision to treat FIP in such cats must first depend on the accuracy of the initial FeLV test. About 5 in 100 positive in-house FeLV ELISA tests in a healthy cat population will be falsely positive. If the incidence of FeLV in a population of cats coming from the streets is 1%, false positive will be five times more common than true positives. Therefore, it is important that positive ELISA tests be confirmed by another test such as PCR. Owners should also confirm whenever possible that these cats do not have other FeLV-related diseases such as aplastic anemia, lymphoma, or myeloproliferative disorders. Owners of these cats who elect for GS treatment should also share the short- and long-term results of their efforts so that a better prognosis can be obtained on this cohort of FIP.

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