FENDING OFF FeLV

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Feline leukemia virus (FeLV) is an oncornavirus within the family Retroviridae. Despite a reduction in the prevalence of infection over the last 2 decades, FeLV remains an important cause of mortality in cats as a result of its ability to cause immune suppression, bone marrow disorders and hematopoietic neoplasia. The latest data on the prevalence of FeLV infection suggests a prevalence of around 4% in North America, with higher prevalences in some parts of Europe.

Once established as a persistent infection, FeLV infection progresses more rapidly than FIV infection and is more pathogenic, so virtually all cats that have progressive, productive infections ultimately die of FeLV-related disease. However, in contrast to FIV infection, many cats infected with FeLV regress to a permanent state of viral latency (regressive infection). Thus, a positive test result for FeLV in an apparently healthy cat does not always imply that FeLV-related disease and mortality will occur.

FeLV is primarily transmitted through close contact between cats, with biting being a lesser mode of transmission. The lesser role of biting in FeLV infection results in a weaker predisposition in male cats when compared with FIV.

Because of the phenomenon of age-related resistance, most cats with FeLV-associated disease are less than 3 years of age. This contrasts with FIV-associated disease, which is generally identified in geriatric cats because of the very slow progression of infection.

There are 4 different subtypes of FeLV: FeLV-A, FeLV-B, FeLV-C, and FeLV-T. Each subtype uses a different receptor to enter cells. All cats infected with FeLV-B, FeLV-C, and FeLV-T are co-infected with FeLV-A, and only FeLV-A is transmitted between animals. The other subtypes, which are more pathogenic, arise from FeLV-A. The FeLV subtype influences the clinical expression of disease. For example, FeLV-T, a T-cell tropic variant, is associated with immunodeficiency in cats, whereas FeLV-C is associated with non-regenerative anemia.

The outcome of FeLV infection depends strongly on the virus strain involved and factors that influence host immune function. The virus replicates in oral lymphoid tissue and then circulates in a few monocytes and lymphocytes within peripheral blood. Some cats may develop systemic signs, such as fever, lethargy and lymphadenopathy during this period. A small number of infected lymphocytes then travel to the bone marrow, where the virus infects rapidly dividing precursor cells and subsequently lymphoid and epithelial cells throughout the body. Infection of the bone marrow is a critical step in the pathogenesis of FeLV infection. Once infection of epithelial cells within the intestinal crypts and salivary glands occurs, the virus is shed in massive quantities in the saliva and feces; it can also be shed in urine.

There are several possible outcomes of infection with FeLV. The immune system of some infected cats is able to suppress productive viral infection within a few weeks after infection, before significant infection of the marrow occurs. These cats develop a *regressive infection* whereby proviral DNA is present in the host cell genome but production and shedding of virus no longer occurs. Regressive infection usually occurs for life, but it may be reactivated with immunosuppression. Transfusion of blood from cats with regressive infections to naïve cats has the potential to be followed by reactivation of FeLV in the transfused cat. Cats develop progressive infection once involvement of the marrow is established and persistent viremia and progressive FeLV-related disease results.

Progressive FeLV infection leads to opportunistic infections, neoplasia, anemia, immune-mediated disease, neurological disorders, enteritis, and reproductive disease. The most common types of neoplasia in cats infected with FeLV are lymphoma and leukemia. Anemia in cats infected with FeLV may occur as a result of multiple different mechanisms, including decreased RBC production and increased RBC destruction.

Infection with FeLV is often diagnosed during screening efforts. Screening of healthy cats should be performed with ELISA assays for FeLV antigen. The retrovirus status of all cats should be known regardless of the presence of absence of illness.

Even though some cats that test positive for FeLV antigen have no clinical signs or physical examination abnormalities, a CBC, chemistry panel, and urinalysis should be obtained from these cats (and at a minimum, a complete CBC with blood smear evaluation) to assess for underlying abnormalities that may signal the presence of FeLV-related disorders.

The initial assay of choice for diagnosis of FeLV infection is an ELISA that detects soluble p27 capsid protein antigen in bloodThe most recent study examining the performance of currently available point-of-care (POC) assays for FeLV was published in 2017 (Levy et al, 2017). The investigators took 146 FeLV+ and 154 FeLV- cats as determined using two ELISA assays (ViraChek, Zoetis and Petchek, IDEXX Laboratories). The sensitivity of the IDEXX SNAP, Zoetis WITNESS, Bionote (Anigen), and Zoetis VetScan were 100%, 89%, 92%, and 86%; specificity was 100%, 96%, 96%, and 86%. The biggest problem with any screening assays is the lack of positive predictive value; with an overall prevalence of 1 to 5%, most positive results will be false positive results. However, negative results suggest absence of infection. Confirmation of positive test results is recommended. There are several options to confirm a positive test result:

- Perform another ELISA antigen test using an assay from a different manufacturer. However, it should be remembered that in contrast to FIV infection, cats that test truly positive for FeLV antigenemia early in the course of infection may ultimately still control the infection.
- Perform an IFA assay on peripheral blood smears, because cats with positive IFA results have infection of the bone marrow and are almost always progressively infected. However, IFA is an insensitive diagnostic test.
- Retest with ELISA 1 month later. If the antigen test remains positive, progressive infection is likely. In some cats, antigenemia may persist for 4 months before regressive infection occurs, so the test should be repeated 3 months later or monthly if client finances permit so long as the cat remains healthy.

- Perform a full CBC. If hematological abnormalities exist, progressive infection is likely.
- A more accurate and sensitive way to determine virus load than IFA testing is to quantify quantify viral proviral DNA using the IDEXX quantitative PCR test for FeLV. This was nicely demonstrated in a study published by Beall et al (2021) where naturally-infected FeLV-antigen positive shelter cats were monitored over a 4-year period of time using quantitative PCR. They then showed that there was a strong correlation between survival probability and virus load status, with the median survival time for high-virus load positive cats being 1.37 years; most low-virus load positive cats, like the negative control cats, were still alive and likely had regressive infection instead of progressive infection at the end of the follow up time. This studdy really helped to support use of the IDEXX quant RealPCR test to determine whether a cat that tests positive on a screening ELISA could ultimately control the infection or succumb to FeLV-associated disease. According to IDEXX's algorithm, cats that are ELISA antigen-positive and PCR negative, or cats that are ELISA antigen-positive and have loads less than 100000 copies per mL, are considered regressively infected. The remaining cats are likely progressively infected.
- Laboratories in some other countries also offer assays that detect and quantify viral RNA; high viral RNA loads also suggest progressive infection and indicate active viral replication.

False negative ELISA assay results can occur in the first month after exposure, before sufficient virus can be detected in the peripheral blood. Cats that test negative within 30 days of possible exposure to the virus should be retested 1 to 2 months later. If viral RNA assays are available, these can test positive before ELISA, and can be an option for earlier follow-up testing (1 week later).

IFA assays can be performed on fresh peripheral blood smears or bone marrow. IFA is less sensitive than ELISA and, depending on the laboratory, is more prone to false negative and positive results and so is not recommended for screening purposes. False negative test results can occur in cats with progressive infection when there are inadequate blood cells in the periphery, such as in neutropenic cats. Performance of IFA on bone marrow rather than peripheral blood may help to overcome this problem.

Cats with opportunistic infections and lymphoma can be successfully treated using medications and supportive treatments used for cats that test negative for FeLV. Antiviral agents and immunomodulators have shown limited benefit for treatment of cats with FeLV infections. Cats infected with FeLV should be housed indoors to prevent spread of infection to other cats and minimize exposure of infected cats to other opportunistic pathogens, and raw food diets should not be fed. Cats should be vaccinated with FVRCP vaccines; whether inactivated vaccines are required is controversial because of a lack of evidence of vaccine-associated disease in FeLV-positive cats that are vaccinated with attenuated live vaccines. Some cats with advanced FeLV infection may not respond well to vaccination. Survival may be prolonged in low stress environments, so provision of space, adequate litter boxes, management of co-infections and a proper diet is important.

Survival times vary depending on the stage of infection, host immunity, and the strain of FeLV involved. Nevertheless, virtually all cats that are progressively infected with FeLV die as

a result of FeLV-related disease within 5 years of diagnosis. Many progressively infected cats, especially adult cats, may live for several years with a good quality of life, and so euthanasia is not recommended on the basis of a positive FeLV test alone.

Several vaccines are available for prevention of FeLV infection. No vaccine provides 100% protection against FeLV infection, and even when protection against progressive infection occurs, regressive infections still occur after challenge. However, vaccination can protect cats from progressive FeLV infection, and so it is indicated for all cats that are at risk of infection. In general, vaccination for FeLV is underperformed and owners should be educated on the importance of vaccination. Two doses are given 3 to 4 weeks apart from 8 to 9 weeks of age, followed by a booster at 1 year and then every 1 to 3 years thereafter. Testing for FeLV should be performed before each booster if exposure to FeLV was likely before booster immunization was required (which would be true for most cats vaccinated for FeLV).

References Available on Request