



# Feline Diseases

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## Feline Leukemia

Despite the widespread use of vaccines, feline leukemia virus (FeLV) remains one of the most important causes of morbidity and mortality in cats. It causes a variety of malignancies, but persistent infection can also cause severe immunosuppression and profound anemia. The virus is present worldwide and infects domestic cats and a few other Felidae.

### Etiology and Pathogenesis

FeLV is a retrovirus in the family Oncovirinae. There are 4 FeLV subgroups of clinical importance. Subgroup A viruses are found in all naturally infected cats. FeLV-A, the original, archetypical form of the virus, is efficiently transmitted among cats. FeLV-A viruses tend to be less pathogenic than viruses of the other subgroups. Almost all naturally infected cats are originally infected by FeLV-A. Within the infected cat, in addition to the original FeLV-A mutated forms, FeLV-B, FeLV-C, or FeLV-T exist. FeLV-B increases the frequency of neoplastic diseases, FeLV-C is strongly associated with the development of erythroid hypoplasia and consequent severe anemia, and FeLV-T has the propensity to infect and destroy T lymphocytes, leading to lymphoid depletion and immunodeficiency. Viruses of all 4 subgroups are detected (but cannot be distinguished) by commonly used FeLV diagnostic test kits.

The incidence of FeLV infection is directly related to the population density of cats. Infection rates are highest in catteries and households with multiple cats, especially when cats have access to the outdoors.

Persistently infected, healthy cats are the major reservoir of FeLV. Carriers excrete large quantities of virus in saliva. Lesser amounts of virus are excreted in tears, urine, and feces. Oronasal contact with infectious saliva or urine is the most likely mode of transmission. Nose-to-nose contact, mutual grooming, and shared litter trays and food dishes facilitate transmission. Bite wounds from infected cats are an efficient mode of transmission but occur relatively infrequently in cats kept indoors 100% of the time. Bites may be a more important mode of transmission in indoor-outdoor cats.

Age resistance is significant. Young kittens are much more susceptible than adults. The virus may be transmitted vertically (in utero or by milk) or horizontally (by secretions and excretions). Because FeLV is a fragile, enveloped virus and because of age resistance, horizontal transmission between adults usually requires prolonged, intimate contact. In addition, the dose required for oronasal transmission of the virus is relatively high.

After oronasal inoculation, the virus first replicates in oropharyngeal lymphoid tissue. From there, virus is carried in blood mononuclear cells to spleen, lymph nodes, epithelial cells of the intestine and bladder, salivary glands, and bone marrow. Virus later appears in secretions and excretions of these tissues and in peripheral blood leukocytes and platelets. Viremia is usually evident 2–4 wk after infection. The acute stage of FeLV infection (2–6 wk after infection) is rarely detected. It is typically characterized by mild fever, malaise, lymphadenopathy, and blood cytopenias.

In ~70% of adult cats, viremia and virus shedding are transient, lasting only 1–16 wk. A few cats continue to shed virus in secretions for several weeks to months after they cease to be viremic. Virus may persist in bone marrow for a longer period, but even this latent, or sequestered, infection usually disappears within 6 mo. Some FeLV-exposed cats (~30%) do not mount an adequate immune response and go on to become persistently (ie, permanently) viremic. Persistently viremic cats develop fatal diseases after a variable time period.

### **Clinical and Pathological Findings**

FeLV-related disorders are numerous and include immunosuppression, neoplasia, anemia, immune-mediated diseases, reproductive problems, and enteritis.

The immunosuppression caused by FeLV results in an increased susceptibility to bacterial, fungal, protozoal, and other viral infections. Numbers of neutrophils and lymphocytes in the peripheral blood of affected cats may be reduced, and those cells that are present may be dysfunctional. Many FeLV-positive cats have low blood concentrations of complement; this contributes to FeLV-associated immunodeficiency and oncogenicity because complement is vital for some forms of antibody-mediated tumor cell lysis.

Lymphoid or myeloid tumors (eg, lymphoma, lymphoid leukemia, erythremic myelosis) develop in up to 30% of cats persistently infected with FeLV.

Leukemia is a neoplastic proliferation of hematopoietic cells originating in the bone marrow. The cell lines that become neoplastic are neutrophils, basophils, eosinophils, monocytes, lymphocytes, megakaryocytes, and erythrocytes. In cats, the leukemias are strongly associated with FeLV infection and sometimes (but not always) associated with neoplastic cells circulating in the blood.

The anemia caused by FeLV is usually nonregenerative and normochromic. There is frequently an idiosyncratic macrocytosis.

Immune complexes formed in the presence of moderate antigen excess can cause systemic vasculitis, glomerulonephritis, polyarthritis, and a variety of other immune disorders. In FeLV infected cats, immune complexes form under conditions of antigen excess, because FeLV antigens are abundant and anti-FeLV IgG antibodies are sparse. These conditions are ideal for the development of immune-mediated disease.

Reproductive problems are common; 68–73% of infertile queens have been reported to be FeLV-positive, and 60% of queens that abort are FeLV-positive (although abortion is a relatively uncommon cause of feline infertility). Fetal death, resorption, and placental involution may occur in the middle trimester of pregnancy, presumably as a result of in utero infection of fetuses by virus transported across the placenta in maternal leukocytes. Occasionally, infected queens give birth to live, viremic kittens. Latently infected (ie, nonviremic) queens may pass virus on to their kittens in milk.

Enteritis, resembling feline panleukopenia both clinically and histopathologically, may develop. Clinical signs include anorexia, depression, vomiting, and diarrhea (which may be bloody). Because of the concurrent immunosuppression associated with FeLV infection, septicemia may develop.

Other disorders may also develop. FeLV occasionally causes a neuropathy leading to anisocoria, urinary incontinence, or hindlimb paralysis. Certain FeLV-induced lymphomas can produce identical clinical signs. If antineoplastic therapy is planned, it is important to distinguish neoplasia from neuropathy. FeLV can also cause quasineoplastic disorders such as multiple cartilaginous exostoses (osteochondromatosis).

## Diagnosis

Two types of tests are readily available for clinical use. The immunofluorescence assay (IFA) tests for the presence of FeLV structural antigens (eg, p27 or other core antigens) in the cytoplasm of cells suspected to be FeLV-infected. In clinical practice, peripheral blood smears are usually used for the IFA, but cytologic preparations of bone marrow or other tissues can also be used. The IFA is considered to be the most reliable but requires submission to a commercial laboratory, so results are delayed. IFA-positive cats are considered to be persistently viremic and have a poor longterm prognosis.

The more convenient ELISA can be performed in the veterinary clinic and tests for the presence of soluble FeLV p27. FeLV antigen may be present in the absence of intact, infectious viral particles because excess FeLV antigens are released from infected cells free of viral particles. The ELISA detects antigenemia rather than viremia. Several different test kits are available; most have sensitivities and specificities of 98%. Accuracy can be improved by running both the IFA and ELISA on the same cat.

Diagnosis of FeLV-induced neoplasia is similar to that of other tumors. Cytologic examination of fine-needle aspirates of masses, lymph nodes, body cavity fluids (eg, pleural effusion), and affected organs may reveal malignant lymphocytes. Bone marrow examination may reveal leukemic involvement, even when the peripheral blood appears normal. Biopsy and histopathologic examination of abnormal tissues is often necessary for diagnostic confirmation.