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Information Bulletin

Feline Immunodeficiency Virus

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Feline immunodeficiency virus (FIV) (formerly called feline T-lymphotropic lentivirus, or FTLV) is a recently identified member of the virus family Retroviridae. Within the Retroviridae are placed three virus subfamilies: Oncovirinae, Spumavirinae, and Lentivirinae. The Oncovirinae subfamily includes the *oncogenic* (cancer-causing) retroviruses, such as feline leukemia virus (FeLV) and feline sarcoma virus (FeSV). The Spumavirinae subfamily includes the *syncytium-forming viruses* of a number of species (including the cat); to date, those viruses have not been shown to cause disease. The Lentivirinae subfamily comprises several retroviruses associated with nononcogenic disease processes. Those viruses include the causative agents of progressive pneumonia of sheep, infectious anemia of horses, arthritis-encephalitis of goats, and acquired immunodeficiency syndrome (AIDS) of humans. It is to this subfamily of retroviruses, the lentiviruses, that FIV belongs.

The genome (genetic material) of FIV, in common with that of other retroviruses, is composed of single-stranded *ribonucleic acid (RNA)*. The production of a double-stranded *deoxyribonucleic acid (DNA)* copy of the RNA genome is an essential step in the replication of FIV within host cells. That step requires an enzyme, *reverse transcriptase (RT)*, which is carried into the cell by FIV itself. (All retroviruses must possess their own RT because it is not commonly found in host cells.) One of the criteria by which FIV can be distinguished from FeLV involves a difference in the biochemical requirements necessary for optimal activity of each virus's RT.

The DNA copy of the viral genome is inserted into the chromosomal DNA of the infected host cell. That alien invader, known as a *provirus* or *proviral DNA*, then is replicated whenever the host cell divides and can serve as a template for the intracellular production of new viral particles. A cell infected with a retrovirus such as FIV is infected essentially for its lifetime, as are all of its daughter cells. This is of great significance in light of the persistence of FIV within the cat despite the mounting of an active immune response. In fact, the identification of FIV-infected animals today is based on detection of FIV antibody rather than FIV itself, because any cat that has been infected with FIV and produced antibody to it presumably is infected for life.

Another feature differentiating FIV from FeLV is the morphology, or structure, of the individual virus particles. By using electron microscopy scientists can show that retroviruses are extruded from the outer membrane of infected cells into the surrounding microenvironment. Both FIV and FeLV possess a characteristic outer *envelope*, comprising a portion of the host-cell membrane and certain viral proteins, which forms around the internal *core* of the virus as it exits through the cell membrane. Electron photomicrographs demonstrate that the internal core of the FIV particle is characteristically elongated or cone-shaped (see figure on page 3); the core of FeLV is more spherical.

Immunological data confirm that FIV and FeLV are distinctly different viruses. Antibodies produced by FIV-infected cats do not react with FeLV, nor do antibodies produced by FeLV-infected cats react with FIV. Furthermore, FIV is not cross-reactive with human immunodeficiency virus (HIV), the lentivirus responsible for AIDS in people.

Historical Perspective

Feline immunodeficiency virus was first recovered from cats in California that suffered from an immunodeficiency syndrome similar to human AIDS. Weight loss, unthriftiness, and a variety of chronic diseases—*gingivitis, stomatitis, periodontitis, pustular dermatitis, rhinitis,* and *enteritis*—were observed in these animals. A small number of cats also exhibited neurologic abnormalities resembling those seen in AIDS patients. Feline immunodeficiency virus was isolated in the laboratory by cocultivating leukocytes from an infected cat with leukocytes from an uninfected cat. Morphological criteria and the presence of a magnesium-dependent RT identified FIV as a member of the lentivirus subfamily of retroviruses.

It is now clear that FIV represents a serious health hazard for domestic cats. For many years the major feline virus of concern was FeLV, which produces an immunodeficiency syndrome characterized by several of the same chronic disease processes observed in FIV-infected cats. For nearly as long it had been recognized that a significant number of cats with chronic infections, neurologic abnormalities, and anemias test FeLV-negative; in retrospect, it may be that FIV has been responsible, at least in part, for the disease syndromes noted in some of those animals.

The mechanisms by which FIV infection produces an immunodeficiency state, predisposing cats to development of other chronic infections, remain to be elucidated.

Host Range

In nature FIV infections appear to be restricted to members of the cat family (the Felidae), which includes domestic cats as well as certain exotic species. Evidence of FIV infection has been found in several species of nondomestic cats within zoo populations, including snow leopards, lions, tigers, and jaguars. In addition, FIV infection has been documented in free-roaming populations of Florida panthers and bobcats found in and around the Everglades. The significance of FIV infection in exotic cats is not clear at this time, but it could be of considerable importance in the future management of these endangered species.

Transmission of FIV

The natural means by which FIV is spread has not been identified with certainty, but investigative findings do point to a likely possibility. In nature FIV infections occur most commonly in older male cats that spend the majority of their time outdoors. In infected animals the virus is present in the blood and in salivary secretions, yet studies in which uninfected and infected cats have been housed together for a number of years reveal little or no evidence of virus transmission. Hence casual, nonaggressive contact (such as sharing of food and water bowls and social grooming practices) does not appear to be an efficient means of infection, despite the presence of FIV in saliva. The virus can spread from infected queens to their kittens, but this has not been demonstrated to result from transmission either in utero or via milk or colostrum. A fairly high number of infected cats are neutered, so sexual transmission probably is not a primary means of initiating infection. Taken together, these findings suggest that aggressive biting behavior (as would be expected to occur among free-roaming, territorial male cats), resulting in deposition of virus-laden saliva or infected blood cells into the bite wound, may be the major means of transmission.

The distribution of FIV infection in the feline population is poorly defined, but preliminary surveys suggest that the virus is widespread. Studies in the United States estimate that 1 to 3 percent of normal, healthy cats and 10 to 15 percent of cats with chronic infections are infected with FIV. Infections have also been reported in Canada, Britain, and Japan. In Japanese cats, rates of infection appear to be higher (12 percent of healthy cats and 43 percent of clinically ill cats) than among cats in other countries.

Pathogenesis of FIV Infection

Following initial contact of a cat with FIV, the virus appears to be carried to regional lymph nodes, where it may replicate in a subpopulation of leukocytes known as *T lymphocytes* or *T cells*. (Those cells are suspected to be the primary target cell of FIV, because laboratory culture techniques require the use of feline lymphocytes, presumably T cells, in order to grow the virus.) The virus then spreads to lymph nodes throughout the body, resulting in a generalized lymphadenopathy. That stage of the disease usually passes unnoticed by the owner unless the nodes are markedly enlarged. Some time later—perhaps days but possibly weeks or months—the cat may develop a fever accompanied by a drop in the leukocyte count. A low red-blood-cell count often follows. The cause of the sometimes precipitous drop in cell counts is unknown, but it is most likely due to a loss of precursor cells in the bone marrow. An immunologically mediated anemia in which red blood cells are removed by cells in the spleen also appears to occur in some cats with FIV infection.

Once the leukocyte count decreases, a cat's ability to protect itself against infection is compromised. Bacteria, viruses, protozoa, and fungi common in the cat's everyday environment and generally innocuous to a healthy animal can cause severe illness in an immunosuppressed individual. It is the secondary infections that are believed to be responsible for most of the clinical signs associated with FIV.

A number of FIV-infected cats also are infected with the feline syncytium-forming virus (FeSFV), a member of the Spumavirinae subfamily of retroviruses. That finding is not surprising, considering that the mechanics of transmission of the two viruses appear to share some similarities. Whether such dual infections are of any clinical significance remains to be determined.

Clinical Signs of FIV Infection

Cats infected with FIV develop antibodies to the virus usually within two to five weeks. Most develop generalized lymphadenopathy during that period, soon followed by fever. Lymphadenopathy persists for a period of three to six months, after which time most cats appear to remain outwardly healthy for at least two years. Such a lengthy period of asymptomatic infection is common in many lentivirus infections, including AIDS. It is still too early, however, to define a characteristic mean duration of asymptomatic FIV infection, that is, the length of time between signs of acute infection (fever, lymphadenopathy) and the development of the immunodeficiency syndrome.

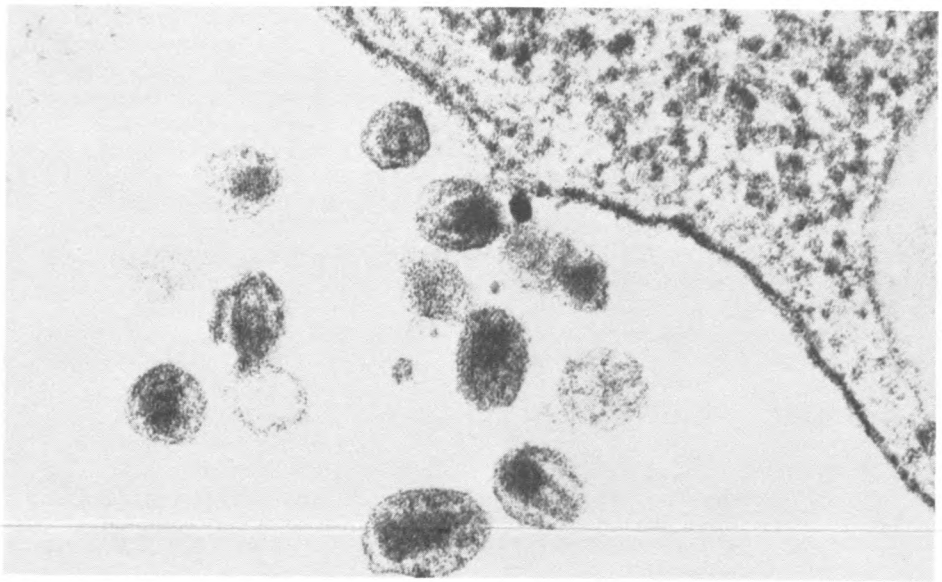
Clinically, FIV-associated disease may actually have been seen for years, because the immunodeficiency syndrome with its multiplicity of secondary infections, anemia, and low leukocyte counts is indistinguishable from certain non-oncogenic syndromes associated with FeLV infection. Prior to the discovery of FIV many cats were thought to have an FeLV-associated disease even when repeat tests for FeLV were negative. Now that a test for FIV is available, it has become apparent that about 10 to 15 percent of FeLV-negative, symptomatic cats are infected with FIV. About 1 to 2 percent of healthy FeLV-negative cats appear to be infected with FIV.

The clinical signs associated with the disease are diverse because of the variety of secondary infections that may be contracted. General unthriftiness and poor coat condition are frequently the only outward signs of disease. Fever of at least 103° F often is present in the later stages of disease. A very common presenting complaint is loss of appetite or evidence of pain when eating because of infections of the mouth (gingivitis, stomatitis). Those conditions can lead to periodontitis and eventual tooth loss. Chronic or recurrent infections of the skin, urinary bladder, and upper respiratory tract also are seen. Persistent diarrhea due to enteritis is a frequent problem. Abortion or other reproductive disorders have been reported in infected queens. Some infected cats have experienced seizures or other neurologic disorders.

It is suspected that some cats identified as FIV-positive may have been infected for several years. A few such cats have had histories of recurrent illness with periods of relatively good health between episodes. In such cases, *leukopenia* (low white-blood-cell count) and anemia appear in a cyclic manner, with episodes of low cell counts followed by periods of near normality. However, the general trend tends to be progressive, with cell counts dropping lower during each succeeding episode. Slow but progressive weight loss also takes place; severe wasting occurs late in the disease process.

Diagnosis of FIV Infection

Current testing procedures screen for the presence of antibody to the virus in a serum sample; the presence of antibody is equated with persistent FIV infection. Kits for in-office veterinary testing are now available, making detection of FIV-infected cats no more difficult than FeLV testing. (This is in stark contrast to the case with feline infectious peritonitis virus, in which a diagnostic test for carrier cats is unavailable). Because a small number of false-positive reactions may occur, positive results obtained by in-house test kits ideally should be confirmed by another assay, such as a



Electron photomicrograph of multiple FIV particles released from an infected cell (× 68,000)

plate ELISA, immunofluorescence, or a Western blot (available at some diagnostic laboratory facilities, such as the New York State Diagnostic Laboratory at Cornell).

Occasionally cats with FIV infections may not mount an appropriate antibody response to the virus or may be in the early antibody-negative stage of the infection at the time of testing; in such cases screening tests will be falsely negative. Unfortunately there is not yet an available assay that can detect the virus itself. Periodic retesting of antibody-negative cats may be indicated if FIV infection is suspected persistently or if recognized exposure to FIV has taken place.

Treatment and Control

Treatment for illnesses resulting from FIV infection is based on the clinical signs. Antimicrobial therapy for secondary bacterial or fungal infections is moderately successful but must be continued on a long-term basis or reinstituted as new infections arise. Supportive measures such as intravenous fluid therapy, blood transfusions, and feeding a high-calorie diet are often required. Corticosteroids or other anti-inflammatory drugs may be needed in some cases to control gingivitis and stomatitis. Recently megestrol acetate has been used to combat weight loss and wasting in human AIDS patients; no information is available at this time on its use in cats with FIV infection.

None of those therapies is directed at FIV itself. To date no safe and effective antiviral drug has been discovered. Zidovudine (azidothymidine, AZT), which has been found useful in AIDS therapy, may have some efficacy against FIV, but its side effects in cats appear to be even more severe than those seen in human beings. Drugs designed to enhance or modify the immune response, such as the interferons, may eventually prove valuable in treating FIV and other lentivirus infections.

Presently cat owners can protect their pets only by preventing contact with infected cats. Pets kept indoors and away from free-roaming cats are highly unlikely to contract FIV infection. Owners of catteries and multiple-cat households should ensure an antibody-negative status in all their cats by testing for FIV and removing or isolating all positive animals. Once an all-negative status has been achieved, prospective additions should be tested negative prior to introduction into the household.

Immunization against FIV

A vaccine against FIV is not available. Certain aspects of the virus-host interaction make the outlook for development of a traditional type of vaccine somewhat bleak. Several other lentiviruses, such as HIV and equine infectious anemia virus, undergo frequent molecular variation in the proteins found in their surface envelopes; the immune response thus has to adapt constantly to those altered proteins in order to suppress the infection. Whether such molecular variation occurs with FIV is not yet known. In addition, lentiviruses are able to avoid the immune response altogether by hiding within cells in provirus form and by spreading directly from one cell to another. As if that were not enough, lentiviruses infect and replicate in some of the very cell types that are most important in immunity against viruses. Taken together, all of those mechanisms probably play a role in protecting the virus from the immune response that would be induced by traditional immunization methods. New techniques for producing immunity to viruses such as FIV and HIV are now being explored, but it will likely be some time before any significant advances are achieved.

Public-Health Aspects of FIV

Although FIV is similar to HIV and causes an AIDS-like illness in cats, it is highly species-specific. Feline cells alone have been found to support its replication in culture. There is no immunologic cross-reactivity between FIV and any of the other lentiviruses, including HIV. In addition, initial studies of human beings who have had close contact with FIV-infected cats show absolutely no evidence of FIV infection. As of this writing, therefore, FIV does not appear to represent a health hazard for human beings.

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About the Cornell Feline Health Center

The ultimate purpose of the Cornell Feline Health Center is to improve the health of cats by developing methods to prevent or cure feline diseases and by providing continuing education to veterinarians and cat owners. The Cornell Feline Health Center is a nonprofit organization supported largely by private contributions. Correspondence may be directed to:

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