Feline Immunodeficiency Virus
Margaret Barr, D.V.M.

Feline immunodeficiency virus (FIV), previously called feline T-lymphotropic lentivirus (FTLV), is a recently recognized feline virus belonging to the family Retroviridae. Although FIV is related to the retrovirus feline leukemia virus (FeLV), FIV does not cause tumors and it is not classified in the oncornavirus subfamily. Instead, the morphology and biochemistry of FIV closely resemble the characteristics of the retroviruses that are associated with non-malignant disease processes. These viruses, the lentiviruses, include the causative agents of maedi-visna and ovine progressive pneumonia, equine infectious anemia, caprine arthritis-encephalitis, and human acquired immunodeficiency syndrome (AIDS).

Clinically, the disease caused by FIV may have been recognized for years. However, the immunodeficiency-like syndrome is indistinguishable from some of the non-neoplastic syndromes associated with FeLV infection. Prior to the isolation of FIV, FeLV-associated disease was diagnosed in many cats, even when repeated tests for the virus were negative. It now appears that about 20 percent of these FeLV-negative, immunosuppressed cats are infected with the feline lentivirus.

The similarity between certain disease manifestations of feline immunodeficiency virus and feline leukemia virus, and because they belong to the same broad family of viruses, leads to an obvious question. How do we know that FIV is not just a mutant strain of FeLV? One difference between FIV and FeLV is the morphology of the virion. When infected cells are examined by electron microscopy, viruses can be seen budding from the outer surface of the cell into the surrounding environment. Both FIV and FeLV have a characteristic outer envelope, comprised of a portion of the host cell's membrane and some viral proteins, that is incorporated by the virus as it exits the cell. However, the internal structure of the FIV particle is elongated or cone-shaped while that of FeLV is more circular.

The genome of FIV, as with other retroviruses, consists of single-stranded ribonucleic acid (RNA). The production of a double-stranded deoxyribonucleic acid (DNA) copy of the viral genome is an essential step in the replication of this virus within the host cell. This step requires the activity of an enzyme, reverse transcriptase (RT), that is carried into the cell as one of the viral proteins. This enzyme is cation-dependent under assay conditions: FIV RT prefers Mg++ and FeLV RT prefers Mn++. The double-stranded DNA provirus integrates into the host cell's chromosomal DNA where it may remain latent for some time before replication of new virus particles occurs.

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An additional proof that FIV and FeLV are only distantly related is that they are antigenically unrelated. Antibodies produced in cats infected with FIV do not recognize FeLV antigens, and antibodies to FeLV do not bind to FIV particles. Furthermore, FIV is not antigenically cross-reactive with human immunodeficiency virus (HIV), the lentivirus responsible for AIDS in people.

Pathogenesis of FIV Infection

Very little is known about the initial pathogenesis of FIV. The primary mode of transmission is also unknown. Transmission through bite wounds is the most likely method of virus spread since free-roaming male cats are most frequently infected. Other types of salivary contact, such as the use of contaminated food and water bowls and social grooming practices, may also play a role in transmission. However, casual, nonaggressive contact such as this does not appear to be an efficient route of infection. Transmission from an infected queen to her kittens can occur, but it is unknown whether this happens in utero or postpartum through ingestion of infected milk. Experimentally, sexual transmission has not been demonstrated and a fairly high percentage of naturally-infected cats are neutered; therefore, sexual transmission probably is not a primary method of initiating infection.

Following the initial contact of the cat with FIV, the virus appears to be carried to regional lymph nodes, where it may replicate in T-lymphocytes. These cells are suspected of being the primary target of FIV since laboratory culture techniques originally required the use of feline T-cells in order to grow the virus. The virus then spreads to lymph nodes throughout the body, resulting in a generalized lymphadenopathy. This stage of the disease usually goes unnoticed by the cat’s owner unless the nodes are greatly enlarged. Lymphocytosis may be observed during this stage of the infection. Some time later, perhaps days but possibly weeks to months, the cat may develop a fever accompanied by a drop in the white-blood-cell count. This decrease in white cells is primarily due to a neutropenia that may progress eventually to a panleukopenia. Anemia may also develop. The cause of this sometimes precipitous drop in blood cells is unknown, although it may be due to a loss of precursor cells in the bone marrow.

Feline Immunodeficiency Syndrome

The clinical signs associated with the disease are diverse because numerous secondary infections may be contracted by the immunosuppressed cat. General unthriftness and poor coat condition are frequently the only outward sign of a problem. Fever of at least 103°F is often present in the later stages of disease and may be much higher at times. A very common presenting complaint is a loss of appetite or evidence of pain when eating due to gingivitis, stomatitis, and periodontitis. Chronic, nonresponsive or recurrent infections of the skin (including severe generalized dermatophytosis and demodicosis), urinary bladder, and upper respiratory tract are commonly seen. Concurrent infections with FeLV, feline infectious peritonitis virus, Toxoplasma, and Hemobartonella are common. Persistent diarrhea due to intestinal tract infection or damage is
also a frequent problem. Abortion of kittens or other reproductive failures have been seen in infected queens. Some infected cats have experienced seizures, dementia, and other neurologic disorders.

Hepatomegaly, splenomegaly, and cardiomegaly have been reported in some FIV-infected cats. Histopathology frequently has revealed moderate to severe infiltration of the tissues with lymphocytes and plasma cells. Lymphocytic infiltration of many other tissues, including the kidneys and gastrointestinal tract, has been seen also. Lymph nodes may be hyperplastic in earlier stages of the disease, while lymphoid depletion is seen frequently in advanced cases.

It is suspected that some of the cats identified as FIV-positive have been infected for several years. Many of these cats have histories of recurrent illnesses with periods of relative health between episodes. In such cases, leukopenia and anemia appear to be cyclic, with episodes of low cell counts followed by near normal levels. However, the general trend seems to be progressive with cell counts dropping lower during each subsequent episode. Slow but progressive weight loss is common, with severe wasting occurring late in the disease process.

Treatment of FIV-Associated Disease

Treatment for illnesses caused by FIV is based on clinical signs. Antibiotic therapy for secondary bacterial and fungal infections is moderately successful but must be continued long-term or resumed as new infections occur. Supportive treatments such as intravenous fluids, blood transfusions, and feeding of high calorie dietary supplements are frequently required. The use of corticosteroids and other anti-inflammatory drugs may be indicated in some cases to control gingivitis and stomatitis. Anabolic steroids may help to combat weight loss and wasting.

Some research has been done using interferon or other immunomodulatory drugs to control the virus, but it is too early to know if the results will be promising. The drug AZT, used in therapy for AIDS patients, may be useful against FIV, but its side effects are apparently greater in cats than in humans. Other antiviral drugs are currently being tested against retroviruses in humans and animals, but none have been able to completely eliminate the infections.

Prevention of Infection with FIV

Presently, vaccination of cats against FIV is not possible. Certain aspects of virus pathogenesis may make the production of a traditional type of vaccine difficult or impossible. Human immunodeficiency virus and equine infectious anemia virus are known to undergo frequent antigenic variation in the proteins found on their envelopes. Therefore, the host's immune response is constantly adapting to these changed proteins in order to fight the infection. In addition, lentiviruses can avoid the immune response altogether by remaining latent in target cells or by spreading directly from cell to cell. Finally, these viruses infect and replicate in some of the cell types that are important in immunity against most other viruses. All these mechanisms play a role in protecting the virus from the antibodies induced by traditional vaccination methods. New methods of inducing immunity to viruses such as FIV and HIV are being explored, but it may be many years before a breakthrough is achieved.

Pet owners can protect their cats only by preventing contact with potentially infected cats. Pets kept indoors and away from free-roaming cats are highly unlikely to contract the disease. Catteries and multiple-cat households should test all cats in the colony. Once a negative status is established, all new additions should be tested prior to introduction to the household. Current testing procedures look for the presence of antibody to the virus in a serum sample. It should be noted that development of detectable antibody levels may take 8-12 weeks or longer after exposure to FIV. Kits for in-house veterinary testing are now available (CITE - Agritech Systems), making detection of infected cats no more difficult than FeLV testing.

Public Health Significance

Although FIV is closely related to the human immunodeficiency virus and causes a disease similar to AIDS in the cat, it is highly species-found to support its replication. There is no antigenic cross-reactivity between FIV and any (continued on page 8)
Dr. Saidla Is Appointed
Feline Extension Veterinarian

The Cornell Feline Health Center and the College of Veterinary Medicine at Cornell University are pleased to announce the appointment of Dr. John E. Saidla of Auburn, Alabama to the newly established position of feline extension veterinarian effective October 1, 1988. Dr. Saidla will also serve as assistant director of the Feline Health Center and will be responsible for coordinating the extension and continuing education activities of the College of Veterinary Medicine and Feline Health Center in the area of feline medicine and surgery.

Dr. Saidla is a 1961 graduate of the College of Veterinary Medicine at Auburn University. For the past 22 years he has owned and operated the Auburn Veterinary Hospital as a sole proprietorship. While conducting his practice in the shadow of a veterinary college, he has been involved in many activities with Auburn University including a number of committees and has interacted with students in various capacities. In early 1988 he was appointed as an adjunct assistant professor in the department of pathobiology.

He has had extensive involvement in local, regional, state, and national organized veterinary medicine. Some of the offices he has held include: president, Alabama Academy of Veterinary Practice; president, East Alabama Veterinary Medical Association; chairman, Medical Records Committee of A.A.H.A.; and treasurer, A.A.H.A. for 3 years. He has a special interest in computerized medical records for veterinary hospitals. Currently he is serving on the A.V.M.A. Standard Nomenclature and Coding Committee, and is editor of SNOCLIN (Standard Nomenclature of Clinical Practice).

Dr. Saidla is author or coauthor of 29 publications. He has presented 37 lectures or seminars to professional audiences, and over 50 lectures or seminars to veterinary students. He has been involved in several research projects.

For his outstanding contributions to veterinary medicine, Dr. Saidla has been recognized with several awards including: A.V.M.A. Practitioner Research Award (1981), Alabama A.V.M.A. Distinguished Service Award (1983), Alabama Academy of Veterinary Practice Annual Award (1983), A.A.H.A. Southeast Regional Practitioner of the Year (1984), A.A.H.A. Charles E. Bild Practitioner of the Year (1985), and Alabama Academy of Veterinary Practice Service Recognition (1988).
Salmonella Implicated as Cause of Song Bird Fever

Fredric W. Scott, D.V.M., Ph.D.

This spring's bird migration to the Northeastern United States was associated with a high incidence of diseased songbirds. States primarily involved were Vermont, New Hampshire, and Massachusetts, with some cases in Maine, Connecticut, and eastern New York. Several species of songbirds were affected during this outbreak. Pine siskins were the most frequently involved species, but black-capped chickadees, evening grosbeaks, common redpolls, American goldfinches, cardinals, boat-tailed grackles, cowbirds, and house sparrows were also affected. Cats that preyed on diseased birds or frequented bird feeder areas developed acute febrile illnesses lasting 2 to 7 days. Affected cats were usually adult outdoor hunting cats of any age. Most had good vaccination histories. Many had known histories of catching wild songbirds 2 to 5 days before clinical signs appear.

Clinical Disease

Clinical disease in cats had a sudden onset with acute depression and complete anorexia. Initially, vomiting sometimes occurred, and enteritis, often hemorrhagic, developed in many cases. High fever was a consistent finding usually 104-105°F, but with reported cases of temperatures as high as 108°F. Frequently, clinical signs mimicked either poisoning or panleukopenia. The incubation period was 2 to 5 days, and the course of the disease varied from 2 to 7 days. Recovery was usually rapid and uneventful. However, some cats required up to three weeks to regain weight and normal eating habits. Most cats responded to antibiotic and supportive treatment unless there were complicating factors. For example, three fatal cases occurred in one practice out of about 30 total cases. One cat tested positive for feline immunodeficiency virus (feline T-lymphotropic virus) and another cat was positive for hemobartonellosis.

Transmission of the infective organism appeared to be by ingestion of contaminated birds, or apparent infection from frequenting contaminated bird feeding areas. There have been no reported cases of in-hospital transmission.

Clinical Pathological Findings

Many cats had severe leukopenia of all components with total leukocyte counts in the 2,000 to 4,000 range (one case was as low as 1,100). There was a marked left shift with numerous band cells as the disease progressed. Leukocyte counts returned to normal within 3 to 7 days after the fever subsided. Platelet counts were slightly depressed in some cases, and total bilirubin was elevated. Most cats were not sufficiently ill to warrant blood diagnostic tests.

Gross and histopathological changes on a limited number of cats have been rather unremarkable with no specific diagnosis possible.

Etiology

There is reasonably good evidence that the causative agent is *Salmonella typhimurium* which was cultured from two cats and one diseased bird by our Diagnostic Laboratory. One practitioner, responding to the survey, cultured type B *Salmonella* from 5 of 7 cases in cats. However, other cases have been cultured extensively and salmonella was not isolated. Histopathological changes do not necessarily confirm salmonellosis. The inconsistent enteritis is also puzzling, although this could be caused by the variable dose of salmonella organisms received from the contaminated bird. The original source of the infection in birds is unknown, but the spread of infection from feeder to feeder is undoubtedly due to fecal contamination of bird seed at the feeder site.

Tissues from two cats that died during the outbreak were negative for cytopathic viruses. Serum samples obtained from cats during the acute disease had high virus neutralizing antibody
titers against feline parvovirus, thus discounting feline parvovirus as the causative agent.

Treatment

Isolation, general supportive treatment, and good nursing care are indicated. Antibiotic treatment of enteritis caused by salmonella is not recommended since this will enhance the salmonella colonization by reducing the normal gut flora. However, antibiotic treatment of septicemic cases is indicated. Gentamicin, ampicillin, and chloramphenicol are the preferred drugs. The salmonella strains isolated to date from this outbreak are not particularly resistant and are susceptible in vitro to these antibiotics.

Control and Prevention

Songbird fever can be controlled by breaking the infection cycle in the bird and preventing the cat from eating birds or frequenting contaminated areas. Bird feeders should be thoroughly cleaned and disinfected with Clorox, and bird feeding should be discontinued for the spring and summer. Cats should be confined indoors.

The disease outbreak in the spring of 1988 was self-limiting when the migration season for the birds was concluded. We do not know if reoccurrences will be seen during the fall migration, or in the spring 1989 migration.

Public Health Concerns

There is reason for concern about possible human infection if the organism is salmonella. There are no documented human infections associated with this disease in cats, although there may be human infections from handling infected birds. Owners should be advised of possible risks and special precautions should be exercised in handling these cats, their litter pans, and other contaminated material. Prudent washing of hands is a must. Disinfection of litter pans and food dishes with dilute Clorox (1:32 or 4 ounces per gallon of water) or other disinfectant should be done routinely for at least four months after infection. Many infected cats will shed salmonella organisms for three to four weeks, and some will shed as long as three to four months. Fecal samples (not rectal swabs) should be cultured for salmonella using enrichment techniques at least three times over a 10 day period. If all cultures are negative, then the cat is considered to be free of salmonella.

Survey

As part of the service to professional members of the Feline Center, a disease alert and survey were mailed in mid May to veterinarians located in New England, New York, Pennsylvania, and New Jersey. One hundred fifty six (18.8%) of the questionnaires were returned. Fifteen of the returned questionnaires reported multiple cases in cats that were consistent with songbird fever, with 128 cases reported. Additional conversations with several nonmember veterinarians disclosed several additional cases of songbird fever cases occurring in cats, with one clinic having over 100 affected cats during March and April.

Fredric W. Scott, DVM, PhD, is the director of the Cornell Feline Health Center and professor of veterinary virology at Cornell.

References:
3 Reed, N. Vermont Institute of Natural Science, Woodstock, Vermont, 1988
A two-year-old, castrated male, domestic long-haired cat was presented to the Small Animal Clinic at the College of Veterinary Medicine at Cornell on July 25, 1986. Prior to admission, he had a 10 day history of progressive anorexia, weight loss, lethargy, and vomiting. He was an exclusively indoor cat with no history of exposure to toxins and was feline leukemia negative.

The physical exam showed a thin (7 pounds), dehydrated (5 to 8%) cat with a rough haircoat, pale mucous membranes, and gingival bleeding. His kidneys were small and irregularly shaped on abdominal palpation. The results of the initial laboratory tests (Table 1) confirmed the cat's state of dehydration and severe azotemia. Based on these findings, a presumptive diagnosis of chronic renal failure was made.

Lactated ringers solution, supplemented with B-vitamins, was given to restore hydration status and allow diuresis. Initially, the fluids were administered at 25 ml/hr or 600 ml/day. Although he was offered a variety of foods to encourage him to eat, his caloric intake was inadequate and a concentrated dietary supplement was force fed. The primary cause of the renal failure was unknown. However, amoxicillin (10 mg/lb BID, PO) was administered to treat an infection, if present.

Further diagnostic tests included serial blood chemistry and ultrasound tests to evaluate the efficacy of treatment. The BUN and serum creatinine levels continued to decrease with fluid therapy (Table 2).

On ultrasonographic examination at initial presentation, the kidneys were bilaterally involved. They appeared small, with little cortical tissue visualized, and an altered appearance to the medullary region suggesting fibrosis or an infiltrate. The ultrasonographic exam was repeated 18 months later with similar results. The ultrasonographic image does not suggest an etiology, but is representative of chronic renal disease.

Intravenous fluids were gradually decreased and subcutaneous fluids were given when the cat's condition had stabilized. On August 5, the patient was discharged from the hospital. His home care included subcutaneous fluids, amoxicillin for 8 weeks, and dietary management using a low protein, low phosphorous, restricted sodium diet. Over the next two months, the subcutaneous fluids were gradually tapered off. His blood parameters stabilized at a BUN of 35 mg/dl, and a serum creatinine level of 3.2 mg/dl. He developed the ability to concentrate urine to a specific gravity of 1.030-1.035. He regained approximately two pounds of body weight and a good quality haircoat. To date, he has continued to do well with conservative management dietary management. His blood chemistry parameters are checked bimonthly, and remain stable.

Caroline Griffitts, DVM, is a 1988 graduate of the veterinary college at Cornell.

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Table 1. Diagnostic Test 7/25/86

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Feline Immunodeficiency Virus

(continued from page 3)

of the other lentiviruses, including HIV. In addition, initial studies show that veterinarians, pet owners, and researchers who have had close contact with FIV-infected cats have absolutely no evidence of infection. Of course, careful research will continue to explore the relationship of the animal lentiviruses to the human lentivirus in an effort to increase the understanding of the pathogenesis, epidemiology, and potential control methods of this very important group of viruses.

Margaret (Peggy) Barr, DVM, is currently working on the feline immunodeficiency virus for her PhD project in veterinary virology.

Further Reading:


