CHAPTER 22

Feline Leukemia Virus Infection

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Overview of Feline Leukemia Virus Infection

First Described: Scotland, 1964 (Jarrett et al.)[1]

Cause: Feline leukemia virus (family Retroviridae, subfamily Orthoretrovirinae, genus *Gammaretrovirus*)

Affected Hosts: Domestic and some wild Felidae

Geographic Distribution: Worldwide

Mode of Transmission: Prolonged close contact with salivary secretions; to a lesser extent biting, transplacental transmission, transmission through milk, and through blood transfusion

Major Clinical Signs: Lethargy, fever, pallor, stomatitis, signs of underlying lymphoma or leukemia, signs of immune-mediated disorders or opportunistic infections

Differential Diagnoses: FIV infection is the primary differential diagnosis for cats with signs of immunosuppression; feline calicivirus infection, or FIV infection are differential diagnoses for cats with stomatitis; primary immune-mediated disease and other bone marrow diseases are differential diagnoses for cats with immune-mediated diseases and cytopenias

Human Health Significance: FeLV does not infect humans.

Etiology and Epidemiology

FeLV is an enveloped RNA virus that belongs to the genus *Gammaretrovirus* of the family Retroviridae. FeLV infection remains an important cause of mortality in domestic cats through its ability to cause immune suppression, bone marrow disorders, and hematopoietic neoplasia. FeLV also causes disease in wild felids such as the highly endangered Iberian lynx.[2]

FeLV infection progresses more rapidly than FIV infection and is more pathogenic, so most cats that develop progressive infections ultimately die of FeLV-related disease. However, in contrast to FIV infection, many cats in the early state of FeLV infection regress to a permanent state of viral latency ("regressive infection"). It is possible that some cats, after exposure to a low dose of FeLV, may eliminate the infection altogether ("abortive infection"), although this appears to be a rare outcome. Regardless, a positive test result for FeLV infection in an apparently healthy cat does not always imply that FeLV-related disease and mortality will occur.

The structure of FeLV is similar to that of FIV, except that the capsid is icosahedral rather than cone shaped (Figure 22-1). There are three main subtypes of FeLV: FeLV-A, FeLV-B, and FeLV-C. Each subtype uses a different receptor to enter cells (Table 22-1). All cats infected with FeLV-B and FeLV-C are co-infected with FeLV-A, and only FeLV-A is transmitted between animals. FeLV-B and FeLV-C are more pathogenic than FeLV-A. FeLV-B arises through recombination of FeLV-A proviral DNA with endogenous FeLV sequences present in host cellular DNA.[3] FeLV-C arises from accumulation of mutations or insertions in the *env* (SU) gene of FeLV-A.[4,5] The FeLV subtype influences the clinical expression of disease (see Table 22-1). For example, FeLV-C is associated with nonregenerative anemia. Even within an FeLV subtype, mutations in the SU and the LTR regions of the viral genome affect disease outcome.[6,7] An additional subtype, FeLV-T, has been associated with immunodeficiency.

Transmission of FeLV-A primarily results from close contact with salivary secretions, such as through licking, mutual grooming, and shared food and water dishes. Other routes of transmission, such as by biting, blood transfusion, in milk, and possibly by fleas, can also occur.[8-10] The virus survives poorly outside the cat and is readily inactivated by disinfectants, soap, and desiccation. The overall prevalence of FeLV infection has declined over the past two decades with more extensive testing and vaccination. Before the institution of widespread testing and vaccination, more than 30% of cats in some catteries were infected.[11] In the early 1990s, the overall prevalence of infection was 13% in nearly 28,000 sick cats from North

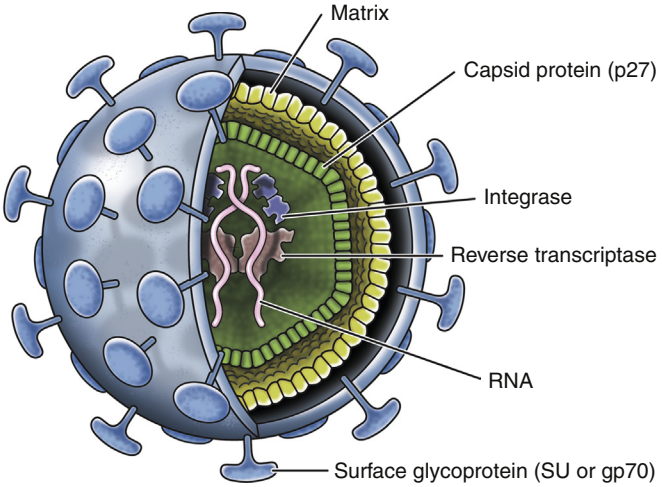

FIGURE 22-1 Structure of feline leukemia virus. Gammaretroviruses contain two identical strands of RNA and associated enzymes, which include reverse transcriptase, integrase, and protease, packaged into a core composed of the capsid protein (p27) with a surrounding matrix, all enclosed by a phospholipid membrane envelope derived from the host cell. The envelope contains a gp70 glycoprotein and the transmembrane protein p15E.

TABLE 22-1

Host Cellular Receptors Involved in FeLV Infection

FeLV Subtype	Receptor	Receptor Function	Comments
FeLV-A	FeTHTR1*	Thiamine transporter protein	Present in all cats with FeLV; transmitted exogenously
FeLV-B	FePit1 or FePit2†	Inorganic phosphate transporter protein	Results from recombination between FeLV-A and feline endogenous FeLV-related retrovirus sequences; may accelerate development of lymphoma or enhance neuropathogenicity
FeLV-C	FLVCR‡	Heme transporter protein	Arises from point mutations in FeLV-A *env* gene; associated with nonregenerative anemia

*Mendoza R, Anderson MM, Overbaugh J. A putative thiamine transport protein is a receptor for feline leukemia virus subgroup A. J Virol 2006;80(7):3378-3385.

†Anderson MM, Lauring AS, Robertson S, et al. Feline Pit2 functions as a receptor for subgroup B feline leukemia viruses. J Virol 2001;75(22):10563-10572.

‡Keel SB, Doty RT, Yang Z, et al. A heme export protein is required for red blood cell differentiation and iron homeostasis. Science 2008;319(5864):825-828.

America that were at risk for exposure.[12] The prevalence was just 7% in a similar population of approximately 1400 cats in 2006.[13] The prevalence of FeLV infection in European cats has also declined markedly.[14] Currently, the overall prevalence of infection in mixed populations of cats is 1% to 6%.[13,15-19] Cats with access to the outdoors; those that have contact with other cats; cats that are male, aggressive, or intact; and cats that are co-infected with FIV are at increased risk of FeLV infection.[12,13,15,17] Male cats are less strongly predisposed to FeLV infection than to FIV infection, and in some studies,[20] no male predisposition has been recognized. Adult cats are more likely to be infected with FeLV than cats aged less than 6 months,[13,17] but the median age of cats infected with FeLV is 3 years,[15] which is lower than that for FIV. This reflects a) the greater degree of pathogenicity of FeLV than FIV and its ability to significantly reduce lifespan; and b) the phenomenon of age-related resistance to FeLV, whereby exposure of cats that are less than 4 months of age to the virus is much more likely to lead to progressive infection than exposure of adults.[21] When 12- to 16-week old kittens are exposed to a multicat household with endemic FeLV infection, between 60% and 70% of kittens will become infected within a 5-month time period. In contrast, less than 5% of cats aged 6 months or older will become infected over the same time period; over a 2-year period, 40% to 50% of these adult cats will become infected. Infection of adult cats can also still occur with exposure to high doses of the virus or when there is underlying host immune compromise.

Clinical Features

Signs and Their Pathogenesis

The outcome of FeLV infection is extremely variable and depends strongly on the virus strain involved, the challenge dose, the route of inoculation, and factors that influence host immune function such as age, genetics, co-infections, stress, and treatment with immunosuppressive drugs. After oronasal exposure to the virus, the virus replicates in oral lymphoid tissue and then circulates in a few monocytes and lymphocytes within peripheral blood. Some cats develop systemic signs, such as fever, lethargy, and/or 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. This infection of the bone marrow is considered a critical step in the pathogenesis of FeLV infection. Once infection of epithelial cells in the salivary glands occurs, the virus is shed in massive quantities in saliva; low quantities of virus can also be shed in urine and feces.

Possible outcomes of infection with FeLV are shown in Figure 22-2. The immune system of some infected cats suppresses viral replication 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 (see Chapter 21). This may occur after the initial period of viremia, or viremia may never be detectable.[22] Regressive infection can persist for life and may be reactivated with immunosuppression, such as might occur during pregnancy or following treatment with immunosuppressive drugs.[23] Later in life, an unknown percentage of cats with regressive infections may develop FeLV-negative malignancies as a result of integration of viral DNA within host cellular oncogenes. Most cats with regressive infection, however, never develop clinical signs related to FeLV infection. Viral genome sequences may eventually be incompletely replicated, and as a consequence, reactivation of virus replication will become impossible in some cats over time. In *abortive infections*, no viremia occurs after infection, and virus cannot be detected using any method. Cats with abortive infections have been exposed to low doses of FeLV, and although they fail to develop viremia, they will develop antibodies to the virus.[24] Some cats that never test antigen-positive may have *focal infections*, that is, evidence of proviral DNA in some tissues but not in blood or bone marrow.[9] Cats develop *progressive infection* once involvement of the marrow is established and cellular destruction by the virus exceeds the ability of the host's immune system to suppress viral replication. Persistent viremia and progressive FeLV-related disease result (Box 22-1).

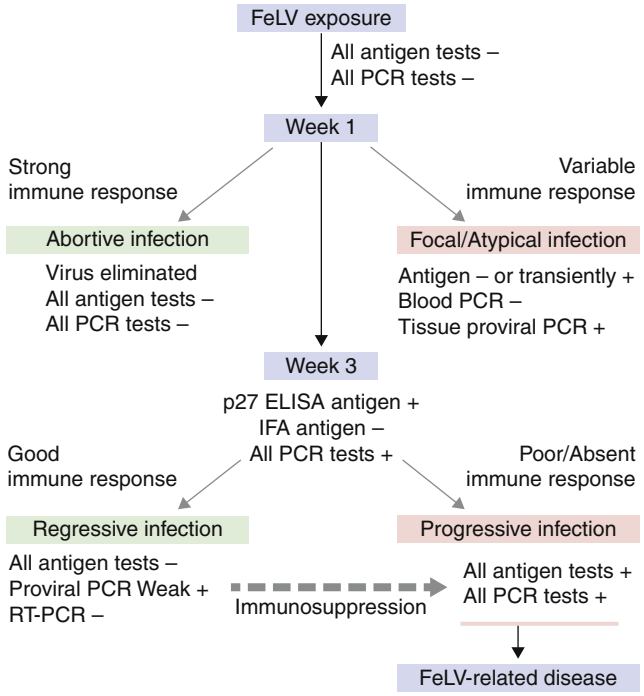

FIGURE 22-2 Outcomes of infection with FeLV. In the first week of infection, cats test negative with all antigen assays (i.e., p27 ELISA and IFA assays), RT-PCR for viral RNA, and PCR for proviral DNA. Rarely, cats exposed to low levels of virus eliminate the infection before or at this time point *(abortive infection)*. Soluble antigen assays and proviral PCR assays become positive from about the third week after infection, and virus is shed in saliva, tears, urine, and feces. After this time point, productive viral infection is suppressed by the host immune response *(regressive infection)* or the virus multiplies rapidly in the bone marrow and a progressive infection occurs, which is characterized by persistently positive antigen ELISA, IFA, viral RNA, and proviral DNA assay results. Cats with *focal or atypical infection* are never or transiently antigen positive and test negative using PCR assays on blood or bone marrow, but some tissues (such as the mammary gland or bladder) are positive with proviral PCR. The latter occurs in only a small percentage (e.g., < 5%) of infected cats.

Opportunistic Infections

Opportunistic infections may develop in FeLV infections as a result of myelo suppression or an acquired cell-mediated immunodeficiency. The immunosuppressive properties of FeLV are not fully understood but have been linked in part to the viral envelope peptide, p15E, which inhibits T and B cell function, inhibits cytotoxic lymphocyte responses, alters monocyte morphology and distribution, and has been associated with impaired cytokine production and responsiveness.[25-28] Kittens with progressive FeLV infection have impaired T cell and, to a lesser extent, B cell function.[29-32] Infected cats may develop lymphopenia, thymic atrophy, and depletion of lymphocytes within lymph node paracortical zones. CD4+ T cell malfunction may contribute to a decreased humoral and cell-mediated immune response in affected cats,[33,34] and the response to vaccination may also be impaired. Impaired neutrophil function compounds the effect of neutropenia in some infected cats.[35-37] Opportunistic infections that result include bacterial infections of the upper and lower urinary tract, hemoplasmosis, upper respiratory tract infections, feline infectious peritonitis, chronic stomatitis, toxoplasmosis, dermatophytosis, and cryptococcosis (Figure 22-3). The prevalence of some of these infections in cats with FeLV infection does not differ significantly from that in cats not infected with FeLV, but clinical signs are more severe and refractory to therapy. Infection with FeLV is an established risk factor for hemoplasma infection. In one study, it was also a risk factor for *Bartonella henselae* infection, but no evidence of clinical disease was identified in the cats infected with *B. henselae*.[38]

BOX 22-1

Clinical Outcomes of Progressive FeLV Infection

Neoplasia, especially lymphoma, leukemia and fibrosarcomas (with FeSV)
Opportunistic infections
Pure red cell aplasia
Aplastic anemia, myelodysplasia, or myelofibrosis
Immune-mediated disease (immune-mediated hemolytic anemia, thrombocytopenia, glomerulonephritis, polyarthritis, uveitis)
Peripheral lymphadenopathy
Neurologic disease (e.g., anisocoria, urinary incontinence)
Reproductive failure
Gastrointestinal disease (uncommon)
Other (e.g., osteochondromatosis, cutaneous horns)

FeSV, feline sarcoma virus.

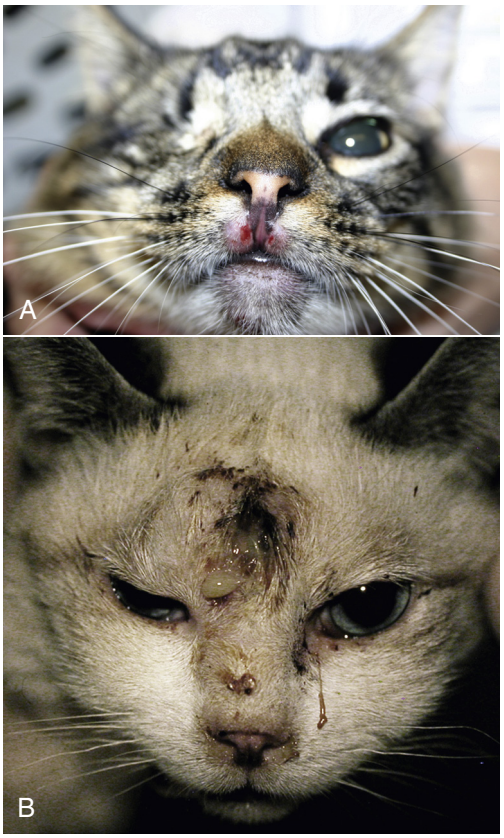

FIGURE 22-3 Opportunistic infections in cats with progressive FeLV infection. **A,** Ulceration of the nasal planum in a 6-month-old male neutered domestic medium hair cat with progressive FeLV infection as defined by positive ELISA antigen and IFA assays on peripheral blood. Stomatitis was also present, and feline calicivirus infection was suspected. **B,** Severe nasal cryptococcosis in a Siamese cat from a cattery with endemic FeLV infection.

Neoplasia

FeLV causes neoplasia in cats primarily as a result of insertional mutagenesis, by which the virus activates proto-oncogenes (especially *c-myc*, but also others such as *flit-1*) or disrupts tumor suppressor genes.[39] The most common types of neoplasia in cats infected with FeLV are lymphoma and leukemia. Cats infected with FeLV are more than 60-fold more likely to develop lymphoma than cats not infected with FeLV; this compares with approximately 5-fold for FIV.[40] Lymphoma or leukemia can be detected in nearly one quarter of cats with progressive FeLV infection at necropsy.[41] In the 1980s, as many as 70% of cases of feline lymphoma were associated with FeLV infection, but with improved control measures and vaccination, the vast majority of cats (more than 80% to 90%) seen at veterinary clinics with lymphoma now test negative for FeLV antigen.[42-44] The most common types of lymphoma in cats infected with FeLV are thymic (mediastinal), multicentric, spinal, renal, or ocular lymphoma. FeLV-associated lymphomas are mostly of T-cell origin, but B cell lymphoma can also occur. In contrast, FIV-associated lymphomas tend to be of B-cell origin.[42] Approximately 80% of cats with thymic lymphoma test positive for FeLV antigen, whereas fewer than 10% of cats with gastrointestinal lymphoma are FeLV antigen-positive. Large granular lymphoma is rarely associated with FeLV infection.[45] Cats with thymic lymphoma typically develop clinical signs of lethargy, tachypnea, and sometimes regurgitation. Most FeLV-positive cats with lymphoma are less than 4 years of age.[14]

Cats with regressive infection appear to be at greater risk for development of lymphoma than cats that were never exposed to FeLV. FeLV-negative cats that live with cats that test positive for FeLV antigen have a more than 40-fold increased risk of lymphoma compared to that expected without exposure to FeLV.[46] Several studies have investigated the prevalence of FeLV proviral DNA in tumor cells from cats that test negative for FeLV antigen. Some studies (including more recent studies that used real-time PCR assays) found no evidence of FeLV proviral DNA in feline lymphomas.[14,47,48] In older studies that used conventional PCR, more than 20% of antigen-negative lymphomas tested positive.[49,50] Additional studies from a variety of geographic locations that use multiple real-time PCR assays are required to clarify the role that FeLV plays in lymphomas and leukemias that develop in cats that test negative for FeLV antigen.

FeLV is responsible for the majority of myelogenous leukemias, erythroleukemias, megakaryocytic, and lymphoid leukemias in cats, although not all cats with these tumors test positive for FeLV antigen. Most FeLV-associated leukemias are acute. FeLV infection can underlie chronic eosinophilic leukemia,[51] chronic myelomonocytic leukemia,[52] and chronic lymphocytic leukemia. However, most cats with chronic lymphocytic leukemia are seronegative for FeLV antigen.

FeLV infection can result in the development of multiple fibrosarcomas in young cats. These occur when FeLV-A recombines with cellular oncogenes (such as *c-fes*, *c-fms*, or *c-fgr*) to form feline sarcoma viruses (FeSV). These viruses then develop mutations in these oncogenes that, when reinserted into cellular DNA, cause malignant transformation.[53,54] To replicate, FeSV requires the presence of FeLV-A, which supplies proteins such as those encoded by the *env* gene. Thus, all cats infected with FeSV test positive for FeLV antigen. FeSV-associated fibrosarcomas are characterized by multifocal, locally invasive, often ulcerated cutaneous masses that metastasize readily to the lung and other sites with a poor prognosis. FeLV-FeSV DNA sequences have been detected in some uveal melanomas from cats,[55] but other studies have failed to identify an association between FeSV and ocular melanomas or sarcomas in cats.[56,57] FeLV infection does not appear to be important in the pathogenesis of solitary fibrosarcomas or injection-site sarcomas in cats.[58,59]

Other tumor types that are variably associated with FeLV infection are feline olfactory neuroblastomas, cutaneous horns, and osteochondromatosis (multiple cartilaginous exostoses).[60] Feline olfactory neuroblastomas are rare and aggressive tumors of the nasal cavity that can lead to signs of rhinosinusitis and neurologic signs. Osteochondromatosis is characterized by benign cartilage-capped exostotic growths that arise from the surface of a bone, which can cause pain, lameness, disfigurement, and paresis due to spinal cord compression. Cutaneous horns occur as a result of benign keratinocyte hyperplasia.

BOX 22-2

Mechanisms of Anemia in Cats Infected with FeLV

Decreased RBC Production
- Pure red cell aplasia (FeLV-C)
- Aplastic anemia
- Leukemia (myelophthisis)
- Myelofibrosis
- Anemia of inflammatory disease

RBC Loss
- Thrombocytopenia secondary to immune-mediated or bone marrow disease

Increased RBC Destruction
- FeLV-associated IMHA
- Co-infection with hemoplasmas

IMHA, immune-mediated hemolytic anemia.

Anemia and Bone Marrow Disorders

Multiple mechanisms can lead to anemia in cats infected with FeLV (Box 22-2). Approximately 90% of FeLV-associated anemias are nonregenerative.[61] A variety of bone marrow disorders lead to decreased red blood cell production. FeLV-C infection results in pure red cell aplasia, a severe nonregenerative anemia associated with erythrocyte macrocytosis and depletion of erythroid precursors in the bone marrow. This occurs because FeLV-C binds to and interferes with a heme exporter protein, which results in subsequent heme toxicosis to the developing erythrocyte.[62] The presence of macrocytosis in the absence of reticulocytosis should thus raise suspicion for FeLV infection. FeLV infection can also lead to aplastic anemia in some cats, which is a deficiency in all cell lineages (platelets, myeloid, and erythroid) in the bone marrow, and replacement of the bone marrow space by adipose tissue. Anemia and bone marrow dysfunction may also result from myelophthisis secondary to leukemia, myeloid and/or erythroid dysplasia, or myelofibrosis (progressive replacement of the marrow with collagenous connective tissue) (Figure 22-4). Myelodysplasia is characterized by disordered maturation of marrow precursors, which in some

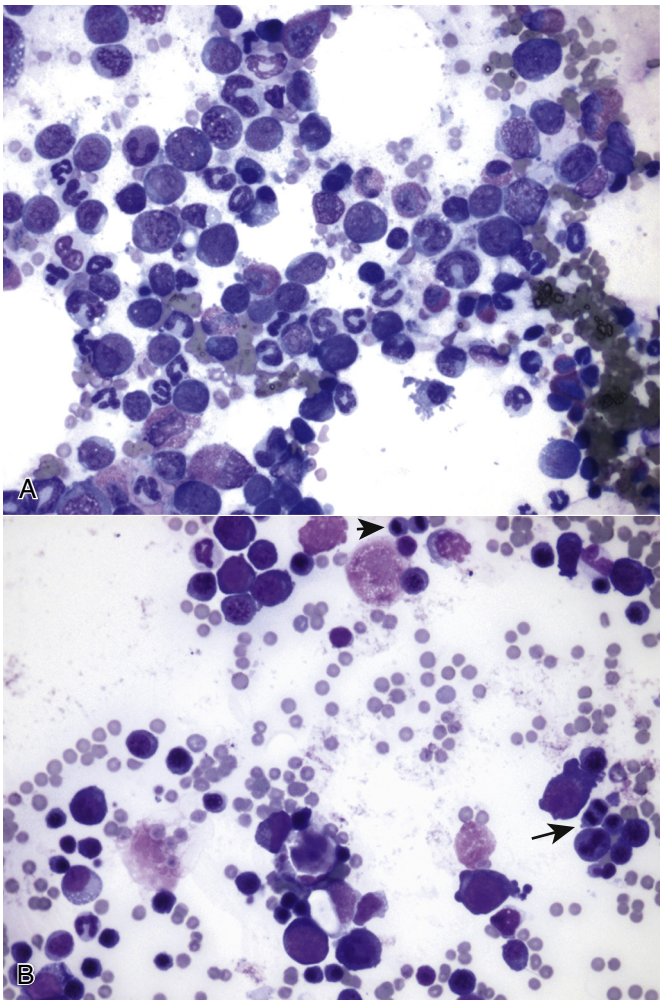

FIGURE 22-4 Bone marrow abnormalities in cats with FeLV infection. **A,** Bone marrow aspirate cytology from a 6-month old male neutered domestic shorthair cat that was evaluated for lethargy and fever. Acute leukemia, marked erythroid aplasia, marked granulocytic dysplasia, and increased eosinophilopoiesis is present. Megakaryocytic dysplasia was also identified. The G:E ratio was approximately 2950:1 with marked erythroid aplasia. Wright's stain. **B,** Bone marrow aspirate cytology from a 1-year-old male neutered domestic shorthair. Severe megaloblastic erythrodysplasia and mild megakaryocytic dysplasia were identified. The myeloid series is present but markedly decreased in all stages; the myeloid to erythroid ratio was estimated at 1:6.5 *(compare with A)*. Nuclear to cytoplasmic asynchrony (megaloblastic change) is present, with immature nuclei in cytoplasm with hemoglobinization. Mitotic figures are present in moderate numbers and are seen in the late stages of the erythroid series *(arrows)*.

cases precedes emergence of leukemia. FeLV infection underlies many myelodysplastic syndromes (MDS) and leukemia in cats.[63] However, over the past two decades, 50% of 28 cats with myelodysplasia and 44% of 41 cats with leukemia seen at the University of California, Davis, tested negative for FeLV antigen in peripheral blood, and only 36% of 34 cats with dysmyelopoiesis seen at the University of Minnesota were positive for FeLV antigen.[64] Several different classification systems have been used to describe feline MDS.[64] The French-American-British (FAB) classification scheme used for humans has been modified for dogs and cats. This divides MDS into 2 groups: 1) MDS with refractory cytopenia (less than 6% myeloblasts in the bone marrow, MDS-RC) and 2) MDS with excessive numbers of myeloblasts (6% to 30% myeloblasts, MDS-EB). The presence of more than 30% blasts indicates leukemia. The most common form of MDS in cats is MDS-EB.[64] Regressive FeLV infections have been detected by proviral DNA PCR in some cats with bone marrow disorders,[65] but the relationship between the presence of proviral DNA and the pathogenesis of disordered marrow function is unclear.

Anemia in cats with FeLV infection may also result from anemia of inflammatory disease, which can be triggered by opportunistic infections or neoplastic disease. Erythrocyte destruction occurs in some FeLV-infected cats as a result of secondary immune-mediated hemolytic anemia (IMHA) or co-infection with hemoplasmas (see Chapter 41). Hemorrhage as a result of thrombocytopenia or defective platelet function may also contribute to anemia. Mechanisms of thrombocytopenia include immune-mediated thrombocytopenia (ITP) and bone marrow dysfunction. Similarly, neutropenia can result from myeloid hypoplasia, myelofibrosis, myelodysplasia, myelophthisis, or maturation arrest at the myelocyte or metamyelocyte stages. In some cases, peripheral neutropenia accompanied by myeloid hyperplasia reflects underlying immune-mediated neutropenia.

Immune-Mediated Disorders

In addition to immune-mediated cytopenias, other immune-mediated disorders that can occur in association with progressive FeLV infection are glomerulonephritis,[66] uveitis,[67] and polyarthritis.[68] Circulating immune complexes have been detected in infected cats.[69-71] Because primary immune-mediated disorders are otherwise rare in cats, retrovirus testing is essential in cats that are diagnosed with these conditions before immunosuppressive drug treatment is initiated.

Neurologic Disorders

Neurologic disorders in cats with progressive FeLV infections may occur secondary to central nervous system (CNS) neoplasia, opportunistic infections, or FeLV infection itself. The envelope protein of FeLV may be neurotoxic.[72,73] Anisocoria, mydriasis, Horner's syndrome, and urinary incontinence can occur. FeLV infection may be one of the most frequent causes of urinary incontinence in cats, an otherwise uncommon condition. A myelopathy has been described in FeLV-infected cats that showed various neurologic signs such as disorientation, lethargy, increased vocalization, progressive ataxia, paresis, paralysis, hyperesthesia, urinary incontinence, recurrent constipation, and anisocoria with diminished pupillary light reflexes.[74] At necropsy, abundant FeLV antigen was detectable within neurons, endothelial cells, oligodendroglia, and astrocytes within the spinal cord.[74]

Gastrointestinal Disease

Uncommonly, FeLV causes enteritis that clinically and histologically resembles that caused by feline panleukopenia virus (FPV), except that lymphoid depletion is absent.[75] Clinical signs include vomiting, acute or chronic diarrhea that may be hemorrhagic, inappetence, weight loss, and dehydration. FeLV-infected cats with "panleukopenia-like syndrome" have intestinal crypt destruction and pancytopenia that results from myeloid destruction (Figure 22-5).[76] Although now very rare, co-infections with FeLV and FPV can also occur, and the 2 viruses may enhance each other's pathogenicity.[77] Co-infections with FeLV and other enteric viruses, such as feline coronavirus, also occur.[78] In most cases, diarrhea in cats infected by FeLV results from an etiology other than FeLV alone.

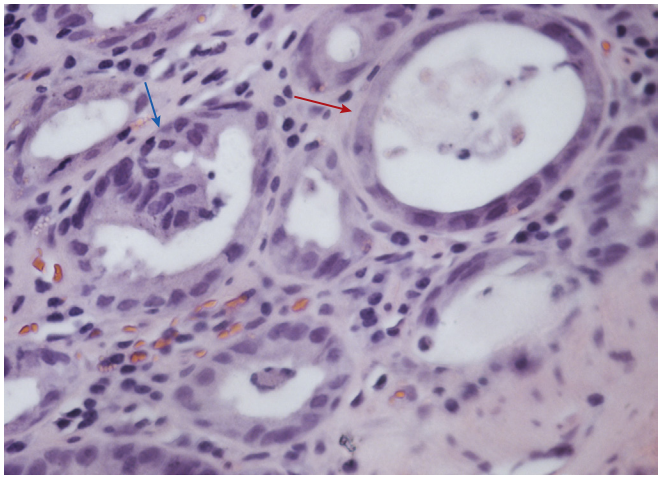

FIGURE 22-5 Histopathology of a colonic biopsy specimen from a 6-year-old intact male FeLV+ domestic shorthair with a 1-week history of anorexia, weight loss, lethargy, fever, and bloody mucoid diarrhea. Severe, diffuse, plasmacytic colitis was present with crypt epithelial necrosis and regeneration. One crypt is dilated, lined with attenuated epithelium, and contains necrotic debris *(red arrow)*. An adjacent crypt shows evidence of regeneration *(blue arrow)*. A tissue gram stain showed a mixed population of bacteria on the luminal surface, but not within crypts. A CBC showed thrombocytopenia (22,000 platelets/μL) and neutropenia (2700 neutrophils/μL) with neutrophil toxicity. A fecal parvovirus antigen test was negative, and bone marrow aspirate cytology showed evidence of myelodysplasia. Remarkably, this cat lived another 3 years with transfusion support, but ultimately was euthanized because of acute granulocytic leukemia with secondary sepsis.

Reproductive Disorders

Transplacental spread of FeLV can lead to fetal resorption, abortion, neonatal death, and fading kitten syndrome.[76] Fetal loss may also result from secondary endometritis. Kittens infected in late gestation or after birth develop thymic atrophy, failure to nurse, dehydration, lethargy, and death within the first 2 weeks of life.

Physical Examination Findings

Physical examination findings in cats with progressive FeLV infection vary dramatically depending on the stage of infection and the secondary disease process present. There may be no abnormalities, or cats may show signs of lethargy, pyrexia, mucosal pallor, petechial hemorrhages, dehydration, peripheral lymphadenomegaly, thin body condition, stomatitis, subcutaneous abscesses, or upper respiratory tract disease. Anemic cats may have a hemic murmur, tachypnea, or tachycardia, or they may be icteric. Cats with severe anemia can be laterally recumbent or comatose and hypothermic. Cats with thymic lymphoma may be tachypneic and have decreased lung and cardiac sounds on thoracic auscultation as a result of malignant pleural effusion, or heart sounds may be displaced caudally. Decreased compressibility of the cranial thorax may also be detected. Splenomegaly, hepatomegaly, renomegaly, intestinal masses, and/or abdominal lymph node enlargement may be detected on abdominal palpation of cats with multicentric lymphoma. Neurologic signs are detected infrequently when compared with signs of anemia or thoracic or abdominal lymphoma and include ataxia, anisocoria, and mydriasis. Although also relatively uncommon, uveitis may be identified, or there may be other ocular abnormalities as a result of intraocular lymphoma or co-infections with other pathogens.

Diagnosis

Infection with FeLV is often diagnosed when healthy cats are screened for infection. Screening should be performed with ELISA or related immunochromatographic in-house assays for free FeLV antigen in serum, because these assays are sensitive, specific, rapid, widely available, and most well understood. The retrovirus status of all cats should be known regardless of the presence of absence of illness.[79] The indications for retrovirus testing are described in Chapter 21 (see Box 21-1).

Even though many 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 could signal the presence of FeLV-related disorders. Subtle hematologic abnormalities, such as erythroid macrocytosis or monocytopenia, may be present in the absence of overt clinical signs and can signify a poorer long-term outcome. Additional diagnostic tests indicated in infected cats that are anemic include a reticulocyte count, Coombs' test, and PCR assay for hemoplasmas. Bone marrow aspiration and core biopsy are indicated in cats with pancytopenia or persistent nonregenerative anemias.

Laboratory Abnormalities

Complete Blood Count

The CBC may be normal or show regenerative or nonregenerative anemia, neutropenia, lymphopenia, monocytopenia, and/or thrombocytopenia. Evidence of agglutination may be present in cats with IMHA. Moderate to marked leukocytosis and increased band neutrophils may also be present. Large numbers of circulating blasts, megakaryocytes or dysplastic cells (such as erythrocytes with giant Howell-Jolly bodies) can be found in cats with leukemia or MDS. When compared with uninfected cats, FeLV-infected cats were nearly 3.8-fold more likely to be anemic, 5-fold more likely to be thrombocytopenic, 3.6-fold more likely to be neutropenic, and 2.8-fold more likely to have lymphocytosis.[80]

Serum Biochemical Tests and Urinalysis

Findings on serum biochemistry analysis and urinalysis are nonspecific and reflect underlying disease processes. Hyperbilirubinemia and bilirubinuria may be present in cats with immune-mediated hemolytic anemia or hemoplasmosis. Cats with glomerulonephritis may be proteinuric. Some cats have evidence of bacterial urinary tract infections. Urine culture and susceptibility testing of a urine specimen obtained via cystocentesis are indicated in cats with suspected urinary tract infection.

Bone Marrow Cytology and Histopathology

Both bone marrow aspirate and core biopsy specimens should be obtained in cats with pancytopenia or nonregenerative anemia. If aspirate results are not diagnostic, the core biopsy should be submitted for interpretation. This is because bone marrow aspirates from cats with aplastic anemia or myelofibrosis are typically of low cellularity. Bone marrow findings in cats with FeLV infection include evidence of neoplastic lymphoid, erythroid, or myeloid cells (which circulate in the peripheral blood of cats with leukemia); myelodysplasia; hypoplasia or aplasia of erythroid, myeloid, or megakaryocyte cell lines; erythroid, myeloid, and megakaryocyte hyperplasia despite peripheral cytopenias; and megakaryocyte hypoplasia. Cytochemical stains

that identify cells of the myeloid lineage (such as alkaline phosphatase, peroxidase, Sudan black B, and nonspecific esterase), immunocytochemistry, or flow cytometry using antibodies that target cell surface cluster of differentiation (CD) molecules may be needed to definitively identify the cell type involved in some acute undifferentiated leukemias.

Diagnostic Imaging

Imaging findings in cats with FeLV infection reflect the underlying disease process and are extremely variable. Cats with FeLV-associated thymic lymphosarcoma have a mediastinal mass on thoracic radiography that may be accompanied by mild to severe pleural effusion (Figure 22-6). Abdominal sonography in cats with multicentric lymphoma may reveal hypoechoic and enlarged abdominal lymph nodes and enlargement, hypoechogenicity, or mottling of the spleen, liver, or kidneys. Increased hepatic echogenicity can also occur with lymphoma. Intestinal masses with loss of normal bowel wall layering may also be detected. Splenomegaly may be detected in cats with immune-mediated cytopenias.

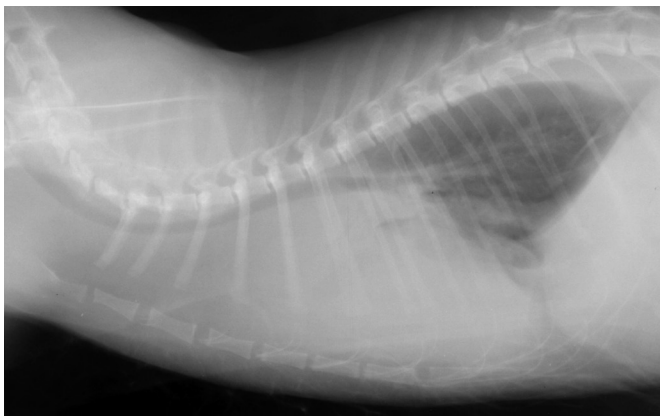

FIGURE 22-6 Lateral thoracic radiograph from a 5-year-old male neutered domestic shorthair cat with mediastinal lymphoma 11 months after it tested positive for circulating FeLV antigen. The cat was tachypneic and had muffled heart sounds that were displaced caudally. There is evidence of pleural effusion and dorsal displacement of the trachea. Cytologic examination of pleural fluid revealed large numbers of malignant lymphocytes.

Microbiologic Tests

Diagnostic assays available for FeLV infection are listed in Table 22-2.

Antigen Assays

The initial assay of choice for diagnosis of FeLV infection is an ELISA or a similar immunochromatographic test that detects soluble p27 capsid protein antigen in blood. The term *soluble* is used to distinguish these assays from assays such as IFA, which detect fixed antigen within cells. In most cats, the presence of circulating antigen correlates with viremia, although a few cats have viremia in the absence of detectable antigen or antigenemia in the absence of detectable viremia.[79] In-practice lateral flow assays are available that detect antigen in anticoagulated whole blood, plasma, or serum. In the past, the use of whole blood generated less reliable results than when plasma or serum was used, but with new-generation tests, whole blood is considered an acceptable alternative.[79] When a choice is available, serum is the preferred specimen. The use of tears or saliva is not recommended, because errors are more likely to occur. When virus isolation in culture was used as the gold standard, the sensitivity of seven different assays ranged from 92.1% to 96.8%, and the specificity ranged from 95.4% to 99.2%.[81]

TABLE 22-2

Diagnostic Assays Available for Feline Leukemia Virus Infection

Assay	Specimen Type	Target	Performance
ELISA or similar immunochromatographic tests for soluble FeLV antigen	Serum, plasma, whole blood	FeLV p27 antigen	Confirmation of positive results is recommended in healthy cats with a second test from a different manufacturer. Positive antigen test results do not signify progressive infection, and the assay must be repeated in 1 to 3 months or an IFA performed. False negatives can occur in the first month of infection.
IFA	Serum, bone marrow	FeLV antigen in blood cells	Less sensitive than ELISA. Positive results indicate infection of the bone marrow and therefore progressive infection. False positives may occur if nonspecific fluorescence is interpreted as a positive result.
PCR	Blood, bone marrow, saliva (RT-PCR); bone marrow, tissue, lymph node aspirates (PCR)	FeLV RNA (RT-PCR) or proviral DNA	Sensitivity and specificity may vary between laboratories. Never use in the absence of antigen testing. Assays that have demonstrated sensitivity and specificity may be useful to detect cats with regressive infection for elimination from blood donor programs, or to resolve the results of discordant ELISA and IFA assays. False-negative test results may occur when variant strains are present.
Virus isolation	Blood, bone marrow	Replication-competent FeLV virus	Difficult, not widely available. Requires a specialized laboratory. Used primarily as a research tool.

IFA, immunofluorescent antibody; RT, reverse transcriptase.

When ELISAs are used as screening tests, confirmation of positive test results is recommended because of the low prevalence of infection in healthy cats and the higher possibility that false-positive test results may occur. Positive test results in the absence of FeLV antigen have the potential to occur rarely as a result of operator error or nonspecific reactivity.[82] As for FIV infection, it is especially important to immediately confirm positive test results if they are likely to result in euthanasia or rehoming for disease control purposes. 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 antigen early in the course of infection (i.e., before involvement of the bone marrow) may ultimately control the infection. Thus a single positive test result does not imply progressive infection, even if it is immediately repeatable using a test from a different manufacturer. If the cat has signs consistent with FeLV-related disease, a single positive test result is more likely to mean that progressive infection is present.
- Perform an IFA assay on peripheral blood smears, because cats with positive IFA results have infection of the bone marrow and, with rare exceptions, are almost always progressively infected. Cats that test negative with IFA assays may be in a transient viremic phase that may result in either progressive or regressive infection, or they may have progressive infection but the sensitivity of IFA is too low to detect it. In this case, both ELISA and IFA assays, or the ELISA assay alone, could be repeated in 1 to 4 months.
- Retest with ELISA 6 months later. If the antigen test remains positive, progressive infection is likely. In some cats, antigenemia persists for 16 weeks before regression occurs, so the test could be repeated earlier than 6 months (e.g., 12 weeks later) or monthly if client finances permit so long as the cat remains healthy.
- Perform a full CBC. If hematologic abnormalities are present, progressive infection is likely.

Negative ELISA results can occur in the first month after exposure to FeLV, before sufficient antigen is detectable 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. Because development of antibodies to FIV can take up to 2 months, it is usually most practical to retest for both viral infections 2 months after possible exposure. Kittens can be tested at any time, because maternal antibody does not interfere with FeLV testing.

Immunofluorescent Antibody or Immunoperoxidase Staining

IFA assays are widely offered by veterinary diagnostic laboratories and can be performed on fresh peripheral blood or bone marrow. At least two fresh smears (without anticoagulant) should be air-dried and mailed to the laboratory. IFA is less sensitive than ELISA and, depending on the laboratory, is more prone to false-negative and false-positive results and so is not recommended for screening purposes. The presence of detectable virus using IFA in circulating blood cells indicates progressive infection more than 90% of the time. Cats with early viremia (before the bone marrow is infected) test IFA-negative but ELISA-positive. Cats with regressive infection test negative with both IFA and ELISA assays (see Figure 22-2). Negative IFA test results can occur in cats with progressive infection when there are inadequate blood cells in the periphery, such as in neutropenic cats. Performing IFA on bone marrow rather than peripheral blood may help to overcome this problem. False-positive results can occur when inexperienced laboratory personnel interpret nonspecific fluorescence as a positive test result. They also have the potential to occur when the antibody conjugates bind nonspecifically to eosinophil granules, so eosinophils must be excluded in interpretation of fluorescing cells.[83]

Some cats with clinical abnormalities that strongly suggest FeLV-related disease (such as leukemia or myelodysplasia) test negative for circulating antigen using ELISA but have bone marrow cells that test positive for FeLV antigen using IFA. For example, at the author's teaching hospital, 8 of 18 cats with leukemia or MDS that tested negative for soluble FeLV antigen had bone marrow smears that were positive using IFA; the remainder tested IFA negative. This phenomenon may reflect either false-positive IFA assay results, or true infection with undetectable levels of antigen in the peripheral blood. The use of PCR on bone marrow may help to resolve the FeLV status in at least some of these cats.

Immunohistochemistry can also be used to detect viral antigen in tissue specimens or bone marrow core biopsies, although it may be less sensitive than IFA.

Molecular Diagnosis Using the Polymerase Chain Reaction

Several different PCR assays have been developed for detection of FeLV nucleic acid. Currently the major clinical indications for PCR are (1) to screen potential blood donors in conjunction with antigen testing or (2) to test for regressive infection when FeLV is strongly suspected as the cause of neoplasia but antigen tests are negative.

PCR assays may detect FeLV RNA (reverse transcriptase–polymerase chain reaction [RT-PCR]) or proviral DNA and must be carefully designed so that they do not detect endogenous FeLV sequences. At the current time, PCR assays should *never* be used in the absence of antigen testing in order to screen for or diagnose FeLV infection. The clinician needs to understand if the assay used detects proviral DNA, viral RNA, or both (some laboratories run both assays), because the clinical significance of a positive viral RNA assay (i.e., productive viral infection) differs from that of a positive proviral DNA assay (which suggests nonproductive viral infection for cats with negative antigen tests). After infection, RT-PCR assays may be positive several weeks before antigen tests or virus isolation become positive,[84] and depending on the assay, PCR for viral RNA can be more sensitive than soluble antigen tests. High viral RNA loads in blood and saliva appear to be associated with progressive infection, whereas low loads may be associated with regressive infection (Figure 22-7).[84]

PCR assays for proviral DNA can be used on blood, buffy coats, bone marrow, or tissues of cats that test negative for FeLV antigen. Cats with a positive proviral PCR test result but negative soluble antigen test, which in one study represented about 10% of cats with negative antigen test results, have regressive infection.[85,86] These cats are probably not infectious to other cats but may reactivate virus shedding with severe stress or immunosuppression, or transmit the virus through blood transfusion or vertical transmission. Proviral DNA appears to be present at much lower levels in cats with regressive infection than in those with progressive infection.[86,87] The cell types that contain FeLV proviral DNA also may differ for antigen-negative and antigen-positive cats. The proviral DNA of one FeLV strain was

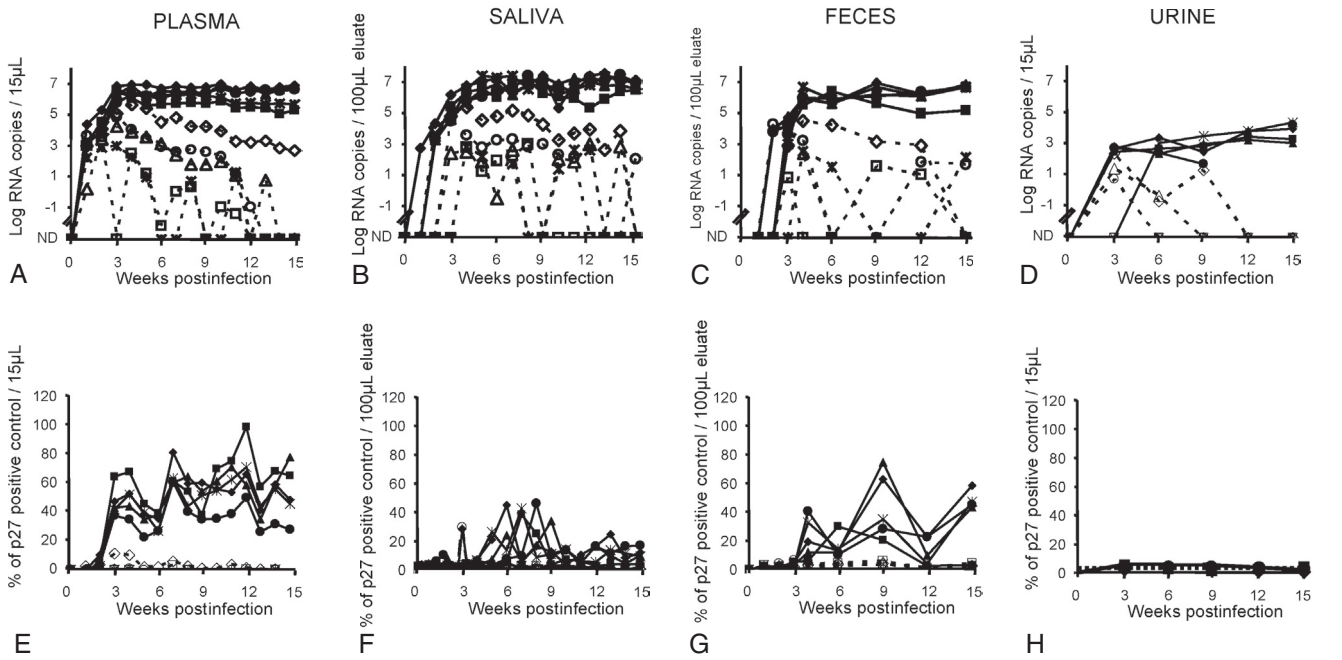

FIGURE 22-7 Viral RNA (**A-D**) and p27 antigen (**E-H**) loads in plasma (**A** and **E**), saliva (**B** and **F**), feces (**C** and **G**), and urine (**D** and **H**) in 10 cats experimentally infected with FeLV. Each line represents observations for a single cat. Continuous lines represent data from cats with progressive infection, and broken lines represent data from cats with regressive infection. (Modified from Cattori V, Randon R, Riond B, et al. The kinetics of feline leukemia virus shedding in experimentally infected cats are associated with outcome. Vet Microbiol 2009;133(3):292-296, Figure 1.)

found only in the lymphocytes of antigen-negative cats, whereas antigen-positive cats had high loads within all leukocyte types, including lymphocytes, monocytes, and granulocytes.[86,87] The use of bone marrow or tissue specimens, rather than whole blood, may increase sensitivity for detection of proviral DNA.

The sensitivity and specificity of commercially available PCR assays are likely to vary with assay design, and the usefulness of assays offered commercially has not been published, so until more information is available, great caution is warranted when interpreting the results of PCR assays for FeLV infection. Retroviruses have high rates of mutation, and the presence of sequence variations may lead to false-negative results. False-positive results occur in some PCR laboratories as a result of contamination or manual loading errors, or poor assay design. Because FeLV vaccine virus is inactivated or recombinant, it does not replicate or integrate into the host genome, so vaccination should not lead to false-positive PCR results.

Virus Isolation

FeLV can be readily isolated in cell culture. The cell culture supernatant can then be tested for production of FeLV using antigen assays or viral RNA PCR. Because growth requires several days and specialized techniques, cell culture is not routinely used for clinical diagnosis.

Antibody Assays

Although not useful for diagnosis of FeLV infection, detection of antibody responses to FeLV infection is performed on a clinical research basis with virus neutralization assays and IFA assays that detect antibodies against feline oncornavirus cell membrane–associated antigen (FOCMA).[24,48,84,88,89] Positive antibody test results in cats that test negative for FeLV antigen indicate previous exposure followed by abortive or regressive infection. Cats with progressive infections and high viral loads usually fail to develop antibody responses.[24,48,88] Antibody responses may occur after vaccination with FeLV vaccines.

Pathologic Findings

Gross and histopathologic findings in cats with FeLV infection usually reflect secondary disease processes. Lymphoma and evidence of myelodysplasia or leukemias are the most common findings, but opportunistic infections may also be detected. The intestinal tracts of cats with FeLV-associated enteritis reveal crypt cell necrosis and regeneration, lymphoplasmacytic infiltrates, and blunting and fusion of villi (See Figure 22-5).[90] Reactive lymphoid hyperplasia is also a common finding. CNS lesions include loss of axons and dilated myelin sheaths within the spinal cord.[74] Immunohistochemical stains may be applied to tissue sections to confirm the presence of FeLV antigen in association with lesions.

Treatment and Prognosis

Cats with opportunistic infections and lymphoma can be successfully treated using the same medications and supportive treatments used for FeLV negative cats with these problems. Opportunistic infections may require longer periods of treatment or, in some cases, lifelong treatment with antimicrobial drugs. Hemoplasma infections should be treated with doxycycline (see Chapter 41). Cats with nonregenerative anemias may require periodic blood transfusions. Serum erythropoietin concentrations are already high in these cats, and in many cases, treatment with darbepoetin or human recombinant erythropoietin is unsuccessful but could be attempted. The efficacy of treatments such as filgrastim is not known and may be complicated by the formation of antibodies (see Chapter 7). The management of cats with stomatitis is discussed in Chapter 21. In general, glucocorticoids and other immunosuppressive drugs

TABLE 22-3

Suggested Medications for Treatment of Cats with Feline Leukemia Virus Infection

Drug	Dose	Route	Interval (hours)	Comments
Zidovudine (AZT)	5 mg/kg	PO	12	Monitor CBC weekly during treatment for the first month, then monthly.
Feline recombinant interferon omega	1 million U/kg	SC	q24h for 5 consecutive days starting on days 0, 14, and 60	
Human recombinant interferon alpha	1 to 50 U/cat	PO	24	

should be avoided unless immune-mediated cytopenias are suspected. Some cats with FeLV-associated IMHA respond well to treatment with glucocorticoids, and glucocorticoid treatment may be unavoidable.

Antiviral agents and immunomodulators are of limited benefit for treatment of cats with FeLV infections (see Chapter 7 for more information) (Table 22-3). The use of feline recombinant IFN-ω improved clinical scores and survival times in cats with FeLV infection over a short time period (2 months) in one study.[91] Beneficial outcomes have also been described after treatment with low-dose oral human recombinant IFN-α. Zidovudine (AZT) has not performed as well for treatment of sick cats with FeLV infections as it has for those with FIV infections, and the results of some studies have shown minimal benefit. In other studies, AZT improved oral cavity inflammation, reduced antigenemia, and prolonged life span in naturally and experimentally infected cats with FeLV infection.[92,93] Controlled studies of the efficacy of other treatments, such as lymphocyte T-cell immunomodulator (T-cyte Therapeutics, Inc.) and acemannan, are required. Antivirals that show promise for treatment of FeLV infection include fozivudine (which is closely related to AZT) and the integrase inhibitor raltegravir, which has been used to treat gammaretrovirus infections in humans and inhibits FeLV replication in cell culture.[94] The safety of these drugs in cats remains to be determined.

Cats infected with FeLV should be housed indoors to prevent spread of infection to other cats. Indoor housing also minimizes exposure of infected cats to other opportunistic pathogens. Raw food diets should not be fed. Survival may be prolonged in low-stress environments, so provision of space, adequate litter boxes, management of co-infections, and a proper diet are important. Vaccines administered for prevention of respiratory viruses and FPV should be inactivated. Some FeLV-infected cats may not respond as well to vaccination as noninfected cats.

Prognosis

Survival times vary considerably depending on the stage of infection, host immunity, and the strain of FeLV involved. Nevertheless, virtually all cats that are progressively infected with FeLV go on to develop FeLV-related disease within 5 years of diagnosis.[95] A comparison of more than 800 FeLV-infected cats and 8000 controls revealed a median survival time of 2.4 years for FeLV-infected cats versus 6.3 years for controls.[79] 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. Some cats with FeLV-associated lymphoma may have long-term remissions when treated with standard chemotherapy protocols. Some, but not all, studies suggest that FeLV infection is a negative prognostic indicator in cats with lymphoma.[96] One of the authors has treated a cat that initially tested positive for FeLV antigen using ELISA and had evidence of IFA-positive, severe megaloblastic erythroid dysplasia in the marrow and IMHA, yet subsequently became ELISA-negative and remained in clinical remission while being treated with glucocorticoids more than 4 years later.[97] The prognosis is least favorable for cats with leukemia, which generally survive less than a few weeks.

Immunity and Vaccination

Several parenteral vaccines are available for prevention of FeLV infection, which include adjuvanted inactivated whole virus vaccines; nonadjuvanted canarypox vectored virus vaccines that incorporate the *env* and *gag* genes of FeLV (Purevax and Eurifel, Merial); and a recombinant subunit vaccine that contains p45, the nonglycosylated form of gp70 (Leucogen, Virbac). The recombinant canarypox vaccine available in Europe is a different product than that licensed for use in the United States. Studies that have used highly sensitive PCR assays have shown that vaccination does not produce sterilizing immunity (that is, complete absence of viral RNA, DNA, antigenemia, and viremia after challenge).[98] In other words, cats develop regressive or even progressive infections, but not abortive infections after challenge.[98] Nevertheless, vaccination with recombinant subunit, canarypox vectored, and whole virus vaccine prevented progressive infection in 87%, 78%, and 44% of cats when compared with controls, respectively. One vaccine protected 83% of cats against antigenemia after challenge as long as 2 years after vaccination.[99]

In summary, no vaccine provides 100% protection against FeLV infection, and even when protection against progressive infection occurs, regressive infections still occur. However, because vaccination protects cats from progressive infection, it is indicated for all at-risk cats, such as those with outdoor exposure or those that reside in households with other FeLV antigen-positive cats. The American Association of Feline Practitioners (AAFP) highly recommends that all FeLV antigen-negative kittens be vaccinated for FeLV, because of the potential that some of these kittens may escape or become outdoor cats, even when the intention of the owner is to keep the kitten indoors.[100] Vaccination is also recommended for cats entering shelters that are likely to be housed with other cats.[79] Two doses are given in

the left pelvic limb as distally as possible, 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, although more information is required on the duration of immunity for FeLV vaccines. The European Advisory Bureau on Cat Diseases (ABCD) suggests a booster every 2 to 3 years for cats older than 3 to 4 years of age, in light of the lower susceptibility of adult cats to infection.[101] Annual boosters are required for recombinant vaccines. Acutely ill cats should not be vaccinated, but it is acceptable to vaccinate cats with chronic diseases, such as chronic kidney disease. Testing for FeLV should be performed before each booster if exposure to FeLV was likely before the booster was required (which should apply for most cats vaccinated for FeLV). Vaccination with FeLV vaccines has been associated with injection-site sarcomas, so only cats that are likely to be exposed should be vaccinated.

Prevention

Prevention of FeLV infection involves indoor housing of cats away from other cats infected with FeLV, testing and removal (or separation) of cats that test antigen-positive from other cats, vaccination, and proper screening of blood donor cats with soluble antigen assays *and* PCR. Routine hand-washing precautions are indicated for hospitalized cats, and precautions should be taken (such as the wearing of gloves) to protect FeLV-infected cats from nosocomial pathogens. Fomites such as food and water bowls and litter boxes should not be shared between FeLV antigen-negative cats and cats with unknown or antigen-positive FeLV status. Neutering can prevent roaming and reduce the likelihood of FeLV infection. When a cat from a multicat household tests antigen-positive, all cats should be tested and retested and positive cats should be separated from other cats if possible. Euthanasia is recommended for sick, FeLV-positive cats that enter shelters.[101] People who adopt cats that have unknown retrovirus status from shelters should be educated about the disease and the need for quarantine and testing after adoption.

Public Health Aspects

Although FeLV can replicate in human cell culture lines, no conclusive evidence of natural infection with FeLV has ever been detected in humans.

CASE EXAMPLE

Signalment: "Hamster" a 6-year-old female spayed domestic shorthair from Fairfield, CA.

History: Hamster was brought to the University of California, Davis, Veterinary Medical Teaching Hospital for the problems of fever, lethargy, anorexia, diarrhea, and vomiting. The diarrhea had been present for 3 days and was greenish, mucoid, and occurred once to twice daily. The owner reported that Hamster had vomited yellow fluid at least three times during this period and was completely inappetent. Her urination habits had not changed. Hamster was taken to a local veterinary clinic on the first day of illness, where a physical examination revealed pyrexia (105.1°F or 40.6°C). She was treated with clavulanic acid–amoxicillin and a single intramuscular injection of enrofloxacin but there was no clinical improvement. Hamster had tested positive for FeLV antigen 1.5 years ago, after which time she had been housed exclusively indoors. She lived with some caged birds and three other FeLV-positive cats. None of the other cats were ill. Hamster played with elastic bands, but there was no known toxin exposure and no recent changes in her environment. Her diet usually consisted of a commercial dry cat food.

Physical Examination:

Body Weight: 6.9 kg

General: Quiet, alert, responsive, hydrated, T = 104.4°F (40.2°C), HR = 220 beats/min, RR = 36 breaths/min, mucous membranes pink, CRT = 1 s. Haircoat unkempt.

Eyes, Ears, Nose, and Throat (with Dilated Fundoscopic Examination): The only abnormality noted was mild gingivitis.

Musculoskeletal: Body condition score 7/9. Normal ambulation was present.

Cardiovascular and Respiratory: No clinically significant abnormalities were detected.

Gastrointestinal and Urogenital: The cat resented palpation of her cranial abdomen. The perianal region was stained with green fecal material.

Lymph Nodes: All lymph nodes were <1 cm in diameter.

Laboratory Findings:

CBC:

HCT 24.6% (30%-50%).
MCV 48.4 fL (42-53 fL), MCHC 32.1 g/dL (30-33.5 g/dL)
Reticulocytes 7800 cells/μL
WBC 11,470 cells/μL (4500-14,000 cells/μL)
Neutrophils 10,438 cells/μL (2000-9000 cells/μL)
Band neutrophils 459 cells/μL
Lymphocytes 344 cells/μL (1000-7000 cells/μL)
Monocytes 229 cells/μL (50-600 cells/μL)
Platelets 122,000 platelets/μL (180,000-500,000 platelets/μL). The neutrophils showed slight toxicity, and there were a few macroplatelets

Serum Chemistry Profile:

Sodium 148 mmol/L (151-158 mmol/L)
Potassium 3.8 mmol/L (3.6-4.9 mmol/L)
Chloride 110 mmol/L (117-126 mmol/L)
Bicarbonate 18 mmol/L (15-21 mmol/L)
Phosphorus 2.9 mg/dL (3.2-6.3 mg/dL)
Calcium 9.5 mg/dL (9.0-10.9 mg/dL)
BUN 15 mg/dL (18-33 mg/dL)
Creatinine 1.2 mg/dL (1.1-2.2 mg/dL)
Glucose 169 mg/dL (63-118 mg/dL)
Total protein 7.0 g/dL (6.6-8.4 g/dL)
Albumin 2.6 g/dL (2.2-4.6 g/dL)
Globulin 4.4 g/dL (2.8-5.4 g/dL)
ALT 72 U/L (27-101 U/L), AST 121 U/L (17-58 U/L)
ALP 12 U/L (14-71 U/L), γ- GGT 0 U/L (0-4 U/L)
Cholesterol 104 mg/dL (89-258 mg/dL)
Total bilirubin 0.2 mg/dL (0-0.2 mg/dL).

Urinalysis (Cystocentesis): SGr 1.020; pH 7.0, 1+ protein, 2+ hemoprotein, 0-1 WBC/HPF, 0-2 RBC/HPF, rare rods, few amorphous crystals.

Imaging Findings:

Plain Abdominal Radiographs: The small bowel was diffusely gas- and fluid-filled with normal intestinal diameter. The colon was relatively empty with a small amount of fluid. No masses were identified. There was renal asymmetry with poor visualization of the right kidney. Abdominal serosal detail appeared normal.

Abdominal Sonography: The right kidney could not be identified. The left kidney appeared normal and measured 4.2 cm in length. A small amount of fluid was present in the colon. The remainder of the abdomen was unremarkable.

Microbiologic and Virologic Testing: Aerobic bacterial urine culture: negative

Point-of-care ELISA serology for FeLV antigen and FIV antibody: positive for FeLV antigen

PCR for *Mycoplasma haemofelis* and *Candidatus* Mycoplasma haemominutum (whole blood): negative

Diagnosis: Progressive FeLV infection with suspected acute pyelonephritis (characterized by fever, gastrointestinal signs, bacteriuria, neutrophilia with a left shift, and mild thrombocytopenia). Right renal agenesis (likely congenital).

Treatment: Hamster was hospitalized and treated with intravenous fluids, enrofloxacin (5 mg/kg, slow IV, q24h) and ampicillin (20 mg/kg, IV, q8h) (note that the parenteral use of enrofloxacin in this cat was off-label and has the potential to cause irreversible blindness). Her temperature normalized within 24 hours, and there was no more vomiting or diarrhea. After 48 hours, the hematocrit was 27.6%, neutrophil count was 5759 cells/μL with no bands or toxicity, and lymphocyte count was 917 cells/μL. She was discharged from the hospital with instructions to continue antibiotic treatment for 1 month. Two weeks after the antibiotics had been discontinued, she was apparently healthy and a physical examination, CBC, kidney panel, urinalysis, and aerobic bacterial urine culture showed no abnormalities. Her hematocrit was 38.9%, white cell count was 4620 cells/μL, and platelet count was 220,000/μL. One year later, she remained clinically healthy and a CBC showed a hematocrit of 38.2%, white cell count of 4500 cells/μL, neutrophil count of 3362 cells/μL, lymphocyte count of 905 cells/μL, and a monocyte count of 45 cells/μL. Despite the mild cytopenias present, Hamster remained alive and well with a normal CBC 4 years after she was initially seen for gastrointestinal signs. She died 2 years after that, 7.5 years after she first tested positive for FeLV infection.

One of the other cats in the household, a 5-year-old, male neutered domestic medium hair cat, was euthanized 1.5 years after Hamster was initially evaluated. He developed severe normocytic, normochromic nonregenerative anemia (HCT 10.5%, with 5200 reticulocytes and 11 nucleated RBC/HPF) with neutropenia (1320 cells/μL) in association with circulating blast cells.

Comments: Even though this cat was initially seen for moderately severe illness in association with progressive FeLV infection, she made a full recovery with treatment and remained alive and well for 6 additional years. The nonregenerative anemia likely resulted from inflammatory disease. The negative urine culture may have resulted from recent treatment with antimicrobial drugs, and renal ultrasound is insensitive for diagnosis of pyelonephritis. The age of this cat, the strain of FeLV involved, and the challenge dose, as well as other environmental and genetic factors, probably all played a role in the course of disease. This case clearly demonstrates that other treatable diseases may be present in FeLV-infected cats and that search for the underlying cause of clinical signs and adequate treatment is always recommended. The second cat in the household likely also had progressive FeLV infection; the development of anemia suggested infection with FeLV-C.

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