Updates in the diagnosis and management of feline leukemia virus (FeLV)

Not all feline leukemia virus (FeLV) infected cats are the same. There are different stages of infection, different outcomes, and different disease manifestations. Some infected cats will go on to live a nearly normal lifespan while others may die within months to a few years. If each FeLV-infected cat is different, how do you evaluate them beyond a positive screening result?

IDEXX Reference Laboratories is pleased to announce the availability of the FeLV Quant RealPCR™ Test. This test, in combination with the FeLV Antigen by ELISA, can help to assess the current stage of infection, inform decisions about introduction to multi-cat households, monitor changes in the stage of infection with illness, and encourage pet owners to maintain regular care for an FeLV-infected cat. With proper preventive health care and good husbandry, many FeLV-infected cats may live for years.

Evolving understanding of FeLV transmission and disease stages

Feline leukemia virus is a well-known retrovirus of cats, yet our understanding of this infection continues to evolve. As a retrovirus, FeLV uses its reverse transcriptase enzyme to create a DNA copy of its RNA viral genome. This proviral DNA copy is then inserted into the genomic DNA of the infected feline cell when it divides. As long as that cell survives or gives rise to new cells, the FeLV proviral DNA persists and leaves behind a blueprint for infectious virus. Studies using polymerase chain reaction (PCR) for detecting proviral DNA copies of FeLV indicate that most cats are unlikely to eliminate this infection.[1,2]

FeLV is a highly contagious virus spread primarily via saliva among cats in casual close contact. Mutual grooming, shared food/water bowls, and aggressive behaviors can be a means of transmission. Depending upon the age, health, and immune status of the cat exposed to the virus, the infection may become progressive, regressive, or be aborted.[3,4]

- An **abortive infection** occurs when the cat's immune system eliminates the virus prior to proviral DNA integration in dividing lymphocytes.
- A cat with a **regressive infection** has controlled the spread of infection prior to a secondary viremia. These cats are at reduced risk of shedding the virus and developing FeLV-related disease.
  - –**Latent infection:** Bone marrow infection present but no/minimal evidence of secondary viremia.
  - –**Focal infection:** Control occurs prior to bone marrow infection, thereby limiting infection to focal lymphoid or other organ systems.
- A cat with a **progressive infection** has undergone infection of the bone marrow and a secondary viremia and is at increased risk of shedding the virus and developing FeLV-related disease.

If the immune response does not eliminate the virus after initial exposure, FeLV spreads to the bone marrow and infects hematopoietic precursor cells.[1] FeLV infection in the hematopoietic and lymphoid tissues can cause either cellular proliferation (resulting in lymphoma or leukemia) or myelosuppression.[1] This can cause immune dysregulation and the increased susceptibility to opportunistic infections and coinfections seen in progressive FeLV infections.

Diagnosis of FeLV infection

The American Association of Feline Practitioners (AAFP) recommends screening all cats for FeLV infection at the time they are acquired, before initial vaccination, after potential exposure to FeLV-infected cats, and as part of a diagnostic workup for any illness. ELISA tests directed against the FeLV p27 protein are available both in-clinic and at the reference laboratory. In-clinic tests for FeLV p27 antigen using whole blood, serum, or plasma are commonly used to screen for FeLV infection in veterinary clinics and animal shelters.[4] Confirmation of positive in-clinic screening results is recommended. Historically, an immunofluorescence assay (IFA) was used to confirm FeLV infection but has been shown to yield a high number of false-negative and false-positive results.[1,3] The limitations of IFA in detecting FeLV have been well-documented.[4–6] The IDEXX FeLV Antigen by ELISA, performed at the reference laboratory (preferably on plasma), is a highly sensitive and specific test that is recommended for confirmation of FeLV infection.[7,8] Real-time PCR (FeLV RealPCR™ Test) detects proviral DNA and, therefore, is useful to confirm the presence of FeLV infections that have progressed to the bone marrow.[1,2] Due to additional transmission risks, any cat used as a blood donor or for breeding should be tested with both the FeLV Antigen by ELISA and an FeLV RealPCR Test for proviral DNA. Ideally these tests should be performed twice at least 3–6 months apart.[4]

Staging of confirmed FeLV infections

Recently, studies of FeLV-infected cats have demonstrated a correlation between outcome of infection and viral RNA and proviral DNA loads.[7,8] A practical approach to follow-up testing is needed along with the understanding that FeLV may be better represented as a disease spectrum that can be a chronic, yet manageable disease rather than a static disease state. Staging FeLV infections reflect the disease state at the time of testing, and the stage can change over time depending upon a cat's health and immune status, similar to other chronic viral infections. Prognosis for cats with progressive infections is variable depending upon current immune status, stress, or concurrent disease. Some progressive cats may remain nonclinical for several years. Similarly, cats with a regressive infection may remain nonclinical or may revert to a progressive infection with immunosuppression, stress, or concurrent disease. Regressively infected cats may mount an effective immune response and eventually become PCR and/or antigen negative. **A single-point-in-time test may not be enough to determine the long-term outcome of a FeLV infection in a cat.**

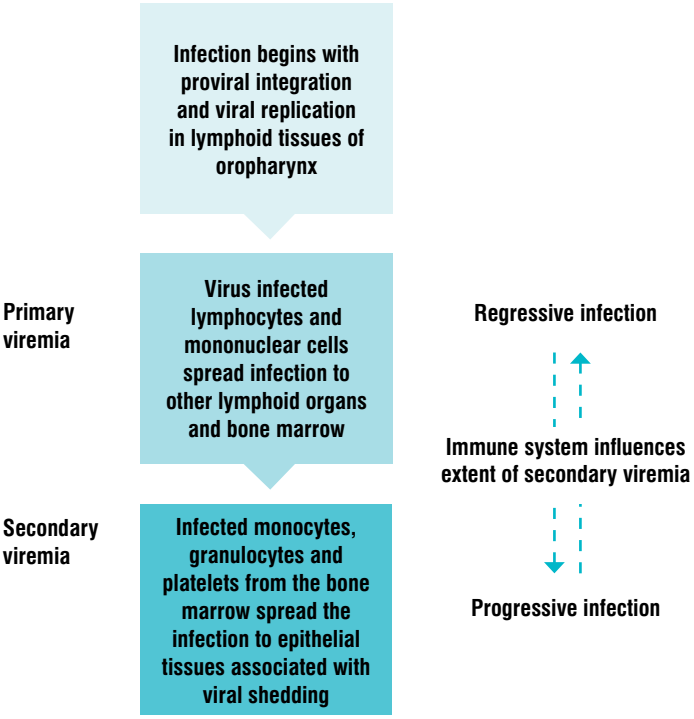


Figure 1. FeLV stages

The presence of FeLV p27 antigen on a screening ELISA, when confirmed by the FeLV Antigen by ELISA, indicates that an FeLV infection is present. It does not indicate the stage of the infection. Using a multimodal testing approach with both FeLV Antigen by ELISA and quantitative real-time PCR for staging potentially infected FeLV patients is recommended.

High viral RNA and proviral DNA loads have been associated with progressive infections, while low loads have been associated with regressive infections.[1,2,9] Likewise, a positive correlation between these molecular measures and levels of p27 antigen have been documented.[1,2,8,9] Using the correlation between proviral DNA loads and concentrations of p27 antigen, we have defined a cut-off for the quantitative FeLV real-time PCR to be 1×10^6 copies/mL. Copies at this level and greater are most likely consistent with a progressive infection (high proviral DNA and high antigen). Copies less than 1×10^6 copies/mL are most likely consistent with a regressive infection (low proviral DNA and low antigen).

Results from the combined diagnostic methodologies of FeLV Antigen by ELISA and quantitative real-time PCR provide more objective information for staging and monitoring of FeLV infections.

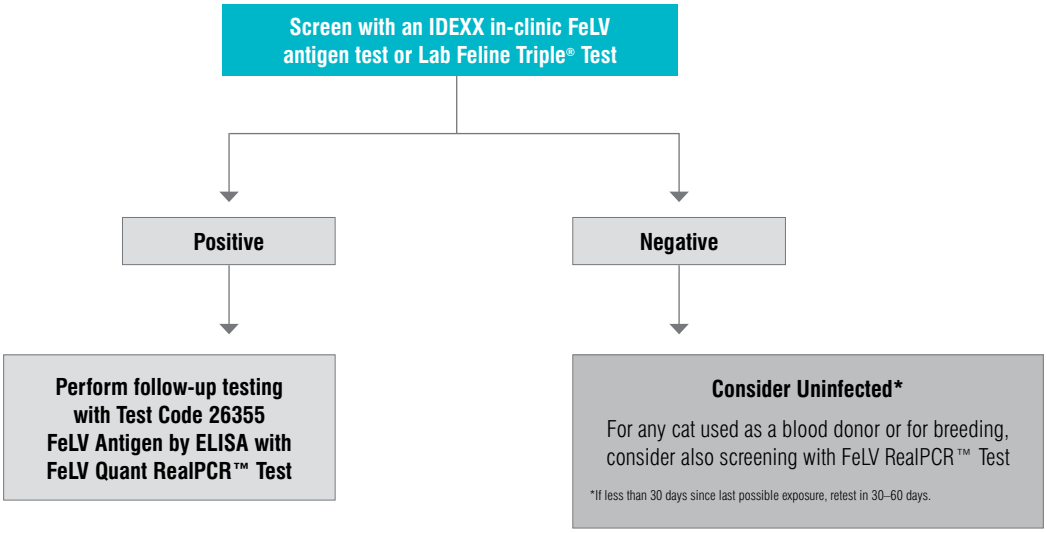
IDEXX introduces the FeLV Quant RealPCR Test

IDEXX Reference Laboratories is pleased to announce the introduction of the FeLV Quant RealPCR™ Test. This quantitative real-time PCR test detects integrated proviral FeLV virus, confirming infection. When positive for FeLV, quantitation of the FeLV proviral DNA (copies/mL) is also provided. When considered along with the clinical history and FeLV Antigen by ELISA results, the quantitative values may assist in staging an infected cat as either regressively infected or at risk for progressive disease (table 1). Evaluating changes in quantitative values over time may also be useful for monitoring a cat for reversion from regressive to progressive disease, which may be a concern in times of stress or concurrent disease. The FeLV Quant RealPCR Test is available in combination with the IDEXX FeLV Antigen by ELISA or as a stand-alone PCR test. The FeLV Antigen by ELISA with FeLV Quant RealPCR Test, test code 26355 (or add-on test code 263551 when ordered with a CBC/chemistry profile), is recommended as a confirmatory and staging test following an in-clinic screening FeLV antigen test. The stand-alone FeLV Quant RealPCR Test, test code 26354, may be used following a positive FeLV Antigen by ELISA or for monitoring progression over time. Quantitation of a prior positive nonquantitative FeLV RealPCR™ Test is also available as an add-on test (test code 263541).

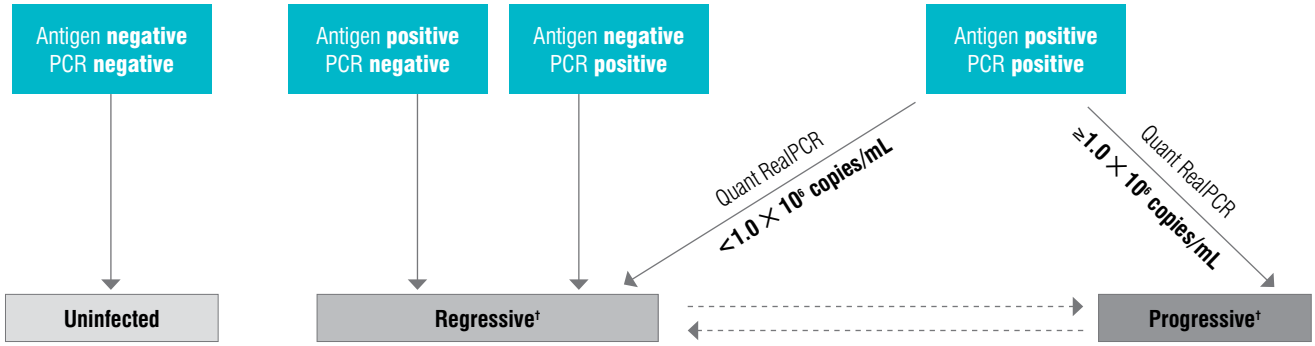
Stage of infection	FeLV Antigen by ELISA	FeLV Quant™ RealPCR
Uninfected (Abortive)	Negative	Negative
Regressive	Positive	Negative
	Negative	Positive ($<1 \times 10^6$ copies/mL)
	Positive	Positive ($<1 \times 10^6$ copies/mL)
Progressive	Positive	Positive ($\geq 1 \times 10^6$ copies/mL)

Table 1. Expected FeLV Antigen by ELISA and FeLV Quant RealPCR Test results for each FeLV disease stage

Diagnostic algorithm for diagnosis and staging of FeLV infection



Interpreting your ELISA and Quant RealPCR results



†If clinical signs develop, retesting with quantitative real-time PCR is recommended to confirm evidence of progression versus comorbidity with another disease.

Management of FeLV-positive cats

Understanding the current stage of infection allows veterinarians to guide proper placement of cats in multi-cat households, provide recommendations on husbandry, and educate clients on appropriate steps to help monitor the health of their cat.

- **Placement**—Avoid placing progressively infected cats with other cats that have a compromised immune system. This includes kittens under 6 months of age and senior or geriatric cats with chronic diseases.
- **Comorbidities**—Cats with FeLV infections may become ill because of conditions unrelated to their FeLV infection. Determining their current stage may help to distinguish comorbidities from progressive FeLV disease.
- **Outcome**—Regressively infected cats are expected to have a longer survival time than cats with progressive infections. However, some cats with progressive infections may live for years.
- **Owner education**—FeLV-infected cats should either be kept indoors or have controlled access to outdoor space. The number of cats in the household should be managed to minimize stress and create a stable environment. Limit the introduction of new cats to help control opportunistic infections particularly for progressively infected cats. Good nutrition is a must, and progressively infected cats should have their weight monitored regularly. Cats with progressive infections should be seen immediately by a veterinarian if any signs of illness appear so that opportunistic infections or other illnesses can be caught early and treated.
- **Antiretroviral therapy and immune modulators**—These are only indicated in exceptional cases because of the lack of proven efficacy and potential for toxicity. More studies are needed to demonstrate clinical benefits, and their effectiveness are still under investigation.[3,4]

Ordering information

Test code	Test name and contents
26355	**FeLV Antigen by ELISA with FeLV Quant RealPCR™ Test** Includes quantification of FeLV viral particles if PCR positive.
263551	**FeLV Antigen by ELISA with FeLV Quant RealPCR™ Test Add-on** Includes quantification of FeLV viral particles if PCR positive.
26354	**FeLV Quant RealPCR™ Test** Includes quantification of FeLV viral particles if PCR positive **Note:** Serology (SNAP® tests or reference laboratory ELISA) is recommended for initial screening for FeLV infections.
263541	**FeLV RealPCR™ Quantification Add-on** This test can be used to request quantification of a previously reported positive (nonquantitative) FeLV RealPCR™ Test.

Specimen requirements: 2 mL EDTA whole blood (LTT); keep refrigerated. If requesting a panel that includes an FeLV Antigen by ELISA, please submit 1 mL plasma (preferred) or serum in addition to the whole blood specimen.

Turnaround time: 1–4 days

Ordering your tests online

Did you know that you can search for diagnostic tests, create requisitions, and review status and results on **vetconnectplus.com**?

Customer support services

IDEXX supports your practice with our customer support, technical support, and medical consulting services teams, including our diagnostic support veterinarians and board-certified veterinary specialists.

1-888-433-9987

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Published October 2019