Retrovirus Educational Toolkit







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American Association of Feline Practitioners

Retrovirus Educational Toolkit



Retrovirus Educational Toolkit

This toolkit was developed from the AAFP Retrovirus Testing and Management Guidelines. Feline leukemia virus (FeLV) and feline immunodeficiency virus (FIV) infections are found in cats worldwide. Both infections are associated with a variety of clinical signs and can impact quality of life and longevity. Key points include:

- 1. The retrovirus status of every cat should be known.
- Cats should be tested as soon as possible after they are acquired, following exposure to an infected cat or a cat of unknown infection status, before vaccination against FeLV or FIV, and whenever clinical illness occurs.
- 3. It may not be possible to determine a cat's infection status based on testing at a single point in time; repeat testing using different methods could be required.
- 4. Although vaccines are available for FeLV in many countries and FIV in some countries, identification of infected cats remains an important factor for preventing new infections.
- 5. Although FeLV and FIV infections can be associated with clinical disease, some infected cats, especially those infected with FIV, can live for many years with good quality of life.
- There is a paucity of data evaluating retroviral and immunomodulatory treatments for infected cats.
- Management of infected cats should focus on effective preventive healthcare strategies, prompt identification and treatment of illness, and limiting the spread of infection.

Table 1 Prevalence of FeLV antigen and FIV antibody by region in samples submitted to a referral laboratory (2008–2016)				
Region (number of cats tested)	FeLV antigen prevalence (%)	FIV antibody prevalence (%)		
North America (2.5 million)	4	5		
Caribbean (6882)	9	13		
Latin America (9984)	13	7		
Northern Europe (95,800)	7	7		
Southern Europe (206,157)	12	12		
Middle East/Africa (4787)	14	14		
Asia-Pacific (81,201)	6	13		

Risk factor	FeLV	FIV
Increasing age	xx	XXX
Male sex	xx	XXX
Sexually intact status	xx	XXX
Outdoor access	xxx	XXX
Close contact with infected cats	xxx	xx
Inter-cat aggression	xx	XXX
Illness (especially oral disease, abscess tract disease)	, respiratory xxx	XXX
Kitten born to an infected gueen	XXX	×

Instructions for Use

This educational toolkit is an implementation tool for veterinary professionals to access and gather information quickly. It is not intended as a complete review of the scientific data for retrovirus testing and management. We recommend that you familiarize yourself with the AAFP Retrovirus Testing and Management Guidelines prior to using this toolkit.

To use the toolkit, click the tabs at the top in the blue navigation bar to access each page and read more information about each area including transmission, outcomes of infection, diagnosis, prevention, management, treatment, frequently asked questions (FAQs), and client resources. Each page also has an associated printable PDF that you can use in your practice. Additionally, a link to a printable version of the entire toolkit, which contains information from each page, is included in the left side bar.

Acknowledgments

The AAFP would like to thank **IDEXX Laboratories** for their educational grant to develop this toolkit, and for their commitment to help the veterinary community improve the lives of cats. We also would like to thank Dr. Kelly St. Denis for chairing the Toolkit development and the AAFP Retrovirus Testing and Management Guidelines panel for all their hard work in developing the information.

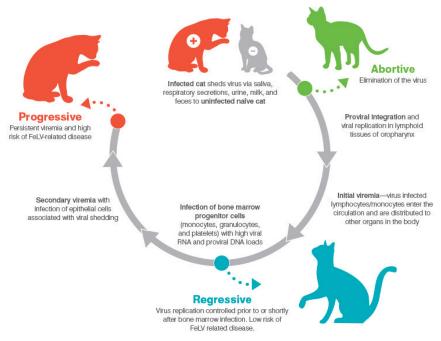


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Transmission

FeLV Transmission Principles

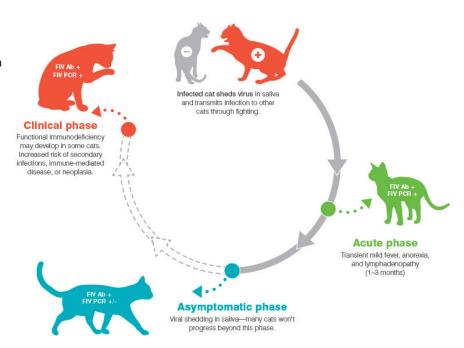
- Infected cats may begin to shed virus within 30 days of exposure
- · Shed in saliva
- Less commonly shed in nasal secretions, milk, urine, or feces
- Transmitted mainly via oral nasal route and less commonly via bite wounds
- Spread horizontally among cats that live together or fight
- Spread vertically and horizontally from infected queens to their kittens
- Kittens more susceptible to becoming progressively infected than adult cats



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FIV Transmission Principles

- Infected cats may begin to shed virus within 14 days of exposure
- · Shed in saliva
- Spread horizontally via bite wounds and FIV-infected white blood cells
- Transmission from queens to kittens is uncommon in natural infection
- Transmission between cohabitating cats is uncommon without fighting
- Sexual transmission is uncommon



Courtesy of IDEXX. Copyright © 2018, IDEXX Laboratories, Inc. All rights reserved. Used with permission. Reference: Hosie MJ, Addie D, Belák S, Boucraut-Baralon C, Egberink H, Frymus T, Gruffydd-Jones T, Hartmann K, Lloret A, Lutz H, Marsilio F, Pennisi MG, Radford AD, Thiry E, Truyen U, Horzinek MC. Feline immunodeficiency. ABCD guidelines on prevention and management. J Feline Med Surg. 2009 Jul;11(7):575-84.





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Outcomes of Infection

FeLV

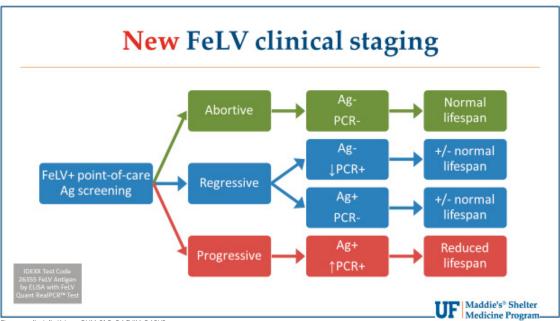


Figure credit: Julie K. Levy, DVM, PhD, DACVIM, DABVP

Abortive Infection

- Characterized by negative test results for culturable virus, antigen, viral RNA and proviral DNA
- · Only indication of FeLV infection is the presence of antibodies
- · Not common after experimental infection but seems to be more common in the field
- FeLV antibodies in the absence of detectable viral RNA, proviral DNA, or anitgen, and without having received FeLV vaccines

Regressive Infection

- Viral shedding does not occur, but the virus does integrate into the cat's genome
- Can transmit infection if used as blood donors
- Low risk of developing FeLV-associated diseases
- · Small risk of reactivation of the virus
- Integration into the DNA can lead to lymphoma or bone marrow suppression

Progressive Infection

- FeLV not contained during the early stage
- Extensive viral replication first in lymphoid tissue, then bone marrow and subsequently in mucosal and glandular epithelial tissues
- Mucosal and glandular infection associated with excretion of infectious virus, mainly in saliva, but also other secretions
- Insufficient FeLV-specific immunity, neutralizing antibodies are not typically detectable
- Shorter survival time and succumb to FeLV-associated diseases within several years



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Outcomes of Infection continued

FIV

FIV Disease Pathogenesis

- Acute phase following exposure: often goes unnoticed
- Immune response: suppression of circulating virus
- Asymptomatic phase: slow, progressive dysfunction of the immune system
- FIV-related disease phase: patient developed FIV related clinical symptoms and disease

FIV Acute Phase

- Transient fever, lymphadenopathy, and lymphopenia
- Signs can be subtle and transient: +/-fever, +/- general malaise, +/- lymphadenopathy
- Often goes unnoticed
- Virus detectable in high concentrations in the blood by culture and PCR
- CD4+ and CD8+T cell numbers decline

FIV Immune Response

- FIV antibodies produced by 60+ days post infection
- Circulating virus suppressed
- CD8+T cells increase above pre-infection levels
- Inversion of CD4:CD8 ratio
- Over time both CD4 and CD8 lymphocytes gradually decrease in numbers

FIV Asymptomatic Phase

- Can last for many years
- Increased risk of chronic and recurrent infections
- Neoplasia is 5x more likely
- Cell-mediated immunity more affected than humoral immunity
- Hyperglobulinemia may occur
- Survival time similar to that of non-FIV infected cats

FIV Clinical Phase

- May never develop FIV-related clinical signs in their lives
- Clinical signs are related to immunodeficiency and/or immunostimulation
- Related conditions include chronic gingivostomatitis, chronic rhinitis, lymphadenopathy, immune-mediated glomerulonephritis, and weight loss
- Neoplasia may occur including (but not limited to): B cell lymphosarcomas, myeloproliferative disease, and squamous cell carcinoma
- Concurrent infections: viral, bacterial, fungal, protozoal, parasitic (e.g. Demodex)



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Diagnosis

When to Test

- As soon as possible after they are acquired
- Following exposure to an infected cat or a cat of unknown infection status
- Prior to vaccination against FeLV or FIV
- Whenever clinical illness occurs, regardless of previous testing status

Both Viruses Together

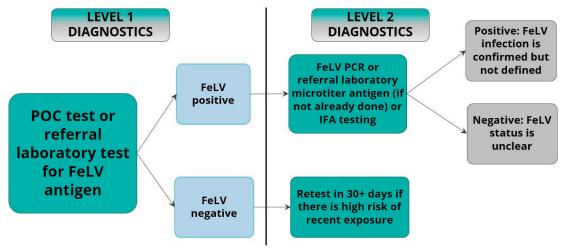
- A single testing protocol is difficult to recommend for all cats.
- Infected cats may not present with signs of disease.
- ALL sick cats should be tested.
- It is not always possible to determine infection status with single test.
- Repeat tests using different methods may be necessary.

FeLV

Testing for FeLV: Interpreting Results

- Results of FeLV testing may be discordant.
- Abortive infection: negative on the POC test.
- Progressive infection: positive on the POC test 30+ days after exposure.
- Regressive infection: negative OR positive on the POC test.
- PCR testing may be positive in both progressively and regressively infected cats.
- Other testing results (microwell, IFA, etc.) may be positive depending on stage and class of infection.

Preventive Healthcare – Retrovirus Management FeLV Testing



Level 1 diagnostics might be sufficient in circumstances where the test results are consistent with the patient's signalment and clinical signs. Level 2 diagnostics can be appropriate to clarify infection status in some patients.



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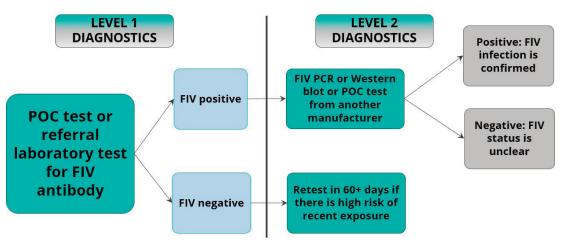
Diagnosis continued

FIV

Testing for FIV: Interpreting Results

- A positive POC for FIV test indicates the presence of FIV antibodies.
- Infected cats will be positive for FIV antibodies 60+ days post-infection.
- If the patient test is negative, the patient should be retested for FIV in 60 days.
- Confirmatory testing is ideal and may include a different manufacturer's POC test, a PCR test, or a Western Blot test.

Preventive Healthcare - Retrovirus Management FIV Testing



Level 1 diagnostics might be sufficient in circumstances where the test results are consistent with the patient's signalment and clinical signs. Level 2 diagnostics can be appropriate to clarify infection status in some patients.

About FIV Vaccinates

- FIV vaccine is no longer available in North America since 2015.
- Vaccinated cats may retain antibodies against FIV for 7+ years post vaccination.
- FIV vaccinates may be positive for FIV antibodies.
- Vaccinated cats may continue antibody positive on some POC tests for 7+ years.
- Cats testing positive still need to be assessed for previous vaccination.
- Some POC tests are able to differentiate between antibodies of truly infected versus vaccinated cats. See AAFP Retrovirus Guidelines "https://catvets.com/retroviruses"

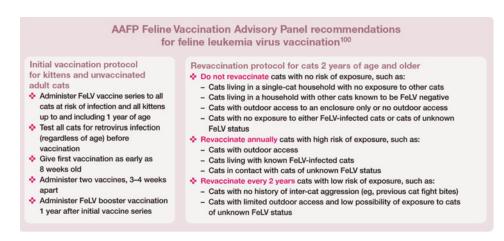


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Prevention

Vaccination

- Vaccination against FeLV does not diminish the importance of testing to identify and isolate cats that are progressively infected.
- It cannot be concluded that FeLV vaccination protects against all outcomes of FeLV infection. Nevertheless, several current vaccines are still of great clinical importance because they appear to be efficacious at preventing progressive infection and, thus, curtailing FeLV-associated diseases.
- Vaccines against FIV are no longer available in North America since 2015, but vaccinated cats may still live in this region.



Limiting Transmission in the Veterinary Practice

- Hospitalized retrovirus-infected cats can be kept in the general hospital wards, but should not be allowed to have direct contact with other hospitalized cats.
- Retrovirus infected cats should not be housed in isolation with other sick cats as their immunocompromised status could increase their risk of nosocomial infection.
- Cats used for blood or tissue donation should be screened and confirmed to be negative for FeLV antigen by ELISA and FeLV provirus by PCR, as well as for FIV antibodies.
- There is little risk of retrovirus transmission among cats by indirect exposure when simple precautions and routine cleaning procedures are followed.
- Reusable dental and surgical instruments should be cleaned according to appropriate sterility principles.

Considerations for Multi-Cat Environments

- All cats entering shelters should be considered potentially retrovirus infected, regardless of the environment from which they originated.
- Retrovirus infected cats should not be housed in isolation with other sick cats as their immunocompromised status could increase their risk of nosocomial infection.
- It is broadly recommended that all cats be tested for retroviral infection, but an exception exists for free-roaming stray and feral community cats in trap-neuter-return (TNR) programs.
- The presence of infection can vary within individual litters, community cat colonies, and households. It is not appropriate to conserve costs by testing one cat as a proxy for others or by pooling samples from a group of cats.

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Management

Management of infected cats should focus on effective preventive healthcare strategies, prompt identification and treatment of illness, and limiting the spread of infection.

Healthcare

- Infected cats can live for many years with a high quality of life.
- Follow consistent preventive healthcare strategies.
- Promptly identify and treat illness.
- Prevent, identify, and limit the spread of infectious disease.
- Euthanasia of positive cats is not recommended.

Management of Retrovirus Infected Cats: Multi-Cat Households

- FIV: transmission limited where cohabitating cats do not fight or reproduce
- FeLV: transmission via shared food and water bowls, allogrooming and alloplay
- Reduce stress by resource and environmental needs management.
- House infected cats indoors or with access to enclosed outdoor structures only.
- Longevity appears to be best in cats living in low-density household.



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Treatment

Antiretroviral Agents

- Long-lasting benefits have not been demonstrated.
- Long-term use is costly with mild to severe toxic side effects.
- Zidovudine (AZT) may be beneficial in reducing retroviral load, particularly in cats with stomatitis or neurologic signs.
- Consider these in cases where clinical illness is thought to be attributable to retroviral infection.
- AZT: 5-10 mg/kg PO q12h
- A higher dose should be used in caution with FeLV patients due to risk of non-regenerative anemia.

Immunomodulatory Antiviral Drugs

- Well-designed trials are lacking or have failed to show benefit.
- Parenteral feline interferon omega may provide some clinical improvement.
- No controlled studies using oral feline interferons exist to date.



Retrovirus Educational Toolkit

Veterinary Professionals FAQs

Confirming retrovirus status can be challenging in some situations. Understanding what to do with test results is confounded by multiple factors, including patient status, lifestyle, recent exposures, and test sensitivities and specificities. The FAQ includes commonly asked questions and dilemmas as they are often encountered by clinicians.

Can I vaccinate for FeLV before testing? Does the FeLV vaccine interfere with test results?

Vaccination against FeLV does not interfere with testing for viral antigen using available point-of-care ELISA tests. However, there is no therapeutic value in administering FeLV vaccination to infected cats, and the vaccine would be unnecessary. Therefore, it is strongly recommended to test a patient prior to vaccination.

Do I need to test vaccinated cats for FeLV?

The FeLV status of cats, including those that have been vaccinated, should be known. Regardless of vaccination status, if a patient falls in the at-risk category, or has presented in ill health, the patient should be tested. Although commercially available FeLV vaccinations have been shown to have good efficacy, the protective effect is not 100%. As such, vaccinated cats may still be at a small risk of infection.

How soon after exposure can I test for FeLV?

The point-of-care FeLV ELISA test assesses for the presence of FeLV p27 viral antigen. Once exposed to the virus, patients who become infected will most likely become viral antigen positive by 30 days post-infection. There are some exceptions to this, and any questionable situations should be re-evaluated over longer time periods or with additional laboratory testing (e.g. PCR).

How soon after exposure can I test for FIV?

The point-of-care FIV ELISA test assesses for the presence of antibodies against FIV. Most patients who become infected will develop antibodies as early as 60 days post-infection. Any questionable situations should be re-evaluated over longer time periods or with additional laboratory testing (e.g. PCR).

Can I pool blood or saliva samples from a group of cats that are housed together to test for FeLV?

Pooling samples from multiple patients is not recommended. Technically, saliva testing using point-of-care ELISA tests is less sensitive than testing blood or serum. Saliva samples are a sensitive sample source when testing for FeLV by RT-PCR. If pooled samples are used for point-of-care antigen testing, false negatives might occur, and infected cats in a group will be missed. If pooled samples are used for ELISA or RT-PCR testing, a positive sample does not identify the infected cat, thus necessitating retesting of all cats in the group individually. The ideal rule of thumb for FeLV testing is 'one cat, one test.'

Can I pool blood or saliva samples from a group of cats that are housed together to test for FIV?

Pooling samples from multiple patients is not recommended for FIV testing. The point-of-care FIV ELISA test assesses for the presence of antibodies against FIV. Most patients who become infected will develop antibodies as early as 60 days post-infection. If pooled samples are used for point-of-care antibody testing, false negatives might occur, and infected cats in a group will be missed. If pooled samples are used for testing, a positive sample does not identify the infected cat, thus necessitating retesting of all cats in the group individually. The ideal rule of thumb for FIV testing is 'one cat, one test.'



Retrovirus Educational Toolkit

Veterinary Professionals FAQs continued

Why do indoor cats need testing for retroviruses?

Indoor cats are not exempt from a history of possible exposure from their queen or previous cat-cat interactions prior to acquirement. They are not exempt from the potential for exposure to retroviruses if living with other cats. While testing in most cases has good sensitivity, there are periods during a cat's infection when testing may be negative, and thus an infection missed. The retrovirus status of all at-risk and all sick cats should be known.

Why isn't one test enough to rule out FeLV?

There are three factors to consider when testing for FeLV post-exposure. The first is the time to become positive for viral p27 antigen, as detected on point-of-care ELISA testing. This can take 30 days or longer, such that a recent exposure may result in a false negative test, missing infection. The second and third factors to consider are the testing type and patient infection class. As cats that have been infected with FeLV may become regressively or progressively infected, some patients may not be positive for FeLV viral p27 antigen but may still be infected. Thus, other types of testing such as PCR testing for FeLV proviral DNA will further elucidate the infection status of the patient.

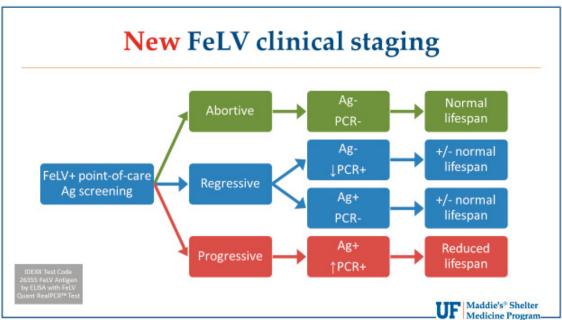


Figure credit: Julie K. Levy, DVM, PhD, DACVIM, DABVP

Why isn't one test enough to rule out FIV?

The point-of-care FIV ELISA test assesses for the presence of antibodies against FIV. Most patients who become infected will develop antibodies as early as 60 days post-infection. When testing for FIV, recent exposure will not be evident by antibody testing, leading to false negatives. Further testing is necessary to elaborate on infection risks and status.

Should I test new stomatitis cases for FIV/FeLV even if previous tests were negative?

Yes. Even with previous testing, recent exposures or previous false negatives may exclude proper identification of retrovirus infected cats. Inflammatory oral disease is associated with an increased risk of retrovirus infection in naturally infected cats.



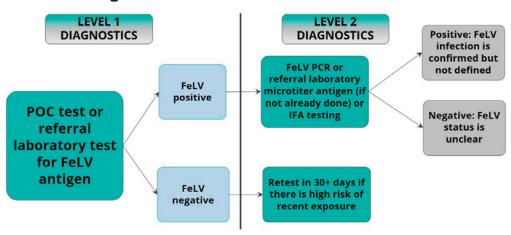
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Veterinary Professionals FAQs continued

I have a patient with discordant FeLV test results, now what?

A single testing protocol is difficult to recommend for all cats. Depending on which tests were run on your patient and when, further testing, the timing of testing, and what tests to run will vary. In the case where Level 2 Diagnostics have been performed, and the patient's status still remains unclear, additional Level 2 Diagnostic tests or repeat testing over time may help. During the time that the patient's status remains unclear, the patient should be considered infectious.

Preventive Healthcare - Retrovirus Management **FeLV Testing**

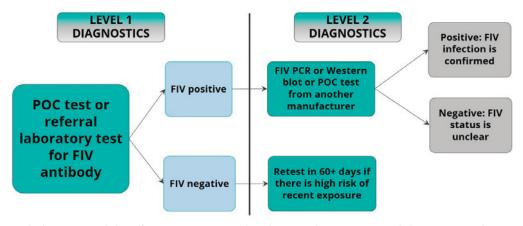


Level 1 diagnostics might be sufficient in circumstances where the test results are consistent with the patient's signalment and clinical signs. Level 2 diagnostics can be appropriate to clarify infection status in some patients.

I have a patient with discordant FIV test results, now what?

A single testing protocol is difficult to recommend for all cats. Depending on which tests were run on your patient and when, further testing, the timing of testing, and what tests to run will vary. In cases where Level 2 diagnostics have been performed and the patient's status remains unclear, additional Level 2 Diagnostic tests or repeat testing over time may help. During the time that the patient's status remains unclear, the patient should be considered infectious.

Preventive Healthcare - Retrovirus Management **FIV Testing**



Level 1 diagnostics might be sufficient in circumstances where the test results are consistent with the patient's signalment and clinical signs. Level 2 diagnostics can be appropriate to clarify infection status in some patients.

13



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Veterinary Professionals FAQs continued

What does the quantitative real-time PCR test for FeLV tell us?

Cats that are infected with FeLV may become regressively or progressively infected. The type of infection that occurs is dependent on the patient's immune status at the time of testing. This impacts the levels of active provirus (antigen) and/or proviral DNA. High levels of proviral DNA and antigen-positive tests are most commonly associated with progressive infections, while low levels of proviral DNA with antigen-positive or antigen-negative tests are most commonly associated with regressive infections. The quantitative real-time PCR for proviral DNA can measure the number of copies of proviral DNA, which will clarify whether the patient has a regressive or progressive infection. Regressively infected patients will have fewer than 1 million copies of proviral DNA per mL, while those patients that are progressively infected will have more than 1 million copies of proviral DNA per mL.

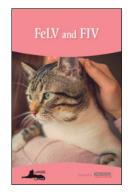
Stage of Infection	FeLV Antigen by ELISA	FeLV Quant™ RealPCR
Uninfected (Abortive)	Negative	Negative
Regressive	Positive	Negative
	Negative	Positive (<1 x 10 ⁶ copies/mL)
	Positive	Positive (<1 x 10 ⁶ copies/mL)
Progressive	Positive	Positive (≥1 x 10 ⁶ copies/mL)

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

Courtesy of IDEXX. Copyright © 2019, IDEXX Laboratories, Inc. All rights reserved. Used with permission. Reference: Beall et al. Evaluation of a quantitative enzyme-linked immunosorbent assay for feline leukemia virus p27 antigen and comparison to proviral DNA loads by realtime polymerase chain reaction. Comp Immunol Microbiol Infect Dis. doi:10.1016/j.cimid.2019.101348

I work in a shelter. I'd like more information on when to test for FeLV.

- www.maddiesfund.org/felv-what-you-need-to-know-for-shelter-decision-making.htm
- $\hbox{ } www. idexx. com/files/updates-diagnosis-management-felv. pdf$



What recommendations do you have for communicating with clients who insist on trying unvalidated treatments found on the internet?

The AAFP and affiliates offer many client-based resources to help owners of retrovirus-infected cats sift through and look past online unvalidated treatments.

- AAFP Client Brochure (download/print): https://catvets.com/guidelines/client-brochures
- Catfriendly.com Webpage: FeLV (https://catfriendly.com/felv)
- Catfriendly.com Webpage: FIV (https://catfriendly.com/fiv)

FeLV and FIV





You are an important member of your cat's healthcare team.
You are instrumental in helping with the success of
treatments and improved healthcare for your cat.



FeLV and FIV





Feline immunodeficiency virus (FIV) and feline leukemia virus (FeLV) can cause many types of illness as well as death in infected cats. These viruses do not infect humans or other animals.

FELINE IMMUNODEFICIENCY VIRUS

Feline immunodeficiency virus is more commonly found in male cats that are not neutered and in cats that fight with other cats. It is found less often in kittens and neutered adult cats. The virus is spread through the saliva and is usually passed to other cats by bite wounds. In North America, about 3 to 5% of tested cats are found to be infected with FIV. In Latin America, up to 25% of tested cats are found to be infected.

FELINE LEUKEMIA VIRUS

Feline leukemia virus infection is more commonly spread among cats that live together. The virus can also be spread from mother to kittens, and among cats that fight. It is mainly spread through saliva when cats groom each other, and when food and water bowls are shared. In North America, about 4% of tested cats are found to be infected with FeLV. In Latin America, up to 42% of tested cats are found to be infected.

SIGNS OF INFECTION

A cat newly infected with FIV may show mild illness, with fever or a drop in appetite. These changes do not last more than a day or two before the cat is back to normal. After the early days of



infection, the cat may not be sick for months or years. These cats can still infect other cats. Later in life, the cat's infection may become active again, and the cat will show signs of sickness. When the virus is active, it can weaken the immune system, leaving the cat at risk for different infections. The virus can also cause cancers in infected cats. As it can take many years for the virus to become active again, many cats infected with FIV can live long and healthy lives.

When first exposed to FeLV, a cat might not show any signs of illness. Some cats that are exposed to FeLV can clear the virus completely from their body. Other cats are able to control the infection, preventing illness. In some cats, the infection will become active in their body and they will develop problems such as low red blood cells (anemia) or cancer. These problems can be severe and even fatal.

DIAGNOSIS

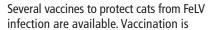
Your cat can be tested for FIV or FeLV infection. There are many times in your cat's life when your veterinarian will recommend testing. Any time your cat is sick, your cat should be tested for FIV and FeLV infection. If your cat goes outdoors, or fights with other cats, your veterinarian may recommend regular testing. If your cat is new to the family or you adopt another cat, testing is

advised before introducing the new cat to other cats in the household.

If your cat tests positive for FIV or FeLV, further tests may be reommended by your veterinarian. Even if your cat's first test result is negative, your veterinarian may still advise repeat testing in the future.

PREVENTION

There are no vaccines available in the United States or Canada that can protect cats from FIV infection. FIV vaccines are only available in a few countries in the world.



recommended for all kittens, again one year later, and regularly for cats that have access outdoors. Adult indoor-only cats living alone or with uninfected cats may not need to be vaccinated after the first 2 years. Your veterinarian will help assess your cat's vaccination needs.



There are no treatments for either virus that will get rid of the infection. Infected cats should visit their veterinarian for regular check-ups as this will help the cat live as long as possible with good health. Your veterinarian will advise on blood testing, vaccinations, and parasite prevention. High-quality commercial diets are recommended; raw food diets may cause serious infections.

Infected pet cats should live indoors so they don't infect other cats. Other cats in the same household should be tested for FeLV and FIV. In some cases, cats that live together may need to be separated to avoid the spread of infection. Your veterinarian

will help you determine what the best plan is for you and your cat(s).

Stress may play a role in triggering the virus to become active again. If there are other cats in the home, or a shortage of food bowls, water bowls, and litter

boxes, it may cause stress because most cats do not like to share. Keeping litter boxes, and food and water bowls clean is also important. More information about what your cat needs to feel safe and secure indoors can be found at www.catfriendly.com/healthyenvironment.

Your veterinarian is your partner in caring for your infected cat. With regular healthcare checkups and a low-stress life, cats infected with FIV or FeLV may live happy and healthy lives for many years.



