STOP THE SPREAD
Feline leukemia virus vaccines prevent viral shedding and progressive infection and decrease the opportunity for at-risk cats to become infected or seriously ill.

VACCINATION STATION

Feline Leukemia Virus

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Feline leukemia virus (FeLV) is a gammaretrovirus and one of the most common causes of infectious disease in cats worldwide. Various studies estimate the prevalence of FeLV to be between 2% and 3.5% in the United States and Canada. The development and use of accurate diagnostic tests and vaccinations has led to a decrease in the prevalence of FeLV since its discovery more than 50 years ago; however, the seroprevalence has not changed in the past decade.[1,2]

FeLV infection can spread rapidly in the feline population if vigilant preventive and early diagnostic protocols are not maintained. The course of FeLV infection is a delicate balance between the cat's immune system and the virus, and possible outcomes include progressive, regressive, abortive, or focal infection. Following recommended guidelines for diagnosing and preventing FeLV will help prevent a resurgence of this disease.

FELINE LEUKEMIA VIRUS

Exposure and Transmission

FeLV is an enveloped virus with a single-stranded RNA genome that uses reverse transcriptase to convert the viral RNA genome into a DNA form. The DNA form is then integrated into the host's cells by the enzyme integrase. This integrated DNA is known as the "provirus."[3]

Primary transmission of FeLV is through salivary shedding, although it can also be found in urine, feces, and milk. FeLV is not stable in the environment, so transmission is generally through communal contact between cats who are socially friendly, groom each other, and share resources, or aggressive interactions between cats that result in bite wounds. In addition to horizontal transmission, FeLV can be transmitted vertically from an infected queen to her kittens. The virus may also be spread via blood transfusions.

Male cats, as well as cats that live outdoors or are intact, are at a higher risk for exposure. FeLV infection is much more prevalent in sick cats, and if healthy cats are eliminated from survey results, the prevalence of FeLV increases to 38%.[3]

Outcomes

FeLV replicates in the tonsils and local lymph nodes of exposed cats and then spreads through the body via infected lymphocytes and monocytes. This is the primary viremia stage. Eventually the virus infects the

bone marrow and is integrated into neutrophils and platelets, which then circulate in the bloodstream. This is the secondary viremia stage.[1,4]

While cats of all ages can become infected with FeLV, kittens are much more likely to develop a progressive infection. Cats with progressive FeLV infections are persistently viremic, constantly shed millions of viral particles in their saliva, and are an infection risk to other cats. They should be kept separately from FeLV-naïve cats, even if the infected cat appears otherwise healthy. Cats with progressive FeLV infections are most likely to develop FeLV-associated disease, such as lymphoma, bone marrow disorders, immune-mediated diseases, or susceptibility to secondary infections. These cats frequently die within 3 years of diagnosis.[3,5]

Older cats usually develop a regressive or abortive infection, and if they develop a progressive infection, they appear to have milder signs.[3] Cats diagnosed with a regressive infection have recovered from the primary viremia and generally avoid infection of the bone marrow. Antigenemia typically clears within 3 months, though the FeLV provirus still circulates in peripheral blood. These cats usually do not develop FeLV-associated disease, although the potential exists for the virus to be reactivated if the cat becomes immunocompromised, and viral shedding could recur.[4] The potential for reactivation decreases over time after exposure, although it is never completely eliminated.[3]

Cats with an abortive FeLV infection can be harder to diagnose. The virus is contained before provirus integration takes place, and the cats never become viremic. These cats develop FeLV-neutralizing antibodies and a strong immunity to FeLV. They will not develop FeLV-associated disease, and they have the same life expectancy as cats that have never been exposed to FeLV.[3]

Focal or atypical FeLV infections are very rare and can be challenging to diagnose because they may cause discordant test results. A queen with a focal infection in the mammary glands could pass the infection to her kittens during nursing. The neonates may then develop fading kitten syndrome and die soon after birth.[5]

Diagnostic Tests and Interpretation

A variety of tests are available to diagnose FeLV, and it is important to understand what the results signify to determine a prognosis and management plan for an infected cat. The American Association of Feline Practitioners (AAFP) recommends screening all cats for FeLV at any of the points listed in **BOX 1**.

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Most point-of-care (POC) tests are based on enzyme-linked immunosorbent assay or rapid immunomigration methodologies. If a cat tests positive on a POC test, additional testing is recommended, particularly if the cat is considered at low risk for infection. Repeated testing may be needed to determine if a cat has progressive or regressive infection.[1] A cat with a regressive infection will generally no longer test positive on a POC test within 12 weeks of exposure to FeLV.

An FeLV provirus DNA polymerase chain reaction (PCR) test can be done to confirm a positive POC test or to help differentiate between progressive and regressive infection. Cats with regressive, abortive, or focal infections usually have high levels of anti-FeLV antibodies.[3] Neither maternal antibodies nor FeLV vaccines interfere with POC screening tests, although a

BOX 1 When to Screen Cats for Feline Leukemia Virus (FeLV)[6]

- At time of acquisition
- Before initial vaccination against FeLV
- After exposure to an infected cat
- When clinically ill
- Before introducing a new cat to an environment
- To diagnose potential FeLV shedders in a multicat environment

blood sample collected immediately after FeLV vaccine administration may contain FeLV antigen from the vaccine itself; therefore, blood samples should be collected before vaccination.[5]

VACCINES

Vaccinating cats against FeLV contributed to the decrease in disease prevalence. Unvaccinated cats with bite wounds are 7.5 times more likely to be infected with FeLV than vaccinated cats with bite wounds, suggesting that FeLV vaccination provides some level of protection.[1] It is most likely, based on current studies, that FeLV vaccines prevent antigenemia and progressive infection, although they do not prevent proviral integration. In general, vaccinated cats appear to be protected from FeLV-associated disease and the related shortened lifespan.[5]

Types and Efficacy

Several types of FeLV vaccines are available (**BOX 2**), but their relative efficacy remains controversial. Inactivated vaccines contain a "killed" version of FeLV, so the virus cannot replicate in the host. They contain adjuvants that help to promote an adequate immune response. Adjuvants have been implicated in adverse reactions, though the evidence is mixed.[6] Recombinant vaccines encode a part of an immunogenic FeLV antigen that undergoes limited replication in the host and stimulates a protective immune response. They may trigger a more rapid onset of immunity, and they do not contain adjuvant. Conflicting evidence in the literature regarding the efficacy and safety of inactivated versus recombinant vaccines makes it difficult to recommend one type over the other.[6]

Published vaccine efficacy trials are funded by manufacturers, and challenge testing protocols vary widely among studies.[5] One study divided a group of cats into control and vaccinated groups and then used methylprednisolone to suppress the immune system before challenging with FeLV. Another study challenged the control and vaccinated groups with intraperitoneal injections of FeLV.[7,8] Neither study approximates real-world exposure. Other studies determined efficacy by measuring for the presence or absence of antigenemia, level of proviral loads, or presence of anti-FeLV antibodies.[9,10] No study has definitively shown that one type of vaccine is superior. Independent studies with standardized challenge and testing protocols are needed to determine if one type of vaccine is truly more efficacious than another.

Duration of immunity (DOI) is also difficult to know. Several studies have shown that the DOI is at least 12 months, and in many cases, it is 24 to 36 months.[1,5]

All cats should be tested before vaccination. There is no benefit to vaccinating cats that have FeLV, and unnecessary vaccinations carry risk. If a vaccinated cat's status is unknown before immunization and the cat later develops a progressive infection, the vaccine's efficacy could be inappropriately questioned and vaccine failure may be incorrectly assumed.[1]

Administration Schedule

Feline vaccines are divided into core (recommended for every cat) and non-core. FeLV vaccines are considered core for kittens and non-core for adults; therefore, each cat's health status, lifestyle, environment, and risk factors should be evaluated annually to determine if the cat should be vaccinated against FeLV.

In kittens and at-risk adult cats, the AAFP recommends that the FeLV vaccine initially be administered as 2 doses given 3 to 4 weeks apart, starting at 8 weeks of age, then as a single dose in 1 year. After that, cats at high risk should be revaccinated annually (unless product licensure indicates a longer interval). Cats at low risk may be vaccinated every 2 to 3 years, and cats at minimal risk do not need to be revaccinated.[6]

Adverse Events

Post-vaccination adverse events are rare in cats. The most common adverse events are lethargy, fever, decreased appetite, and inflammation at the vaccination site. Anaphylaxis is very rare and may manifest as vomiting, diarrhea, respiratory distress, pruritus, facial

BOX 2 Types of Available Feline Leukemia Virus Vaccines

- Adjuvanted inactivated whole virus vaccine
- Recombinant subunit vaccine
- Genetically engineered subunit recombinant canarypox vector vaccine

swelling, or collapse. If a cat has an anaphylactic reaction to the FeLV vaccine, discontinuation of administration may be advised. If revaccination is warranted, then the cat should be premedicated with an antihistamine and glucocorticoid 20 to 30 minutes before vaccine administration.[6]

The most serious adverse event is the development of a feline injection site sarcoma (FISS) at the vaccination site. Because of this, the AAFP recommends that FeLV vaccines be administered distal to the left stifle. The distal tail is an alternative location. If a lump develops at the vaccine site, the AAFP recommends following the 3-2-1 rule. This rule states that biopsy of any mass should be performed if the mass is present 3 months after vaccination, is larger than 2 cm in diameter, or is increasing in size 1 month after vaccination.[6] This will facilitate clean margins if amputation is required as part of the treatment plan for the FISS.[6,11]

CONCLUSION

FeLV remains a serious disease, and veterinarians should continue to follow existing guidelines for vaccination and prevention to lower its prevalence. FeLV vaccines prevent viral shedding and progressive infection and decrease the opportunity for at-risk cats to become infected or seriously ill. Adverse events following vaccination are rare. Every cat's individual risk should be evaluated annually to determine need for vaccination. More studies are required to determine if certain vaccine types are safer or more efficacious than others. TVP

References

1. Little S, Levy J, Hartmann K, et al. 2020 AAFP feline retrovirus testing and management guidelines. *J Feline Med Surg*. 2020;22(1):5-30.
2. Burling AN, Levy JK, Scott HM, et al. Seroprevalences of feline leukemia virus and feline immunodeficiency virus infection in cats in the United States and Canada and risk factors for seropositivity. *JAVMA*. 2017;251(2):187-194.
3. Hartmann K, Hofmann-Lehmann R. What's new in feline leukemia virus infection. *Vet Clin North Am Small Anim Pract*. 2020;50(5):1013-1036.
4. Hofmann-Lehmann R, Hartmann K. Feline leukaemia virus infection: a practical approach to diagnosis. *J Feline Med Surg*. 2020;22(9):831-846.
5. Hartmann K. Feline leukemia virus infection In: Sykes JE, Greene CE, eds. *Infectious Diseases of the Dog and Cat*. 4th ed. Philadelphia, PA: Elsevier Saunders; 2011:108-136.
6. Stone AE, Brummet GO, Carozza EM, et al. 2020 AAHA/AAFP feline vaccination guidelines. *J Feline Med Surg*. 2020;22(9):813-830.
7. Pederson N. Immunogenicity and efficacy of a commercial feline leukemia virus vaccine. *J Vet Intern Med*. 1993;7(1):34-39.
8. Hofmann-Lehmann R, Tandon R, Boretti FS, et al. Reassessment of feline leukaemia virus (FeLV) vaccines with novel sensitive molecular assays. *Vaccine*. 2006;24(8):1087-1094.
9. Westman M, Norris J, Malik R, et al. Anti-SU antibody responses in client-owned cats following vaccination against feline leukaemia virus with two inactivated whole-virus vaccines (Fel-O-Vax® Lv-K and Fel-O-Vax® 5). *Viruses*. 2021;13(2):240.
10. Grosenbaugh DA, Frances-Duvert V, Abedi S, et al. Efficacy of a nonadjuvanted recombinant FeLV vaccine and two inactivated FeLV vaccines when subject to consistent virulent FeLV challenge conditions. *Biologicals*. 2017;49:76-80.
11. Saba CF. Vaccine-associated feline sarcoma: current perspectives. *Vet Med (Auckl)*. 2017;8:13-20.

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