The Cat with FIV:
The Vaccine and Diagnostic Testing

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In July 2002, the first licensed vaccine against feline immunodeficiency virus\textsuperscript{1} (FIV) was introduced in the United States. Although few articles have addressed FIV in the clinical literature over the past few years, most clinicians would agree that the consequences of FIV infection in the individual cat are significant and justify the need for an FIV vaccine. The disease referred to as “FIV” is caused by one of a number of retroviruses known to infect domestic cats worldwide. Characterized by a long latent period, infected cats gradually experience deterioration of immune function associated with declining numbers of T helper lymphocytes (CD4+). [REF: Levy, 2000] The consequences are manifest as a wide spectrum of vague clinical features, none of which are diagnostically distinctive.

The principle serological test for FIV infection used throughout the world is the determination of FIV antibody in serum. The enzyme-linked immunosorbent assay (ELISA) and immunoblot (Western Blot) methods used to detect FIV antibody have become the mainstay for diagnosing infected cats and conducting surveys among populations of cats at risk for infection. Epidemiological studies using these tests have provided good evidence for horizontal transmission of FIV among cats and have identified adult male cats living outdoors as those at greatest risk of infection. Since the virus can be recovered from the saliva of infected cats, bite wounds sustained during fighting are believed to be a principle means of virus transmission. On the other hand, casual contact among infected and non-infected cats is an unlikely means of transmission. Although it appears possible that FIV can be sexually transmitted, as the virus has been recovered from the semen of infected cats, this mode of transmission appears to be uncommon in nature. Likewise,

\textsuperscript{1} Fel-O-Vax FIV, Fort Dodge Animal Health
transmission from infected queen to fetus (vertical transmission) is possible, but rare. On the other hand, it is more likely that infected queens will transfer FIV antibody, not virus, via colostrum to nursing kittens. Since colostral FIV antibody may persist in kittens for several months, it is customary to disregard a “positive” FIV antibody test result in healthy kittens under 6 months of age.

Yet, the introduction and use of the killed FIV vaccine will substantially change the approach clinicians use to assess potentially infected cats. Of particular importance is the fact vaccination is known to be associated with development of FIV antibodies that interfere with all FIV tests on the market today. The consequences are not insignificant. Until an alternative, reliable, and accessible laboratory test for FIV infection is made available, veterinarians have lost the ability to distinguish between a vaccinated cat and an infected cat.

**The Vaccine**

The current FIV vaccine is a killed, whole virus vaccine containing two virus subtypes, or clades, of FIV called clade A (Petaluma strain) and clade D (Shizuoka strain). The manufacturer recommends a vaccination schedule that entails administration of 3 doses initially, 2-3 weeks apart, followed by annual revaccination. Each 1 ml dose is administered subcutaneously to cats 8 weeks of age or older. The vaccine is adjuvanted.

**Vaccine Efficacy and Safety**

Based on experimental studies submitted to the USDA, the FIV vaccine has a good efficacy and safety profile. Efficacy (challenge) studies showed that 4 of 24 (16%) vaccinated cats were infected following challenge while 17 of 19 (90%) unvaccinated (control) cats were infected following challenge. This represents an 82% preventable fraction. (NOTE: FIV Subtypes A and B are the most common in the United States. Experimental FIV vaccines have not demonstrated cross-protection between subtypes). In clinical safety studies, over 2000 doses were administered to 689 cats (299 were less than 12 weeks of age). Reactions such as pain at the injection site, lethargy, and fever, were reported in 1.1%. There were no fatalities reported.
...but what about the test?

FIV antibody testing has become the hallmark of serologic tests used to identify cats infected with FIV. In fact, FIV testing has become so widely used in practice that an advisory panel organized by the American Association of Feline Practitioners and Academy of Feline Medicine recently published revised guidelines on feline retrovirus testing and implications for managing cats determined to be positive for FIV antibody. [REF: Guidelines]. In summary, the advisory panel recommended that all cats be tested for both FeLV and FIV infection. With respect to FIV antibody testing, emphasis is placed on the importance of testing all sick cats regardless of negative results of previous FIV tests.

Regarding test selection, the advisory panel has published that ELISA and other immunochromatographic tests available in clinical practice, are the preferred screening tests to be used in the initial assessment of any sick cat. It is further recommended that all positive screening test results be confirmed by the Western blot test.

Here’s the problem...all cats vaccinated with the killed FIV vaccine are expected to develop FIV antibodies following administration of the first dose. Antibodies are known to persist for at least 1 year. Vaccine-induced antibodies interfere with all antibody tests commercially available in the US and Europe:

- SNAP® FeLV Antigen/FIV Antibody Combo (IDEXX Laboratories)
- PetCHEK® FIV (IDEXX Laboratories)
- All Western Blot tests

In addition, kittens of vaccinated queens are likely to have a positive test result due to passively acquired vaccine-induced antibody. Negative test results for antibody may still be interpreted as negative for exposure and infection.

With the introduction of the FIV vaccine, and loss of the ability to identify FIV-infected cats in clinical practice, a substantial effort is underway to identify an alternative diagnostic test that is reasonably priced and accurate.
Alternative Testing

*Virus isolation* (VI) has been suggested as possible means of distinguishing vaccinated cats from infected cats. However, virus stability during transport, availability, and cost are such significant limiting factors that VI is not a reasonable consideration for veterinarians in clinical practice. Isolating FIV from infected cats is well suited to experimental laboratories where the sample collection and virus isolation methods can be highly controlled.

On the other hand, *polymerase chain reaction* (PCR)-based tests for identification of RNA and proviral DNA\(^2\) have received considerable attention, subsequent to the release of the killed FIV vaccine, as “the” alternative test for detecting infected cats...whether or not they’ve received prior vaccination. While it is possible to identify FIV, in both vaccinated and unvaccinated cats, using PCR technology, the ability to provide widespread diagnostic services to practitioners through commercial laboratories has not yet been accomplished. In the long run, this may prove to be quite problematic given the nature of PCR technology.

PCR technology must *not* be viewed as simply another “new and improved” means of detecting FIV antibody. In fact, it doesn’t detect antibody at all...but that’s just the beginning. The “family” of feline immunodeficiency viruses, is varied and their expression, once they’ve infected a cat, is quite complex. That, combined with the inherent sensitivities of PCR-based test methods make turning a PCR test into *the* replacement test for FIV antibody, and doing so at the levels of reliability and consistency we have enjoyed, a major technological challenge.

Although most clinicians will not be especially interested in all of the technical and methodological issues pertaining to PCR testing, it is important to understand that PCR, discovered just within the last 20 years, is an exceptionally accurate method for rapidly manufacturing unlimited copies of

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\(^2\) *Proviral DNA:* feline retroviruses are RNA viruses. The use of the term "DNA" in reference to FIV may be confusing. However, during retrovirus infection, through production of the unique enzyme reverse transcriptase, FIV is able to duplicate its own single-stranded viral RNA making
DNA. In effect, PCR has made it possible to identify unique sequences of DNA even when the sample size is miniscule. Obviously, such technology would be of considerable value in diagnosing infection, particularly viral infections, where the virus quantity can be quite small and the genetic features of the virus quite distinct. Recently, the ability of a novel quantitative polymerase chain reaction (qPCR) method to detect proviral DNA in FIV-infected cats was described in 1999. While using the Taqman® PCR to detect FIV provirus is a significant fact, incorporating the technology into routine use in the clinical setting will take time.

Even if PCR testing for FIV does become commercially available in the near future, the clinician must understand and appreciate the fact that the incredible sensitivity of PCR method has direct and important implications on test results. For example, in-hospital PCR testing for FIV, or anything else, is simply not feasible today. An outside laboratory must analyze all specimens. In addition to contending with the risk of sample transport and contamination (with extraneous nucleic acid), it will become critical (at least it should be) for all laboratories offering PCR testing for FIV to use standardized, validated reagents and testing protocols. The process of validating test methods will require documenting the accuracy of PCR against various FIV field strains (variants of virus subtypes) seen in the United States. At this writing, the means of standardizing PCR tests for veterinary medicine simply doesn’t exist. Then, with all that said, it’s a matter of price.

**Conclusion**

Over the next year, it is anticipated that commercial PCR testing for FIV will become increasingly more available to veterinarians in clinical practice. However, until significant refinements to conventional PCR-based tests can be assured, clinicians must appreciate the implications that FIV vaccination will have on our ability to survey the at-risk population of cats for FIV infection.

For the future, what may be even more important that developing PCR testing for commercial FIV testing purposes is the development and

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*Note: A double-stranded provirus. This is referred to as "proviral DNA." Specific proviral DNA sequences are the target of the PCR test for FIV.*
introduction of a recombinant FIV vaccine. Recombinant vaccine technology has already been introduced into veterinary medicine and promises to be an important, perhaps critical, contribution to vaccine safety and efficacy in the future. A recombinant FIV vaccine offers the prospect of inducing a protective, sustained cell-mediated immune response, but without antibody. Distinguishing infected cats from vaccinated would again be possible.
Suggested Reading


