PREVALENCE AND RISK FACTORS
Worldwide prevalence of feline immunodeficiency virus (FIV) varies from 1 to 31% in healthy cats and is generally higher in sick cats, but the exact prevalence depends on the study design used. In a US-based study, Levy et al. surveyed 345 veterinary clinics (FIV-positives - 3.1% of 9970 cats) and 145 animal shelters (FIV-positives - 1.7% of 8068 cats; Levy, 2006). Prevalence figures for Canada and Japan are as follows: Canada – 4.3% of 11,144 cats tested in 2007 (Little, 2011); Japan – 23.2% of 1770 outdoor cats (Nakamura, 2010). The major risk factors for FIV infection are as follows: Age – adult; Gender – male (MN 4.3%, MI 3.3%) and intact status; Lifestyle – free-roaming/outdoor access; and Health status – Current illness (6.1%; Levy, 2006). Of shelter cats studied by Levy et al. (2006), 1.4% were owner relinquished, 1.6% were stray and 3.9% were feral.

TRANSMISSION
By far the most common mode of transmission is via bite wounds from infected cats. Also documented but much less common is vertical transmission from an infected mother to kittens during pregnancy, birth or lactation, although this seems to occur more commonly with laboratory viral strains rather than field strains. FIV transmission can also be achieved via blood donation from an infected cat. Mucosal transmission via oral, rectal or vaginal mucosa has only been demonstrated under laboratory conditions and mucosal infection requires up to 10,000x more virus than other routes (Dandekar 1992). Fomite transmission is not an important route for FIV as FIV quickly loses infectivity outside the host and is susceptible to all commonly used disinfectants. There can be viral strain differences in the relative ease of transmission via various routes. In one recently published study of a large ‘mixed’ household of FIV-positive and FIV-negative cohabiting cats, FIV transmission did not occur over years of exposure and vertical transmission of FIV was not demonstrated in 19 kittens born to 5 FIV-positive queens (Litster, 2014).

PATHOGENESIS
Acute infection
Initial infection is often clinically silent, although there can be mild fever and/or lymphadenopathy. During this phase there are large amounts of virus circulating and CD4 (helper) and CD8 (cytotoxic) T-lymphocytes decline. The host response to initial infection, results in production of anti-FIV antibodies, reducing the circulating viral load. There is also increased CD8 T-lymphocyte count, so that CD4:CD8 ratio is reduced.

Long asymptomatic period
After initial infection, there is an extended asymptomatic period, during which progressive dysfunction of immune system can occur. CD4 T-lymphocyte count generally declines, resulting in reduced CD4:CD8 ratio, but does not always cause clinical signs. Non-regenerative anemia, lymphopenia and neutropenia can also occur. Because cell-mediated immunity is reduced, antibody-mediated immunity can be stimulated, with an accompanying increased serum globulin concentration. FIV-positive cats respond adequately to vaccination, unless advanced disease is present.

AIDS-related complex phase and terminal phase
These stages do not always/usually occur and many FIV-infected cats can live long and healthy lives, especially if regular veterinary attention is provided. Clinical signs, if they occur, might take years to develop and clinical signs are generally seen in older cats. These can include chronic inflammation of the oral cavity and skin; secondary infections (viral, bacterial, fungal, protozoal); neoplasia, especially lymphoma; signs of neurological or renal disease; and slow, progressive weight loss.

DIAGNOSIS
Diagnosis – Antibody tests
Most cats produce antibodies within 60 days of exposure, but it may take much longer (12 months) if viral exposure is low. Point-of-care testing is available to be performed on serum, plasma or whole blood. It is highly sensitive and specific and detects antibodies to FIV core proteins. The Western blot test is a laboratory-based test which has previously been used to confirm an ELISA-positive result, but might not be as sensitive or specific as the original SNAP test (Levy, 2004). Positive FIV antibody test results can sometimes occur in uninfected cats as antibody tests cannot distinguish between antibodies that are produced in response to a natural infection and those that are produced in
response to FIV vaccination. Vaccine-induced antibodies can persist for at least 1 year after vaccination and perhaps over 9 years (Crawford and Levy, 2007). Positive antibody test results can also be produced in uninfected kittens (<6 months old) when their mother is FIV-positive (infected or vaccinated).

**Diagnosis – Antigen tests**

These tests detect FIV viral protein. A commercially available FIV PCR test can potentially distinguish cats that are vaccinated but FIV-uninfected from FIV-infected cats. This test relies on adequate amounts of certain amino acid sequences from field strains of FIV being ‘recognized’ by the test. Strain information is also provided. Virus isolation testing can be performed at reference laboratories and is a ‘reference standard’ method that takes at least 28 days to perform.

**Diagnosis – Which cats to test**

The following cats should be tested for FIV - sick cats; cats and kittens that will be group housed; cats and kittens at adoption, and a minimum of 60 days later if negative; cats with recent exposure to FIV-positive cat or cat of unknown FIV status, especially if there is a bite wound, and a minimum of 60 days later if negative. Cats living with FIV-infected cats should be tested annually. High-risk cats, such as outdoor, free-roaming cats, cats with bite wounds should also be considered for FIV testing. Testing should always be performed before considering vaccination against FIV and in blood donor cats before blood collection.

**TREATMENTS FOR FIV**

There have been a few published reports of treatments targeting the immune system or the virus in FIV-infected cats. In one study, an 8-week course of recombinant feline interferon in 7 naturally infected FIV-positive cats (3 healthy, 4 unhealthy) and 5 untreated FIV-positive cats were enrolled as controls (Doménech, 2011). In the FIV-infected group, the healthy/mildly unhealthy cats remained stable (4 cats) and the unhealthy cats had improved clinical scores (3 cats). Recombinant feline interferon is not available in the USA. Another study used oral human interferon as a low-dose oral treatment (Pedretti, 2006) in 30 naturally-infected unhealthy FIV-positive cats (24 treated, 6 placebo) over a 14 month treatment period. Investigators documented clinical improvement in the first 2 months and treated cats had significantly longer survival than placebo-treated cats, but there was no change in CD4:CD8 ratio or other hematological parameters. Hartmann, et al., (1992) used zidovudine (AZT) to treat FIV-infected cats in a placebo-controlled study with a 3-week treatment period. Stomatitis and CD4:CD8 improved, but AZT can cause dose-dependent anemia which often resolves in the first 3 weeks of treatment and is not suitable for cats with signs of bone marrow suppression. Additionally, AZT-resistant strains of FIV could potentially arise. Nine-(2-phosphonylmethoxyethyl) adenine (PMEA) was also used by the same group and was associated with clinical improvement in a placebo-controlled study conducted over a 3-week treatment period. PMEA caused more severe anemia than AZT-treated cats.

**VACCINATION AGAINST FIV**

FIV vaccination is classified as a non-core vaccine by the AAFP Vaccine Guidelines (AAFP, 2013), only to be administered to cats in specific risk categories, such as outdoor cats that fight and cats living with FIV-positive cats in unstable relationships. It should be remembered that FIV antibody tests cannot distinguish between vaccinated and infected cats, so FIV vaccination should be performed in conjunction with microchipping so that cats are properly identified. The currently available FIV vaccine is an inactivated (killed) vaccine against subtypes A and D, which also cross-protects against subtype B. Published challenge studies have shown 20-100% ‘preventable fraction’ (proportion protected by vaccination in excess of proportion that is naturally resistant; Yamamoto et. al., 2007). The AAFP Vaccine Guidelines do not recommend FIV vaccination for shelter use and it is widely agreed that resources are better used elsewhere, such as spay/neuter/rabies vaccination programs. FIV vaccination requires 3 doses to be effective and protection is strain-dependent (Yamamoto et. al., 2007). Additionally, reduced aggression in spayed/neutered cats makes FIV transmission less likely. Free-roaming cats are more likely to be presented as strays at veterinary hospitals and shelters where it might be assumed that they are FIV-infected which could result in a negative outcome for the FIV-positive uninfected cat.

**FACTORS ASSOCIATED WITH DISEASE PROGRESSION**

Clinical staging for FIV is not well characterized or widely adopted. CD4 T-lymphocyte count and CD4:CD8 decline in the terminal stages of disease, accompanied by decreased IL-2 and increased TNF-α. During the course of infection, errors also occur during viral replication, resulting in ‘evolution’ of the virus over time. During this process, ‘natural selection’ of viral variants that resist the host immune response and lead to progression of disease can
potentially occur. One study evaluated 33 naturally infected cats that were divided into high and low viral load groups at enrollment (Goto, 2002). The survival of the high viral load group was significantly reduced compared to the low viral load group over the next 4 years and viral loads increased just prior to death.

PROGNOSIS

There have been a number of retrospective studies of cats naturally infected with FIV. One study described a closed household with endemic FIV, FeLV and feline coronavirus observed over 10 years (Addie, 2000). Nine of 26 cats were initially infected with FIV; 6 additional cats became infected with FIV by the end of the 10-year study period. FIV infection did not adversely affect life expectancy in this household. In a retrospective Canadian study (Ravi, 2010), 39 FIV-positive cats were compared with 22 FIV-negative cats over approximately 8 years. The survival time of FIV-positive cats after diagnosis was not different from FIV-negative cats.

References
Addie D Vet Rec 2000;146:419.

Additional reading