FELINE LEUKAEMIA VIRUS

Aetiology Epidemiology Diagnosis Prevention and Control Potential Impacts of Disease Agent Beyond Clinical Illness References

AETIOLOGY

Classification of the causative agent

Feline leukaemia virus (FeLV) is an exogenous gammaretrovirus (enveloped, single-stranded RNA) enzootic to domestic cats. The course of disease is somewhat variable pending the infectious strain of FeLV (FeLV-A, -B, or -C) and what endogenous retroviruses are present in the host's genome. It is the recombination of these retroviruses within the host that influence pathogenicity. The surface glycoprotein and promoter region sequence of the infecting FeLV strain are the two most significant pathogenic determinants.

Resistance to physical and chemical action

Inactivated using standard heat-sterilisation protocols, e.g., autoclaving
Not determined
Inactivated by most commercial detergents and disinfectants
Unstable in the environment

EPIDEMIOLOGY

Hosts

- Domestic cats (*Felis catus*)
- Infections of wild free-ranging felids are rare and are often associated with interactions with feral domestic cats. Susceptible species include:
 - Pallas' cats (Otocolobus manul)
 - Puma subspecies, namely the Florida Panther (*Puma concolor coryi*)
 - European wildcats (*Felis silvestris*)
 - Iberian lynx (*Lynx pardinus*)
 - Far-eastern leopards (*Panthera pardus orientalis*)
 - Far-eastern wildcats (*Prionailurus bengalensis euptilurus*)
 - Sand cats (*Felis margarita*)
- It is believed ocelots (*Leopardus pardalis*), oncillas (*L. tigrinus*), and guignas (*L. guigna*) can be infected but resist development of clinical disease
- There is insufficient data to suggest wild free-ranging bobcats (*Lynx rufus*), jaguarundis (*Puma yagouaroundi*), lions (*Panthera leo*) and cheetahs (*Acinonyx jubatus*) are infected with FeLV however, captive animals of these species have been infected and developed clinical disease

Transmission

- The virus targets monocytes and lymphocytes within oral or pharyngeal lymphoid tissues which then migrate and transport the virus to peripheral tissues
- Viral particles are shed from bodily fluids such as saliva when biting or grooming

• Neonates can become infected by ingesting milk from infected mothers

Sources

• Other infected felids; free-roaming individuals, adults, and males are at a higher risk of infection due to behavioural components of transmission

Occurrence

FeLV is found in domestic cats worldwide. Many countries have documented significant declines in disease incidence for domestic cats due to effective vaccination and testing protocols, but epidemiologic data for free-ranging wild felids is lacking. Clinical latency and lifelong infection are significant complicating factors in efforts to control the virus.

Prevalence in wild free-ranging felids is not fully understood and appears to be related to the degree of interaction with free-ranging domestic cats; there have been documented cases in wild felids in North America, South America, Africa, Europe, and Asia. It is believed FeLV was a significant contributor to the population decline of the endangered Iberian lynx in the early 2000s. FeLV has also been documented as a contributing cause of death in multiple Florida panthers, which has impacted management practises to assist this endangered species.

For more recent, detailed information on the occurrence of this disease worldwide, see the OIE World Animal Health Information System - Wild (WAHIS-Wild) Interface [http://www.oie.int/wahis_2/public/wahidwild.php/Index].

DIAGNOSIS

Clinical diagnosis

Although infection with FeLV is lifelong, some individuals will be "regressively" infected, and the individual's immune response is intermittently able to suppress virus replication. During these periods, the animal is unable to shed and transmit virus. Animals with regressive infections do not typically die of complications secondary to FeLV.

Animals that are consistently viral antigen positive are "progressively" infected, and therefore have marked viral replication in lymphoid tissues, bone marrow, and epithelial tissues including mucosa. Virus is shed from bodily fluids, namely saliva. Complications secondary to FeLV infection are common and often deadly. Antigenemia is detectable in blood at approximately 1 month post-exposure, but the time between infection and clinical disease presentation is highly variable.

Rarely, an exposed individual remains uninfected.

Lesions

The known pathogenesis of FeLV stems from its disease course in domestic cats; this information is translated to wild felids and used as a foundation for studying and treating the disease in other felid species. There are four main presentations of FeLV infection known:

Feline lymphosarcoma

- Typically T-cell in origin
- Firm, homogenous pale tissue that is often multicentric, thymic, or located in the eyes/CNS
- There are 4 forms based upon the location of the primary tumour
 - <u>Multicentric</u> tumours originate from many lymphoid and non-lymphoid tissues
 - <u>Thymic</u> originate from the thymus; most often seen in neonates
 - <u>Alimentary</u> originate from gastrointestinal lymphoid tissues and/or mesenteric lymph nodes; most often seen in older individuals
 - <u>Unclassified</u> all tumours originate in non-lymphoid tissue (skin, eyes, CNS); uncommon

Feline myeloproliferative diseases and anaemia

- Transformation of one or more bone marrow cell types
- There are 4 forms recognised based on the lineage targeted
 - Erythremic myelosis erythroid progenitors
 - Granulocytic leukaemia granulocytic myeloid progenitor, often neutrophil lineage
 - Erythroleukaemia granulocytic myeloid and erythroid progenitors
 - <u>Myelofibrosis</u> malignant proliferation of fibroblasts and cancellous bone; causes medullary osteosclerosis and myelofibrosis
- Clinical findings may include abundant neoplastic cells in bone marrow, a nonregenerative anaemia, and/or immunosuppression
- Transformed erythropoietic cells may induce other cytopenias

Immunopathologic disease associated with FeLV infection

- Prolonged, high levels of viral antigen in the blood can bind antibody and form antigen/antibody complexes that become trapped in glomerular capillaries, inducing glomerulonephritis
- Antibody-dependant cytotoxicity against viral antigens expressed on lymphocyte surfaces may lead to lymphocyte depletion, increasing the animal's susceptibility to inflammatory and infectious diseases

Feline fibrosarcoma

- Fibrosarcoma may or may not be virus-associated
 - If FeLV associated, it is typically seen in younger individuals and is very proliferative with frequent metastases
- This form, referred to as feline sarcoma virus, is replication defective and cannot be transmitted

Differential diagnoses

- Feline immunodeficiency virus (FIV)
- Feline infectious peritonitis (FIP)
- Feline panleukopenia virus
- Hemoparasite infection (e.g, Mycoplasma haemofelis)
- Toxoplasmosis
- Cataracts, glaucoma, retinal detachment
- Glomerulonephritis
- Non-viral lymphosarcoma
- Non-viral fibrosarcoma
- Multiple myeloma, myelophthisis

• Other causes of immunosuppression

Laboratory diagnosis

Although infection is lifelong, some infected animals may be intermittently negative for viral antigen and virus isolation in blood. In these cases, confirming the presence of "provirus" in blood leukocytes via PCR may be necessary.

Samples

For isolation of agent

- Lymphoid tissue
- Salivary gland
- Intestinal tract

Serological tests

- Whole blood
- Saliva
- Bone marrow

Procedures

Identification of the agent

- Virus isolation is possible but not often performed outside of a research setting.
- PCR is sensitive and is typically regarded as a confirmatory test.
- IFA may be used, but is prone to false positives.

Serological tests

- Point-of-care ELISA screening kits for FeLV's viral capsid protein gp27
 - Can detect gp37 in blood 1 month post-exposure, but the test may need to be repeated to ensure antigenemia was not missed.
- May get discortant test results pending variability in response to infection, time since exposure, etc.; in these cases, retesting is indicated.

PREVENTION AND CONTROL

Sanitary prophylaxis

- Detergents and disinfectants are very effective decontaminants.
- Do not intermix positive/negative cats in captive facilities.

Medical prophylaxis

• Vaccination may not be protective against infection, but may lessen severity and progression of disease

- Inactivated, subunit, and recombinant vaccines (+/- adjuvant) are available for domestic cats and are effective for at least 1 year following administration.
 - It is unclear whether current FeLV vaccines which utilise the gp27 subunit are effective in wild free-ranging felids. However, gp70 subunit vaccines designed for domestic cats are successful in increasing antibody titres in cheetahs, tigers, and servals.
- Do not vaccinate already infected cats.
- Identification and removal of infected cats in at-risk populations
- Do not allow neonates in captive facilities to nurse from infected mothers.
- Avoid sharing of communal food/water in captive facilities.

POTENTIAL IMPACTS OF DISEASE AGENT BEYOND CLINICAL ILLNESS

Risks to public health

- FeLV is not believed to be a health risk to humans.
- FeLV is a potential threat to biodiversity and the health of wild free-ranging felid populations.

Risks to agriculture

• There are currently no identified risks to the agricultural industry.

REFERENCES AND OTHER INFORMATION

 American Association of Feline Practitioners. (2008). Feline Retrovirus Management Guidelines. Retrieved from

https://www.catvets.com/public/PDFs/PracticeGuidelines/RetrovirusGLS-Summary.pdf

- Briggs, M. B. and Ott, R. L. (1986). Feline leukemia virus infection in a captive cheetah and the clinical and antibody response of 6 captive cheetahs to vaccination with a subunit feline leukemia vaccine. *Journal of the American Veterinary Medical Association, 189*(9), 1197–1199.
- Brown, M. A., Cunningham, M. W., Roca, A. L., Troyer, J. L., Johnson, W. E., and O'Brien, S. J. (2008). Genetic characterization of feline leukemia virus from Florida Panthers. *Emerging Infectious Disease*, *14*(2), 252-259.
- Citino S. B. (1988). Use of a subunit feline leukemia vaccine in exotic cats. *Journal of the American Veterinary Medical Association, 192*(7), 957–959.
- Duarte, A., Fernandes, M., Santos, N., and Tavares, L. (2012). Virological survey in free-ranging wildcats (*Felis silvestris*) and feral domestic cats in Portugal. *Journal of Veterinary Microbiology*, 158, 400-404.
- Fenner, F. J. (2011). Feline Leukemia and Sarcoma Viruses. In N. J. MacLachlan & E. J. Dubovi (Eds.), *Fenner's Veterinary Virology* (4th ed., pp. 259-262). Elsevier.
- Filoni, C., Helfer-Hungerbuehler, A. K., Catão-Dias, J. L., Marques, M. C., Torres, L. N., Reinacher, M., and Hofmann-Lehmann, R. (2017). Putative progressive and abortive feline leukemia virus infection outcomes in captive jaguarundis (*Puma yagouaroundi*). *Virology Journal*, *14*(1), 226.
- Guimaraes, A., Brandão, P., De Moraes, W., Cubas, Z., Santos, L., Villarreal, L., et al. (2009). Survey of Feline Leukemia Virus and Feline Coronaviruses in Captive Neotropical Wild Felids from Southern Brazil. *Journal of Zoo and Wildlife Medicine, 40*(2), 360-364.
- Helfer-Hungerbuehler, A. K., Widmer, S., Kessler, Y., Riond, B., Boretti, F. S., Grest, P., Lutz, H., and Hofmann-Lehmann, R. (2015). Long-term follow up of feline leukemia virus infection and characterization of viral RNA loads using molecular methods in tissues of cats with different infection outcomes. *Virus Research*, *197*, 137-150.

- Hofmann-Lehmann, R., Fehr, D., Grob, M., Elgizoli, M., Packer, C., Martenson, J. S., O'Brien, S. J., and Lutz, H. (1996). Prevalence of antibodies to feline parvovirus, calicivirus, herpesvirus, coronavirus, and immunodeficiency virus and of feline leukemia virus antigen and the interrelationship of these viral infections in free-ranging lions in east Africa. *Clinical and Diagnostic Laboratory Immunology*, *3*(5), 554-562.
- Ostrowski, S., Van Vuuren, M., Lenain, D. M., and Durand, A. (2003). A Serologic Survey of Wild Felids from Central West Saudi Arabia. *Journal of Wildlife Diseases*, *39*(3), 696-701.
- Naidenko, S. V., Pavlova, E. V., and Kirilyuk, V. E. (2014). Detection of seasonal weight loss and a serologic survey of potential pathogens in wild Pallas' cats (*Felis [otocolobus] manul*) of the Daurian Steppe, Russia. *Journal of Wildlife Diseases*, 50(2), 188-194.
- Naidenko, S. V., Hernandez-Blanco, J. A., Pavlova, E. V., Erofeeva, M. N., Sorokin, P. A., Litvinov, M. N., Kotlyar, A. K., Sulikhan, N. S., and Rozhnov, V. V. (2018). Primary study of seroprevalence to virus pathogens in wild felids of South Primorie, Russia. *Journal of Canadian Zoology, 96*, 839-846.
- Leutenegger, C. M., Hofmann-Lehmann, R., Riols, C., Liberek, M., Worel, G., et al. (1999). Viral infections in free-living populations of the European wildcat. *Journal of Wildlife Diseases, 35*(4), 678-686.
- Marker, L., Munson, L., Basson, P. A., and Quackenbush, S. (2003). Multicentric T-cell lymphoma associated with feline leukemia virus infection in a captive Namibian cheetah (*Acinonyx jubatus*). *Journal of Wildlife Diseases, 39*(3), 690-695.
- Meli, L. M., Cattori, V., Martinez, F., Lopez, G., Vargas, A., Palomares, F., Lopez-Bao, J. V., Hofmann-Lehmann, R., and Lutz, H. (2010). Feline leukemia virus infection: a threat for the survival of the critically endangered Iberian lynx (*Lynx pardinus*). *Veterinary Immunology and Immunopathology*, 134(1-2), 61-7.
- Mora, M., Napolitano, C., Ortega, R., Poulin, E., and Pizarro-Lucero, J., (2015). Feline immunodeficiency virus and feline leukemia virus infection in free-ranging guignas (*Leopardus guinga*) and sympatric domestic cats in human perturbed landscapes on Chiloé Island, Chile. *Journal of Wildlife Diseases*, *51*(1), 199-208.
- Munson, L., Marker, L., Dubovi, E., Spencer, J. A., Evermann, J. F., and O'Brien, S. J. (2004). Serosurvey of viral infections in free-ranging Namibian cheetahs (*Acinonyx jubatus*). Journal of Wildlife Diseases, 40(1), 23-31.
- Osofsky, S., Hirsch, K., Zuckerman, E., and Hardy, W. (1996). Feline Lentivirus and Feline Oncovirus Status of Free-Ranging Lions (*Panthera leo*), Leopards (*Panthera pardus*), and Cheetahs (*Acinonyx jubatus*) in Botswana: A Regional Perspective. *Journal of Zoo and Wildlife Medicine*, 27(4), 453-467.
- Pinches, M. D. G., Helps, C. R., Gruffydd-Jones, T. J., Egan, K., Jarrett, O., and Tasker, S. (2005). Diagnosis of feline leukaemia virus infection by semi-quantitative real-time polymerase chain reaction. *Journal of Feline Medicine and Surgery*, *9*(1), 8-13.
- Ramanathan, A., Malik, P. K., and Prasad, G. (2007). Seroepizootiological Survey for Selected Viral Infections in Captive Asiatic Lions (*Panthera leo persica*) from Western India. *Journal of Zoo and Wildlife Medicine*, *38*(3), 400-408.
- Riley, S. P., Foley, J., and Chomel, B., (2004). Exposure to feline and canine pathogens in bobcats and gray foxes in urban and rural zones of a national park in California. *Journal of Wildlife Diseases, 40*(1), 11-22.
- Sleeman, J. M., Keane, J. M., Johnson, J. S., Brown, R. J., and Vande Woude, S. V. (2001) Feline Leukemia Virus in a Captive Bobcat. *Journal of Wildlife Diseases, 37*(1), 194-200.
- Thalqitzer, S., Wachter, B., Robert, N., Wibbelt, G., Mueller, T., Lonzer, J., Meli, M. L., Bay, G., Hofer, H., and Lutz, H. (2010). Seroprevalences to viral pathogens in free-ranging and captive cheetahs (*Acinonyx jubatus*) on Namibian farmland. *Clinical and Vaccine Immunology*, *17*(2), 232-238.

- The International Society of Feline Medicine and The American Association of Feline Practitioners. (2013). Disease information fact sheet: Feline leukemia virus. *Journal of Feline Medicine and Surgery*, *15*, 785-808.
- Westman, M. E., Malik, R., and Norris, J. M. (2019). Diagnosing feline immunodeficiency virus (FIV) and feline leukemia virus (FeLV) infection: an update for clinicians. *Australian Veterinary Journal*, 97(3), 47-55.



The OIE will periodically update the OIE Technical Disease Cards. Please send relevant new references and proposed modifications to the OIE Science Department (<u>scientific.dept@oie.int</u>). Last updated 2019. Written by Marie Bucko and Samantha Gieger with assistance from the USGS National Wildlife Health Center.