

Leucemia e Inmunodeficiencia felina: Claves Diagnósticas

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Virus de la Leucemia felina (FeLV)



Es un gammaretrovirus responsable de la aparición de enfermedades no neoplásicas como anemia no regenerativa, inmunosupresión y neoplásicas como linfomas, leucemia y trastornos mieloproliferativos. La prevalencia es muy variable dependiendo de la zona o núcleo de población estudiado (albergues, gatos de ciudad...)

Patogénesis:

- 1º Adsorción vírica a la superficie de la célula diana.
- 2º Fusión de la envuelta vírica con la pared celular y liberación de la nucleocápside con ARN vírico.
- 3º El ARN vírico se transcribe a ADN por acción de la transcriptasa inversa. El ADN vírico es transportado al núcleo celular donde se integra. Se forma así el PROVIRUS.
- 4º Durante la mitosis celular, las células hijas heredan el provirus (ADN vírico integrado). Por ello las infecciones por retrovirus son de por vida.
- 5º Producción de nuevas partículas víricas: El ADN integrado, produce ARNm, proteínas de la cápside (gag y pol) y ARN de nuevas partículas. El virión se ensambla bajo la membrana celular donde se encuentran proteínas de la envuelta necesarias para su salida de la célula por gemación. Este proceso no conlleva muerte celular.

Diagnóstico:

a. Pruebas diagnósticas:

En FeLV las proteínas internas son muy inmunógenas y antigénicamente idénticas para todos los subgrupos de FeLV. La proteína de la cápside vírica gag, p27, se sintetiza en gran cantidad y se encuentra tanto en el citoplasma celular como en el medio extracelular como antígeno libre.

ELISA: Detecta antígeno vírico extracelular libre en plasma (proteína de la cápside vírica p27).

Tiene alta sensibilidad (90%) y alta especificidad.

+ Un positivo por si solo no tiene por qué indicar viremia persistente.

IFD (Inmunofluorescencia Directa): Detecta antígeno vírico intracelular p27 en el citoplasma de neutrófilos y plaquetas de sangre y médula ósea. Los neutrófilos y las plaquetas se liberan infectados a sangre desde la médula osea invadida por el virus.

Necesita sangre entera con anticoagulante y refrigerada, o bien se remite frotis de sangre entera.

+ Un positivo indica viremia persistente.

- Falsos negativos: gato virémico con leucopenia (neutropenia y trombocitopenia) donde sólo un pequeño porcentaje de leucocitos periféricos están infectados.

PCR: Sobre células mononucleares de sangre periférica y médula ósea.

- **Real time PCR DNA** que detecta y cuantifica el número de copias de Provirus (DNA vírico integrado en célula). Detecta viremia persistente (ELISA+, RT-PCR+) Y virus latente (ELISA -, RT-PCR +). Especificidad: muy alta. Necesitan un buen laboratorio
- **Real time PCR ARN:** Permite la cuantificación de virus sin necesidad de células. Se realiza sobre sangre entera, suero, plasma, **saliva**, heces. Demuestra viremia al detectar ARN vírico pero no detecta latencia ya que estos gatos no producen RNA detectable en plasma, saliva o heces. Es de utilidad en colonias para detectar positivos en gatos poco manejables utilizando saliva, ya que es muy sensible.

b. Patogenia e interpretación de resultados

Se produce Infección oronasal mediante contacto con saliva, heces, leche, orina y secreción nasal.

Ocurre replicación en tejido linfático local y área orofaríngea.

- Gatos inmunocompetentes: gracias al sistema inmune mediado por células el virus se elimina completamente. El virus en ellos nunca se disemina sistémicamente y no se detecta la infección ya que no hay antígeno.
- Gato no inmunocompetente: El virus se replica en linfocitos y monocitos y se disemina por todo el organismo: **VIREMIA PRIMARIA**. El gato se encuentra mal, con fiebre y linfadenopatía. El virus se disemina al timo, bazo, nódulos linfáticos y

glándulas salivares por lo que es infeccioso. Esta fase dura entre 3 y 16 semanas y en algunas ocasiones hasta un año.

Viremia primaria
ELISA +
IFD –
RT-PCR +

Tras la viremia primaria:

- **VIREMICO TRANSITORIO o REGRESOR:** El sistema inmune puede eliminar el virus antes de que éste llegue a Médula Osea. Ocurre en el 30-40% de los gatos infectados. Desarrollan respuesta inmune eficaz por neutralización con anticuerpos que le protege frente a futuras infecciones pero no tiene una duración de por vida. Se deberán vacunar anualmente de leucemia felina para aumentar su inmunidad natural

Virémico transitorio (pruebas en sangre)
1º ELISA +, RT-PCR + y tras meses del primero se hace el
2º ELISA -, RT-PCR -, IFD –

- **VIRÉMICO PERSISTENTE (viremia secundaria)** El sistema inmune NO puede eliminar el virus, y éste llega a Médula Osea (ocurre en un 30-40% de los gatos infectados). Las células hematopoyéticas producen granulocitos y plaquetas infectadas que circulan por el cuerpo. El virus se encuentra integrado en el DNA celular en forma de provirus, por lo que la división celular resulta en células hijas que también contienen virus. Esta es la causa de que se mantengan durante años en el gato tras la invasión de la médula ósea. Para eliminar la infección todas las células deberían ser detectadas y eliminadas, pero eso supondría la eliminación de todo el pool hematológico y del sistema inmune. La viremia es máxima con niveles altos de virus (1 ml. de saliva con 1 millón de virus). Se trata de un
1º ELISA +
2º ELISA +, IFD + (en plaquetas y granulocitos con p27 tras afectación de médula osea). RT-PCR + (sangre y médula)

Tras la invasión de la médula osea:

- Desaparece la viremia, pero la médula persiste infectada. **PORTADOR LATENTE EN MEDULA OSEA:** La viremia desaparece, pero no así el virus del organismo, ya que se encuentra integrado en el DNA de algunas células de la médula ósea en forma de PROVIRUS DNA. En estos gatos no se producen copias víricas libres ya que la información del DNA no se transfiere a producción de proteínas víricas. La división de esas células producirá nuevas células con PROVIRUS pero no se producen copias víricas. Ocurre en un porcentaje bajo de gatos y cuanto más tiempo permanece la viremia 2º menos probable es que esto suceda.

ELISA – (No encuentra antígenos de la cápsula)
IFD – (No puede encontrar antígenos de la cápsula)
RT-PCR – (sangre) RT-PCR + (médula)

No son infecciosos. Pero la Infección latente **se puede reactivar** ante inmunosupresión y estrés intenso como el producido durante la preñez y durante lactación donde puede aparecer viremia eliminación de virus por saliva y leche. Pero cuanto más tiempo transcurra entre infección latente y posible inmunosupresión o estrés, menos probable será la reactivación ya que se producen errores en el material genético vírico y no es posible producir proteínas víricas viables. Se cree que la latencia puede ser un método de eliminación del virus.

¿Produce sintomatología un virus latente en médula ósea?. Puede originar mielosupresión o malignidad hematopoyética debido a que FeLV se puede integrar en lugares del genoma responsables de la regulación correcta de la división celular. Puede que el provirus integrado altere la función celular y contribuya a la patogénesis de la mielosupresión.

OTROS TIPOS DE LATENCIA: Debido a la realización cada vez más frecuente de RT-PCR, se ha observado que un 10% de las muestras de sangre resultan RT-PCR + pero ELISA -. Son **PORTADORES LATENTES** y es más frecuente de lo que se creía. La causa está en que un sistema inmune eficaz que consiga eliminar la viremia, no es capaz de eliminar completamente el virus de todas las células del cuerpo.

En un estudio reciente (Dr.Hans Lutz, Universidad de Zurich, ESFM Feline Congress 2008) se ha observado que esto ocurre tanto en gatos no vacunados como vacunados con posterior exposición al virus de leucemia. Ninguna vacuna utilizada en el estudio era capaz de proteger de la integración del virus como provirus en células y de una mínima replicación, pero si de la viremia. Este provirus puede permanecer durante años y la reactivación puede ocurrir pero el riesgo es muy bajo.

Muestra de sangre:

ELISA –

RT-PCR ADN +

RT-PCR ARN + (pero muy bajo número de copias)

Nota: RT-PCR ARN es capaz de detectar FeLV en un número pequeñísimo de células, al ser más sensible que ELISA.

¿Qué efectos clínicos puede tener?: Se han encontrado provirus en células tumorales de gatos FeLV negativo (ELISA), por lo que puede estar involucrado en la patogénesis del tumor.

- **GATOS DISCORDANTES:** El virus no permanece en médula ósea ni en sangre, sino en otros órganos donde se replica de forma intermitente o permanece latente en vejiga, ojos, tejido mamario. Ocurre en un 5% de los gatos y explica resultados discordantes o alternancia de ELISA

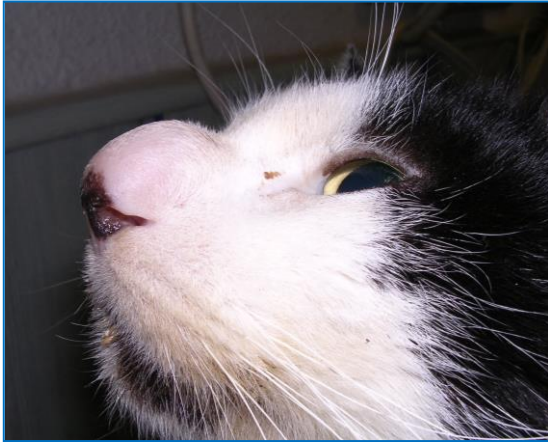
positivos y negativos. Puede haber madres que transmitan infección a sus hijos a través de la leche, pero que ellas resulten negativas.

Pruebas en sangre:

ELISA + variable (al eliminarse p27 a la circulación de forma intermitente).

PCR -

Virus de la Inmunodeficiencia felina (FIV)



Es un retrovirus del género Lentivirus, responsable de la aparición de cuadros de SIDA (Síndrome de Inmunodeficiencia Adquirido) como consecuencia de la muerte de linfocitos T CD4+. En esta fase sobreviene la muerte debido al desarrollo de un síndrome crónico de consunción (pérdida de peso y deterioro físico), enfermedad neurológica, neoplasia y/o infecciones oportunistas sistémicas.

Existen **5 subtipos** genéticamente distintos en todo el mundo: **A, B, C, D y E**: Los subtipos identificados más frecuentemente son el subtipo A y B. En Europa se ha observado mayoritariamente el subtipo A y B. En Estados Unidos, el subtipo A es el predominante excepto en la costa este, que es el B, pero también están presentes los otros subtipos. Un mismo gato puede ser infectado por varios subtipos.

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Fases de la enfermedad

1. **Fase de viremia:** En esa fase se produce la replicación del virus en ganglios regionales y una posterior viremia. Aparecen signos inespecíficos de anorexia, letargia, linfadenopatía y leucopenia transitoria.

2. **Fase asintomática o de latencia clínica.** En esta fase no hay signos de enfermedad ya que la carga viral se reduce pero la viremia no desaparece. La infección viral progresa durante este periodo sufriendo el sistema inmune una disminución progresiva del cociente T CD4/CD8.

3. **Fase de inmunodeficiencia.** En esta fase se produce una disminución severa del cociente de linfocitos T CD4+/ CD8+ y una alteración de su función dando lugar al desarrollo del Síndrome de Inmunodeficiencia Adquirido (SIDA).

Diagnóstico

b. Pruebas diagnósticas:

ELISA: Detecta anticuerpos anti-FIV contra tres proteínas estructurales del virus: p15 y p24 (proteínas de la nucleocápside) y gp40 (glicoproteína de la envoltura) en suero, plasma o sangre entera.

Tiene alta sensibilidad del 99.3% y alta especificidad 99.8%.

Falsos positivos si...

- Detecta anticuerpos vacunales, por lo que no debe utilizarse en el caso de sospechar que un gato esté vacunado frente a FIV (Confirmar con PCR).
- Detecta anticuerpos maternos, por lo que en un gato menor de 8 meses pueden obtenerse falsos positivos (Repetir tras los 8 meses de vida y confirmar con PCR).

Falsos negativos si...

- Hay una carga viral escasa debido a una infección temprana (Confirmar con PCR).
- Secuestro de complejos inmunes debido a enfermedad inmunomediada (Confirmar con PCR).
- Inmunosupresión severa (Confirmar con PCR).

Western Blot: Detecta anticuerpos anti-FIV para cada proteína individual del virus, al separar éstas mediante electroforesis. Se realiza en suero, plasma o sangre entera.

Es el *gold-standard* para el diagnóstico de la infección de FIV.

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PCR: sobre cualquier tejido. Las diferentes técnicas de PCR disponibles (rt-PCR, RTPCR, PCR anidada, PCR convencional) permiten detectar el subtipo A, pero el resto de subtipos son detectados de forma más variable.

Falso negativo si...

- En el caso de realizarlo en la fase asintomática con una reducida carga viral, puede obtenerse un falso negativo dependiendo de la sensibilidad de la técnica (Buscar laboratorios con una elevada calidad y confirmar con Western Blot siempre tras los 8 meses de vida).
- Un transporte inadecuado de la muestra puede dar lugar a falsos negativos al degradarse el ac. Nucléico (Confirmar con Western Blot siempre tras los 8 meses de vida).
- El PCR no está detectando el subtipo viral. (Pedir al laboratorio que especifique qué subtipo detecta su PCR y pedir PCR para el resto de subtipos y confirmar con Western Blot siempre tras los 8 meses de vida).

Falso positivo si...

- La vacunación de gatos frente a FIV, puede aumentar el número de falsos positivos pero se desconocen las causas ya que la vacuna se supone que no debe provocar replicación vírica.
- Contaminación del PCR con pruebas anteriores en laboratorios no cuidadosos (Repetir y confirmar con Western Blot).

Tratamiento FeLV/FIV

Hasta el día de hoy no existe un tratamiento curativo para esta enfermedad, sólo se pueden utilizar tratamientos paliativos que aumenten la calidad y esperanza de vida.

1. Tratamiento precoz, agresivo y más duradero de complicaciones bacterianas, parasitarias... a las que son más susceptibles debido a la inmunosupresión que padecen aunque no sea detectable ya que la respuesta inmune mediada por anticuerpos está afectada en todos los gatos infectados por FeLV.
2. Tratamiento de linfoma con tratamiento quimioterápico específico. Puede dar supervivencias de hasta dos años en algunos gatos.
3. Antiviarles:

- AZT: Bloquea la transcriptasa inversa. Sólo en infección temprana (en las tres primeras semanas tras infección) se ha observado en estudios experimentales que evita la llegada del virus a médula ósea. En infecciones naturales sin embargo, no se obtienen tan buenos resultados como en el tratamiento de FIV donde consigue reducciones en el título viral en plasma.
Mejorar el estado clínico y la calidad de vida, mejorando la esperanza de vida en algunos gatos.

Dosis: 5-10 mg/kg cada 12 horas oral en ciclos de 6 meses continuado o bien 6 meses alternos (descansos de un mes).

Efectos secundarios sobre todo en la dosis mayor: Anemia no regenerativa es un efecto secundario frecuente. Hay que hacer analíticas semanales.

Si el Ht llega a un 20% hay que parar el tratamiento. La anemia se recuperará en unas semanas.

Si durante las primeras 4 semanas no hay anemia, hacer analíticas una vez al mes.

No tratar a gatos con anemia por aplasia medular.

Otros efectos como vómitos y anorexia se presentan de forma muy esporádica.

- Otros antivirales inhibidores de la transcriptasa (STAMP, PME9, AMD3100), inhibidores de proteasa, Ac. Valproico y Lamiduvide han mostrado eficacia variable, algunos son tóxicos y muchos de los tienen una disponibilidad limitada en medicina veterinaria.

4. Inmunomoduladores.

- Interferón omega felino: mejora la sintomatología clínica y aumenta la vida, pero no ayuda a revertir la viremia. El protocolo en cuadros de anemia e Inmunosupresión recomendado por el laboratorio es de:
1 MU/kg/sc durante 5 días. Esperar 14 días y repetir hematología.
Si se han recuperado los valores repetir el ciclo 5 días más. Repetir el ciclo en recaídas. No tiene efectos secundarios.

Manejo de gatos FeLV + y FIV +

De los gatos que conviven con el positivo:

- Testar a todos los gatos de casa
- Informar del riesgo para los gatos negativos y de que lo mejor para no infectar es aislarlos.
- Esterilizar a todos los gatos.
- No introducir a nuevos gatos
- El riesgo para los gatos que ya vivían con un FELV + no es muy alto ya que han sido infectados antes y pueden ser inmunes para una nueva infección. Se estima que el riesgo es de un 10-15% si es FeLV- habiendo vivido con el FeLV+ durante varios meses.

De todos modos, la neutralización de virus por anticuerpos no es duradera de por vida, por lo que un gato que inicialmente es inmune, con los años puede llegar a infectarse.

- El virus FIV se transmite básicamente por mordeduras o heridas en peleas, por lo que la probabilidad de transmisión dentro de grupos estables y pacíficos es prácticamente nula.
- Se deberá vacunar anualmente de leucemia felina para aumentar la inmunidad natural y prevenir de que la vacuna no protege al 100%
- Controlar bien a otros gatos enfermos para que no contagien al gato infectado por FIV.
- Evitar corticoides en gatos negativos que conviven con positivos a FeLV ya que hay riesgo de reactivación de infección latente.

Del gato infectado:

- No debe salir a la calle para no diseminar la infección.
- Mantener una buena nutrición y evitar carnes crudas por riesgo de contagio de *Toxoplasma*.
- Mantener programa de vacunación para prevenir infecciones. Se ha comprobado que su sistema inmune no responde tan eficazmente como un gato libre de infección vírica ante la vacunación de rabia.
- Desparasitar interna y externamente
- Revisiones cada 6 meses para curar cualquier posible patología de forma temprana: hacer analítica de sangre, radiografía, ecografía, analítica de orina. Revisar frecuentemente la boca para evitar infecciones crónicas orales.
- Pesar rutinariamente ya que la pérdida de peso es indicativo de enfermedad aunque no se detecte otro signo.

Bibliografía

PALMERO, M. CARBALLÉS, V *Leucemia Felina*. Enfermedades Infecciosas Felinas. (5-99) Servet. 2010.

PALMERO, M. CARBALLÉS, V *Inmunodeficiencia Felina*. Enfermedades Infecciosas Felinas. (99-143) Servet. 2010.

HORZINEK, M. ADDIE, D. BELAK, S et al. *ABCD guidelines on Feline Leukaemia virus*. European advisory Board on Cat Diseases. October 2007

HORZINEK, M. ADDIE, D. BELAK, S et al. *ABCD guidelines on Feline Immunodeficiency virus*. European advisory Board on Cat Diseases, March 2008

LUTZ, H. HOISE, M.. *Feline Retrovirus infections*. ESFM Feline Congress 2008. Edimburg.

LUTZ.H AND HOSIE.M. *Feline retrovirus infections: FeLV/FIV*. ESFM feline congress 2008.September, Edinburgh. 25-28

STÜTZER.B, MÜLLER.F, MAJZOUB.M et al. *Role of latent feline Leukemia Virus Infection in nonregenerative Cytopenias of cats*.Journal of Veterinary Internal Medicine, Nov 2009

CATTORI.V, PEPIN A.C, TANDON. R et al. *Real-time PCR investigation of feline leukemia virus proviral and viral RNA loads in leukocyte subsets*, Veterinary immunology and immunopathology, pages 124-128, Volume 123, May 2008

TORRES. A.N, O'HALLORAN. K.P, LARSONA. L.J et al. *Development and application of a quantitative real-time PCR assay to detect feline leukemia virus RNA*, Veterinary immunology and immunopathology, pages 81-89, Volume 123, May 2008

HARTMANN.K, GRIESSMAYR.P, SCHULZ.B et al. *Quality of different in-clinic test systems for feline immunodeficiency virus and feline leukaemia virus infection*. Journal of feline medicine and surgery, pages 439-445, Volume 9, December 2007

GROAT. R et al. *Upgraded IDEXX Diagnostic Products for Simultaneous Detection of Antibodies to Feline Immunodeficiency Virus (FIV) gag and env Proteins in Feline Blood Samples*. IDEXX Laboratories, Inc., Research & Development

DIEZ.N. *Exploración ecográfica del tracto digestivo*. XXVII congreso anual de AMVAC. Madrid, 26,27 y 28 de Febrero de 2010

WOLF.A.M. *Care of the FeLV/FIV infected cat*. Atlantic Coast Veterinary Conference, 2002

DE MARI K. et al. *Effects of a recombinant Feline Omega Interferon on the survival and clinical signs of ill FeLV and/or FIV-infected cats*. IFRR Symposium, Amelia Island, USA, 2002

DE MARI K. et al. *Therapeutic effects of recombinant Feline Omega Interferon on FeLV-infected and FeLV/FIV-coinfected symptomatic cats*. Journal of Veterinary Internal Medicine, 18, pages 477-482, 2004

DE MARI K. and SANQUER.A. *Effects of a recombinant Feline Omega Interferon on a population of FeLV and/or FIV infected cats suffering from anemia*. 7th International IFRR Symposium, Pisa, Italy, 2004

GINGERICH D.A. *Lymphocyte T-Cell immunomodulator (LTCl): Review of the immunopharmacology of a new veterinary biologic*. The International Journal of Applied Research of Veterinary Medicine. Vol 6, N^o2, 2008

SCHERK.M. *Vaccination and the Immune Status of the Cat*. Waltham Feline Medicine Symposium 2002

SPARKES A.H. *Feline leukaemia virus and vaccination*. Journal of feline medicine and surgery, volume 5, pages 97-100, April 2003

LANGHAMMER.S, HÜBNER.J, KURTH.R et al. *Antibodies neutralizing feline leukaemia virus (FeLV) in cats immunized with the transmembrane envelope protein p15E*, Immunology, pages 229-237, February 2006

SCHULTZ.R.D. *Vaccines, Vaccination Programs and Methods to Determine Their Effectiveness*, 21st Forum of American College of veterinary internal medicine, 2003

HOFMANN-LEHMANN.R, TANTDON.R, BORETTI F.S et al . *Reassessment of feline leukaemia virus vaccines with novel sensitive molecular assays*. Vaccine. Pages 1087-194, February 2006

HOFMANN-LEHMANN.R, CATTORI.V, TANDON. R et al. *How molecular methods change our views of FeLV infection and vaccination*. Veterinary immunology and immunopathology, Vol 123, pages 119-123, May 2008

GROAT R. et al. *Upgraded IDEXX Diagnostic Products for Simultaneous Detection of Antibodies to Feline Immunodeficiency Virus (FIV) gag and env Proteins in Feline Blood Samples*. IDEXX Laboratories, Inc., Research & Development.

LEVY , J., CRAWFORD, C., HARTMANN, K. et al. 2008 *American Association of Feline Practitioners' feline retrovirus management guidelines*. Journal of Feline Medicine and Surgery, 2008, pp. 300-316.

RICHARDS, J.R. *Feline immunodeficiency virus vaccine: implications for diagnostic testing and disease management*. Biologicals, December 2005.

BERLINSKI, P.J., GIBSON, J.K., FORESTER, J.K. *et al.* *Further Investigation into the Increased Susceptibility of Cats to Feline Immunodeficiency Virus (FIV) After Vaccination with Parenteral Vaccines.* 21st Annual Forum of American College of Veterinary Internal Medicine, 2003.

LEVY, J.K., CRAWFORD, P.C., SLATER, M.R. *Effect of vaccination against feline immunodeficiency virus on results of serologic testing in cats.* Journal of American Veterinary Medical Association. November 2004.

GROAT, R., CURATO, J., SEYMOUR, C. *et al.* *FELINE Antibody Response to Fort Dodge Fel-O-Vax FIV Vaccine Interferes with FIV Diagnostic Tests.* 21st Annual Forum of American College of Veterinary Internal Medicine, 2003.

Etiology and Epidemiology.

Feline immunodeficiency virus. Feline immunodeficiency virus (FIV) is an exogenous, single-strand RNA virus in the family Retroviridae, subfamily Lentivirinae. The virus is morphologically similar to the human immunodeficiency

virus (HIV) but it is antigenically distinct. Like FeLV, FIV produces reverse transcriptase to catalyze the insertion of

viral RNA into the host genome. Multiple subtypes of the virus exist, and some isolates have differing biologic

behavior. For example, immune deficiency is induced much more quickly by some isolates, and clinical diseases,

such as uveitis, are induced by some but not all isolates.

Aggressive biting behavior is thought to be the primary route of transmission of FIV; older, male, outdoor cats with

clinical signs of disease are most commonly infected. The prevalence of FIV antibodies in North America was 2.5%

in a recent study (Levy et al., 2006). FIV is present in semen and can be transmitted by artificial insemination.

Transplacental and perinatal transmission occurs from infected queens to kittens. Arthropod transmission appears to

be unlikely. Transmission by routes other than biting is less common because high levels of viremia are of short duration.

FIV replicates in several cell types, including T-lymphocytes (CD4+ and CD8+), B-lymphocytes, macrophages, and

astrocytes. The primary phase of infection occurs as the virus disseminates throughout the body, initially leading to

low-grade fever, neutropenia, and generalized reactive lymphadenopathy. A subclinical, latent period of variable

length then develops; the length of this period is related in part to the strain of virus and the age of the cat when

infected. The median age of healthy, naturally infected cats and clinically ill naturally infected cats is approximately 3

years and 10 years, respectively, suggesting a latent period of years for most strains of FIV. Chronic experimental

and naturally occurring infection results in a slow decline in circulating CD4+ lymphocyte numbers, response to

mitogens, and decreased production of cytokines associated with cell-mediated immunity, such as interleukin (IL)-2

and IL-10; neutrophil function and natural killer cell function are also affected. Humoral immune responses are often

intact, and a polyclonal gammopathy develops from nonspecific B-lymphocyte activation. Within months to years, an

immune deficiency stage similar to acquired immunodeficiency syndrome (AIDS) in human beings develops.

Coinfection with FeLV potentiates the primary and immune deficiency phases of FIV. However, coinfection with

Mycoplasma haemofelis, *Toxoplasma gondii*, feline herpesvirus, and feline calicivirus, as well as immunization, failed

to potentiate FIV-associated immunodeficiency in research studies.

Feline leukemia virus. Feline leukemia virus (FeLV) is a single-strand RNA virus in the family Retroviridae,

subfamily Oncovirinae. The virus produces reverse transcriptase, which catalyzes the reaction, resulting in the

formation of a DNA copy (provirus) of FeLV viral RNA in the cytoplasm of infected cells; the provirus is inserted into

the host cell genome. On subsequent host cell divisions the provirus serves as a template for new virus particles formed in the cytoplasm and is released across the cell membrane by budding. FeLV is composed of several core and envelope proteins. Envelope protein p15e induces immunosuppression. Core protein p27 is present in the cytoplasm of infected cells, peripheral blood, saliva, and tears of infected cats; detection of p27 is the basis of most FeLV tests. The envelope glycoprotein 70 (gp70) contains the subgroup antigens A, B, or C, which are associated with the infectivity, virulence, and disease caused by individual strains of the virus. Neutralizing antibodies are produced by some cats after exposure to gp70. Antibodies against feline oncornavirus-associated cell membrane antigen (FOCMA) are formed by some cats but are generally not used clinically. The principal route of infection by FeLV is prolonged contact with infected cat saliva and nasal secretions; grooming or sharing common water or food sources effectively results in infection. Because the organism does not survive in the environment, feces, or urine, fomite and aerosol transmission is unlikely. Transplacental, lactational, and venereal transmission is less important than casual contact. FeLV infection has worldwide distribution; the seroprevalence of infection varies geographically and by the population of cats tested. Infection is most common in outdoor male cats between ages 1 and 6 years. In a recent study (Levy et al., 2006) the prevalence of FeLV antigenemia in cats in North America was 2.3%. FeLV can be detected in feces of infected fleas for 2 weeks (Vobis et al., 2006). However, the prevalence rates for FeLV vary little across regions of the United States with high and low prevalence rates of fleas, so this is an unlikely route of infection. The virus replicates first in the oropharynx, followed by dissemination through the body to the bone marrow. If persistent bone marrow infection occurs, infected white blood cells and platelets leave the bone marrow with ultimate infection of epithelial structures, including salivary and lacrimal glands. Whether infection occurs after natural exposure to FeLV is determined by the virus subtype or strain, the virus dose, the age of the cat when exposed, and the cat's immune responses. Using realtime PCR and antigen ELISA results, four classes of FeLV infection were defined (Torres et al. 2005; Levy et al. 2008). Some FeLV-exposed cats can eliminate the infection (abortive) whereas others progress to clinical illness and persistent viremia (progressive). Other FeLV-exposed cats will develop regressive infection characterized by antigen-negative results and lower transiently positive realtime PCR results. Latent FeLV infections are transiently antigen positive but have persistently positive realtime PCR results. Latent and regressive infections can be potentially activated by the administration of glucocorticoids or other immunosuppressive drugs. The pathogenesis of various syndromes induced by FeLV is complex but includes induction of lymphoma from activation of oncogenes by the virus or insertion of a provirus into the genome of lymphoid precursors; subgroup C induction of aplastic anemia from increased secretion of tumor necrosis factor- α -lymphocyte depletion (both CD4+ and CD8+ lymphocytes) or dysfunction; neutropenia; neutrophil function disorders;

malignant transformation; and viral induction of bone marrow growth-promoting substances leading to myeloproliferative diseases.

Clinical Features.

Feline immunodeficiency virus. Clinical signs of infection with FIV can arise from direct viral effects or secondary infections that ensue after the development of immunodeficiency. Most of the clinical syndromes diagnosed in FIV-seropositive cats also occur in FIV-naïve cats, which makes proving disease causation difficult during the subclinical stage of infection. A positive FIV antibody test does not prove immunodeficiency or disease from FIV and does not necessarily indicate a poor prognosis. The only way to determine accurately whether an FIV-seropositive cat with a concurrent infectious disease has a poor prognosis is to treat the concurrent infection. Primary (acute) FIV infection is characterized by fever and generalized lymphadenopathy. Owners commonly present FIV-infected cats in the immunodeficiency stage for evaluation of nonspecific signs such as anorexia, weight loss, and depression or for evaluation of abnormalities associated with specific organ systems. When a clinical syndrome is diagnosed in a cat seropositive for FIV, the workup should include diagnostic tests for other potential causes.

Clinical syndromes reportedly from primary viral effects include chronic small-bowel diarrhea, nonregenerative anemia, thrombocytopenia, neutropenia, lymphadenopathy, pars planitis (inflammation in the anterior vitreous humor), anterior uveitis, glomerulonephritis, renal insufficiency, and hyperglobulinemia. However, in one recent report of naturally infected cats, FIV was associated with proteinuria but not renal azotemia (Baxter et al, 2012).

Behavioral abnormalities, with dementia, hiding, rage, inappropriate elimination, and roaming, are the most common neurologic manifestations of FIV infection. Seizures, nystagmus, ataxia, and peripheral nerve abnormalities may occasionally be attributable to primary viral effects. Lymphoid malignancies, myeloproliferative diseases, and several carcinomas and sarcomas have been detected in FIV-infected, FeLV-naïve cats, suggesting a potential association between FIV and malignancy; FIV-infected cats are at higher risk for the development of lymphoma (Madgen et al, 2011).

Feline leukemia virus. Owners generally present FeLV-infected cats for evaluation of nonspecific signs such as anorexia, weight loss, and depression or abnormalities associated with specific organ systems. Of the FeLV-infected cats evaluated at necropsy, 23% had evidence of neoplasia (96% lymphoma/leukemia); the remainder died from nonneoplastic diseases (Reinacher, 1989). Specific clinical syndromes can result from specific effects of the virus or from opportunistic infections caused by immunosuppression. A positive FeLV test result does not prove disease induced by FeLV. When a clinical syndrome is diagnosed in a FeLV-seropositive cat, the workup should include diagnostic tests for other potential causes. The opportunistic agents discussed for FIV also are common in FeLV-infected cats.

Bacterial or calicivirus-induced stomatitis occurs in some FeLV-infected cats as a result of immunosuppression. FeLV infection can result in vomiting or diarrhea from a form of enteritis clinically and histopathologically resembling

panleukopenia, from alimentary lymphoma, or from secondary infections attributable to immunosuppression. Icterus in FeLV-infected cats can be prehepatic from immune-mediated destruction of red blood cells induced by FeLV or

secondary infection by *Mycoplasma haemofelis* or "*Candidatus Mycoplasma haemominutum*"; hepatic from hepatic

lymphoma, hepatic lipidosis, or focal liver necrosis; or posthepatic from alimentary lymphoma. Some FeLV-infected

cats with icterus may be concurrently infected by FIP virus or *T. gondii*.

Clinical signs of rhinitis or pneumonia occur in some FeLV-infected cats as a result of secondary infections. Dyspnea or dysphagia from mediastinal lymphoma occurs in some cats. These cats are generally younger than 3 years and

may have decreased cranial chest compliance on palpation as well as muffled heart and lung sounds if pleural

effusion is present.

Mediastinal, multicentric, and alimentary lymphomas are the most common neoplasms associated with FeLV;

lymphoid hyperplasia also occurs. Alimentary lymphoma most commonly involves the small intestine, mesenteric

lymph nodes, kidneys, and liver of older cats; most cats with alimentary lymphoma are FeLV negative. Renal

lymphoma can involve one or both kidneys, which are usually enlarged and irregularly margined on physical

examination. Fibrosarcomas occasionally develop in young cats coinfecting with FeLV and feline sarcoma virus.

Lymphocytic, myelogenous, erythroid, and megakaryocytic leukemia all are reported with FeLV infection;

erythroleukemia and myelomonocytic leukemia are the most common. The history and physical examination findings

are nonspecific.

Renal failure occurs in some FeLV-infected cats from renal lymphoma or glomerulonephritis. Affected cats are

presented for evaluation of polyuria, polydipsia, weight loss, and inappetence during the last stages of disease.

Urinary incontinence from sphincter incompetence or detrusor hyperactivity occurs in some cats; small-bladder

nocturnal incontinence is reported most frequently.

Some FeLV-infected cats are presented for miosis, blepharospasm, or cloudy eyes from ocular lymphoma. Aqueous

flare, mass lesions, keratic precipitates, lens luxations, and glaucoma are often found on ocular examination. FeLV

does not likely induce uveitis without lymphoma. Neurologic abnormalities associated with FeLV infection include

anisocoria, ataxia, weakness, tetraparesis, paraparesis, behavioral changes, and urinary incontinence.

Nervous

system disease is likely to develop as a result of polyneuropathy or lymphoma. Intraocular and nervous system

disease in FeLV-infected cats can occur from infection with other agents, including FIPV, *Cryptococcus neoformans*,

Bartonella spp., or *T. gondii*.

Abortion, stillbirth, or infertility occurs in some FeLV-infected queens. Kittens infected *in utero* that survive to birth

generally develop accelerated FeLV syndromes or die as part of the kitten mortality complex.

Some FeLV-seropositive cats present for lameness or weakness from neutrophilic polyarthritis attributed to immune

complex deposition. Multiple cartilaginous exostoses occur in some cats and may be FeLV related.

Diagnosis.

Feline immunodeficiency virus. Neutropenia, thrombocytopenia, and nonregenerative anemia are common

hematologic abnormalities associated with FIV infection. Monocytosis and lymphocytosis occur in some cats and may be caused by the virus or chronic infection with opportunistic pathogens. Cytologic examination of bone marrow aspirates may reveal maturation arrest (i.e., myelodysplasia), lymphoma, or leukemia. A progressive decline in CD4+ lymphocytes, a plateau or progressive increase in CD8+ lymphocytes, and an inversion of the CD4+/CD8+ ratio occurs in experimentally infected cats over time. A multitude of serum biochemical abnormalities is possible depending on what FIV-associated syndrome is occurring. Polyclonal gammopathy can occur in some FIV infected cats. No pathognomonic imaging abnormalities are associated with FIV infection. Antibodies against FIV are detected in serum in clinical practice most frequently by enzyme-linked immunosorbent assay (ELISA). Comparisons between different tests have shown the results of most assays are comparable (Hartmann et al., 2007). Clinical signs can occur before seroconversion in some cats and some infected cats never seroconvert; thus false-negative reactions can occur. Results of virus isolation or RT-PCR on blood are positive in some antibody-negative cats. False-positive reactions can occur with ELISA; therefore positive ELISA results in healthy or low-risk cats should be confirmed by Western blot immunoassay or RT-PCR. Kittens can have detectable, colostrum-derived antibodies for several months. Kittens younger than 6 months that are FIV seropositive should be tested every 60 days until the result is negative. If antibodies persist at 6 months of age, the kitten is likely infected. Virus isolation or PCR on blood can also be performed to confirm infection. The biggest problem with FIV RT-PCR assays to date is lack of standardization among laboratories and the potential for both false-positive and falsenegative results (Crawford et al., 2005). A vaccine against FIV has been licensed in the United States. This vaccine induces antibodies that cannot be distinguished from those induced by naturally occurring disease with currently available tests (see below). Detection of antibodies against FIV in the serum of cats that have not been vaccinated against FIV documents exposure and correlates well with persistent infection but does not correlate with disease induced by the virus. Because many clinical syndromes associated with FIV can be caused by opportunistic infections, further diagnostic procedures may determine treatable etiologies. For example, some FIV-seropositive cats with uveitis are coinfecting by *T. gondii* and often respond to the administration of anti-*Toxoplasma* drugs. **Feline leukemia virus.** A variety of nonspecific hematologic, biochemical, urinalysis, and radiographic abnormalities occur in FeLV-infected cats. Nonregenerative anemia alone or in combination with decreases in lymphocyte, neutrophil, and platelet counts is common. The presence of increased numbers of circulating nucleated red blood cells or macrocytosis in association with severe nonregenerative anemia occurs frequently; examination of bone marrow often documents a maturation arrest in the erythroid line (erythrodysplasia). Immune-mediated destruction of erythrocytes can be induced by FeLV and occurs in cats coinfecting with hemoplasmas; regenerative anemia, microagglutination or macroagglutination of erythrocytes, and a positive result on the direct Coombs test are common

in these cats. Neutropenia and thrombocytopenia occur from bone marrow suppression or immune-mediated destruction. In a recent study, 37 cats with non-regenerative cytopenias were evaluated for latent FeLV in the bone marrow by RT-PCR assay and 2 cats were positive (Stützer et al, 2010). FeLV-infected cats with the panleukopenialike syndrome have gastrointestinal tract signs and neutropenia and are difficult to differentiate from cats with panleukopenia virus infection or salmonellosis. In addition, cats with FeLV-induced panleukopenia-like syndrome usually have anemia and thrombocytopenia, abnormalities rarely associated with panleukopenia virus infection. Azotemia, hyperbilirubinemia, bilirubinuria, and increased activity of liver enzymes are common biochemical abnormalities. Proteinuria occurs in some FeLV-infected cats with glomerulonephritis. Cats with lymphoma have mass lesions radiographically depending on the organ system affected. Mediastinal lymphoma can result in pleural effusion; alimentary lymphoma can cause obstructive intestinal patterns. Lymphoma can be diagnosed by cytologic or histopathologic evaluation of affected tissues. Because lymphoma can be diagnosed cytologically and treated with chemotherapy, cats with mediastinal masses, lymphadenopathy, renomegaly, hepatomegaly, splenomegaly, or intestinal masses should be evaluated cytologically before surgical intervention. Malignant lymphocytes are also occasionally identified in peripheral blood smears, effusions, and CSF. Most cats with suspected FeLV infection are screened for FeLV antigens in neutrophils and platelets by immunofluorescent antibody (IFA) testing or in whole blood, plasma, serum, saliva, or tears by ELISA. Serum is the most accurate fluid to assess in ELISA tests. IFA results are not positive until the bone marrow has been infected. The results of IFA testing are accurate more than 95% of the time. False-negative reactions may occur when leukopenia or thrombocytopenia prevents evaluation of an adequate number of cells. False-positive reactions can occur if the blood smears submitted for evaluation are too thick. A positive IFA result indicates that the cat is viremic and contagious; approximately 90% of cats with positive IFA results are viremic for life. The rare combination of IFA-positive and ELISA-negative results suggests technique-related artifact. Negative ELISA results correlate well with negative IFA results and an inability to isolate FeLV. Comparisons of different antigen tests have shown the results of most assays to be comparable (Hartmann et al., 2007). The virus can be detected in serum by ELISA before infection of bone marrow and can therefore be positive in some cats during early progressive stages of infection or during early latent infection even though IFA results are negative. Other possibilities for discordant results (ELISA positive, IFA negative) are false-positive ELISA results or falsenegative IFA results. Cats with positive ELISA results and negative IFA results are probably not contagious at that time but should be isolated until retested 4 to 6 weeks later because progression to persistent viremia and epithelial cell infection may be occurring. ELISA-positive cats that revert to negative have developed latent infections or regressive infection. Virus isolation, IFA performed on bone marrow cells, immunohistochemical staining of tissues for FeLV antigen, and PCR can be used to confirm latent or regressive infection in some cats. Cats with latent or regressive infection are not likely

contagious to other cats, but infected queens may pass the virus to kittens during gestation or parturition or by milk.

Cats with regressive or latent infection can be immunodeficient and may become viremic (IFA and ELISA positive)

after receiving corticosteroids or after extreme stress.

A delay of 1 to 2 weeks generally occurs after the onset of viremia before ELISA tear and saliva test results become

positive; therefore these test results can be negative even when results with serum are positive and so are not

recommended for use. Antibody titers to FeLV envelope antigens (neutralizing antibody) and against virustransformed

tumor cells (FOCMA antibody) are available in some research laboratories, but the diagnostic and prognostic significance of results from these tests is unknown. Realtime PCR assays are more sensitive than

conventional PCR for FeLV infections, but validated and standardized assays are not currently available in the United

States (Torres et al. 2005).

Treatment.

Feline immunodeficiency virus. Because FIV-seropositive cats are not necessarily immunosuppressed or

diseased from FIV, the cat should be evaluated and treated for other potential causes of the clinical syndrome. Some FIV-seropositive cats are immunodeficient; if infectious diseases are identified,

bacteriocidal drugs administered at

the upper end of the dosage should be chosen. Long-term antibiotic therapy or multiple treatment periods may be

required. The only way to determine if an FIV-seropositive cat with a concurrent infection has a poor prognosis is to

treat the concurrent infection.

A number of anti-lentiviral drugs may be effective for the treatment of FIV infected cats but controlled studies are

largely lacking (Mohammad et al, 2012). Administration of interferons has shown clinical benefit in some studies

(Domenech et al, 2011). Oral administration of 10 IU/kg of human interferon-alpha led to improved clinical signs and

prolonged survival compared with a placebo-treated control group in one study (Pedretti et al., 2006). In another

study feline recombinant interferon was administered at 10⁶ U/kg/day SQ for 5 days in three series (starting on days

0, 14, and 60) and was shown to improve clinical signs early in the study and prolong survival in treated cats (de Mari

et al., 2004). Administration of antiviral agents such as the reverse transcriptase inhibitor azidothymidine (AZT) has

had mixed success in the treatment of FIV. Use of AZT at a dosage of 5 mg/kg PO or SQ q12h improved overall

quality of life and stomatitis in FIV-infected cats and is believed to aid in the treatment of neurologic signs (Hartmann

et al., 1995a, 1995b). Cats treated with AZT should be monitored for the development of anemia. The anti-viral

compound plerixafor was used in a study of naturally infected cats and was shown to lessen pro-viral load but did not

improve clinical outcomes (Hartmann et al, 2012). When combined with 9-(2-phosphonylmethoxyethyl) adenine

(PMEA), intolerable side-effects occurred. Administration of bovine lactoferrin by mouth was beneficial in the

treatment of intractable stomatitis in FIV-seropositive cats (Sato et al., 1996). Removal of all premolar and molar

teeth has also been effective for treatment of intractable stomatitis in some FIV-seropositive cats.

Immunomodulators

have not been shown to have reproducible clinical effect, but owners sometimes report positive responses. Human

recombinant erythropoietin administration increased red blood cell and white blood cell counts, did not increase viral load, and had no measurable adverse clinical effects in FIV-infected cats compared with placebo (Arai et al., 2000).

In contrast, although administration of human recombinant granulocyte-monocyte colony-stimulating factor (GM-CSF) to FIV-infected cats increased white blood cell counts in some treated cats, it also induced fever, anti-GM-CSF antibodies, and increased viral load. GM-CSF therefore appears to be contraindicated for the treatment of FIV in cats.

Feline leukemia virus. Several antiviral agents have been proposed for the treatment of FeLV; the reverse transcriptase inhibitor AZT has been studied the most. Unfortunately, administration of AZT to persistently viremic cats does not appear to clear viremia in most, and it had minimal benefits for clinically ill cats in a recent study

(Hartmann et al., 2002). Interferons have an effect against FeLV in vivo and in vitro (Collado et al., 2007; de Mari et

al., 2004). Immunotherapy with drugs such as *Staphylococcus* protein A, *Propionibacterium acnes*, or acemannan

improves clinical signs of disease in some cats, but controlled studies are lacking.

Chemotherapy should be administered to cats with FeLV-associated neoplasia. Opportunistic agents should be

managed as indicated; the upper dose range and duration of antibiotic therapy are generally required.

Supportive

therapies such as hematinic agents, vitamin B₁₂, folic acid, anabolic steroids, and erythropoietin generally have been

unsuccessful in the management of nonregenerative anemia. Blood transfusion is required in many cases.

Cats with

autoagglutinating hemolytic anemia require immunosuppressive therapy, but this may activate virus replication. The

prognosis for persistently viremic cats is guarded; the majority die within 2 to 3 years.

Prevention and Zoonotic Aspects.

Feline immunodeficiency virus. Housing cats indoors to avoid fighting and testing new cats before introduction to

an FIV-seronegative, multiple-cat household will prevent most cases of FIV. Transmission by fomites is unusual

because the virus is not easily transmitted by casual contact, is susceptible to most routine disinfectants, and dies

when out of the host after minutes to hours, especially when dried. Cleaning litter boxes and dishes shared by cats

with scalding water and detergent inactivates the virus. Cats with potential exposure from fighting should be retested

60 days after the potential exposure (Goldkamp et al, 2008). Cats that are FIV infected should be housed indoors at

all times to avoid exposing FIV-naïve cats in the environment to the virus and to lessen the affected animal's chance

of acquiring opportunistic infections. Kittens queened by FIV-infected cats should not be allowed to nurse to avoid

transmission by ingestion of milk. Kittens queened by FIV-infected cats should be shown to be serologically negative

at 6 months of age to document failure of lactogenic or transplacental transmission before being sold. A killed

vaccine containing immunogens from two FIV isolates is licensed for use in some countries (Boehringer-Ingelheim).

The American Association of Feline Practitioners considers the vaccine noncore. However, vaccination of high risk,

FIV seronegative cats should be considered. In addition, the vaccine induces antibodies that cannot be distinguished

from those induced by natural exposure by antibody assays currently available in the United States. FIV RT-PCR assays can be attempted to differentiate FIV infection from vaccination and a positive test result will document infection. However, since FIV induces only low level viremia, a negative RT-PCR assay result does not exclude the infection. HIV and FIV are morphologically similar but antigenically distinct. Antibodies against FIV have not been documented in the serum of human beings, even after accidental exposure to virus-containing material (Butera et al., 2000; Dickerson et al, 2012). Cats with FIV infection resulting in immunodeficiency may be more likely to spread other zoonotic agents into the human environment; clinically ill, FIV-seropositive cats should therefore undergo a thorough diagnostic evaluation.

Feline leukemia virus. Avoiding contact with FeLV by housing cats indoors is the best form of prevention. Potential fomites such as water bowls and litter pans should not be shared by seropositive and seronegative cats.

Testing and removal of seropositive cats can result in virus-free catteries and multiple-cat households. Because of variations in challenge study methods and the difficulty of assessing the preventable fraction of a disease with a relatively low infection rate, long subclinical phase, and multiple field strains, the efficacy of individual vaccines continues to be in question. Vaccination of cats not previously exposed to FeLV should be considered in cats at high risk (i.e., contact with other cats), but owners should be warned of the potential efficacy of less than 100%.

Vaccination should be considered for kittens because of increased risk for progressive infection and then whether to boost the vaccine evaluated 1 year later. Variable recommendations have been given on whether to use a prolonged interval (> 1 year) for FeLV vaccination in cats at risk for infection. There is one vaccine available in some countries labelled for a 2 year interval (Merck Animal Health). Cats with persistent FeLV viremia do not benefit from vaccination and so FeLV serology should be assessed prior to vaccination. Vaccination is related to the development of injection site sarcoma in some cats. Cats developing these tumors may be genetically predisposed (Banerji et al., 2007).

FeLV-infected cats should be housed indoors to avoid infecting other cats and avoid exposure to opportunistic agents. Flea control should be maintained to avoid exposure to hemoplasmas, and *Bartonella* spp. FeLV-infected cats should not be allowed to hunt or be fed undercooked meats to avoid infection by *T. gondii*, *Cryptosporidium parvum*, *Giardia* spp., and other infectious agents carried by transport hosts.

Antigens of FeLV have never been documented in the serum of human beings, suggesting that the zoonotic risk is minimal. However, FeLV-infected cats may be more likely than FeLV-naïve cats to pass other zoonotic agents, such as *C. parvum* and *Salmonella* spp., into the human environment.