FIV and FeLV: An update on vaccination and diagnostics for NZ clinicians

Dr Mark Westman, University of Sydney

Virbac

Shaping the future of animal health

THE UNIVERSITY OF SYDNEY

Outline of webinar

What we will cover:

1. FIV and FeLV infection – Pathogenesis
2. FIV and FeLV infection – Disease associations
3. FIV and FeLV prevalence – Australia and NZ
4. FIV and FeLV infection – Diagnostic challenges
5. FIV and FeLV vaccination

Image courtesy of Lynda du Cross

My background

Image courtesy of Linda Warlond, Clique Photography

RSPCA®

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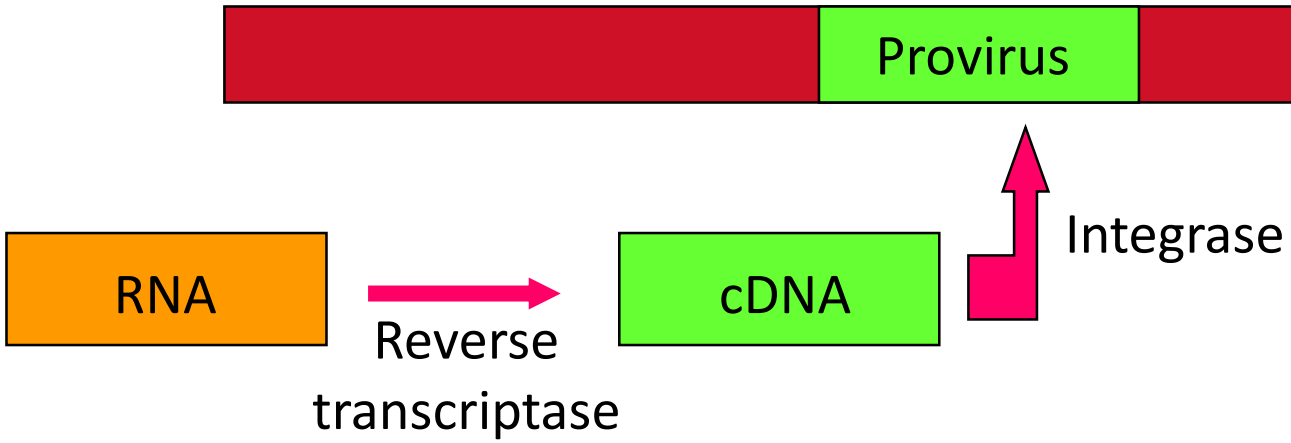
ANIMAL WELFARE LEAGUE NSW

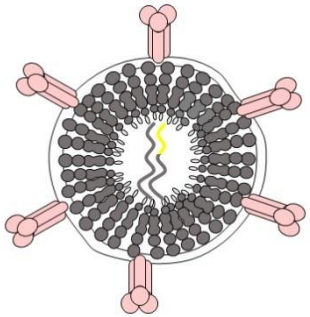
'because every animal is special'

Pets in the Park

Helping the homeless care for their pets

1. Retroviruses – A review of pathogenesis

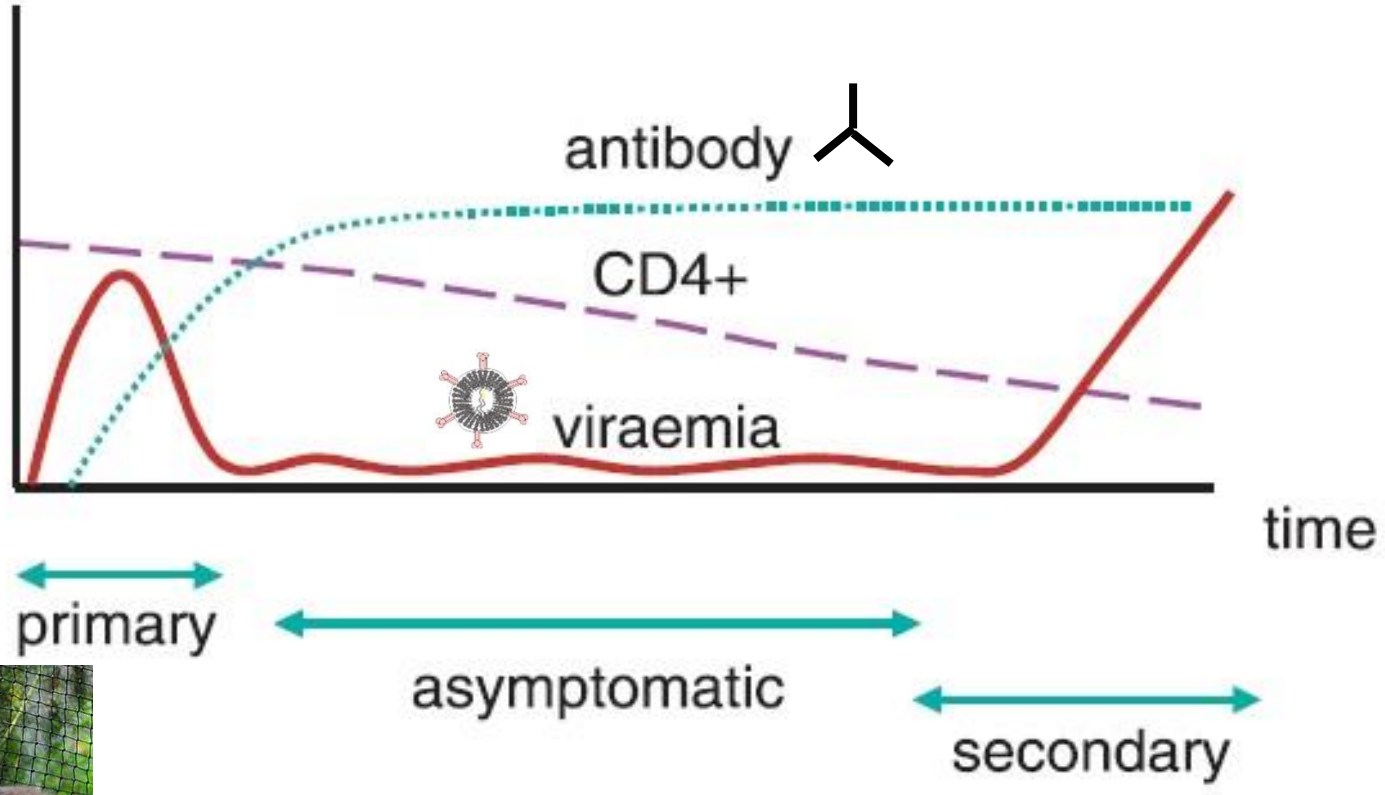




A retrovirus

Retrovirus image courtesy of Prof Brian Willett

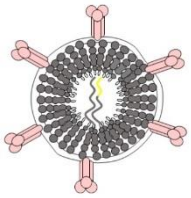
1. FIV pathogenesis



Hosie and Beatty 2007[1]

Image courtesy of Lynda du Cross

1. FeLV pathogenesis

FeLV 

a) Abortive infection

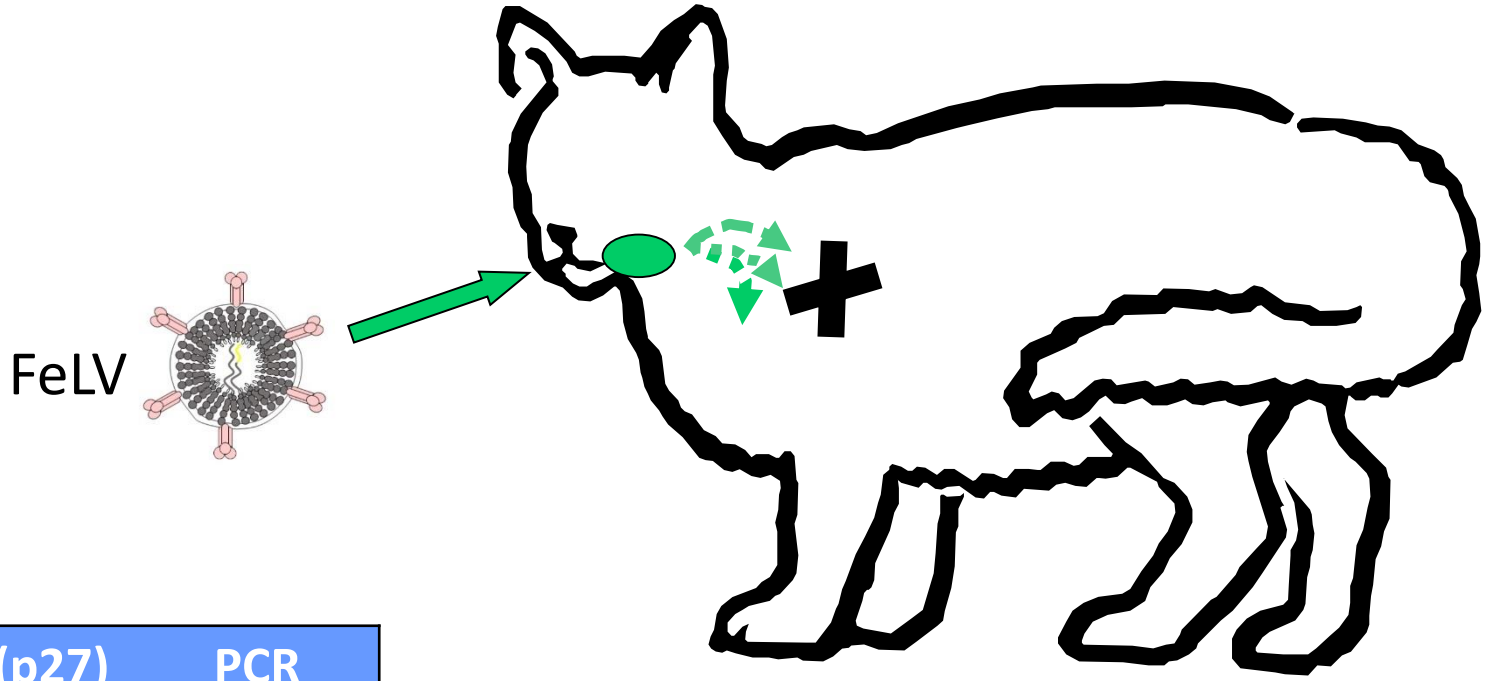
b) Progressive infection

c) Regressive infection

Image courtesy of Lynda du Cross

1. FeLV pathogenesis

a) Outcome of FeLV exposure: ABORTIVE infection

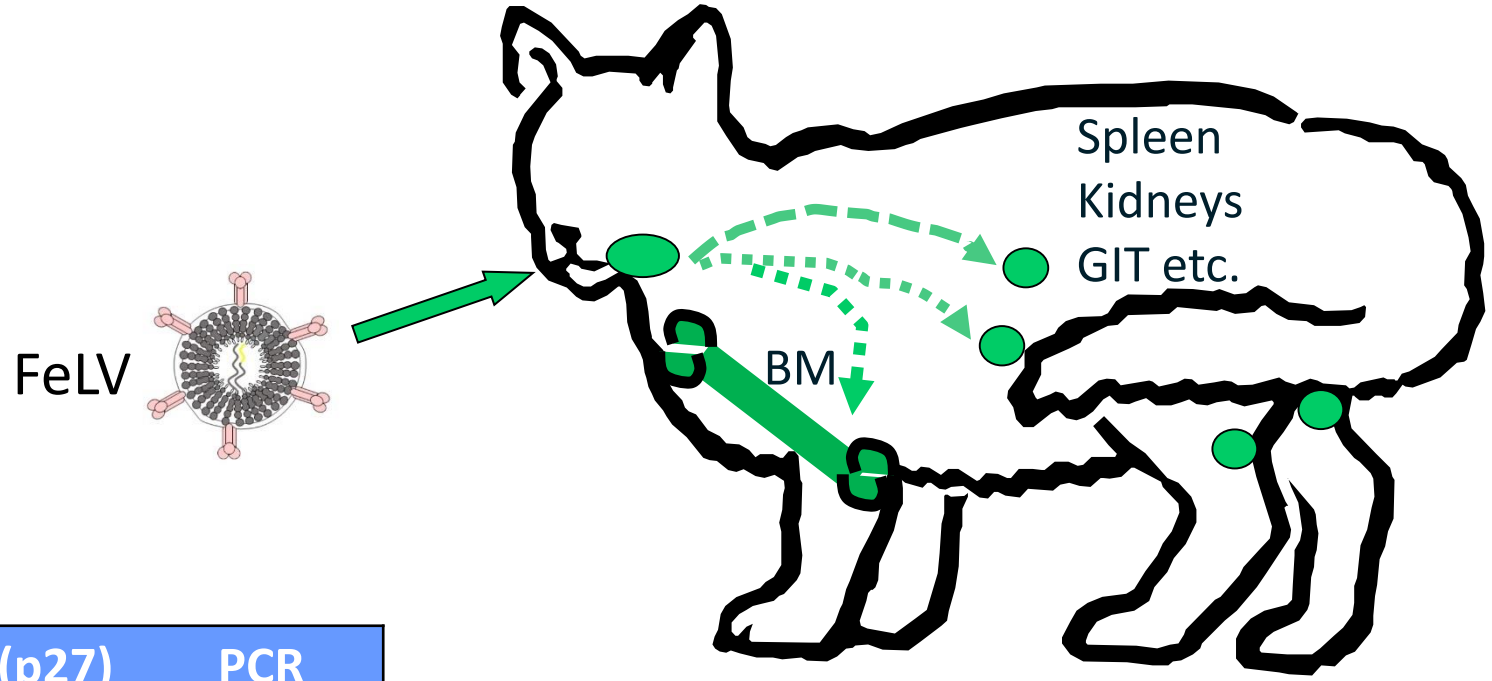


Antigen (p27)	PCR
✗	✗

Image courtesy of Prof Vanessa Barrs

1. FeLV pathogenesis

b) Outcome of FeLV exposure: PROGRESSIVE infection

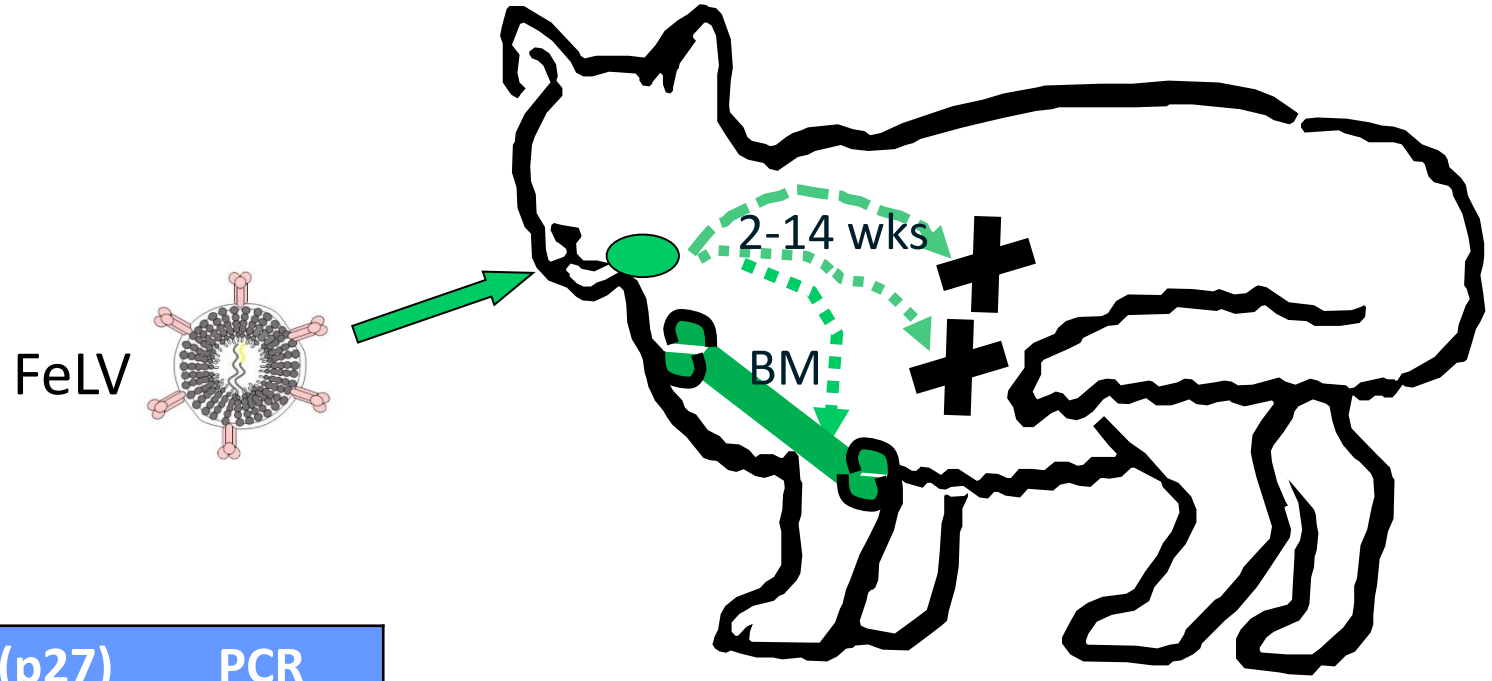


Antigen (p27)	PCR
✓	✓

Image courtesy of Prof Vanessa Barrs

1. FeLV pathogenesis

c) Outcome of FeLV exposure: REGRESSIVE infection



Antigen (p27)	PCR
✓ then ✗	✓

Image courtesy of Prof Vanessa Barrs

2. FIV disease associations

1/17 cats in Group 1 (Chicago) died from hypertrophic cardiomyopathy

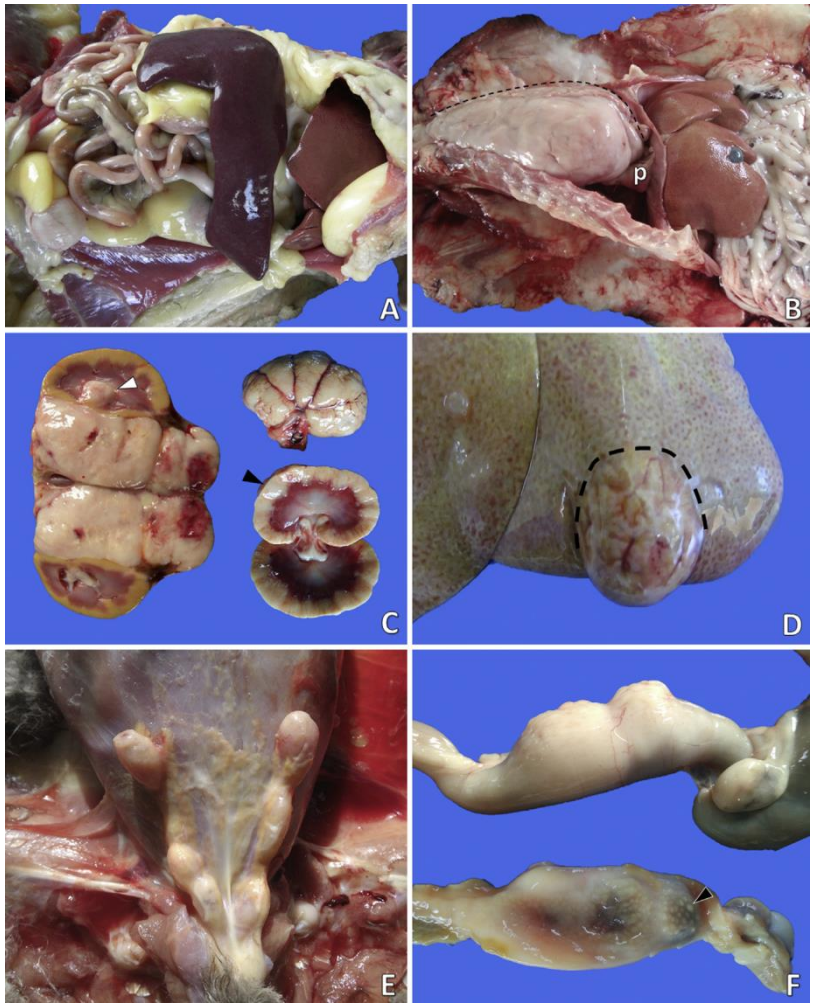
17/27 cats in Group 2 (Memphis) died, of which 9 died from lymphoma and 13 had some evidence of lymphoid disease (lymphoma, lymphoid hyperplasia or lymphoid depletion)

"Therefore, it appears that FIV infection is more likely to progress in cats kept in crowded shelter conditions compared to those living in spacious environments"[2]

2. FIV disease associations

USA study - FIV-infected cats were **six times more likely** to develop leukaemia or lymphoma than FIV-uninfected cats[3]

2. FeLV disease associations (progressive)



Cristo *et al.* 2019[2]

Brazil - 57% (30/53) of lymphomas from FeLV-positive cats[4]

USA study - FeLV-infected cats **62 times more likely** to develop leukaemia or lymphoma than FeLV-uninfected cats[3]

2. FeLV disease associations (progressive)

"…most will develop disease. Of these, 70 – 90% will have died within 18 months – 3 years"

BUT

"Some may remain healthy for many years before one of the FeLV-related diseases develops, and occasional cases remain permanently healthy"[5]

Images courtesy of Lynda du Cross

2. Re-homing progressively FeLV-infected cats

FeLV Adoption Center

About the FeLV Adoption Center

The FeLV Adoption Center provides a home for cats that have been diagnosed with Feline Leukemia, with the ultimate goal of finding each FeLV cat a home to call their very own.

Feline Leukemia (FeLV) is a virus that impacts the immune system and may shorten the lifespan of an infected cat to just 2-4 years after diagnosis. Because of the contagious nature of disease, FeLV+ cats are kept isolated from other cats who are not infected.

The quarantine combined with the estimated lifespan means that our FeLV cats have a harder time getting adopted, and thus are often the first to be euthanized when they test positive at shelters. However, ***APA! believes that these cats and kittens deserve a chance*** – even if it's a chance for just a few years.

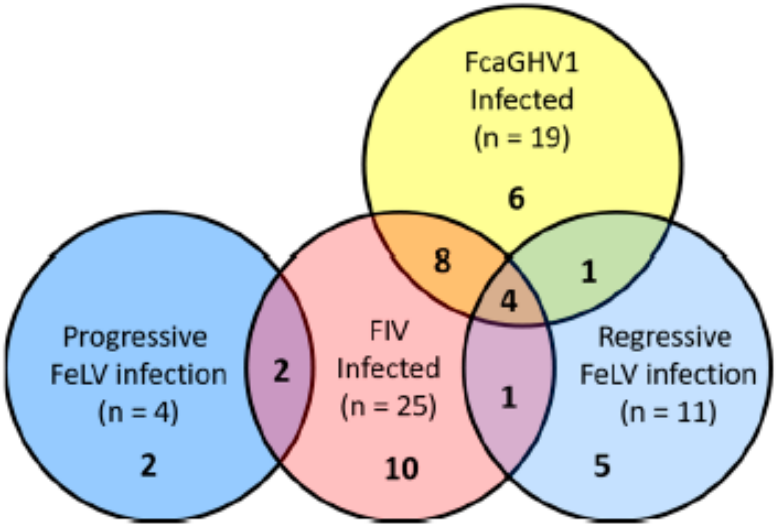
Because FeLV+ cats and kittens are often hard to place and they can't be placed in the cattery with non-infected cats, APA! has created a special place that these kitties can call home until their forever family finds them.

Program Accomplishments

- The FeLV Adoption Center placed 65 cats in their forever homes in 2016
- The average Length of Stay for a FeLV cat in 2017 is currently just 90 days, proving that *not only can these cats be adopted, but they don't stay with us for long before finding a home*

https://www.austinpetsalive.org/about/programs/felv-adoption/

2. FeLV disease associations (regressive)



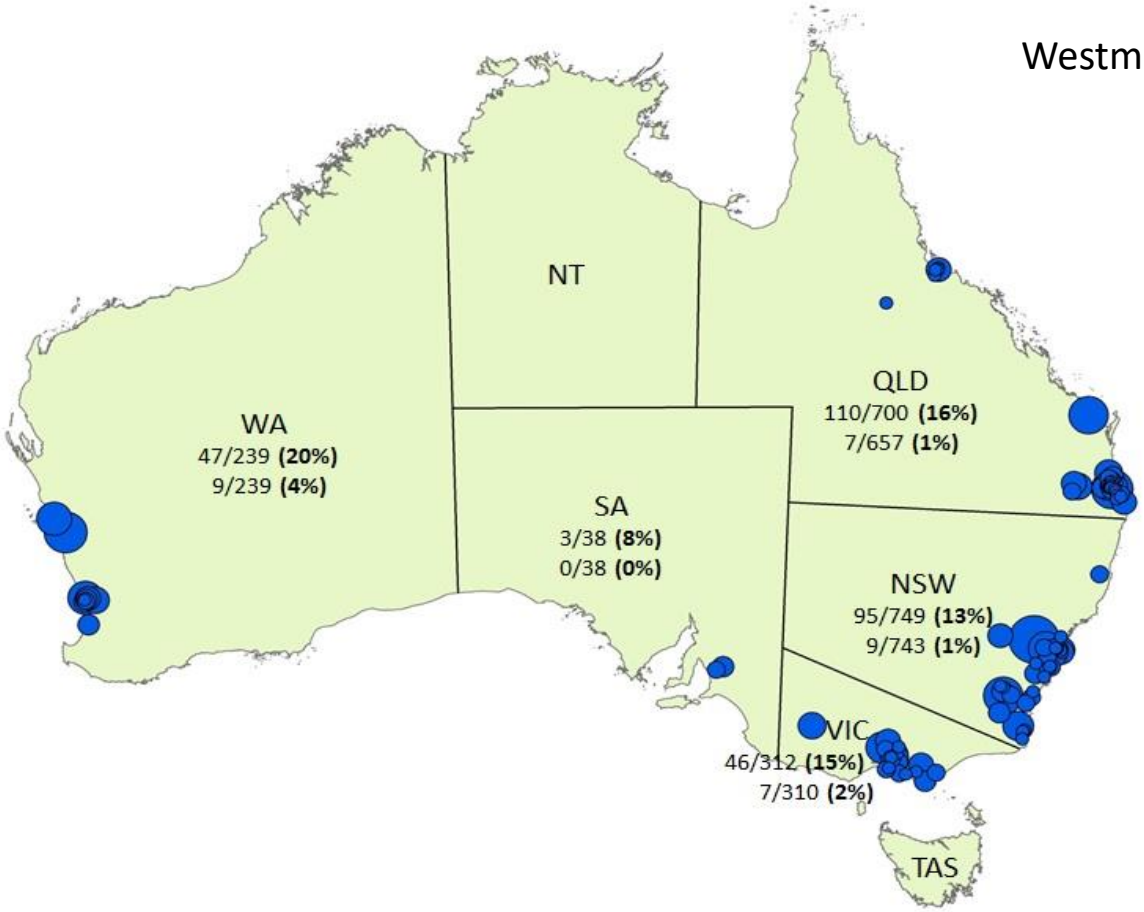
McLuckie *et al.* (2018) – 42 cases of lymphoma in cats with formalin-fixed, paraffin embedded tissue available, as well as FeLV/FIV PoC testing and FeLV PCR testing (note figure shows results for 59 cats)[6]

- 11/42 (26%) cats diagnosed with <u>regressive</u> FeLV infection (Ag-, PCR+)
- 2/42 (5%) cats diagnosed with <u>progressive</u> FeLV infection (plus two more lymphoma cases with only blood samples available)

"Our results [from Australia] support further investigation of a role for regressive FeLV infection in tumorigenesis in cats"[6]

3. FIV and FeLV prevalence - Australia

Westman *et al.* 2016[7]



FIV

305/2,083 (15%) in 2011-13[7]

Progressive FeLV

32/2,032 (2%) in 2011-13[7]

3. FIV and FeLV prevalence – NZ

Original Article

Journal of Feline Medicine and Surgery
15(12) 1063–1069

DOI: 10.1177/1098612X13488384
jfms.com
SAGE

Prevalence and risk factor analysis of feline haemoplasma infection in New Zealand domestic cats using a real-time PCR assay

FIV

20/200 (10%) – published 2013[8]

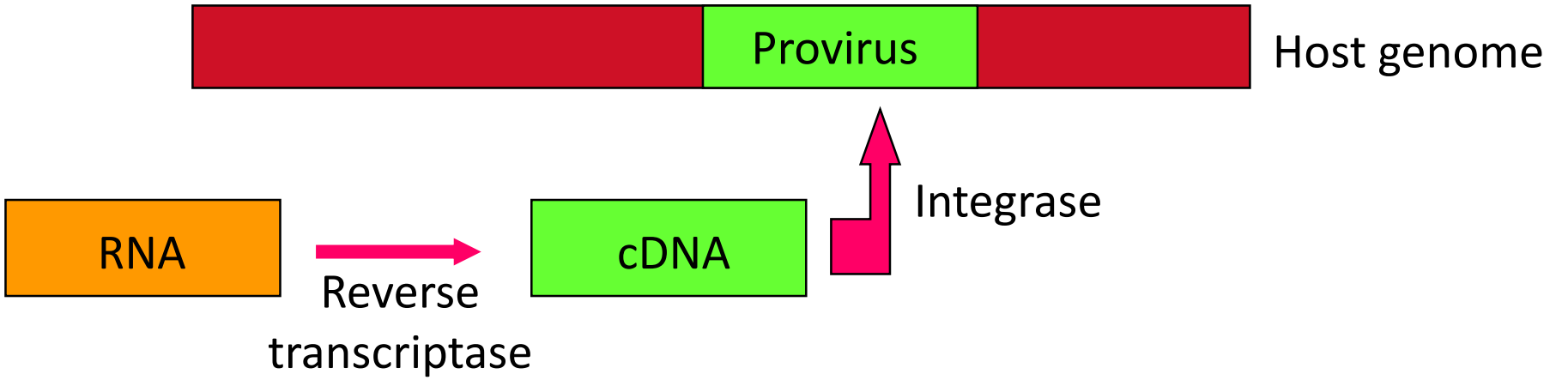
Progressive FeLV

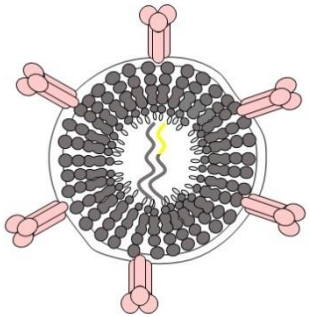
11/200 (5.5%) – published 2013[8]

3. Regressive FeLV prevalence

Country	FeLV-infected	
	Progressive infections	Regressive infections
Switzerland[9]	41/597 (7%)	61/597 (10%)
Switzerland[10]	54/445 (12%)	24/445 (5%)
UK[11]	56/465 (12%)	45/465 (10%)
Australia[12]	2/248 (1%)	3/248 (1%)
Germany[13]	9/495 (2%)	6/495 (1%)

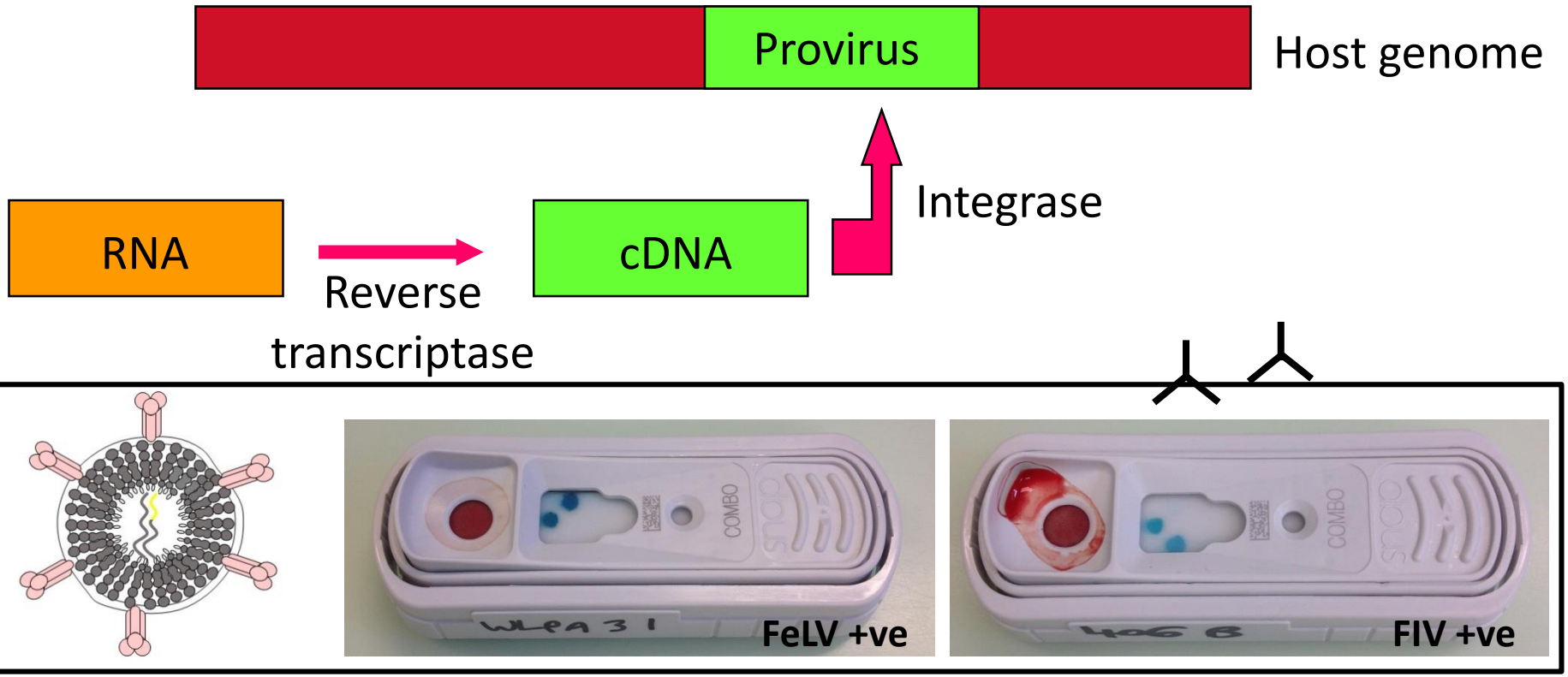
4. FIV/FeLV – A review of diagnosis





FeLV/FIV 1. Antigen testing (FeLV)

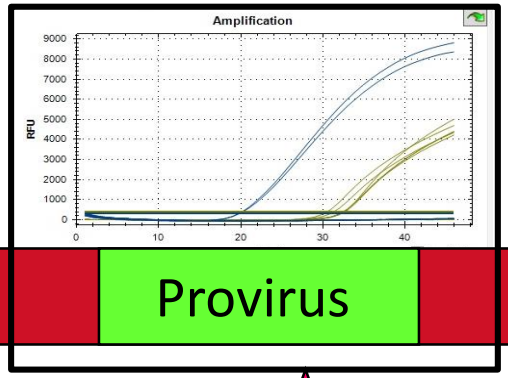
4. FIV/FeLV – A review of diagnosis



FeLV/FIV | 1. Antigen testing (FeLV) | 2. Antibody testing (FIV)

4. FIV/FeLV – A review of diagnosis

3. PCR testing (FIV and FeLV)



Provirus

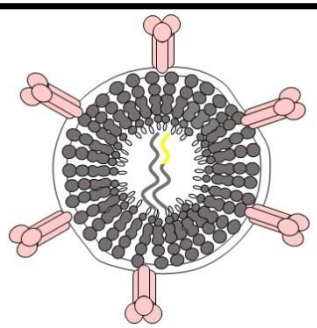
Host genome

RNA

Reverse transcriptase

cDNA

Integrase

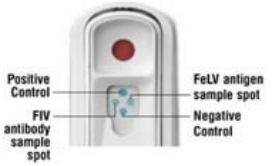


FeLV/FIV

1. Antigen (Ag) testing (FeLV)

2. Antibody (Ab) testing (FIV)

4. Challenges with diagnosis – FIV infection



IDEXX LABORATORIES

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Test	Target Abs	Can differentiate FIV-vaccinated and FIV-infected?[14]
SNAP Combo®	p15, p24 +/- gp40	✗
Witness®	gp40	✓
Anigen Rapid®	gp40	✓

FIV testing – Take home message #1

In areas where FIV vaccination is practiced (currently Australia, New Zealand and Japan), and particularly in shelters where FIV vaccination history is often unknown, screening for FIV infection should be performed using Witness® or Anigen Rapid® FIV test kits[14,15]

BUT beware false-positives can occur for 6 months following primary FIV vaccination (so confirm with FIV PCR testing)[16]

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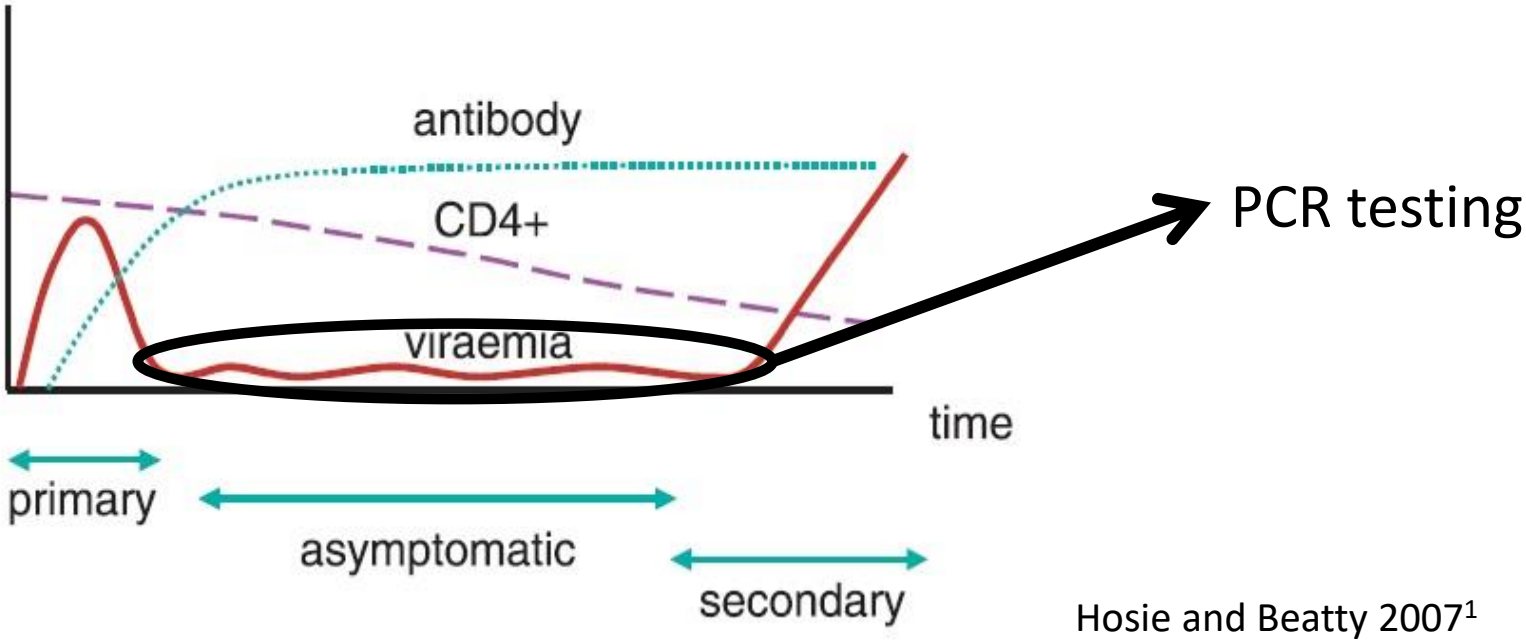
Image courtesy of Lynda du Cross

4. Challenges with diagnosis – FIV infection

FIV antibody-testing (with Witness and Anigen Rapid) is <u>more reliable</u> than PCR testing

2/5 FIV-vaccinated/FIV-infected cats required multiple IDEXX FIV RealPCR™ testing to get a positive result (i.e. some false-negative PCR results)



Hosie and Beatty 2007[1]

4. Challenges with diagnosis – FIV infection

How?

A recent study has shown that the FIV antibodies detected by the test kits are specific to FIV infection.

What does this mean?

A positive FIV test indicates infection only. Any antibodies present due to vaccination will not produce a positive result.

Why use ?

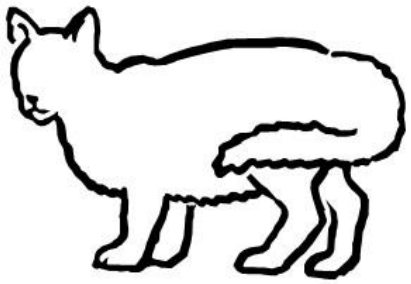
Other test kits can produce false positive results due to vaccination, which can cost time and money, but most importantly, can affect treatment of the patient.

	Vaccinated	Vaccinated and Infected	Infected
	-	+	+
Other kits	+	+	+

Encourage companies to invest in independent research by asking questions and thinking critically!

4. FeLV diagnosis

Outcomes of FeLV exposure:



1. Abortive infection
2. Progressive infection
3. Regressive infection

	Antigen (p27)	PCR
1. Abortive (20-30%)	✗	✗
2. Progressive (30-40%)	✓	✓
3. Regressive (30-40%)	✓ then ✗	✓

4. Challenges with diagnosis - progressive FeLV

IDEXX Laboratories, SNAP FIV/FeLV Combo®

Sensitivity (progressive FeLV) 98.6%
Specificity (progressive FeLV) 98.2%[17]

***** What is the positive predictive value? (PPV) *****

4. Challenges with diagnosis - progressive FeLV

Prevalence	2.0%		
Sensitivity	98.6%		
Specificity	98.2%		
Test population	1000		
	Test positive	Test negative	Total
True positive	19.72	0.28	20
True negative	18	962.36	980
Total	37.36	962.64	1000
PPV/NPV	52.8%	100.0%	

https://uwsheltermedicine.com/library/resources/positive-and-negative-predictive-value-calculator-for-diagnostic-testing

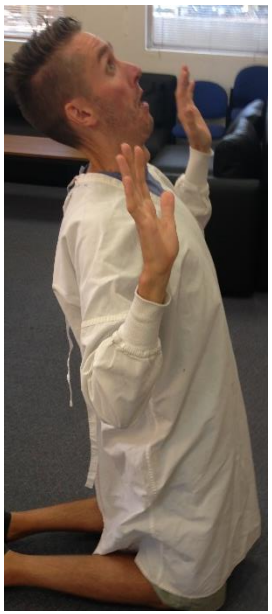
4. Challenges with diagnosis - progressive FeLV

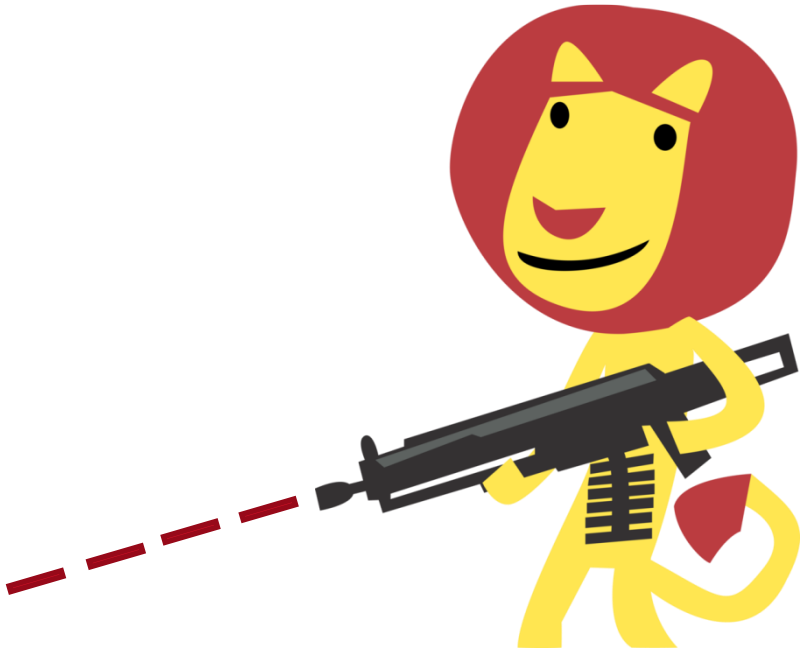
Prevalence	5.5%		
Sensitivity	98.6%		
Specificity	98.2%		
Test population	1000		
	Test positive	Test negative	Total
True positive	54.23	0.77	55
True negative	17	927.99	945
Total	71.24	928.76	1000
PPV/NPV	76.1%	99.9%	

https://uwsheltermedicine.com/library/resources/positive-and-negative-predictive-value-calculator-for-diagnostic-testing

FeLV testing – Take home message #2

A positive FeLV result with rapid (point-of-care) testing should ALWAYS be followed by PCR testing[5]





‘Randy’
No FeLV PCR?

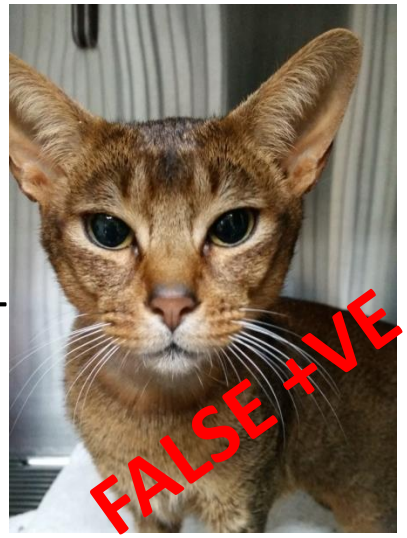
FeLV testing: examples of false-positives

Sick animal – ‘Marcus’

Sick animal (2 different kits) – ‘Skittles’

Healthy animal – ‘Claudia’

Sick animal after blood transfusion – ‘Ranger’



With thanks to Drs Marshall Thornton, Christine Cole and Katherine Briscoe for the images

FeLV testing: examples of false-positives

Original Article

Journal of Feline Medicine and Surgery
15(12) 1063–1069

DOI: 10.1177/1098612X13488384
jfms.com
SAGE

Prevalence and risk factor analysis of feline haemoplasma infection in New Zealand domestic cats using a real-time PCR assay

Kathryn S Jenkins[1], Keren E Dittmer[1], Jonathan C Marshall[1] and Séverine Tasker[2]

Abstract

Haemotropic mycoplasmas (haemoplasmas) are small epierythrocytic bacteria that have the potential to cause severe, life-threatening haemolytic anaemia. The aim of the current study was to evaluate feline haemoplasma prevalence using real-time polymerase chain reaction (PCR) from a convenience sample of New Zealand domestic cats, including blood film examination and a risk factor analysis. DNA was extracted from 200 blood

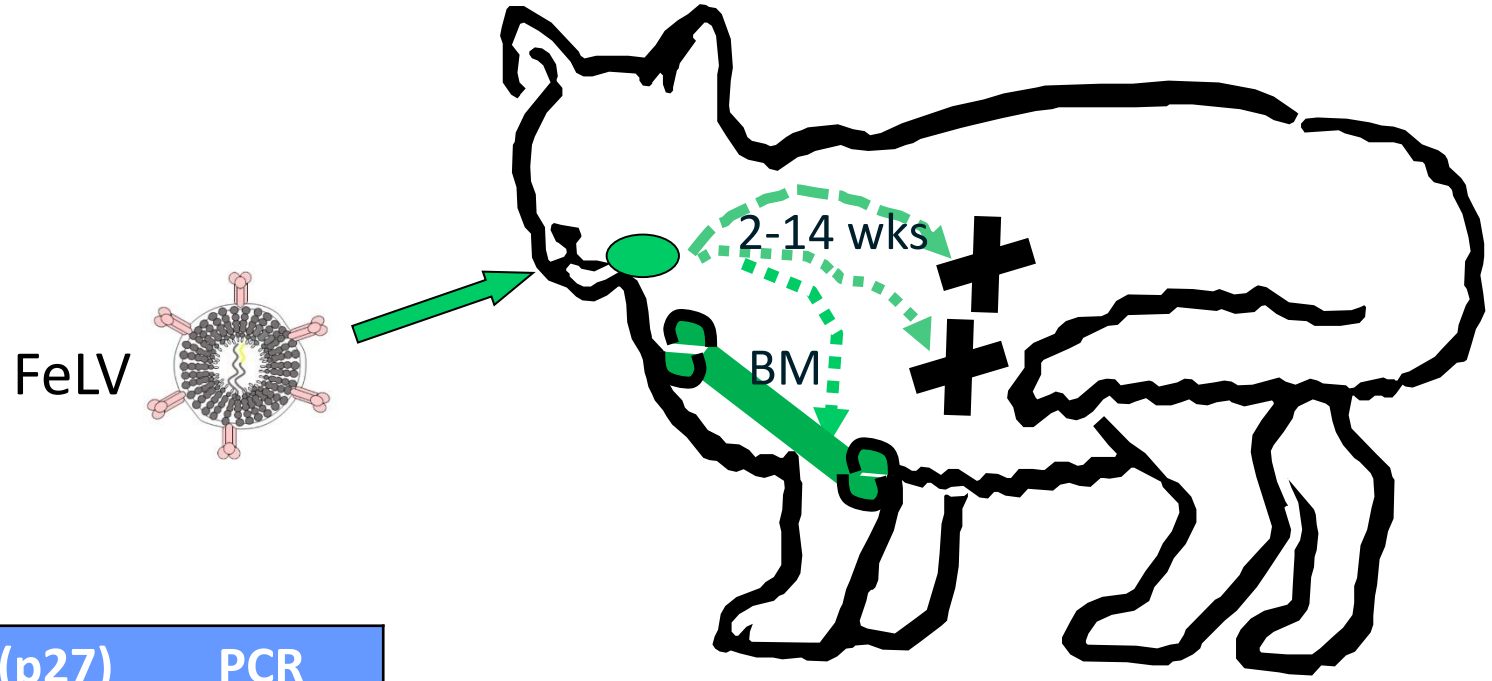
Progressive FeLV

11/200 (5.5%) cats from this study were FeLV antigen positive[8]

None of these 11 samples were FeLV PCR positive (unpublished)

4. Challenges with diagnosis - regressive FeLV

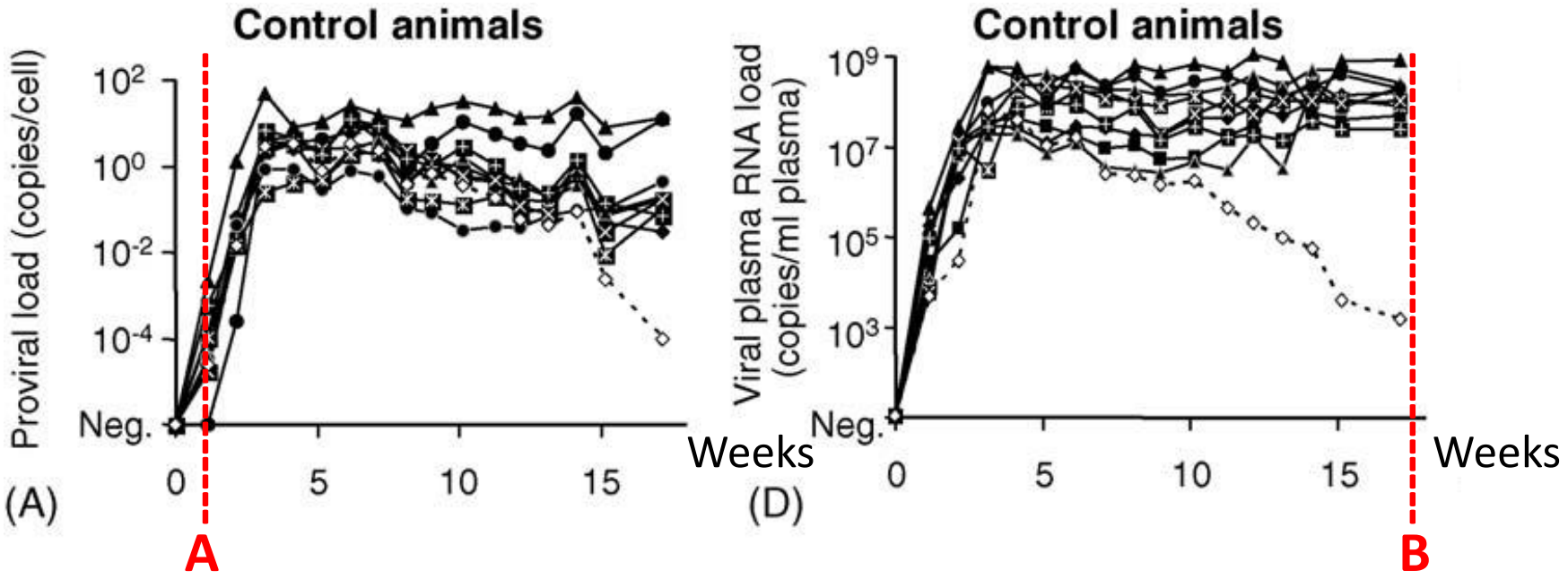
Outcomes of FeLV exposure: REGRESSIVE infection



Antigen (p27)	PCR
✓ then ✗	✓

Image courtesy of Prof Vanessa Barrs

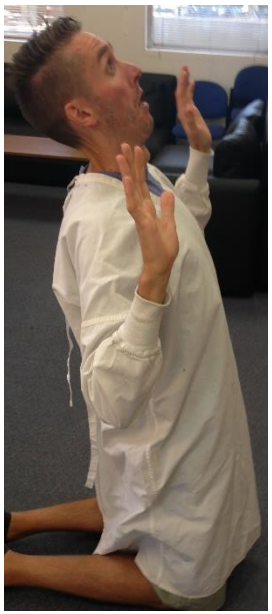
4. Challenges with diagnosis - regressive FeLV

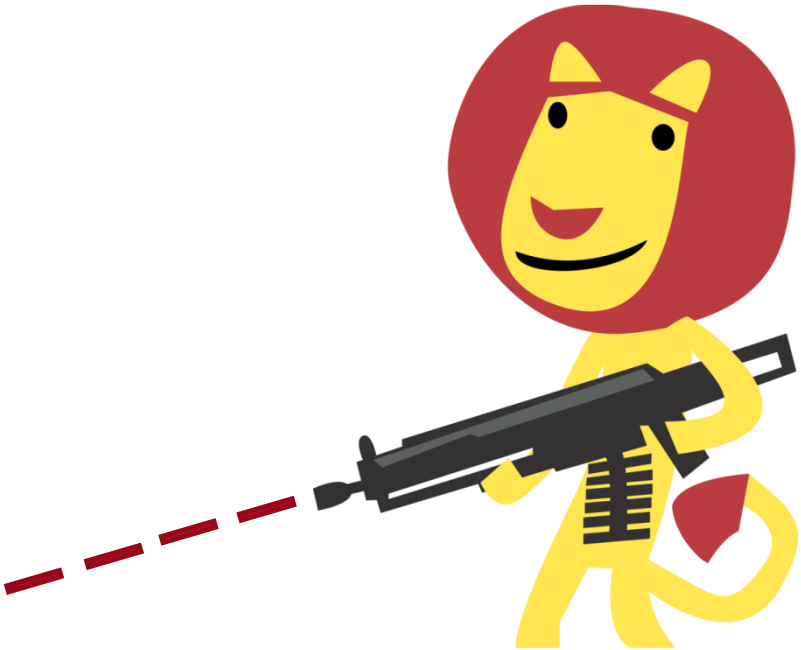


No significant difference was found in the very early phase of the infection between cats that subsequently became progressively FeLV infected and cats that became regressively FeLV infected[18]

FeLV testing – Take home message #3

A positive FeLV result with rapid (point-of-care) testing should ALWAYS be followed by PCR testing[5]





‘Randy’
No FeLV PCR?

And if both are positive, FeLV point-of-care testing should be repeated 3-4 months later[5]

4. Challenges with diagnosis - regressive FeLV

Image courtesy of Dr Duana Mc Bride

10 uninfected cats transfused with blood from regressively FeLV infected cats (Ag-, PCR+)

2/10 of the transfused cats developed progressive FeLV infection, 6/10 developed regressive FeLV infection[19]

FeLV testing – Take home message #4

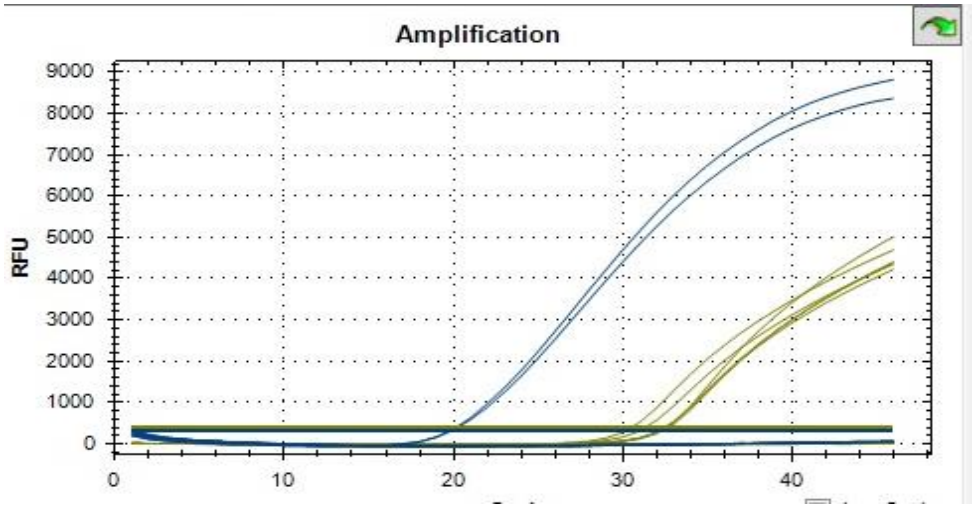
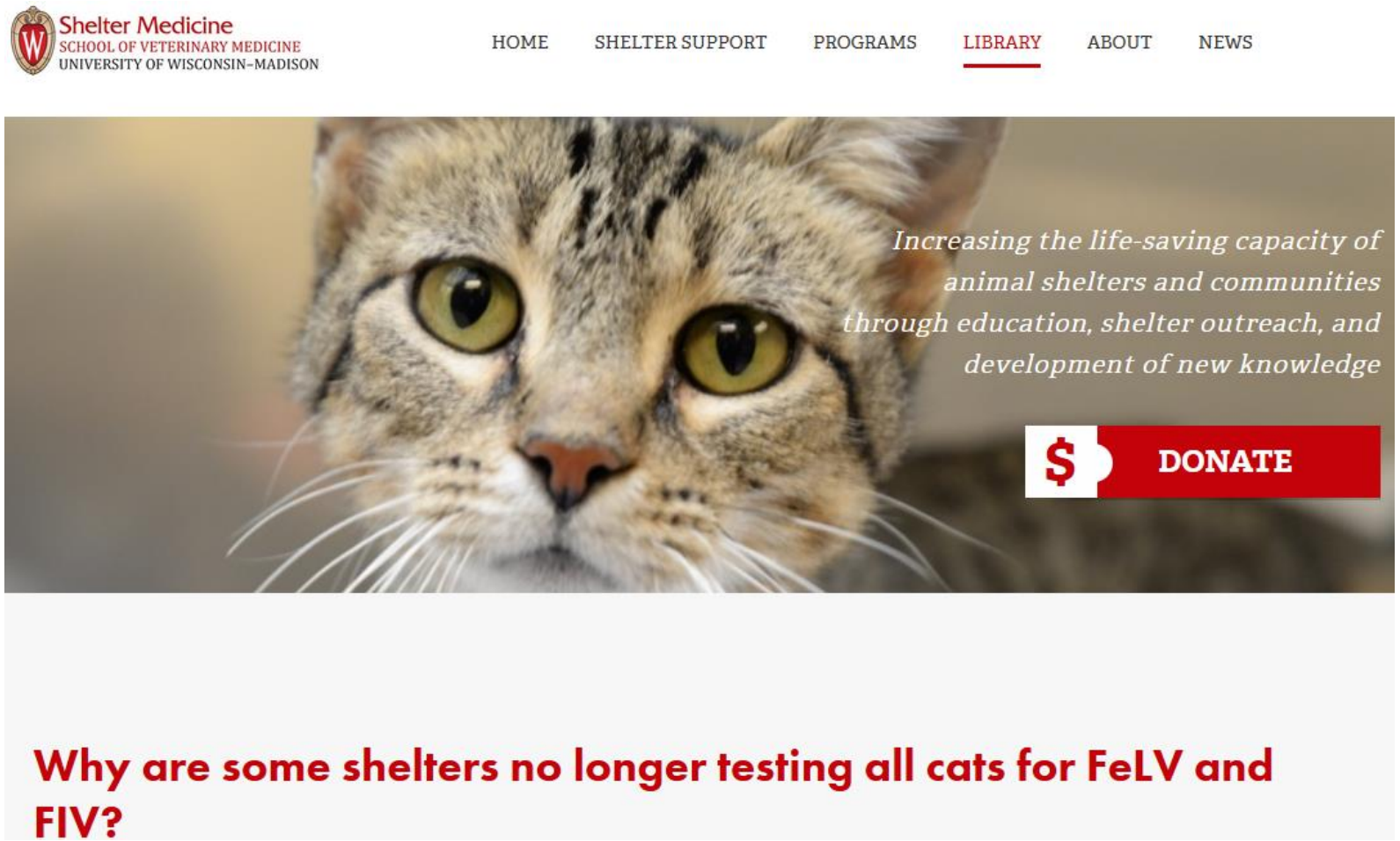


Image courtesy of Dr Duana Mc Bride

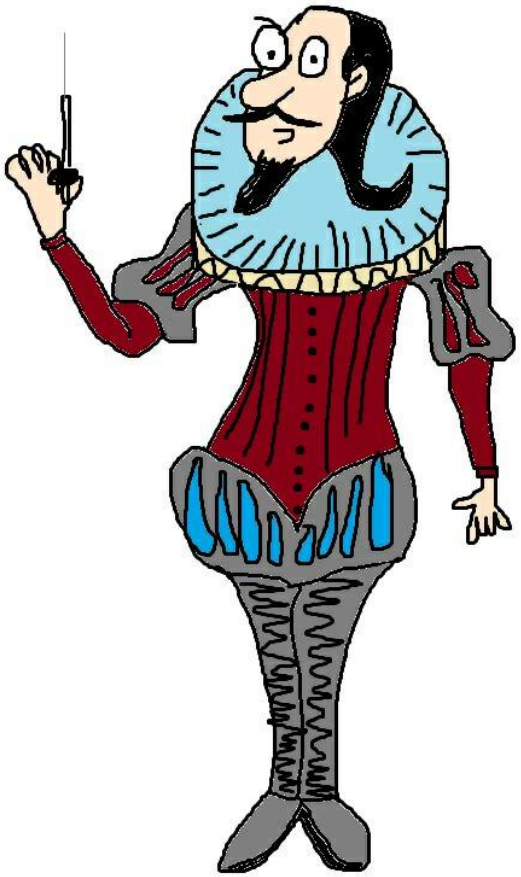
FeLV Ag and PCR testing of all blood donor cats should be performed![20]

4. Challenges with FIV and FeLV diagnosis



https://uwsheltermedicine.com/library/resources/why-are-some-shelters-no-longer-testing-all-cats-for-felv-and-fiv

5. FIV and FeLV vaccination



Q - To vaccinate or not to vaccinate?

5. FIV and FeLV vaccination

GUIDELINES FOR THE VACCINATION OF DOGS AND CATS

**COMPILED BY THE VACCINATION GUIDELINES GROUP (VGG)
OF THE WORLD SMALL ANIMAL VETERINARY ASSOCIATION (WSAVA)**

M. J. Day[1], M. C. Horzinek[2], R. D. Schultz[3] and R. A. Squires[4]

WSAVA Vaccination Guidelines 2015[21]

Both FIV & FeLV vaccination are considered ‘non-core’ (AKA optional)

5. FIV and FeLV vaccination

Things to consider:

- Individual risk factors for the cat
- Local prevalence
- Safety of the vaccine
- Vaccine effectiveness

- FIV vaccine – 56% (Australian field study)[22]
- Jarrett and Ganiere (1996) – combined efficacy for Leucogen was 63%[23]

Jarrett & Ganiere (1996)	Leucat	12	8	−14.3%
	Leucogen	12		52.4%
	Leukocell 2	12		4.8%
Jarrett & Ganiere (1996)	Leucogen	6	6	80%

5. FIV and FeLV vaccination

Things to consider:

- Recommend FIV/FeLV testing prior to annual vaccination using a rapid (point-of-care) test kit to look for ‘vaccine breakthroughs’

Further reading

AUSTRALIAN VETERINARY JOURNAL
AUSTRALIA'S PREMIER VETERINARY SCIENCE TEXT
SMALL ANIMALS

REVIEW

Diagnosing feline immunodeficiency virus (FIV) and feline leukaemia virus (FeLV) infection: an update for clinicians

ME Westman,[a*] R Malik[b] and JM Norris[a]

With the commercial release in Australia in 2004 of a vaccine against feline immunodeficiency virus (FIV; Fel-O-Vax FIV®), the landscape for FIV diagnostics shifted substantially. Point-of-care (PoC) antibody detection kits, which had been the mainstay for diagnosing FIV infection since the early 1990s, were no longer considered accurate to use in FIV-vaccinated cats, because of the production of vaccine-induced antibodies that were considered indistinguishable from those produced in natural FIV infections. Consequently, attention shifted to alternative diagnostic methods such as nucleic acid detection. However, over the past 5 years we have published a series of studies emphasising that FIV PoC test kits vary in their methodology, resulting in differing accuracy in

Structure of FIV and FeLV

Both feline immunodeficiency virus (FIV) and feline leukaemia virus (FeLV) are retroviruses with a similar three-layered structure (Figure 1). The innermost layer consists of the genome–nucleoprotein complex, which contains the viral genetic material (two copies of single-stranded RNA), enzymes essential for viral activity (including integrase, reverse transcriptase and protease) and nucleocapsid protein; the middle layer consists of capsid protein surrounding the genome–nucleoprotein complex, which in turn is surrounded by a matrix protein shell; and the outer layer is the envelope from which glycoprotein 'spikes' project.[1–5]

SMALL ANIMALS

Westman M, Malik R, Norris J. Diagnosing feline immunodeficiency virus (FIV) and feline leukaemia virus (FeLV) infection: an update for clinicians. Aust Vet J. 2019; 97(3): 47-55.

Acknowledgements

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AVA AUSTRALIAN VETERINARY ASSOCIATION

AUSTRALIAN SMALL ANIMAL VETERINARIANS

FELINE HEALTH RESEARCH FUND

Australia Awards Scholarships

Australian Companion Animal Health Foundation

AUSTRALIAN AND NEW ZEALAND COLLEGE OF VETERINARY SCIENTISTS

ENDEAVOUR Scholarships and Fellowships

Acknowledgements

Virbac

Shaping the future of animal health

www.petsinthepark.org.au

Pets in the Park

Helping the homeless care for their pets

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Quiz!

Questions:

1. According to the Jenkins *et al.* study published in 2013, what is the prevalence of FIV infection in New Zealand?

2. According to the Jenkins *et al.* study published in 2013, what is the prevalence of progressive FeLV infection in New Zealand?

3. Witness and Anigen Rapid FIV test kits can differentiate between FIV-vaccinated and FIV-infected cats (Y/N)

4. A regressively FeLV-infected cat by definition tests Ag ___ and PCR ___ (fill blanks +ve or -ve)

5. A low positive predictive value (PPV) and false-positive test results are particularly a concern in ___ disease prevalence populations (low or high)

6. What FIV and FeLV testing should be performed on blood donors?

7. FIV and FeLV vaccination are considered ___ vaccines by the WSAVA?

Image courtesy of Lynda du Cross

Thank you for listening!

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