Vaccination & In-house Diagnosis of FeLV and FIV

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Pathobiology, Veterinary Medicine, KKU
Content

- The diseases
  - Feline Leukemia virus
  - Feline Immunodeficiency Virus

- Vaccine
  - WSAVA guideline
  - Core-, Non-core- and Not-recommended vaccine

- In-house DX for FeLV & FIV
The Diseases

Feline Leukemia Virus
Feline Immunodeficiency Virus
Feline Retroviruses

- Feline Leukemia Virus (FeLV)
- Feline Immunodeficiency Virus (FIV)
### Epidemiology in Thailand

<table>
<thead>
<tr>
<th>Year</th>
<th>Cats</th>
<th>FeLV%</th>
<th>FIV%</th>
<th>FeLV+FIV%</th>
<th>Refs</th>
</tr>
</thead>
<tbody>
<tr>
<td>1988</td>
<td>653</td>
<td>0.9</td>
<td></td>
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<td>Nilkumhang et al., 1988</td>
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<td>1994</td>
<td>28</td>
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<td>Nilkumhang et al., 1994</td>
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<td>1998</td>
<td>145</td>
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<td>32.1</td>
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<td>Pusoonthornthum et al., 1998</td>
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<tr>
<td>2003</td>
<td>115</td>
<td>5</td>
<td>6</td>
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<td>Lister &amp; Nilkumhang, 2004</td>
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<td>2009</td>
<td>746</td>
<td>24.5</td>
<td>20.1</td>
<td>10.1</td>
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<tr>
<td>2013-14</td>
<td>777</td>
<td>16.5</td>
<td>5.4</td>
<td>3.5</td>
<td>Suradhat et al.</td>
</tr>
</tbody>
</table>

Modified from Suradhat et al

Malaysia (2010) FeLV 31.3%, FIV 12.2%, Co-infec 4.3%
Feline Leukemia Virus: FeLV

- Gammaretrovirus
  - 2 key antigens:
    - \( p27 \) (core protein nucleocapsid) : Antigen detection
    - \( gp70 \) (envelope protein), 70b/c and FOCMA are targets for vaccination

Core Proteins
(p10, p12, p15, p27, RT)

Budding Virus/Virus
(Spike – p15e, Knob – gp 70), viral envelop antigens

Adapted from infectious Diseases of the Dog and Cat, 3rd ed. Ed Green. Fig. 13-1 and 13-4.
FeLV

- Risk factors: Outdoors, Aged / Young, Male
- Transmission:
  - Bite wound, Grooming, Trans-placental & Nursing
- Varied clinical presentations
  - Lymphoma, Anemia
- Prevalence 2-30%

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### Clinical signs & key pathomechanism

<table>
<thead>
<tr>
<th>Clinical syndrome</th>
<th>FeLV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tumors</strong></td>
<td>62-times T cell lymphoma</td>
</tr>
<tr>
<td><strong>Bone marrow suppression</strong></td>
<td>Common Anemia, Thrombocytopenia, Neutropenia, Pancytopenia</td>
</tr>
<tr>
<td><strong>Neurologic disorders</strong></td>
<td>Rare</td>
</tr>
<tr>
<td><strong>Immunodeficiency</strong></td>
<td>Common</td>
</tr>
<tr>
<td><strong>Immune-mediated dz</strong></td>
<td>Rare (IMHA)</td>
</tr>
<tr>
<td><strong>Stomatitis</strong></td>
<td>Common</td>
</tr>
</tbody>
</table>

*Modified from Hartmann 2012*
FeLV

Pathogenesis & Pathology

- Oral/pharyngeal lymphoid-associated tissues
- Monocyte & Lymphocyte → Peripheral tissues

  Infected but unable to detect viral Ag / cultivate virus in blood

Regressive infection

+ Immune response
  - Limit viral replication
  - Less shedding
  - +/- Dz

Progressive infection

Insufficient immunity

+++ viral replication:
  - lymphoid tissues, bone marrow, mucosal & glandular epithelial tissues
  - Shed via saliva
  - Dz
ORONASAL Infection (Saliva)

Infection is ‘ABORTED’ NO VIREMIA (uncommon)

Viremic phase 3-6 weeks (<16 weeks)

- Local lymphoid tissue
- Circulating monocyte
- Systemic lymphoid tissue
- Bone marrow

Infection is REGRESSIVE (common)

Viremic Phase if extended beyond 16 weeks Persistent Viremia is expected

Virus contained in Bone marrow Lymphocytes (Latent Infection)

Infection is PROGRESSIVE (less common)

REACTIVATION of VIREMIA is possible
Risk may decline with age

Healthy Cat
Cat clinically healthy based on physical examination

Sick Cat
Cat with clinical signs and/or clinico-pathological findings suggestive of FeLV infection
FeLV: Immunity, Prevention & Control

- Vaccination
  - Not recommended in ag+ or virus+ cat
  - Non-core vaccine

- Testing and prevention of virus spread
  - Removal?

- Sanitary
  - Cleaning with common disinfectant

- Confined, frequent health check

- Tx with corticosteroid or immune suppressive drugs should be used with caution
Feline Immunodeficiency Virus; FIV

- Orthoretrovirinae, Lentivirus

- progressive immune suppression → opportunistic infections

- Asymthomatic → Sick
  - 1. Acute stage: Lymphadenopathy & Fever
  - 2. Subclinical stage: progressive loss of immune function, opportunistic infections, neoplasia
  - 3. Terminal stage: Opportunistic bacterial and fungal infections (mouth, periodontal tissue, cheeks, and tongue), chronic respiratory disease
FIV

- Risk factors
  - Free-roaming, male, aged cat
  - Colostrum & milk

- Transmission:
  - Bite wound, Queen to kittens, Sexual transmission

- Decline in CD+ T cell & Progressive immune dysfunction

- Incubation period: years
  - And remain infected for life
  - Antibody within 2 weeks post-infection
    - *Unable to differentiate* Vac-Ab and Infect-Ab
FIV: Immunity, Control

- Endemic worldwide
  - Higher prevalence in sick cats (vs. healthy)
  - Generally 5-12% prevalence in sick cats
  - 3-4% in healthy cats, with significant variations between countries
  - Can be up to 30% in some groups of cats (e.g. roaming cats)

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FIV: Immunity, Control

- Vaccination: NOT recommended/WSAVA

- Vaccination induces production of antibodies indistinguishable from those developed in response to FIV infection, and interferes with antibody-based FIV diagnostic tests for at least a year following vaccination

- Test & Removal program?
Feline Vaccination Program

Update from WSAVA
Vaccine – Cat-Client & Vet

Vaccine
- Core
- Non-core
- Not-recommended

Cat
- Individual protection
- Herd Immunity

Client
- Cost of preventive medicine
- Annual Health Check
Vaccine – Cat-Client & Vet

Cat
• Individual protection
• Herd Immunity
Individual protection

Vaccination

- Humoral Immunity
  - Protect & Reduce severity

- Cell-mediated immunity
- Memory cells
Herd immunity

Vaccinated > 75%
Non-vaccinated
Herd immunity

Vaccinated

Non-vaccinated
Vaccine – Cat-Client & Vet

Vaccine
- Core
- Non-core
- Not-recommended

Client
- Cost of preventive medicine
- Annual Health Check
Feline vaccination guideline_ WSAVA 2010 & 2015

Core vaccine
- Global significant
- Legislation

Non-core vaccine
- Geographic location
- Lifestyle
- Exposure risk

Not-recommended
- Few Scientific supports
- Interfere with diagnostic test
Feline vaccination guideline_ WSAVA 2010 & 2015

Core vaccine
- Feline Panleukopenia Virus
- Feline Calicivirus
- Feline Herpesvirus-1
- Rabies* (for ASIAN)

Non-core vaccine
- Feline Leukemia virus (FeLV)
- *Chlamydia felis*
- *Bordetella bronchiseptica*

Not-recommended
- Feline Immunodeficiency Virus
- Feline Infectious Peritonitis Virus
GUIDELINES FOR THE

CE Vpat

13 ชม.

WSAVA2010 Vaccination Guideline ฉบับแปลภาษาไทย
โดย ผศ.น.สพ. ดร.วิน สุรเชษฐพงษ์ และ ค.สพ.ญ. ดร.สันนิทตา สุรทัดต์
ดาวน์โหลดได้ที่
http://www.vpathai.org/priv.../WSAVA-2010-guideline_Thai.pdf
... ดูเพิ่มเติม

www.vpathai.org

RECOMMENDATIONS ON VACCINATION FOR ASIAN SMALL ANIMAL PRACTITIONERS: A

REPORT OF THE WSAVA VACCINATION GUIDELINES GROUP
• Feline Panleukopenia Virus
• Feline Calicivirus
• Feline Herpesvirus-1
• Rabies
• Feline Leukemia virus (FeLV)

Feline Immunodeficiency Virus
We should aim to vaccinate every animal with core vaccines, and to vaccinate each individual less frequently by only giving non-core vaccines that are necessary for that animal.
# Feline vaccination Program

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>8 wks</th>
<th>12 wks</th>
<th>16 wks</th>
<th>Booster</th>
</tr>
</thead>
<tbody>
<tr>
<td>Panleukopenia virus, Feline calici, Feline herpesvirus-1</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>q1 year (q3 years)</td>
</tr>
</tbody>
</table>
Remarks

- Use of MLV vaccines is not recommended in:
  - pregnant cats
  - FeLV and/or FIV infected cats
  - Kitten < 4 weeks

- Using international quality-assured MLV vaccines
  - And 3-year licensed DOI

- Using non-core vaccines based on risk of infection
**Remarks (cont.)**

- Minimize adjuvanted vaccines
  - Decrease risk of Feline Injection Site Sarcoma (FISS)

- Site of vaccination

  - ✗ Interscapular region
  - ✓ Skin of the lateral thorax or abdomen
    - ✓ Different site on each occasion
  - ✓ Notify every suspected FISS
Vaccine – Cat-Client & Vet

Client
- Cost of preventive medicine
- Annual Health Check
Client

- Annual check-up and individual healthcare plan
  - Not only for vaccination
  - Age, Breed, Health status, Environment, Lifestyle and travel habits
  - Yearly check for risk diseases
  - Yearly check Protective antibody: Feline Panleukopenia
In-House Tests

FeLV & FIV
Vaccine – Cat-Client & Vet

- Vaccine
  - Core
  - Non-core
  - Not-recommended

- Cat
  - Individual protection
  - Herd Immunity

- Client
  - Cost of preventive medicine
  - Annual Health Check

In-house test kits
Kits usages

- Diagnosis
- Vaccination
- Annual health check & individual health plan
- Blood donor
- Database for risk-based vaccination program
WITNESS® FeLV-FIV

1 drop of sample: anticoagulated whole blood (EDTA, heparin), serum or plasma

3 drops of buffer solution

Result reading and interpretation*: 10 minutes later

* All test result should be interpreted in light of the clinical context (pet history and physical examination) and the knowledge of the disease pathogenesis.

* Pipette and buffer drops should be applied vertically
Clinical diagnosis plus viral antigen or antibody screening:
- RIM™ (Rapid Immuno-Migration™: WITNESS® FeLV-FIV)

Detection of Feline Leukemia Virus Antigen
Identifies p27 core protein of Feline Leukemia virus
- Vaccine and maternally derived antibodies do not influence FeLV Ag tests results.

Detection of Feline Immunodeficiency Virus Antibodies
Identifies anti-FIV antibodies in the blood using a synthetic FIV gp40 peptide from the transmembrane region
- Vaccine and maternally derived antibodies do influence FIV Ab tests results.

Anticoagulated whole blood (EDTA, heparin), serum or plasma

FIV: box of 10 tests; FeLV-FIV combo: box of 5, 10 or 30 tests
WITNESS® FeLV

Rapid Immuno Migration (RIM™) technology, using an antibody directed against an epitope of the p27 core protein.
The WITNESS® FIV test is a simple test, based on Rapid Immuno Migration (RIM™) technology, using a synthetic gp40 peptide from the FIV transmembrane region.
WITNESS FeLV-FIV
New Look + Updates

Building on 14 years of market experience...
To ensure the quality and consistency of the product, two test components were changed related to:

1. the internal gold conjugate,
2. and the chase buffer.

The intent of these changes was to improve sample flow/migration.

Because of the strong performance with laboratory and field testing the biologics (antibodies) are unchanged.

Data on file. USDA submission document October 2013, Zoetis Inc.
Test should be interpreted in light of

- **The clinical context**
  - sick or healthy animal
  - disease prevalence / risks

- **Its procedure**
  - was everything done ok (volume, reading time, etc..) ?
  - problem due to the manipulation / reading?

- **The disease pathogenesis**
  - Including age/vaccination status for FIV
Positive test results should be confirmed, especially in asymptomatic and low-risk cats (low prevalence).

Kittens may be tested at any age.

Vaccine and maternally derived antibodies do not influence FeLV Ag tests results.

WITNESS® FeLV – Interpretation

Healthy Cat
Cat clinically healthy based on physical examination

Sick Cat
Cat with clinical signs and/or clinico-pathological findings suggestive of FeLV infection

- WITNESS FeLV

High risk cat
(e.g. in contact with known FeLV+ cat) highly likely non-infected but cannot rule out recent infection

Low risk cat

Repeat WITNESS® FeLV (>30 days)

Perform confirmatory test (VI*/PCR**)

- NOT INFECTED CAT
  • Can be vaccinated
  • Consider regular screening if cat at risk

+ INFECTED CAT
  • Take appropriate clinical decisions (potentially including euthanasia) and/or start management program (isolation, decreased stress) depending on the disease status (clinically healthy or sick cat)
  • May consider repeat screening if clinically healthy cat

- NOT INFECTED CAT

If high index of clinical suspicion, consider repeating WITNESS® FeLV

* VI: virus isolation
**PCR: polymerase chain reaction

Algorithm developed in collaboration with The Feline Centre, University of Bristol.
FIV: Diagnosis

- Clinical diagnosis plus viral/antibody screening of blood:
  - RIM™ (Rapid Immuno-Migration™: WITNESS® FIV)

Detection of Feline Leukemia Virus Antibodies

- Maternal derived antibodies can lead to false positives if antibody testing is performed in kittens up to 6 months of age
WITNESS® FIV – Interpretation
Algorithm developed in collaboration with The Feline Centre, University of Bristol

Healthy Cat *
Cat clinically healthy based on physical examination

Sick Cat
Cat with clinical signs and/or clinico-pathological findings suggestive of FIV infection

- Highly likely this is a non-FIV infected cat
  - Repeat WITNESS® FIV (>30 days)

+ If high risk of recent exposure
  - If high index of suspicion, consider confirmatory testing
  - Consider other differential diagnosis

WITNESS FIV

- Highly likely this is an FIV infected cat
  - Consider Negative and Non-infected
    - If high risk of recent exposure, consider confirmatory testing
    - Reasons for false negative tests not fully understood

+ Perform Confirmatory test (IFA**/PCR***)

- NOT INFECTED CAT
  - Consider FIV not the cause for the clinical signs in a sick cat
  - Consider other differential diagnosis

+ INFECTED CAT
  - Start FIV management
  - Treat appropriately for any underlying disease

- NOT INFECTED CAT
  - Infected Cat

* Cats under 6 months of age - antibody testing is not appropriate - can consider PCR
** IFA: indirect immunofluorescence antibody test ; ***PCR: polymerase chain reaction
Summary

• Easy to use
  – Minimal training required

• Rapid results
  – Resulting in fewer patients lost to follow-up
  – Quicker treatment for the pet

• Easy to Interpret
  – One line on right = negative
  – Two lines = positive

• Substantial shelf life at room temperatures (in most cases)

• Limited or no need for instrumentation
### WITNESS FeLV Legacy Data (1998-2007)

Note that the test was updated in 2013. Those changes are viewed in a 2014 regulatory filing and in Study Report No. 03-0078-0109, Zoetis Inc.

<table>
<thead>
<tr>
<th>Study</th>
<th>Test #1</th>
<th>Test #2</th>
<th>n</th>
<th>Sensitivity</th>
<th>95% Confidence Interval</th>
<th>Specificity</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pivotal (2006 regulatory document)</td>
<td>WITNESS FeLV</td>
<td>ELISA</td>
<td>341 Plasma</td>
<td>96.9</td>
<td>ND</td>
<td>99.6</td>
<td>ND</td>
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<tr>
<td>Pivotal (2006 regulatory document)</td>
<td>WITNESS FeLV</td>
<td>ELISA</td>
<td>556 whole blood</td>
<td>98.3</td>
<td>ND</td>
<td>99.6</td>
<td>ND</td>
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<tr>
<td>Robinson (1998)</td>
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<td>98.4</td>
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<tr>
<td>Robinson (1998)</td>
<td>WITNESS FeLV</td>
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<td>100</td>
<td>ND</td>
<td>98.6</td>
<td>ND</td>
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<tr>
<td>Hartmann (2001)</td>
<td>WITNESS FeLV</td>
<td>VI</td>
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<td>Hartmann (2007)</td>
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<td>VI</td>
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<tr>
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<td>96</td>
<td>93.9-97.9</td>
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**WB** = Western Blot

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Robinson A, DeCann K, Aitken E. et al. Comparison of a rapid immunomigration test and ELISA for FIV antibody and FeLV antigen testing in cats. **Vet Rec** 1998; 142:491–492.
WITNESS FIV Legacy Data (1998-2007) Note that the test was updated in 2013. Those changes are viewed in a 2014 regulatory filing and in Study Report No. 03-0078-0109, Zoetis Inc.

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<tr>
<td>EU Pivotal (pre2006)</td>
<td>WITNESS FIV</td>
<td>ELISA + WB for discrep</td>
<td>342</td>
<td>98.9</td>
<td>ND</td>
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<tr>
<td>EU Pivotal (pre2006)</td>
<td>WITNESS FIV</td>
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<td>99.0</td>
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<td>ND</td>
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<td>99.7</td>
<td>ND</td>
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<td>Bayesian Statistical</td>
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Vaccine: Core / Non-core /not-recommended?
Vaccine: None adjuvant?
Site of administration?
FeLV +ve ??
Acknowledgment

- Prof. Dr. Sanipa Suradhat
- Dr. Ing. Chuleeporn
- KKU Vet-Teaching Hospital

Thank You for Your Attention