UPDATE ON FIV: WHAT EVERY SHELTER NEEDS TO KNOW

Dr. Annette Litster BVSc PhD FACVSc (Feline Medicine) MMedSci (Clinical Epidemiology)
Director, Maddie’s Shelter Medicine Program
Purdue University
College of Veterinary Medicine

Presentation Outline

• What we know about FIV
  • Epidemiology – Prevalence and risk factors
  • Transmission
  • Diagnosis
  • Clinical signs
  • Vaccination
  • Antiviral treatment
• What we need more evidence about for cats naturally infected with FIV
  • Markers of disease progression
  • Optimal management – For shelters and adopters
  • Prognosis
• What we are learning from the Maddie’s Purdue FIV Study

WHAT WE KNOW ABOUT FIV
EPIDEMIOLOGY
Prevalence and risk factors

Hi I'm Charlie. I don't have FIV but I'm enrolled in the Maddie's Purdue FIV Study because I'm a match for JoJo.

Prevalence and risk factors

- **Worldwide**
  - Prevalence varies 1-14% in healthy cats; higher in sick cats, but exact % depends on study design
  - USA, 2004 – 345 veterinary clinics (3.1% of 9970 cats) and 145 animal shelters (1.7% of 8068 cats)\(^1\)
  - Canada – 4.3% of 11,144 cats tested in 2007\(^2\)

- **Major risk factors**
  - Age - Adult
  - Gender – Male (MN 4.3%, MI 3.3%) and intact status\(^1\)
  - Lifestyle –
    - Free-roaming/outdoor access
  - Shelter – Relinquished 1.4%, Stray 1.6%, Feral 3.9%\(^1\)
  - Health status – Current illness (6.1%)\(^1\)

2. Little et al., Can Vet J 2009; 50:644-648
**TRANSMISSION**

*Hi, I'm Domino. I have FIV and I'm enrolled in the Maddie's Purdue FIV Study.*

---

**Modes of FIV transmission**¹

- Most common
  - Bite wounds
- Also documented but *much* less common
  - Infected mother to kittens – during pregnancy, birth or lactation
  - Blood donation from infected cat
- Only demonstrated under laboratory conditions
  - Mucosal transmission via oral, rectal or vaginal mucosa
  - Mucosal infection requires up to 10,000x more virus than other routes
- Fomite transmission not important
  - FIV loses infectivity outside the host
  - Susceptible to all disinfectants
- Strain differences can be important


---

**Published studies of closed ‘mixed’ populations**

<table>
<thead>
<tr>
<th>FIV-positive (n)</th>
<th>FIV-negative in-contact (n)</th>
<th>In-contact cats infected (n)</th>
<th>Laboratory/ Home</th>
<th>Observation period</th>
</tr>
</thead>
<tbody>
<tr>
<td>18</td>
<td>14</td>
<td>0</td>
<td>Laboratory</td>
<td>4-14 months</td>
</tr>
<tr>
<td>16</td>
<td>31</td>
<td>0</td>
<td>Home</td>
<td>Median 2 years</td>
</tr>
<tr>
<td>5</td>
<td>68</td>
<td>0</td>
<td>Home</td>
<td>3.5 years</td>
</tr>
<tr>
<td>NR</td>
<td>20</td>
<td>1/19 FIV PCR+</td>
<td>Laboratory</td>
<td>2-4 years</td>
</tr>
<tr>
<td>9</td>
<td>17</td>
<td>6</td>
<td>Home</td>
<td>10 years</td>
</tr>
</tbody>
</table>

Maddie’s Purdue FIV Transmission Study

Aim
- To document the FIV serological status of cats living long-term in a stable multi-cat household containing FIV-positive and FIV-negative cats

Hypothesis
- That viral transmission would not occur from FIV-positive to FIV-negative cats

FIV Transmission Study - Protocol

Cats
- Stable multi-cat household of 138 cats with unrestricted access to one another
- All cats indoor except for:
  - 1 FIV-positive indoor/outdoor cat
  - 1 FIV-negative cat that escaped for a 12-month period, then returned

Testing
- FIV SNAP Test 1 - All cats FIV ELISA tested on intake
  - 8 FIV-positive – 6MN 2FS; Median age - 28 months (Range 5mths-10 years)
  - 130 FIV-negative – 71MN 59FS; Median age - 4 months (Range 2mths-12 years)
- All cats FeLV-negative
- FIV SNAP Test 2
  - ELISA testing repeated in 5 FIV-positive and 45 FIV-negative cats (SNAP Test 1 results)
  - FIV SNAP Test 2 performed median 28 months after Test 1 (Range 1-106 months)

Results of FIV SNAP Test 2

FIV ELISA test results in all 50 cats were unchanged from the FIV SNAP Test 1 results
- 5 FIV-positive cats and 45 FIV-negative cats

FeLV ELISA test results from SNAP Test 2 –
- One cat was FeLV-positive FIV-negative

A further 5 of the 50 cats were tested a 3rd time
- Results were the same as at FIV SNAP Test 2 – 1 FIV-positive cats and 4 FIV-negative cats
- The 3rd FIV SNAP test was performed median 3 months after FIV SNAP Test 2 (Range 1-45 months)
- All 5 cats were FeLV-negative
Cumulative exposure to FIV

- Cumulative exposure to FIV-positive cats (n=8) calculated for each FIV-negative cat with ≥2 FIV ELISA test results (n=45)
- Date calculations performed using XL:
  - Entry date to last negative test date for all FIV-negative cats
  - Number of days exposure to each FIV-positive cat calculated individually by comparing residence dates
  - Median cumulative exposure duration of each FIV-negative cat to FIV-positive cats = 11.98 years (3.9-13.7 years)

FIV Transmission Study – Conclusions

- Mutual grooming, mild aggression, shared food bowls, litter boxes etc. did not transmit FIV over many years of cumulative exposure in a mixed group of FIV-negative and FIV-positive cats kept in a stable multi-cat household
- Viral load and phenotype could be important in risk of transmission
- Feline behavior, virology, immunology underpin recommendations for 'mixed' housing

PATHOGENESIS

Hi I’m Clarence.
I don’t have FIV but I’m enrolled in the Maddie’s Purdue FIV Study because I’m a match for Ace. I live with Booth.
Pathogenesis

- **Acute infection**
  - Often clinically silent; perhaps mild fever, lymphadenopathy
  - Large amounts of virus circulating
  - CD4 (helper) and CD8 (cytotoxic) T-lymphocytes decline

- **Response to initial infection**
  - FIV antibody production
  - Reduced amounts of circulating virus
  - Increased CD8 T-lymphocyte count → CD4:CD8 is reduced

- **Long asymptomatic period**
  - Progressive dysfunction of immune system
  - CD4 T-lymphocyte count declines → CD4:CD8 is reduced, but does not always cause clinical signs
  - Non-regenerative anemia, lymphopenia and neutropenia can occur
  - Because cell-mediated immunity is reduced, antibody-mediated immunity can be stimulated → increased serum globulin concentration
  - FIV-positive cats respond adequately to vaccination, unless advanced disease is present

Clinical signs

- Clinical signs might take years to develop, if at all
- 41/89 FIV-positive cats enrolled in the Maddie’s Purdue FIV Study had no clinical signs at enrollment
- Asymptomatic period can last for years and clinical signs are generally seen in older cats
- Chronic inflammation
  - Oral cavity
  - Skin
- Secondary infections
  - Viral, bacterial, fungal, protozoal
- Neoplasia
  - Lymphoma
- Signs of neurological or renal disease
- Slow, progressive weight loss
Hair loss without skin inflammation

Hair loss with inflamed skin

Chronic wounds

Chronic upper respiratory tract disease

Chronic inflammation in the oral cavity

**DIAGNOSIS**

Hi I'm Huckleberry. I don't have FIV but I'm enrolled in the Maddie's Purdue FIV Study because I'm a match for Orangello. I live with Menuchin.
### Diagnosis – Antibody tests

1. **IDEXX SNAP test**
   - In-shelter test on serum, plasma or whole blood
   - Highly sensitive and specific – up to 100%\(^1\)
   - Detects antibodies to FIV core proteins - p15, p24 gag proteins
   - Use within 2 hours of opening foil pack and read in 10 mins

2. **Western blot test**
   - Send-out test
   - Have been used to confirm SNAP-positive result, but might not be as sensitive or specific as the original SNAP test!\(^1\)
   - **When** - Most cats produce antibodies within 60 days of exposure, but it may take much longer (12 months) if viral exposure is low
   - **False positive results** - Positive FIV antibody test results can sometimes occur in uninfected cats -
     - Antibody tests cannot be distinguished between antibodies that are produced in response to a natural infection and those that are
     - Produced in response to FIV vaccination (persist at least 1 year after vaccination; perhaps up to 9 years), or
     - Received by kittens (<6 months old) when their mother is FIV-positive (infected or vaccinated)

---

### Diagnosis – Antigen tests

**Tests that detect FIV viral protein**

- **IDEXX FIV RealPCR™ test**
  - Can potentially distinguish cats that are vaccinated but FIV-uninfected from FIV-infected cats
  - Relies on adequate amounts of certain amino acid sequences from field strains of FIV being 'recognized' by the test
  - Maddie’s Purdue FIV Study found that both the sensitivity and specificity of this test was approximately 94%
  - Strain information is also provided

- **Virus isolation** –
  - Performed at reference laboratories
  - ‘Reference standard’ method that takes at least 28 days to perform

---

Algorithm courtesy of IDEXX Laboratories Inc. 2009

1. Levy et al., JFMS 2008;10:300–316

---

Algorithm courtesy of IDEXX Laboratories Inc. 2009

Diagnosis – Which cats to test

- Sick cats
- Cats and kittens that will be group housed
- Cats and kittens at adoption, and a minimum of 60 days later if negative
- Cats with recent exposure to FIV-positive cat or cat of unknown FIV status, especially if there is a bite wound, and a minimum of 60 days later if negative
- Cats living with FIV-infected cats should be tested annually
- High risk cats – Outdoor, free-roaming cats, cats with bite wounds
- Before considering vaccination against FIV
- Blood donor cats

Hi I’m Menuchin. I don’t have FIV but I’m enrolled in the Maddie’s Purdue FIV Study because I’m a match for Rocky. I live with Huckleberry.

Targeting the immune system

Interferon therapy

- Recombinant feline interferon
  - Not available in US naturally infected FIV-positive cats
  - 7 naturally infected FIV-positive cats; 3 healthy, 4 unhealthy
  - 5 untreated FIV-positive cats as controls; 8-week treatment period
  - Healthy/mildly unhealthy cats remained stable (4 cats)
  - Unhealthy cats had improved clinical scores (3 cats)
- Oral human interferon – low-dose oral treatment
  - 30 naturally infected unhealthy FIV-positive cats; 24 treated, 6 placebo
  - Total 14 months treatment
  - Clinical improvement in the first 2 months
  - Treated cats had significantly longer survival than placebo
  - No change in CD4:CD8 or other hematological parameters

1. Domenech et al., Vet Immunol Immunopathol 2011;143:301-306
Targeting the virus – Anti-viral therapy

- **PMEA and Zidovudine (AZT)** – Work on Step 3
- **Zidovudine (AZT)**
  - Placebo-controlled study showed stomatitis and CD4:CD8 improved; 3 weeks treatment used
  - Can cause dose-dependent anemia; anemia often resolves in the first 3 weeks of treatment
  - AZT-resistant strains of FIV can arise
  - Not suitable for cats with signs of bone marrow suppression
- **PMEA**
  - Associated with clinical improvement in one placebo-controlled study; 3 weeks treatment used
  - Caused more severe anemia than AZT-treated cats


VACCINATION

Hi I'm Cromwell. I have FIV and I'm enrolled in the Maddie's Purdue FIV Study.
Vaccination against FIV

- Classified as a non-core vaccine by AAFP Vaccine Guidelines\(^1\)
  - AAFP Vaccine Guidelines do not recommend shelter use\(^1\)
- Might be considered for cats with high risk lifestyles
  - Outdoor cats that fight
  - Cats living with FIV-positive cats, in unstable relationships
- Antibody tests can’t distinguish between vaccinated and infected cats
- FIV vaccination must be performed in conjunction with microchipping so that cats are properly identified
- Efficacy –
  - Killed vaccine against subtypes A and D
  - Also protects against subtype B
  - Challenge studies have shown 0-82-100% ‘preventable fraction’ (proportion protected by vaccination in excess of proportion that is naturally resistant)

1. Richards et al., JAVMA 2006;229:1405-1441.

FIV Vaccination in Shelters?

FIV vaccination is not recommended for use in shelters or free-roaming cats\(^1\)

- Resources are better used elsewhere, such as spay/neuter/rabies vaccination programs
- FIV vaccination requires at least 3 doses to be effective and protection is strain-dependent
- Reduced aggression in spayed/neutered cats makes FIV transmission less likely
- Free-roaming cats are more likely to be presented as strays at veterinary hospitals and shelters where it might be assumed that they are FIV-infected

1. Levy et al., JFMS 2008;10:300-316

WHAT WE NEED MORE EVIDENCE ABOUT FOR CATS NATURALLY INFECTED WITH FIV

Hi I’m Daddy. I have FIV and I’m enrolled in the Maddie’s Purdue FIV Study.
Hi I'm Newt. I don't have FIV but I'm enrolled in the Maddie's Purdue FIV Study because I'm a match for TJ.

MARKERS OF DISEASE PROGRESSION

Factors associated with disease progression
- Clinical staging not well characterized or widely adopted
- Changes in the immune response
  - CD4 T-lymphocyte count and CD4:CD8 decline in terminal stages
  - Decreased IL-2 and increased TNF-α
- Changes in viral proteins
  - Errors occur during viral replication, resulting in ‘evolution’ of the virus over time
  - ‘Natural selection’ of viral variants that resist the host immune response and lead to progression of disease
- Viral load
  - Study of 33 naturally infected cats divided into High and Low viral load groups at enrollment
  - Survival of High viral load group was significantly reduced over the next 4 years and the viral loads increased just prior to death

1. Kraase et al., Vet Immunol Immunopathol 2010; 134:96-106
2. Goto et al., 2002 J Virol;76:10079

Hi I'm Amos. I don't have FIV but I'm enrolled in the Maddie's Purdue FIV Study because I'm a match for Stormy.

PROGNOSIS
Published evidence on survival in naturally infected cats

- Closed household with endemic FIV, FeLV and feline coronavirus observed over 10 years\(^1\)
  - 26 cats – 9/26 initially infected with FIV; 6 additional cats infected with FIV at the end of 10 years
  - FIV infection did not adversely affect life expectancy
- Retrospective Canadian study\(^2\)
  - 39 FIV-positive cats compared with 22 FIV-negative cats over approximately 8 years
  - Survival time of FIV-positive cats after diagnosis was not different from FIV-negative cats
- Studies have hypothesized that Subtype B might be more host-adapted and therefore less pathogenic\(^2\)

---

2. Ravi et al., Can Vet J 2010;51:271-276

---

OPTIMAL MANAGEMENT
For shelters and adopters

Hi I’m Tac. I don’t have FIV but I’m enrolled in the Maddie’s Purdue FIV Study because I’m a match for Wrigley.

---

Shelter considerations - Testing

- Test all cats before adoption, or before group housing
  - Repeat testing 60 days after initial test and annually for cats kept in long-term group housing
  - Test cats individually; testing representatives of a group or pooled specimens is unreliable
- TNVR Programs
  - Testing optional
- Educate prospective adopters/foster parents
  - Advise them to test a newly acquired cat and resident cats prior to co-housing if testing has not already been performed; follow up testing should be performed after 60 days
Shelter considerations - Management

- Spay/neuter all shelter cats, including FIV-positive cats
- Display FIV status
  - On the cage/room where FIV-positive cats are housed
  - On paperwork for FIV-positive cats
- House FIV-positive cats away from kittens or sick cats
  - To protect the FIV-positive cat as their immune response might be inadequate
- Educate prospective adopters/foster parents
  - House FIV-positive cats indoor-only
  - Monitor FIV-positive cats carefully for clinical signs of disease, especially if there are multiple FIV-positive cats in the same household
  - Provide regular 6-monthly wellness checks with their veterinarian
  - Consider anti-viral therapy if FIV-related disease progresses
  - Explain the possible risks of transmission to FIV-negative cats in the same household
- There is no evidence that FIV can infect humans

WHAT WE ARE LEARNING FROM THE MADDIE’S PURDUE FIV STUDY

Hi I’m Fiona. I have FIV and I’m enrolled in the Maddie’s Purdue FIV Study.

The Purdue FIV Study ‘A Tale of Two Cities’
**Study Protocol**

- Five-year controlled study of naturally-infected FIV-positive cats, starting January 1, 2010
- Data collection every 6 months for FIV-infected cats and every 12 months for age- and sex-matched FIV-negative control cats
- Clinical history, general physical exam, gingival score, serum biochemistry, CBC, CD4/CD8, UA
- Cat owners receive reports to discuss with their regular DVM
- Virology data provided by University of Glasgow Retrovirus Research Laboratory and IDEXX West Sacramento
- Necropsies performed by one pathologist at Purdue
- Memphis FIV-positive cats weighed monthly
- Three-monthly email/phone check-in with all cat owners

**Study Enrollments**

- Two-year enrollment period – January 2010-January 2012
- All cats classified as ‘Healthy’ or ‘Not healthy’ at the time of enrollment
- Healthy = No abnormalities found on a physical examination by AL
- Not healthy = One or more abnormalities found on a physical examination by AL
- All Control cats must be ‘Healthy’
- FIV-positive cats can be ‘Healthy’ or ‘Not healthy’

89 Pairs enrolled
- 38 pairs from Chicago
  - 21 Healthy FIV-positive cats
  - 3 from Shelter X
- 51 pairs from Memphis
  - 20 Healthy FIV-positive cats
  - 17 Not healthy FIV-positive cats
  - 7 from Shelter X
  - 31 Not healthy FIV-positive cats
  - 18 from Household 1
  - 29 from Household 1
Some results so far …

**Mortalities – FIV-positive cats**
- **Chicago** - 4/38 cats enrolled (10.5%) have died
  - Healthy group – 3 cats – 1 death FIV-related, 2 deaths not FIV-related
  - Not healthy group – 1 cat died of FIV-related disease from Shelter X
- **Memphis** - 34/51 cats enrolled (66.7%) have died
  - Healthy group (20 cats enrolled) – 10 cats died of FIV-related disease; 9 were from Household 1 and 1 was from a large, multi-cat household
  - Not healthy group (31 cats enrolled) – 24 cats died of FIV-related disease; all were from Household 1

**Mortalities – FIV-negative cats**
- **Chicago** – 0/51 cats have died
- **Memphis** – 4/51 cats died
  - 2/4 accidental deaths
  - 2 illness-related – One from Household X and one from large multi-cat household

**FIV-Positive Cats - Chicago and Memphis Comparisons**

<table>
<thead>
<tr>
<th></th>
<th>Chicago (n=38)</th>
<th>Memphis (n=51)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at enrollment</td>
<td>Median 4 years (1.5-11)</td>
<td>Median 5.5 years (2-10)</td>
<td>0.02</td>
</tr>
<tr>
<td>No. enrolled in Healthy group</td>
<td>55% (21/38)</td>
<td>39% (20/51)</td>
<td></td>
</tr>
<tr>
<td>No. enrolled in Not Healthy Group</td>
<td>45% (17/38)</td>
<td>61% (31/51)</td>
<td>Not significant</td>
</tr>
<tr>
<td>Time from first FIV diagnosis to enrollment</td>
<td>Median 6 months (1 month-5 years)</td>
<td>Median 2 years (1 month-8 years)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Length of time enrolled</td>
<td>Median 1.9 years (1.3-2.9 years)</td>
<td>Median 3.2 years (1.2-3.2 years)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Housed with &gt;5 cats</td>
<td>10/38</td>
<td>51/51</td>
<td>0.01</td>
</tr>
</tbody>
</table>

FIV-positive cats enrolled in Memphis are older; have been known to be FIV-positive longer; have been enrolled in the study longer; and are housed differently to FIV-positive cats from Chicago.

**More results …**

**Lymphoma**
- Of the 38 FIV-positive cats that have died so far, 13 (34.2%) have had lymphoma identified at necropsy
- 9/13 were from the Not Healthy group and 4/13 were from the Healthy group
- Lymphoma was always found in the bone marrow; often in other sites also

**Weight loss**
- Weight loss usually precedes FIV-related death
- Often >10%/month for at least 3 months

**Viral transmission**
- Three cats originally enrolled in the FIV-negative group have become FIV-positive
- All 3 had significant bite wounds and required hospitalization
- Two were from large multi-cat households with mixed populations
- One was a territorial outdoor cat
Clinical and laboratory results …

**FIV subtypes**
- FIV subtypes A, B, D and F have been identified
- No associations have been made so far between subtype and health status

**Physical exam findings**
- Stomatitis, faucitis, bowel thickening on palpation, allergic skin disease and non-inflammatory alopecia are common in the FIV-positive cats

**Lab results**
- CD4 T-lymphocyte count and CD4:CD8 are lower in FIV-positive cats at enrollment and over the study period so far

Shelter medicine research solving practical problems

- Which factors provide early information about naturally infected cats to predict outcomes so we can advise potential adopters or foster parents?
- Are there particular co-morbidities that are important and/or common in FIV-infected cats?
- Are changes to the immune response and viral loads the cause and/or the result of clinical progression?
- What are the optimal management plans for FIV-infected cats in shelters and adoptive homes?

Acknowledgements

- Maddie’s Fund
- Kristen Hall, Dr. Jamieson Nichols, Dr. John Christian, Becky Bierman, Purdue University College of Veterinary Medicine
- Amber Freiwald
- Fitzhugh B. Crews FIV Cat Sanctuary
- PAWS Chicago
- Tree House Humane Society, Chicago
- IDEXX Laboratories
- University of Glasgow Retrovirus Research Laboratory
- Drennan Animal Hospital, Cordova TN
- Animal Medical Clinic, Jasper GA
- Parkway Village Companion Animal Hospital, Memphis TN
- Maddie’s Purdue FIV Study cats and their owners
Standing on the shoulders of giants …

Dr. Jules Beatty
Dr. Cynda Crawford
Dr. Margaret Hosie
Dr. Julie Levy

Useful resources

- 2008 American Association of Feline Practitioners’ feline retrovirus management guidelines
  - Available for free download at -
    http://jfm.sagepub.com/content/10/3/300.full.pdf+html
- Feline immunodeficiency. ABCD guidelines on prevention and management
  - Use link on right of page at –
    http://www.sheltermedicine.com/node/42

QUESTION TIME

Annette Litster – catvet@purdue.edu

Hi I’m Wrigley. I have FIV and I’m enrolled in the Maddie’s Purdue FIV Study.