I have the following disclosures related to my presentation:

- Funding Sources - None
- Financial Interests - None
- Other Interests - None
I have the following additional disclosures related to my presentation:

- I am a member of the WSAVA Vaccination Guidelines Group, an independent group of academics, whose work is sponsored by MSD Animal Health.
- For attendance at several previous scientific meetings, the cost of my travel, food and accommodation has been covered by Intervet and Boehringer Ingelheim.
- I have in the past undertaken paid teaching work for Merial, Intervet and MSD Animal Health.
- I have undertaken clinical research sponsored by Intervet and Pfizer.

Spoilt for choice...

https://www.phgfoundation.org/blog/16301
**Experimental Hendra virus infection of dogs: virus replication, shedding and potential for transmission**

Dj Middleton, S S Riddell, R Klein, R Arkinson, J Haining, L Frazer, C Mottley, R Evans, D Johnson, J Pallister

First published: 26 January 2017  
DOI: 10.1111/ajv.12552

**Abstract**

**Objective**

Characterisation of experimental Hendra virus (HeV) infection in dogs and assessment of associated transmission risk.

**Methods**

Beagle dogs were exposed oronasally to Hendra virus/Australia/Horse/2008/Redlands or to blood collected from HeV-infected ferrets. Ferrets were exposed to oral fluids collected from dogs after canine exposure to HeV. Observations made and samples tested post-exposure were used to assess the clinical course and replication sites of HeV in dogs, the infectivity for ferrets of canine oral fluids and features of HeV infection in dogs following contact with infective blood.

---

**Clinical management of Brucella suis infection in dogs and implications for public health**

Dr James, G Golovsky, M Thornton, L Goodchild, M Havlicek, P Martin, MB Krockenberger, DJE Marriot, V Ahuja, R Malik, SM Mor

First published: 26 January 2017  
DOI: 10.1111/ajv.12556

**Abstract**

**Background**

Brucellosis caused by Brucella suis is a notifiable disease that has recently emerged in dogs in New South Wales (NSW). Given the potential for zoonotic transmission, euthanasia of affected dogs is recommended, but this action is not mandatory. We report the clinical management of three dogs that underwent treatment at their owner’s request.

**Case reports**

A 14-month-old spayed female crossbreed originally obtained from an urban animal shelter underwent extensive investigations in 2011-12 for lameness and back pain, culminating in decompressive laminectomy. Diagnosis of multifocal discospondylitis and spinal epydymia was made, with B. suis cultured from surgical biopsy specimens. The dog responded to long-term...
Outline of this talk

- Canine leptospirosis – including some unusual clinical presentations
- Parvovirus(es) update, including infections of cats
- An update on feline immunodeficiency and the FIV vaccine
- Update on global companion animal vaccination recommendations

vetcompass.com.au
The VetCompass system brings big data benefits and epidemiology expertise to the companion animal and equine sectors of veterinary science and patient care.

vetcompass.com.au
Outline of this talk

- Canine leptospirosis – including some unusual clinical presentations
- Parvovirus update, including infections of cats
- An update on feline immunodeficiency and the FIV vaccine
- Update on global companion animal vaccination recommendations

Canine leptospirosis – A diversity of clinical presentations
Andy – An Old Classic

- Andy, a 10-year-old male neutered Golden Retriever; lives on a farm
- Referred for icterus and azotaemia
- Presented in late Spring (after rain)
- Oliguric acute to subacute renal failure (< 2ml/kg/hour urine output)
- Developing jaundice
- Initial leptospirosis titres were all < 1:100

Andy: Creatinine and Bilirubin
Case Example: Thor
No jaundice

- 43kg, male, previously healthy German shepherd dog went into oliguric renal failure during a cold winter over the course of 1–2 weeks. “Sub-acute renal failure”.
- No jaundice
- Suburban dog, no known access to toxins
- Slight neutrophilia, mild fever

Thor: MAT Results from Day 3

<table>
<thead>
<tr>
<th>Serogroup</th>
<th>Titre</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hardjo</td>
<td>&lt; 1:100</td>
</tr>
<tr>
<td>Icterohaemorrhagiae</td>
<td>&lt; 1:100</td>
</tr>
<tr>
<td>Canicola</td>
<td>&lt; 1:100</td>
</tr>
<tr>
<td>Grippotyphosa</td>
<td>1:3200</td>
</tr>
<tr>
<td>Pomona</td>
<td>1:800</td>
</tr>
</tbody>
</table>
Leptospira interrogans serovar *grippotyphosa* infection in dogs.


Abstract

Leptospirosis attributed to infection with serovar *grippotyphosa* was diagnosed in 11 dogs. In naturally and experimentally infected dogs, a stereotypic serologic response to infection with Leptospira serovar *grippotyphosa* was detected. Although the highest serum antibody titers developed against serovar *grippotyphosa*, most dogs also had lower titers against serovars *bratislava* and *pomona*. Acute renal failure was evident in 10 dogs. One dog died prior to initiation of treatment; the remaining 10 dogs were treated with antibiotics and fluids. Two dogs were euthanized; 2 dogs recovered without clinical or biochemical evidence of residual renal dysfunction, and 6 dogs recovered but had varying degrees of renal insufficiency. Hepatic involvement appeared to be a minor component of the disease in these dogs. Our results indicate that Leptospira serovar *grippotyphosa* infection is an important problem in dogs and should be considered when evaluating a dog with renal failure.

PMID: 28837647

“Hepatic involvement appeared to be a minor component of the disease in these dogs.”

Clinical and epidemiological features of canine leptospirosis in North Queensland

KI MILLER, SP ROSS, ND SULLIVAN and NR PERKINS


Could there be temporal as well as geographic variation in seroprevalence of the different serogroups / serotypes?
Some fatal leptospirosis cases in very young dogs

Fatal leptospirosis cases in very young dogs

- Young dogs, < 6 months, with a severe hepatic and or renal syndrome
- Despite clinical severity, subtle renal changes on necropsy and histopathology
- Some with and some without jaundice
- Azotaemia more consistently present than jaundice
- Many with pulmonary oedema...

Journal of Veterinary Diagnostic Investigation
2014, Vol. 26(6) 799–804
Lepto? A respiratory pathogen in dogs???

Pulmonary haemorrhage and oedema

SAGE-Hindawi Access to Research
Veterinary Medicine International
Volume 2010, Article ID 928541, 7 pages
doi:10.4061/2010/928541
If this were not leptospirosis, what could it be?

Serial CT features of pulmonary leptospirosis in 10 dogs.
Veterinary Record February 15, 2014.
A large majority of these dogs with serious respiratory disease also have renal involvement (azotaemia)

Haemostatic dysfunction in leptospirosis
The dog whose eye changed colour...

- 7-year-old male castrated Australian shepherd dog. Lives on a farm.
- Sudden change of eye colour, plus lethargy, anorexia.

http://dogtime.com/dog-breeds/australian-shepherd/#slide/7

Initial Presentation

A

After standard treatment for leptospirosis

B

(J Am Anim Hosp Assoc 2011; 47:e162–e167. DOI 10.5326/JAAHA-MS-5590)
Again, the severe azotaemia was diagnostically crucial.

JosiAnne Arfou, DVM, Marie-Claude Blais, DVM, DACVM, Lisa Carlotto, DVM, DVeS, DACVM, Doris Sylvia, DVM, MS,

ABSTRACT

Based on previous research, cats were thought to have been resistant to the development of clinical signs following infection with Leptospira spp. This case report presents three confirmed, naturally infected clinical cases of feline leptospirosis. The cases presented were all individualized cases that were known to the vet. They were also all presented at different stages of renal insufficiency; however, they did not show any liver involvement. The authors suggest that there may be a longer incubation period in cats than dogs and recommend further research in the form of a large, clinical study. /J Am Vet Hosp Assoc 2012;49:255-260. DOI: 10.3385/JAVHAMS.0148.

Cat 1: Hyposthenuria (1.005), marked neutrophilia, azotaemia. Pomona 1:12,800. Complete response to ampicillin & doxycycline.

Cat 2: PU/PD, haematuria, RBC casts, uveitis, forelimb lameness, azotaemia. 1:1600 Pomona & Bratislava. Improved but persistent uveitis.

Cat 3: Collapsed, severe azotaemia, thrombocytopenia, large irregular kidneys, CNS signs, dyspnoea, death. Severe tubulointerstitial nephritis. Bratislava & Autumnalis 1:1600, Pomona & Icterohaemorrhagiae 1:3200

Research update • February 2017

More information on the clinical performance of the SNAP Lepto Test is now available

IDEXX, as a leader in pet health-care innovation, developed an enzyme-linked immunosorbent assay (ELISA) for Leptospira-specific antibodies that can be performed as a point-of-care SNAP test or as an IDEXX Reference Laboratories test. The SNAP-Lepto Test and the Canine leptospira spp. Antibody by ELISA provide fast results at a low cost to assist veterinarians in diagnosing this potentially life-threatening infection. Summaries of two new papers based on research sponsored by IDEXX and published in the (peer-reviewed) International Journal of Applied Research in Veterinary Medicine on the performance of the ELISA for Leptospira-specific antibodies are provided below.

Performance of a recombinant LpL32-based rapid in-clinic ELISA (SNAP Lepto) for the detection of antibodies against Leptospira in dogs.

A broad population of canine samples was tested to evaluate the overall agreement of the SNAP Lepto Test with the microscopic agglutination test (MAT).

Purpose

The purpose of this study was to compare the LpL32-based SNAP Lepto Test to the MAT for detection of anti-Leptospira spp. antibodies.

Study design

The canine serum-samples included in this study were: 460 samples submitted for MAT testing; 150 MAT-negative samples from healthy dogs residing in Alaska; 52 samples positive for anti-Borrelia burgdorferi antibodies, and samples from 28 dogs following Leptospira vaccination.

<table>
<thead>
<tr>
<th>Peak MAT titre</th>
<th>Number of samples</th>
<th>Number of SNAP Lepto test positive</th>
<th>Percent SNAP Lepto test positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>8</td>
<td>5</td>
<td>62.5%</td>
</tr>
<tr>
<td>200</td>
<td>25</td>
<td>11</td>
<td>44.0%</td>
</tr>
<tr>
<td>400</td>
<td>20</td>
<td>21</td>
<td>105.0%</td>
</tr>
<tr>
<td>800</td>
<td>53</td>
<td>57</td>
<td>109.8%</td>
</tr>
<tr>
<td>1600</td>
<td>34</td>
<td>26</td>
<td>76.5%</td>
</tr>
<tr>
<td>3200</td>
<td>13</td>
<td>18</td>
<td>138.5%</td>
</tr>
<tr>
<td>6400</td>
<td>18</td>
<td>16</td>
<td>88.9%</td>
</tr>
<tr>
<td>128000</td>
<td>32</td>
<td>29</td>
<td>90.6%</td>
</tr>
<tr>
<td>256000</td>
<td>14</td>
<td>14</td>
<td>100.0%</td>
</tr>
<tr>
<td>512000</td>
<td>18</td>
<td>18</td>
<td>100.0%</td>
</tr>
<tr>
<td>1024000</td>
<td>19</td>
<td>19</td>
<td>100.0%</td>
</tr>
<tr>
<td>Total</td>
<td>460</td>
<td>256</td>
<td>55.7%</td>
</tr>
</tbody>
</table>

Table 1. SNAP Lepto Test performance with MAT-positive samples by peak titre.
Performance of the new Idexx in-practice SNAP test

<table>
<thead>
<tr>
<th>Criteria for diagnosis</th>
<th>Number of confirmed leptospirosis cases</th>
<th>Number testing positive on SNAP Lepto Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leptospira spp. RealPCR Test positive only (MAT negative)</td>
<td>4</td>
<td>1*</td>
</tr>
<tr>
<td>MAT ≥1.800 on initial testing with no history of Leptospira vaccination</td>
<td>8</td>
<td>7</td>
</tr>
<tr>
<td>MAT titer of ≥1:3200 on initial testing with a previous history of Leptospira vaccination or an unknown vaccination history</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>4-fold increase in MAT titer between acute and convalescent samples</td>
<td>6</td>
<td>6</td>
</tr>
</tbody>
</table>

*Only known Leptospira vaccine in this confirmed leptospirosis category

Table 3. Criteria used to classify the clinical canine population having a differential diagnosis of leptospirosis

Cases may test negative early in the clinical course, seroconverting a little later
Last week

Paper

Evaluation of a rapid IgM detection test for diagnosis of acute leptospirosis in dogs

J. Lizer, M. Grahmann, H. Hapke, S. Velineni, D. Lin, B. Kohn

Recently, a lateral flow assay (LFA) for detection of leptospira-specific IgM in canine sera became commercially available in Europe. The present study aims to evaluate the diagnostic performance of this assay using canine sera from a collection of diagnostic accessions. Diagnostic sensitivity was assessed by testing 37 acute-phase and 9 corresponding convalescent-phase sera from dogs with a confirmed diagnosis of leptospirosis. Specificity was determined by testing sera from sick dogs with non-leptospiral infections (n=15) and healthy dogs with incomplete history of vaccination (n=15). During acute phase of illness, LFA scored positive for 28/37 sera with a sensitivity of 75.7% per cent while only 9/37 (24.3 per cent) samples were positive on microscopic agglutination test. The specificity of the LFA was 98.3 per cent (95/96). This test showed 97.7 and 100 per cent overall agreements with clinical diagnosis for acute-phase and convalescent-phase sera, respectively. The impact of vaccination on the LFA was also determined and vaccine-stimulated IgM responses were negative in 19/25 (76 per cent) dogs at 12 weeks post vaccination. In conclusion, the LFA is a rapid and reliable test for early detection of leptospira-specific IgM during acute phase of canine leptospirosis. However, interpretation of a positive result must be made in the context of clinical signs and vaccination history.

NEWS: Reports Show UK Dogs Are Dying From Lepto Vaccine

Leptospirosis In Dogs / By Dana Scott

UK dog owners are learning what US dog owners have suspected all along...

...the lepto vaccine is much more dangerous than we’re led to believe.

Clinical, serological and echocardiographic examination of healthy field dogs before and after vaccination with a commercial tetravalent leptospirosis vaccine

Andrea M. Speri 1,2, Sabrina Rodrigues-Campos 1, José M. Mafalda 2, Tony M. Figueira 2, Barbara Ricord 1, Claudia E. Roesch 2, Denise Hoffmann Lehmann 1,2 and Barbara Weil 1,2

Abstract

Background

Leptospirosis is a re-emerging bacterial zoonosis caused by spirochetes of the genus Leptospira. Severe disease has been reported in dogs in Europe despite vaccination with bivalent Leptospira vaccines. Recently, a tetravalent canine Leptospira vaccine (Novibacâ® L1) was licensed in Europe. The goal of this study was to investigate clinical signs, microscopic agglutination test (MAT) titres, haematology, blood biochemistry, cardiac (c) Tropinon I levels and echocardiography before and after vaccination with this tetravalent vaccine. Forty-eighty healthy dogs were prospectively enrolled and vaccinated twice, 3–4 weeks apart (T0 and T1). Before vaccination (T0) and 16–31 days after the second vaccination (T2), MAT (n = 4), haematology (n = 48), blood biochemistry (n = 36) and cTropinon I measurement (n = 29) were performed, and MAT was repeated 347–413 days after the second vaccination (T3, n = 44).

Echocardiography was performed before the first and second vaccination (T0 and T1, n = 24).

Review

Reverse Vaccinology: An Approach for Identifying Leptospiral Vaccine Candidates

Odou A. Dellagostin 1,2, André A. Grassmann 1, Caroline Rizzi 1, Rodrigo A. Schuch 1, Sérgio Jorge 1, Thais L. Oliveira 1, Alan J. A. McBride 1 and Daiane D. Hartwig 2

1 Núcleo de Biotecnologia, Centro de Desenvolvimento Tecnológico, Universidade Federal de Pelotas, Pelotas RS 96000-000, Brazil; grassmann.a@gmail.com (A.A.G.); ccrriz@gmail.com (C.R.); schuch.bioteec@gmail.com (R.A.S.); sergiojorgever@hotmail.com (S.J.); thais.laureliveira@gmail.com (T.L.O.); alan.mcbride@ufpel.edu.br (A.J.A.M.);
2 Departamento de Microbiologia e Parasitologia, Instituto de Biologia, Universidade Federal de Pelotas, Pelotas RS 96000-000, Brazil; daianehartwig@gmail.com;
* Correspondence: odor@ufpel.edu.br; Tel.: +55-53-3275-7350

Academic Editor: Christopher Woelfl
Received: 27 October 2016; Accepted: 6 January 2017; Published: 14 January 2017

Abstract: Leptospirosis is a major public health problem with an incidence of over one million human cases each year. It is a globally distributed, zoonotic disease and is associated with significant economic losses in farm animals. Leptospirosis is caused by pathogenic Leptospira spp. that can infect a wide range of domestic and wild animals. Given the inability to control the cycle of transmission among animals.
Outline of this talk

- Canine leptospirosis – including some unusual clinical presentations
- Parvovirus update, including infections of cats
- An update on feline immunodeficiency and the FIV vaccine
- Update on global companion animal vaccination recommendations
Detection of the Canine Parvovirus 2c Subtype in Australian Dogs

Lucy Woolford, Paul Crocker, Hannah Bobrowski, Trevor Baker, and Farhid Hemmatzadeh

Abstract

Canine parvovirus (CPV-2) is an important cause of hemorrhagic enteritis in dogs. In Australia, the disease has been associated with CPV-2a and CPV-2b variants. A third more recently emerged variant, CPV-2c, has not been detected in surveys of the Australian dog population. In this study, we report three cases of canine parvoviral enteritis associated with CPV-2c infection; case 1 occurred in an 8-week-old puppy that died following acute hemorrhagic enteritis. Cases 2 and 3 were an 11-month-old female entire Saint Bernard and a 9-month-old male entire Siberian husky, respectively, both of which had completed vaccination schedules and presented with vomiting or mild diarrhea only. Full genomic sequencing of parvoviral DNA from cases 1, 2, and 3 revealed greater than 99% homology to known CPV-2c variants and predicted protein sequences from the VP2 region of viral DNA from all three cases identified glutamic acid residues at the 425 amino acid residue, characteristic of the CPV-2c variant. Veterinary professionals should be aware that CPV-2c is now present in Australia, detected in a puppy and vaccinated young adult dogs in this study. Further characterization of CPV-2c-associated disease and its prevalence in Australian dogs requires additional research.

Keywords: canine parvovirus 2c, vaccine failure, full genome sequencing

Last year, October...

Too early to comment on disease associations; may be relatively benign
The major cause of death of the kittens was FPV, which accounted for 25%. This is surprising given the good uptake of FPV vaccination in the UK, especially by the cat breeding community, and 56 per cent of the kittens were pedigree.”

Who is infecting who?

FPV & CPV-2 variants
**In vivo**

- FPV-type viruses replicate efficiently in cat tissues and are shed in faeces
- FPV-type viruses replicate in thymus and bone marrow of dogs, not in gut
- CPV-2 variants all replicate efficiently in canine and feline tissues, including intestinal tissues

**CPV-2a, -2b & -2c in felids**

- Domestic cats (all 3)
- Cheetah in Namibia (2b)
- Siberian tiger in Germany (2a)
- Leopard cats in Vietnam and Taiwan (-2a and -2b)
Predominance of *Canine* Parvovirus (CPV) in Unvaccinated Cat Populations and Emergence of New Antigenic Types of CPVs in Cats

Vietnam, Taiwan

“...of feline parvovirus isolates in Vietnam and Taiwan... more than 80% of the isolates were of the canine parvovirus type, rather than feline panleukopenia virus”
CPV was detected in faeces of 32.5% (13/50) of cats in a feline-only shelter and 33.9% of cats in a mixed shelter. All healthy. No FPV!
Persistent CPV infections in cats

• Inside PBMC despite neutralizing antibodies

RAPID COMMUNICATION
Predominance of Canine Parvovirus (CPV) in Unvaccinated Cat Populations and Emergence of New Antigenic Types of CPVs in Cats

Yasuhiro Ikeda,*†, Masanari Mochizuki,† Reiko Naito,† Kazuyuki Nakamura,† Takayuki Miyazawa,* Takashi Mitani,* and Eiji Takahashi*‡


Molecular screening by PCR detects panleukopenia virus DNA in formalin-fixed hearts from cats with idiopathic cardiomyopathy and myocarditis.

Meurs KM. Fox PR. Magnon AL. Liu S. Towbin JA.

Department of Veterinary Clinical Sciences, The Ohio State University College of Veterinary Medicine, Columbus, OH 43210, USA. meurs.1@osu.edu

Cardiovascular Pathology 9(2):119-26, 2000
Molecular screening by PCR detects panleukopenia virus DNA in formalin-fixed hearts from cats with idiopathic cardiomyopathy and myocarditis

“…Panleucopenia virus was identified by PCR in 10 of 31 cats with cardiomyopathy but in none of the controls…”

HUMAN DATA

High Prevalence of Viral Genomes and Multiple Viral Infections in the Myocardium of Adults With “Idiopathic” Left Ventricular Dysfunction

Uwe Kühl, PhD, MD; Matthias Pauschinger, MD; Michel Noutsias, MD; Bettina Seeberg, MD; Thomas Bock, PhD; Dirk Lassner, PhD; Wolfgang Poller, MD; Reinhard Kandolf, PhD, MD; Heinz-Peter Schultheiss, MD

(Circulation. 2005;111:887-893.)

EV=23 (9.4%),
ADV=4 (1.6%),
**PV B19=126 (51.4%)** Parvovirus B19
HHV-6=53 (21.6%),
EBV=5 (2.0%),
HCMV=2 (0.8%),
(27.3% with multiple infections.)
Feline panleukopenia virus in cerebral neurons of young and adult cats

Mutien Garigliani1,2, Gautier Gilliaux1,2, Sandra Jolly1, Tomas Casanova1, Cédric Bayrou1, Kris Gommeren2, Thomas Fieby3, Axel Mayroy1, Benoît Ley3, Dominique Cassart1, Dominique Peeters4, Luc Poncelet4 and Daniel Desnacht2

Abstract

Background: Prenatal infections with feline panleukopenia virus (FPV) have long been known to be associated with cerebellar hypoplasia in kittens due to productive infection of dividing neuroblasts. FPV, like other panleukopenia viruses, requires dividing cells to replicate which explains the usual tropism of the virus for the digestive tract, lymphoid tissues and bone marrow in older animals.

Results: In this study, the necroscopic and histopathological analysis of a series of 28 cats which died from panleukopenia infection in 2013 were performed. Infections were confirmed by real-time PCR and immunohistochemistry in several organs. Strikingly, while none of these cats showed cerebellar atrophy or cerebellar positive immunostaining, some of them, including one adult, showed a bright positive immunostaining for viral antigens in cerebral neurons (dentate gyrus). Furthermore, infected neurons were negative by immunostaining for p21/Waf1, a cell cycle regulatory protein, while neighboring, uninfected neurons were positive, suggesting a possible survival of infected neurons into the mitotic cycle. Next-Generation Sequencing and PCR analyses showed that the virus infecting cat brains was FPV and presented a unique substitution in N51 protein sequence. Given the role played by this protein in the control of cell cycle and apoptosis in other parvoviral species, it is tempting to hypothesize that a cause-effect between this N51 mutation and the capacity of the FPV strain to infect neurons in adult cats might exist.

Conclusions: This study provides the first evidence of infection of cerebral neurons by feline panleukopenia virus in cats, including an adult. A possible re-entry into the cell cycle by infected neurons has been observed. A mutation in the N51 protein sequence of the FPV strain involved could be related to its unusual cellular tropism. Further research is needed to clarify this point.

Risks of cross-species transmission?
Outline of this talk

• Canine leptospirosis – including some unusual clinical presentations
• Parvovirus update, including infections of cats
• An update on feline immunodeficiency and the FIV vaccine
• Update on global companion animal vaccination recommendations

The protective rate of the feline immunodeficiency virus vaccine: An Australian field study

M.E. Westman a, R. Malik b, E. Hall b, M. Harris b, J.M. Norris a,∗

aFaculty of Veterinary Science, The University of Sydney, NSW 2006, Australia
bCentre for Continuing Veterinary Education, The University of Sydney, NSW 2006, Australia
∗Centre for Virus Research, The University of Glasgow, Scotland G12 9QY, United Kingdom

A world-first
A retrospective case-control field study
FIV status was carefully determined
Cats were “observed” for 3+ years

440 cats with outdoor access
139 vaccinated (cases)
301 unvaccinated (controls)
FIV vaccine field study

- Strict inclusion criteria meant numbers were whittled down to:
  - 89 vaccinates
  - 212 unvaccinated controls

- 5/89 (6%) of vaccinates became infected over the study period
- 25/212 (12%) of unvaccinated controls
- Vaccine protective rate = 56%, but...

95% confidence interval for degree of protection extended all the way from -22 to +84%

p = 0.14, so...

“Casts doubt on degree of protection afforded in the field...”
“Retesting before annual revaccination may be prudent...”
FIV vaccine field study

- Power analysis *a priori* assumptions:
  - 3% prevalence in vaccinated cats
  - 16% in unvaccinated controls
- > 5-fold less FIV prevalence anticipated due to vaccination

- Would a lesser degree of protection be of interest to practitioners? To how high a standard should this particular vaccine be held?

Now, a story about myth busting!

- “Point-of-care diagnostic test kits for diagnosis of FIV infection cannot distinguish truly infected from vaccinated, uninfected cats”
- A workaround was developed (apart from PCR) but it was largely ignored
Misconceptions about PCR

- PCR got a “holistic” undeserved reputation for unreliability, emanating from North America, an accident of history...

The variability of serological and molecular diagnosis of feline immunodeficiency virus infection

D. Bianzole, F. Reggerli, X. Wen, S. LiHte, J. Hobson, S. Kruth

Abstract — Diagnosis of feline immunodeficiency virus (FIV) infection by polymerase chain reaction (PCR) has recently become available, but little is known about the performance of this assay. The purpose of this study was to determine the sensitivity and specificity of PCR diagnosis of FIV infection. Replicate aliquots of blood samples from cats identified as FIV positive or negative by 2 previous enzyme-linked immunosorbent assay (ELISA) results, and from clinically healthy dogs, were submitted to different laboratories for FIV serologic diagnosis and PCR. The PCR products obtained in 1 laboratory were sequenced to determine the FIV subtypes. The PCR assays correctly identified 100%, 80%, and 50% of the FIV-positive samples, and 100%, 90%, and 75% of FIV-negative samples. Each dog sample was reported as FIV PCR positive at least once, and FIV subtypes A, B, and C were identified. It was concluded that PCR tests currently available for FIV infection are unreliable, with highly variable sensitivity and specificity.

Determining the feline immunodeficiency virus (FIV) status of FIV-vaccinated cats using point-of-care antibody kits


*Faculty of Veterinary Science, The University of Sydney, NSW 2006, Australia
**Centre for Veterinary Education, The University of Sydney, NSW 2006, Australia

- Those different point-of-care antibody detection tests work quite differently...
Those different p-o-c antibody detection tests detect different things... Whether detection of different proteins has much to do with the clinically important differences in performance between the tests is presently unclear.

Table 1
Summary of the antibodies detected using four different point-of-care FIV antibody test kits.

<table>
<thead>
<tr>
<th>FIV antibody detection kit</th>
<th>FIV target antigen</th>
<th>p15</th>
<th>p24</th>
<th>gp40</th>
</tr>
</thead>
<tbody>
<tr>
<td>SNAP FIV/FelV Combo (Australia, NZ, North America)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SNAP FIV/FelV Combo Plus (Europe)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Witness FIV/FIV</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Argen Rapid FIV/FelV</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Not used in this study, but used by Hartmann et al. [19].

Determining the feline immunodeficiency virus (FIV) status of FIV-vaccinated cats using point-of-care antibody kits

Mark E. Westman1-3, Richard Malik1, Evelyn Hall1, Paul A. Sheehy1, Jacqueline M. Norris1,3

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• Whether detection of different proteins has much to do with the clinically important differences in performance between the tests is presently unclear.
False +ve = vaccinated, uninfected cat.

PPV tells the story best, I think.

Further study...

Table 4
Results of three point-of-care FIV antibody test kits in FIV-vaccinated cats (n = 119). Confidence intervals (95%) are given in brackets.

<table>
<thead>
<tr>
<th>Test kit</th>
<th>SNAP Combo</th>
<th>Witness</th>
<th>Anigen Rapid</th>
</tr>
</thead>
<tbody>
<tr>
<td>True +ve</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>False +ve</td>
<td>114</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>True –ve</td>
<td>0</td>
<td>108</td>
<td>114</td>
</tr>
<tr>
<td>False –ve</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Sensitivity (%)</td>
<td>5/5 = 100</td>
<td>5/5 = 100</td>
<td>5/5 = 100</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>0/114 = 0</td>
<td>106/114 = 95</td>
<td>114/114 = 100</td>
</tr>
<tr>
<td>PPV (%)</td>
<td>5/119 = 4</td>
<td>5/11 = 45</td>
<td>5/5 = 100</td>
</tr>
<tr>
<td>NPV (%)</td>
<td>0/0 = 0</td>
<td>108/108 = 100</td>
<td>114/114 = 100</td>
</tr>
</tbody>
</table>

Abstract
Objectives Recently, two point-of-care (PoC) feline immunodeficiency virus (FIV) antibody test kits (Witness and Anigen Rapid) were reported as being able to differentiate FIV-vaccinated from FIV-infected cats at a single time point, irrespective of the gap between testing and last vaccination (0–7 years). The aim of the current study was to investigate systematically anti-FIV antibody production over time in response to the recommended primary FIV vaccination series.
Further study...

- Looking at cats during or shortly after primary vaccination, it doesn’t work so well.

- 2 weeks post 2nd vaccination:
  - Anigen: 7/12 positive
  - Witness: 8/12 positive

- 1 month after 3rd (final) vaccination:
  - Only 2/12 positive (each test)
  - All negative by 6 months post vaccination

Adult cats in for revaccination...

- There is a need to study what is the situation after annual boosting.
  (Work published to date considered only the primary vaccination program; 3 injections, 4 weeks apart)

“A similar longitudinal study to the current design is required in adult cats prior to and following annual FIV vaccination to determine whether this period of detectable antibody response with PoC test kits such as Witness extends beyond primary FIV vaccination.”
Outline of this talk

- Canine leptospirosis – including some unusual clinical presentations
- Parvovirus update, including infections of cats
- An update on feline immunodeficiency and the FIV vaccine
- Update on global companion animal vaccination recommendations
What are the updated recommendations?

1. Last primary puppy and kitten vaccination goes up from 14 – 16 weeks to 16 weeks plus

2. “First annual booster” (so named) goes from 12 – 16 months to 6 – 12 months

3. FIV vaccine goes from being “not recommended” to “non core"
What are the updated recommendations?

4. “Low risk” and “high risk” situations and feline lifestyles are better defined
5. Updated consideration of anatomical sites for injection of vaccines in cats
6. Much more thoroughly referenced. Quality of evidence considered.

Explaining the updates

Last primary puppy and kitten vaccine goes from 14 – 16 weeks up to 16 weeks plus

“First annual booster” goes from 12 – 16 months to 6 – 12 months

FIV vaccine goes from “not recommended” to “non core”
Effect of interfering maternal antibody

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Original Article

Effects of maternally-derived antibodies on serologic responses to vaccination in kittens

Brian A DiGangi1, Julie K Levy2, Brenda Griffin1, Michael J Reese1, Patricia A Dingman2, Sylvia J Tucker2 and Edward J Dubovi1

Abstract

The optimal vaccination protocol to induce immunity in kittens with maternal antibodies is unknown. The objective of this study was to determine the effects of maternally-derived antibody (MDA) on serologic responses to vaccination in kittens. Vaccination with a modified live virus (MLV) product was more effective than an inactivated (IA) product at inducing protective antibody titers (PMT) against feline parvovirus (FPV), IA vaccination against feline herpesvirus-1 (FHV) and feline calicivirus (FCV) was more effective in the presence of low MDA than high MDA. Among kittens with low MDA, MLV vaccination against FCV was more effective than IA vaccination. A total of 15%, 44% and 4% of kittens had insufficient titers against FPV, FHV and FCV, respectively, at 17 weeks of age. Serologic response to vaccination of kittens varies based on vaccination type and MDA level. In most situations, MLV vaccination should be utilized and protocols continued beyond 14 weeks of age to optimize responses by all kittens.

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4/09/2017

39 dogs
2 vaccines
1:320 highest puppy titre

Veterinary Record (2006)
159, 733-736

Papers & Articles

Comparative trial of the canine parvovirus, canine distemper virus and canine adenovirus type 2 fractions of two commercially available modified live vaccines

J. G. H. E. BERGMAN, M. MUNIZ, D. SUTTON, R. FENSOME, F. LING, G. PAUL

The results of vaccinating two groups of puppies with commercial vaccines, both of which claimed to provide adequate protection with a final vaccination at 16 weeks of age, were compared. Groups of 19 and 20 puppies with similar titres of maternally derived antibodies against canine parvovirus (CPV), canine distemper virus (CDV) and canine adenovirus type 2 (CAV2) at four weeks of age were vaccinated at six and 10 weeks of age and their responses to each vaccination were measured by comparing the titres against CPV, CDV and CAV2 in the serum samples taken immediately before the vaccination and four weeks later. After the vaccination at six weeks of age, all 19 of the puppies in group 1 had responded to CPV and CDV, and 14 had responded to CAV2. In group 2, 17 of the 20 had responded to CPV, 19 to CDV and 15 to CAV2. In both groups the puppies that did not respond to the first vaccination had responded serologically to CPV, CDV and CAV2 at 10 weeks of age.
Comparison of selected canine vaccines for their ability to induce protective immunity against canine parvovirus infection.

Lanson Li, Schulz RD;

Author information

Abstract

OBJECTIVE: To compare the ability of 6 commercially available multicomponent canine vaccines to stimulate antibody production in pups with variable amounts of maternally derived canine parvovirus (CPV) antibody and to induce protective immunity against challenge exposure.

ANIMALS: Sixty-three 5- to 6-week-old Beagle pups with passively acquired CPV antibody titer between 1:20 and 1:320.

PROCEDURE: Pups were assigned to each of 6 vaccine groups and 1 control group. Eight pups in each group were inoculated with vaccine or saline solution twice, with 3 weeks between administrations. The ninth pup served as an unvaccinated control. Serum samples were obtained weekly and tested for CPV antibody by hemagglutination-inhibition assay. All pups were challenge-exposed with virulent CPV-2a and CPV-2b at 14 to 15 weeks of age.

RESULTS: 8 of the vaccines failed to provide protective immunity against challenge exposure because all pups in these groups became infected and most died. A fourth vaccine protected against death, but not infection and disease. Two of the 6 vaccines induced an immune response that was protective against infection and disease.

CONCLUSION AND CLINICAL RELEVANCE: Substantial differences existed among commercial vaccines available in 1994 in their ability to immunize pups with maternally derived CPV antibody. These differences caused many vaccinated pups to be susceptible to CPV disease for variable periods because some vaccines failed to Immunize. Importantly, all 4 of the vaccines that performed poorly have recently been replaced by more effective products so that the 5 vaccines now perform similarly.

...92.2% seroconverted to CPV after the 12-week vaccination. Possible reasons for the non-responsiveness of nearly 10% of the puppies are discussed."
Explaining the updates

Last primary kitten vaccine goes from 14 – 16 weeks up to 16 weeks

“First annual booster” recommendation goes from 12 – 16 months to 26 – 52 weeks

FIV vaccine goes from “not recommended” to “non core”

“First annual booster”

- Change to ~ 26 weeks of age (but guidelines are pragmatic and state up to 52 weeks in this iteration)
- The only immunological rationale for the 12-16 month “booster” (when using modern MLV core vaccines) has been to catch the small percentage of puppies and kittens that fail to respond immunologically at 16 weeks.
- So why leave them open to infection until they are 12 – 16 months of age?
- Absolutely does not preclude a first annual health check
Explaining the updates

1. Last primary kitten vaccine goes from 14 – 16 weeks up to 16 weeks
2. “First annual booster” goes from 12 – 16 months to 6 – 12 months
3. FIV vaccine goes from “not recommended” to “non core”

Explaining the updates?

“Low risk” and “high risk” situations and feline lifestyles are better defined

Updated consideration of anatomical sites for injection of vaccines in cats

Much more thoroughly referenced. Quality of evidence considered.
What is “high risk”?

• Cats that go into boarding catteries should be vaccinated against FCV / FHV-1 annually, with the injection preferably in the months leading up to boarding
FPV, FHV-1, FCV


Despite the title of this paper, vaccinated cats developed more significant illness than did the cats in the much earlier Scott & Geissinger studies. Control cats were worse affected, but protection was limited, esp. against FHV-1
Despite the title of this paper, vaccinated cats developed more significant illness than did the cats in the much earlier Scott & Geissinger studies. Control cats were worse affected than vaccinates, but protection was limited, esp. against FHV-1.
"After primary FeHV-1 infection, cats are largely resistant to disease following further challenge but after six months or more, protection may only be partial."

"Thus in cats with a previously low risk of exposure going into a high risk situation such as a boarding or rescue shelter for example, annual vaccination might still be considered appropriate."

"...the relative efficacy was shown to decrease from 95% shortly after primary vaccination, to 52% after 7.5 years."

Explaining the updates?

“Low risk” and “high risk” situations and feline lifestyles are better defined

Updated consideration of anatomical sites for injection of vaccines in cats

Much more thoroughly referenced. Quality of evidence considered.
Tail vaccination in cats: a pilot study

Cleon G Hendricks¹, Julie K Levy¹, Sylvia J Tucker¹, Shaye M Olmstead², P Cyndis Crawford³, Edward J Dubovi³ and Cathleen A Hanlon⁴

Abstract

Painful injection site reactions affect 1–10 cats per every 10,000 vaccinated and are associated with high mortality. Radical resection may be curative, but is often associated with prolonged recovery, disfiguration and loss of function when tumors occur at commonly recommended injection sites. The objective of this study was to assess alternatives to currently recommended vaccination sites in terms of preference by oncology practitioners, ease of injection and serological responses. Surgical, radiation and medical oncology practitioners were surveyed regarding their preference for vaccination sites based on the ease of tumor resection. A six-point Likert scale was used to measure each cat’s behavioral reaction to vaccination when injected subcutaneously in the distal hind limb or the distal tail. Serum collected before and 1–2 months after vaccination was tested for antibody titer against feline panleukopenia virus (FPV) and rabies virus (RV). The preferred sites for vaccination by 84 oncology practitioners were below the stifle (41%) and the tail (30%). There were no significant differences in the cats’ behavioral reaction to vaccination below the stifle (n = 31) and in the distal tail (n = 29). Of the cats seronegative for FPV at the time of vaccination, 100% developed protective antibody titers (≥40) against FPV 1–2 months following vaccination. For cats seronegative for RV all but one cat (13%) developed acceptable antibody titers (≥0.5 IU/ml) against RV. Tail vaccination was well tolerated and elicited similar serological responses to vaccination in the distal limbs.

Accepted: 22 August 2013

Surprisingly good tolerance reported in this study
Evidence-based guidelines

- Guidelines are much more thoroughly referenced than previously
- Quality of evidence is considered using a specifically developed scale for publications in veterinary vaccinology

**Category 1 evidence**: a recommendation supported by peer-reviewed scientific publication of either experimental or field data. Evidence within this category might still be of variable scientific quality despite peer review, as the peer review process does not conform to a universal standard.

**Category 2 evidence**: a recommendation supported by unpublished commercially sensitive studies submitted as part of a regulatory package for licensed veterinary vaccines. The assumption for this level of evidence is that information appearing on the datasheets of licensed products has been through competent peer review by regulatory authorities.

**Category 3 evidence**: a recommendation supported by commercial or independent experimental or field data that have not been published in the peer reviewed scientific literature or were not included in a formal regulatory package and subjected to scrutiny by regulators.

**Category 4 evidence**: a recommendation unsupported by experimental or field data, but assumed from knowledge of the 'first principles' of microbiology and immunology or supported by widely-held expert opinion.

Lastly...
Comparison of differing cytopathic effects in human airway epithelium of parainfluenza virus 5 (W3A), parainfluenza virus type 3, and respiratory syncytial virus

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Viral growth
Viral shedding
Viral persistence
Multi-layered progeny cells
3-Dimensional (3-D) image reconstruction

ABSTRACT
Parainfluenza virus 5 (PIV5) infects a wide range of animals including dogs, pigs, cats, and humans; however, its association with disease in humans remains controversial. In contrast to parainfluenza virus 3 (PIV3) or respiratory syncytial virus (RSV), PIV5 is remarkably non-syncytial in monolayer cultures of immortalized epithelial cells. To compare the cytopathology produced by these viruses in a relevant human tissue, we infected a cultured bronchial epithelial cell line (SHBE) with PIV5, PIV3 and RSV. The SHBE cell line possesses characteristics of human bronchial epithelial cells and distal airway epithelium. After infection with PIV5, PIV3 and RSV, all infected cell layers, and PIV5 and PIV3 infections were dependent on viral and not other cellular agents. Only PIV3-infected cells showed syncytia. PIV5 infection resulted in a massive loss of infected cells by shedding of infected cells into the culture. These studies revealed striking differences in cytopathology of PIV5 versus PIV3 and RSV and indicate the extent of cytopathology determined in cell lines does not predict events in differentiated airway cells.

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