Rabies Diagnostic Testing and Serology

Susan Moore, Rabies Laboratory/KSVDL/College of Veterinary Medicine/Kansas State University, Manhattan, KS 66502, USA
“head testing”

• Medical urgency, not medical emergency
• direct fluorescent antibody test (dFA) is used to diagnose rabies in brain tissue. The test can only be performed post-mortem.
KANSAS STATE UNIVERSITY

RABIES DIAGNOSTIC REQUISITION

Submitting State:  
1. Kansas  
2. Nebraska  
3. Other

Laboratory Use Only:
Lab No. 

Positive
Negative
Unsuitable
Indeterminate

Signature/Date

Submit to:
Attn: Rabies Laboratory
K-State Veterinary Diagnostic Laboratory
1800 N. Denson Avenue
Mosier Hall
Manhattan, KS 66506-5601
Phone: (785) 532-4483

SPECIMEN SUBMITTED BY

Clinic/Agency ___________________________ Contact ___________________________
Address ____________________________________________________________
City/State/Zip ___________________________ Fax # ____________________________

Do you request a faxed copy of results? □ No □ Yes

SPECIMEN HISTORY

Kind of Animal _______ Breed/Species _______ Age (approx.) _______ Color/Description _______ Gender _______

Animal Location:

Town ___________________________ County ___________________________ Specific Location ___________________________

Submitted animal’s vaccination status:  
1. Current  
2. Unvaccinated  
3. Not Current  
4. Unknown

Was the animal sick or acting strangely? □ No □ Yes

Signs of Rabies:  
1. Neurological disorder  
2. Paralysis  
3. Difficulty swallowing  
4. Dripping  
5. Aggression

Other, describe: ____________________________________________

Date of death: ___________ Manner of death: ___________

Date Submitted: ___________

Owner/complainant: name ___________________________ Phone #: ___________________________

Address ____________________________________________________________
City ___________________________ State/ZIP ___________________________

EXPOSURE HISTORY

Has the animal bitten anyone? □ No □ Yes Name: ___________________________ Date: ___________

If yes, please give details of incident: ____________________________________________

Was this animal in contact with a pet or domestic animal? □ No □ Yes If yes: Date: ___________

If yes: Species ___________________________ Vaccination status:  
1. Current  
2. Unvaccinated  
3. Not Current  
4. Unknown

If yes to any of the above: Name/Owner: ___________________________

Address ____________________________________________________________
Telephone ___________________________

Form 010
K-State Rabies Laboratory
Rabies Diagnostic Testing
1800 N Denison Ave, Mosier Hall
Manhattan KS  66506–5601

Ph: 785-532-4483  fax: 785 532-4474  Email: rabies@vet.k-state.edu

Please call the laboratory prior to submission of samples at 785-532-4481.

Procedure for Submission of Rabies Specimen

Important tip: Healthy dogs, cats, and ferrets (regardless of vaccination status) that have bitten someone and are available for observation may be held for 10 days instead of tested as recommended by the Compendium of Animal Rabies Prevention and Control.

Specimen Preparation:
- Do not submit live animals.
- Ship only the deapapted animal head, unless it is a bat or small rodent.
- A trained, qualified person should separate the animal head from the body as soon as possible. For large animals, the calvarium should be opened and the whole brain should be submitted. To adhere to the National Standard Protocol, the minimum sample is a cross-section of the brainstem and the cerebellum. Specimens without these tissues will be reported as “Unsuitable.” See our website or call for further clarification.
- Immediately chill the specimen(s) to between 32°F and 45°F (e.g., place in a -20 freezer for 1-2 hours).
- FREEZING THE SAMPLE MAY DELAY TESTING. Samples must thaw before commencement of testing.

Instructions for Packaging and Shipping:
- Place each specimen within two seal-able containers (i.e., a primary plastic bag or container and a secondary plastic bag or container sealed securely to contain any fluid).
- Attach identification matching the submission form information to the outside of each double-enclosed specimen. This is essential if more than one specimen per package.
- Place double-enclosed specimen(s) inside an inner container, such as a Styrofoam box.
- Use absorbent packing material, such as newspaper or paper towels, to cushion the specimen(s) and to absorb condensation or potential leaks.
- Place frozen gel/cold packs in the inner container to ensure samples are completely surrounded and will remain cold for at least 48 hours. DO NOT USE DRY ICE! Ice is not recommended but if used, double-bag and seal securely to prevent leakage.
- Close the inner container and place it inside the rigid outer container (cardboard box).
- Place completed rabies submission form(s) in a plastic zip-lock bag. Then place these on top of the closed inner container/box and close the outer container.
- Secure the outer container with packing tape.
- Send the package by overnight courier. A diamond-shaped UN-3373 label on the exterior of the outer container near the “Biological Substance, Category B” statement in the “send to” address is required (see our website). The UN-3373 label must have a minimum dimension of 100 mm x 100 mm (3.9 inches).
- If the package is sent overnight through the United States Postal Service, the sample(s) may be labeled Exempt Animal Specimen.

The Kansas or Nebraska State Health Department as well as the submitting veterinarian will be contacted if a positive or unsuitable specimen is confirmed. When specimens are received by 12:00 pm weekdays, results are normally available by 4:30 pm. Laboratory hours are Monday-Friday, 8:00 am to 5:00 pm, excluding State Holidays.

The Compendium of Animal Rabies Prevention and Control and the Advisory Committee on Immunization Practices provide guidance that administration of rabies post-exposure prophylaxis is a medical urgency, not a medical emergency. Submissions received on Saturday will be tested the next working day. There is no routine testing on Sundays or holidays if the following day is a business day. The need for emergency testing will be evaluated on a case-by-case basis and arrangements MUST be made by telephone in advance.

KANSAS   NEBRASKA

Ingrid Garrison, DVM, MPH, DACVP
State Public Health Veterinarian
KOHE
1000 SW Jackson, Suite 300
Topeka KS 66612
Phone: 913-268-3337

Bryan F Buss, DVM, MPH, DACVP
Acting State Public Health Veterinarian
301 Centennial Mall South
PO Box 95026
Lincoln NE 68509-5007
Phone: 402-471-2937

An updated listing of animal rabies cases in Kansas and Nebraska is available on our website at: www.ksvdl.org/rabies-laboratory

Version 7/2017
Rabies Diagnostic Testing - Sampling

Dorsal view

Lateral view

https://youtu.be/aSEyLw79imA

https://www.youtube.com/watch?v=01gXa8KkuPA
Antigen distribution and quality of staining (4+ to 1+ for positive)

Interpretation, if tissue was adequate and suitable:
1. Test complete / reportable result
   • Positive reading: Positive
   • Negative reading: Negative
2. Test incomplete / results not reported until test is repeated and/or result confirmed.

Interpretation, if tissue was NOT adequate or suitable:
1. Test complete / reportable result
   • Positive reading: Positive
   • Negative reading: Unsuitable
Diagnoses provides surveillance data
Surveillance data helps PEP decisions
Working with rabies

- **Occupational Infections**
- Rabies Laboratory Acquired Infections are extremely rare; two have been documented. Both resulted from presumed exposure to high concentrations of infectious aerosols, one generated in a vaccine production facility, and the other in a research facility.
- Naturally or experimentally infected animals, their tissues and their excretions are a potential source of exposure for laboratory and animal care personnel.
  - Milk has never been shown to transmitted rabies
  - Has been isolated in tears (check!!)
Working with rabies

- When working with infected animals, the highest viral concentrations are present in central nervous system (CNS) tissue, salivary glands, and saliva, but rabies viral antigens may be detected in all innervated tissues.
- The most likely sources for exposure of laboratory and animal care personnel are accidental parenteral inoculation, cuts, or needle sticks with contaminated laboratory equipment, bites by infected animals, and exposure of mucous membranes or broken skin to infectious tissue or fluids.
- Infectious aerosols have not been a demonstrated hazard to personnel working with routine clinical materials or conducting diagnostic examinations.

Biosafety in Microbiological and Biomedical Laboratories 5th Edition
Working with rabies

- BSL-2 and/or ABSL-2 practices, containment equipment, and facilities are recommended for all activities utilizing known or potentially infectious materials or animals. Pre-exposure rabies vaccination is recommended for all individuals prior to working with lyssaviruses or infected animals, or engaging in diagnostic, production, or research activities with these viruses.
- Dedicated laboratory clothing, heavy protective gloves to avoid cuts or sticks from cutting instruments or bone fragments, and a face shield to protect the skin and mucous membranes of the eyes, nose, and mouth from exposure to tissue fragments or infectious droplets.
Working with rabies

- Cleaning and containment of contaminated surfaces or material:
  - Use bleach or 70% alcohol or other virucidal cleaner to disinfect surfaces and instruments
  - Discard contaminated waste in biohazard bags and autoclave before putting in trash containers.
Understanding prophylaxis

• Presence of rabies virus neutralizing antibody is of primary importance in preventing virus from entering the CNS.
  – Non-vaccinated person—passive administration of rabies antibodies and vaccine—bridges the time period between exposure and rise in antibody levels.
  – Previously vaccinated person—vaccine given to boost levels of circulating antibody quickly (secondary response within days) and stimulate cellular immune responses.
• Prophylaxis can be given and effective up until signs and symptoms appear (generally 1-3 months post exposure).
• Type of exposure is a consideration
Time post-infection

US median incubation period is ~35 days

Antibody response

Zone of PEP mediated virus neutralization is at the site of infection

Vaccine induced humoral immune response

Spread and replication of virus in the absence of appropriate PEP

Incubation period (5 days to > 2 years)

Prodrome (0-10 days)

Acute neurologic period (2-7 days)

Coma (5-14 days)

Death

CNS virus

Salivary glands virus

Passive immunity - HRIG

Virus at entry site
Pre-exposure vaccination

- Three vaccines over 21-28 days
- Recommended for those at frequent or continuous risk of rabies exposure, including veterinarians, veterinary technicians, laboratory workers, animal control, travelers to rabies endemic areas.
  1. Protects against unknown exposures
  2. No need for RIG in case of re-exposure.
  3. Begins an anamnestic response immediately.

- Titer checks to determine presence of adequate immunity—every 2 years (frequent risk) or every 6 months (continuous risk)
Post exposure prophylaxis

• Of medical urgency – not emergency
• Complex decisions involving physicians, public health professionals, diagnosticians, veterinarians
  • Animal type (owned, domestic, wild)
  • Type of exposure
  • Availability of biting animal for rabies testing or observation
Post exposure treatment

- Wash the wound
- See a doctor
- Test the animal (if available)
- Contact local health department or animal control.
- Post-exposure treatment (PET) (Essen)
  - Rabies Immune globulin (RIG): Day 0
  - Four IM vaccines: Day 0, 3, 7, and 14
  - Other schedules recognized by WHO: Zagreb, Thai Red Cross
- Previously vaccinated individuals
  - DO NOT get RIG
- Two IM vaccines: Day 0 and 3
Minimum Acceptable RVNA level

• Based on early vaccine clinical trials
  – Measurement of RVNA by mouse neutralization test (MNT) or Rapid Fluorescent Focus Inhibition Test (RFFIT)
  – May depend upon the host, severity of exposure, rabies virus variant
    • A rising immunity is critical to averting productive infection
• Two different levels are recommended:
  – World Health Organization (WHO) – 0.5 IU/mL
  – Advisory Committee on Immunization Practices (ACIP) – complete neutralization of rabies virus at a 1:5 serum dilution in the RFFIT
    • Calculated to IU/mL, this level is approximately 0.1 IU/mL
Titer & IU/mL Calculation from the RFFIT Test Data

- End Point Titer determination
  - Number virus positive fields per 20-field count
  - Calculate titer value using Reed and Muench formula

- IU/mL value is calculated by the following formula:
  - Based on the test serum titer in relation to the assigned WHO reference standard

\[
\frac{\text{Endpoint titer of test serum}}{\text{Endpoint titer of Reference Serum}} \times \text{Assigned Reference Serum Concentration (IU/mL)}
\]
## Guidelines for persons pre-exposure vaccinated and at risk of rabies exposure

<table>
<thead>
<tr>
<th>Agency/Year</th>
<th>Booster vaccination recommended if level is below:</th>
<th>Method of Testing:</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>WHO</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>1992</strong></td>
<td>0.5 IU/mL</td>
<td>MNT or RFFIT; ELISA only with caution</td>
</tr>
<tr>
<td><strong>2005</strong></td>
<td>0.5 IU/mL</td>
<td>RFFIT or FAVN; ELISA if RFFIT not available</td>
</tr>
<tr>
<td><strong>2013</strong></td>
<td>0.5 IU/mL</td>
<td>RFFIT or FAVN; ELISA</td>
</tr>
<tr>
<td><strong>ACIP</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>1976</strong></td>
<td>None, boosters recommended every 2 years</td>
<td>None stated</td>
</tr>
<tr>
<td><strong>1980</strong></td>
<td>1:16 titer or booster every 2 years</td>
<td>RFFIT</td>
</tr>
<tr>
<td><strong>1984</strong></td>
<td>1:5 titer per CDC; 0.5 IU/mL per WHO</td>
<td>RFFIT</td>
</tr>
<tr>
<td><strong>1991</strong></td>
<td>1:5 titer *</td>
<td>RFFIT</td>
</tr>
<tr>
<td><strong>1999</strong></td>
<td>Complete neutralization at a 1:5 serum dilution†</td>
<td>RFFIT</td>
</tr>
<tr>
<td><strong>2008</strong></td>
<td>Complete neutralization at a 1:5 serum dilution‡</td>
<td>RFFIT</td>
</tr>
</tbody>
</table>

*Recommended response 2-4 weeks after either pre- or post-exposure vaccination is complete neutralization at a 1:25 serum dilution which is equivalent to the WHO level of 0.5 IU/mL.

†Recommended response 1-2 weeks after post-exposure vaccination is complete neutralization at a 1:5 serum dilution

‡RVNA titer most properly reported according to a standard as IU/mL
Other factors

- Assay used – difference and relationships between assay characteristics
- Assay performance
- Reporting format – Titer or IU/mL
- Time point of sampling after vaccination
What level is adequate?

• Minimum detectable?
  – **Method validation** is necessary to identify and verify the lowest level of RVNA that can be measured accurately and precisely.
  – The assay should be validated (in each laboratory) to assure minimal false positives or (and) have secondary method to check low positives.

• Is one level appropriate for all situations?
  – Periodic rabies titer check for someone at continuous or frequent risk of rabies exposure
  – Travelers to rabies endemic areas
  – Rabies exposed person having a titer check after recent vaccination
Trends in Core Vaccine Titers in Dogs and Cats – KSVDL 2016

Susan M. Moore, PhD, MS, MT(ASCP)SBB
Kansas State University, KSVDL Rabies Laboratory

ABSTRACT
Measuring antibody titers to core vaccine antigens, while becoming more common in practice remains controversial. In part, this is due to a lack of good quality data that demonstrates protective levels in dogs and cats for periods of time after vaccination. KSVDL began offering a panel of antibody tests to measure neutralizing antibodies to the core vaccines in dogs and cats in the summer of 2015. Compilation of the titer results indicates a large portion of both dogs and cats had adequate titers levels, including rabies titers, but also identified some pets in need of booster vaccination. This demonstrates the utility of checking vaccine titers to ensure each pet has a continuing robust response to vaccination.

INTRODUCTION
Immunity to infectious agents of common risk to dogs and cats can involve both cellular and humoral immunity; antibody testing will only define the humoral immune status. For the common core vaccine antigens, the correlation between antibody level (immediately after vaccination and long-term) and protection from disease has not been adequately studied. This means that though the presence of antibody would imply immunity is sufficiently present to protect against disease, the absence of detected antibody will not necessarily mean sufficient immunity is absent in a vaccinated pet. In addition, tests that do not specifically measure neutralizing antibody can produce results that do not necessarily correlate to protection because the not all specific antibodies to an infectious agent will have neutralizing ability to prevent infection.

For pet owners with concerns about the adverse effects of vaccination, neutralizing antibody titer testing is a tool to demonstrate continued immunity and evidence to avoid an annual vaccination. Many veterinarians would agree that testing is a good idea for dogs and cats with a history of or genetic predisposition to poor responsiveness to a vaccine, or have allergic reactions to or other adverse effect from a vaccine, or have immunosuppression.

RESULTS
A retrospective analysis of core vaccine titers from dog and cats samples submitted to KSVDL from June 2015 to November 2016 was performed. The number of dogs samples tested for the core vaccines distemper, parvovirus, and adenovirus was 6,533; the number of cat samples tested for the core vaccines herpes, calici virus, panleukopenia was 270; and the total samples tested for Rabies titer antibodies was 2,042 (1,796 dogs and 246 cats).

DISCUSSION
The Canine Vaccination Guidelines within the WSAVA Guidelines for the Vaccination of Dogs and Cats (2015) state that, while antibody testing still can be relatively expensive, “The principles of ‘evidence-based veterinary medicine’ suggest that testing for antibody status (for either puppies or adult dogs) should be better practice than simply administering a vaccine booster on the basis that this would be ‘safe and cost less.’”

The 2013 AAFP Feline Vaccination Advisory Panel Report states, “Because antibody titers may not reliably correlate with, or predict, the degree of protection or susceptibility for an individual cat, the Advisory Panel recommends employing defined revaccination intervals rather than measuring antibody titers to assure protection.” According to the report, most cats that have a positive result on a titer test for feline panleukopenia are immune to the disease. Titers for feline herpesvirus-1 and feline calicivirus “may not necessarily correlate well with protective immunity and should not be used to predict protection in the future.” Titers for feline leukemia virus and feline immunodeficiency virus “do not correlate with immunity and should not be used to determine the need for vaccination.”

Most states and many local regulatory bodies have laws requiring rabies vaccination for dogs and cats, for their protection and the protection of humans. Mandatory rabies vaccination is a very effective tool in the prevention and control of rabies. More and more local authorities are allowing proof of continued immunity though rabies titer testing in waiving revaccination requirements in consideration of pet health (history of adverse reactions, current disease medical treatments).

CONCLUSION
Core vaccines are vitally important to pet health, this is absolutely understood. Most immunologists, in general, advise against over-immunization. Neutralizing antibody titer are highly correlated with protection from disease; titer testing is a very useful tool for every small animal practitioner for evaluating the risk of infection in dogs and cats. It is the only available practical method to be certain the animal has developed an immune response to a given core vaccine.

For information on interpretation of core vaccine serology results see:
http://www.ksvdl.org/laboratories/virology/meaning-of-results.html
Challenge studies

*(Rare reports: Vaccinated animals do die from rabies exposure)*
Challenge studies: rabies antibody level in vaccinated animals and survival

• Animals with “detectable” RVNA survive?
  – Mostly…..
  – Rare reports of animals with levels above 0.5 IU/mL dying after challenge

• Animals with no detectable RVNA succumb?
  – Some do, some survive
  – Cellular immunity or undetectable antibody
What we don’t know about rabies serology:

• What level is “significant”?  
  – Protection or seroconversion?
• Timing of blood sample?
• Serology results in challenge studies – are they comparable?
• What is more important: vaccination status or rabies antibody level?
Practical significance of rabies antibodies in cats and dogs.

Aubert MF.

Centre national d'études vétérinaires et alimentaires, Laboratoire d'études sur la rage et la pathologie des animaux sauvages, Malzéville, France.

Abstract

Doubt has sometimes been cast upon the protective effect of rabies antibodies in serum. Animals and humans suffering from fatal rabies often produce high antibody titres, while rabies cases are also observed in vaccinated animals. Cellular immunity is also largely involved in protection. Nevertheless, a large number of laboratory experiments and field observations clearly demonstrate that cats and dogs which develop antibodies after vaccination and before challenge have a very high probability of surviving any challenge, no matter how strong the dose and which virus strain was used. Rabies antibody titration can, therefore, afford a strong additional guarantee to the vaccination certificates accompanying domestic carnivores during transportation between countries. Quarantine rules should also be adapted to the epidemiological features in the exporting country, e.g. statistics of vaccination failure in cats and dogs and host-virus adaptation of the rabies strains circulating in these countries.

Therefore, based on a designated minimal level of neutralising antibodies, and could be proposed as an alternative to quarantine measures. The designated threshold could be based on the results presented in this study. The security of the protection constituted by this threshold would be increased by the extent to which it exceeds the level recognised as effective against experimental challenge in cats and dogs (0.1 IU/ml and 0.2 IU/ml, respectively, measured by RFFIT).
The Relationship Between Rabies Antibody Titers in Dogs and Protection from Challenge

T. O. Bunn and H. D. Ridpath

Table 2 - Relationship Between Antibody Titers and Projected Death Rate

<table>
<thead>
<tr>
<th>Death rate %</th>
<th>Antibody Titer MSNT</th>
<th>Antibody Titer RFFIT</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>.9</td>
<td>1.8</td>
</tr>
<tr>
<td>40</td>
<td>1.3</td>
<td>2.6</td>
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<tr>
<td>30</td>
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</tr>
<tr>
<td>.1</td>
<td>99.7</td>
<td>127.3</td>
</tr>
</tbody>
</table>

MSNT = Mouse Serum Neutralization Test
RFFIT = Rapid Fluorescent Focus Inhibition Test
Exploring a role for titers in rabies vaccination

By Katie Burns

In their rabies challenge studies, Drs. Schultz and Larson found that when exposed to the rabies virus, dogs maintain immunity for up to seven years after vaccination. Although rabies vaccines are killed virus vaccines, which generally don’t provide as long of a duration of immunity as modified-live virus vaccines do, Dr. Schultz described rabies virus as an “excellent antigen.” Some rabies vaccines also have adjuvants to increase efficacy and duration of immunity.

“We’ve used virtually every test available to measure rabies antibodies, and as long as the test was antibody-positive, the dogs challenged were protected from the rabies virus challenge for as long as seven years after vaccination,” he said.
Seroconversion in challenge studies/ evidence of expected vaccine response

<table>
<thead>
<tr>
<th>Reference</th>
<th>Vaccine Used</th>
<th>Vaccination Route</th>
<th>Animal ID</th>
<th>Titer Assay</th>
<th>Seroconversion Cut-off Used</th>
<th>day 14</th>
<th>day 28</th>
<th>day 30</th>
<th>day 32</th>
<th>day 60</th>
<th>day 90</th>
<th>day 90 of challenge</th>
<th>Challenge day</th>
<th>Outcome</th>
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<tr>
<td>1</td>
<td>AedSRRG1</td>
<td>PO</td>
<td>8</td>
<td>FM microtest</td>
<td>not give*</td>
<td>2.8</td>
<td>5.6</td>
<td>5.6</td>
<td>5.6</td>
<td>5.6</td>
<td>5.6</td>
<td>day 90</td>
<td>day 90</td>
<td>S</td>
</tr>
<tr>
<td></td>
<td>AedSRRG1</td>
<td>PO</td>
<td>5M</td>
<td>FM microtest</td>
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<tr>
<td>2</td>
<td>raccoon pox</td>
<td>PO</td>
<td>2</td>
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<td>day 107</td>
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<td>0.3</td>
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<td>day 107</td>
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<td>RFFIT</td>
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<td>0.03</td>
<td>1.2</td>
<td>0.3</td>
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<td>0.3</td>
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<td>day 107</td>
<td>day 107</td>
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<td>RFFIT</td>
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<td>day 107</td>
<td>S</td>
</tr>
<tr>
<td>Control</td>
<td>raccoon pox</td>
<td>PO</td>
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<td>RFFIT</td>
<td>0.15 IU/mL*</td>
<td>0.03</td>
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<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
<td>day 107</td>
<td>day 107</td>
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</tr>
<tr>
<td>Control</td>
<td>raccoon pox</td>
<td>PO</td>
<td>4</td>
<td>RFFIT</td>
<td>0.15 IU/mL*</td>
<td>0.03</td>
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</table>

* results given in IU/mL; results below 0.15 IU/mL were considered negative. The cut-off was determined in a different paper (Smith et al., 1998).**

**levels of antibody were determined by a modified rapid fluorescent focus inhibition test (RFFIT) (Smith et al., 1998).".

Serology - Determination of sero-conversion

- >0.6 unit/mL – Rupprecht, 1986
- >0.2 IU/mL – Hanlon, 1989
- >0.05 IU/mL – Hanlon, 1998
- >0.5 IU/mL – Roscoe, 1998
- >0.06 IU/mL – Blanton, 2007

Data courtesy of Dr. Chris Ellis
Expected titer based on sampling interval

- Studies have shown dogs can reach 0.5 IU/mL RVNA level by day 7
  - In one study 8/8 dogs had titers above 0.5 IU/mL. S. Darkaoui, ClinExpVaccRes, 2016
- Low late-early high responders
- Many reach their peak response between day 14 and 42 for the primary response
- The highest risks of not having a titer of 0.5 IU/mL is a long sampling interval and young animals with only one vaccination
- Is it more important to have a robust response within 30 days or have a titer of >0.5 IU/mL upon exposure?
Serology results vs Vaccination status

• Vaccine licensing requirement for 87% of vaccinated animals to survive challenge, while 80% of control animals succumb.

• Studies show a correlation between antibody level and survival with increasing probability of survival up to 0.5 IU/mL.

• IF: Probability of vaccinated animals surviving rabies challenge = Probability of animals with 0.5 IU/mL surviving rabies challenge

• THEN: Would regulations change to allow serologic monitoring of rabies vaccine response?
Bunn and Ridpath:

It is not the intention of this report to give specific recommendations on how regulations governing vaccine testing or quarantines should be changed, but rather to present the data that indicate serology is a valid indicator of rabies immunity. It is hoped that this information will be analysed by those responsible for such regulations and applied where appropriate.

Dr. Schultz wouldn’t necessarily push for a change in laws, though. He said, “I think the requirement for a three-year revaccination cycle with rabies hopefully will get more dogs immunized. One of the goals for rabies is herd immunity because you always reduce the likelihood of disease by having the greatest number of animals immune as possible.”
Usefulness of rabies serology in animals

• Is used to confirm rabies vaccine response in pets traveling to rabies-free areas
• Can give information on the likelihood of survival from an exposure
• If rabies antibody is detected, it gives information on vaccine status of the animal, however absence of antibody does not rule out previous vaccination (depending on the time interval from vaccination)