

2014 VACCINES & VACCINATION: The *MUST KNOW* Issues

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Over the past decade, Vaccination Guidelines for the dog and cat have moved from a predominantly US perspective to recommendations that address immunization practices in North America, the United Kingdom, Europe, and most recently, Asia. Guidelines for veterinarians practicing in South American countries are being considered at this time.

Today, within the US and Canada, it appears that many practices have incorporated some, or all, of the recommendations put forward in the latest iterations of canine (2011)¹ and feline (2013)² vaccination guidelines. However, as the list of vaccines licensed for use in veterinary medicine continues to grow and vaccine technologies change, veterinarians continue to be challenged with new, sometimes complex, even conflicting, information regarding the selection and use of companion animal vaccines.

For veterinarians who practice in the United States or Canada, the decision to implement either the Canine (AAHA) or Feline (AAFP) Vaccine Guidelines is optional...the Guidelines are recommendations; they are *not* requirements. Also, Canine and Feline Vaccination Guidelines are not intended to represent a universal or standardized protocol applicable to all dogs and all cats. Instead, they are intended to guide decisions leading to the development of a *rational* vaccination protocol.

The notes that follow address key points, and controversies, addressed in published Guidelines. As new information is published, these notes will be revised to reflect new or amended recommendations as they emerge. This manuscript is divided into 2 parts:

PART I: Representative Protocols-Dog and Cat

This section outlines key vaccination recommendations and provides examples of protocols currently used by practices in North America that follow the Canine (AAHA) and Feline (AAFP) Vaccination Guidelines.

PART II: Frequently Asked Questions (FAQs): The Facts v. The Fiction

Several important facts of immunology, and law, have been incorporated into canine and feline vaccination guidelines. The FAQ section of this paper specifically addresses, with references, the "Facts" vs. the "Fiction" behind major vaccination concerns raised by veterinarians: 1) Decisions involved in implementing a protocol; 2) Vaccine safety and adverse reactions; 3) Applications for serologic testing (antibody titers); and...4) Legal concerns regarding the vaccination of dogs/cats.

NOTE: *Published vaccination recommendations for the dog and cat are based, whenever possible, on the results of current scientific studies. The reader is reminded, however, that for some of the recommendations offered, published studies are simply not available. Furthermore, not all recommendations published in the Canine (AAHA) and Feline (AAFP) Vaccination Guidelines fall within the manufacturers' label recommendations.*

¹ 2011 AAHA Canine Vaccination Guidelines are available at www.aahanet.org.

² 2013 AAFP Feline Vaccine Guidelines are available at www.catvets.com.

A. INITIAL VACCINATION of DOGS

CORE Vaccines	Administration	FIRST Booster
MLV or Recombinant Distemper + MLV Parvovirus + MLV Adenovirus-2 (administered as a combination product)	3 doses are recommended between 6 and 16 weeks of age. Example: 8 weeks; and 12 weeks; and 16 weeks of age.	Administer a single dose (of a combination product) not later than 1 year following the last dose in the initial series. A minimum interval of 2 weeks between any 2 doses of vaccine is recommended.
Option: In the US and Canada, parainfluenza virus (CPiV) vaccine is commonly administered in combination with the above vaccines as DA2PPi. (see below)		
Rabies (killed) 1-Year & 3-Year products are available.	Administer a single dose of rabies vaccine not earlier than 12 weeks of age, then... (State/Local/Provincial law applies)	...schedule a second dose of rabies vaccine to be administered not later than 1 year following administration of the 1 st dose, regardless of the dog's age at the time the <i>initial</i> dose is administered. (State/Local/Provincial law applies)
NON-CORE Vaccines	Administration	Booster Recommendations
<i>B. bronchiseptica</i> + parainfluenza virus (intranasal only) (some IN products may also contain CAV-2 antigen)	Single dose (intranasal) at 12 or 16 weeks of age. (optional-some authors recommended 2 doses at 12 and 16 weeks of age). IN vaccine may be administered as early as 3 to 4 weeks of age.	When risk of exposure is sustained, administer a single dose 1 year following the last dose administered.
<i>B. bronchiseptica</i> <u>only</u> (monovalent) Two options are available: > Parenteral (killed-bacterin) –or- > Intraoral (avirulent live) administration.	Parenteral (SQ): Two doses are required, 2 to 4 weeks apart. Intraoral: The manufacturer recommends a single initial dose.	When risk of exposure is sustained, administer a single dose 1 year following the last dose administered.
Leptospirosis (killed) 4-serovar [2-way Leptospirosis vaccines are <i>not</i> recommended by either AAHA or the ACVIM]	2 initial doses, 2 to 4 weeks apart. NOTE: it is not recommended to administer the 1 st dose prior to 12 weeks of age. NOTE: <i>Small Breed Dogs: consider delaying initial doses until the CORE vaccine series has been completed.</i>	Where risk of exposure is sustained, administer a single dose 1 year following completion of the <i>initial</i> 2-dose series.
Lyme disease (recombinant or killed)	2 initial doses, 2 to 4 weeks apart. NOTE: <i>Small Breed Dogs: consider delaying initial doses until the CORE vaccine series has been completed.</i>	Where risk of exposure is sustained, administer a single dose 1 year following completion of the <i>initial</i> 2-dose series.
Canine Influenza Virus (killed)	2 initial doses, 2 to 4 weeks apart are required.	- Manufacture recommends annual re-vaccination where risk of exposure is sustained. - Duration of immunity has not been established.

Canine coronavirus vaccination is not recommended.

Crotalus atrox (rattlesnake) vaccine should only be used in dogs with a defined risk for exposure. Follow the manufacturer's recommendations for dosing.

B. INITIAL VACCINATION of CATS

CORE Vaccines	Administration	FIRST Booster
<p>MLV Panleukopenia + MLV Herpesvirus + MLV Calicivirus</p> <p>When feasible, avoid the use of killed (<u>adjuvanted</u>) vaccines in cats.</p>	<p>NEW: Administer at least 3 (or 4) doses between 6 and 16 weeks (or 20 weeks) of age.</p> <p>Example 8 weeks; and 12 weeks; and 16 weeks of age...<i>with an additional dose at 20 weeks of age</i> where risk of exposure is high.</p>	<p>Not later than 1 year following the last dose in the initial series.</p> <p>16 to 20 weeks for the last dose of the initial series is important to overcome maternally derived antibody.</p>
<p>Recombinant Rabies [non-adjuvanted] Available as a 1-Year product. -or- Killed Rabies [adjuvanted] Available as 1-Year & 3-Year products.</p>	<p>Single dose usually given at 12 <u>or</u> 16 weeks (State, Provincial, or local law applies)</p> <p>(State/Local/Provincial law applies)</p>	<p>Administer a single dose of Rabies vaccine within 1 year following administration of the initial dose.</p> <p>(State/Local/Provincial law applies)</p>
NON-CORE Vaccines	Administration	Booster Recommendations
<p>Recombinant Feline Leukemia Virus (FeLV) [non-adjuvanted]</p> <p>-also available as-</p> <p>Killed Feline Leukemia Virus [adjuvanted]</p>	<p>“Highly Recommended” for <u>all</u> kittens: Administer 1 dose as early as 8 weeks of age followed by a 2nd dose 3-4 weeks later. Booster 1 year later.</p> <p><i>The Au recommends 2 doses at 12 and 16 weeks of age followed by a booster 1 year after completion of the initial series.</i></p>	<p>NEW Where risk of exposure exists...administer a single dose annually thereafter.</p> <p>(some authors recommend revaccination every 2 years for cats considered to be at “low risk” for exposure).</p>
<p>Killed Feline Immunodeficiency Virus (FIV)</p> <p>[Only available as a Killed-adjuvanted]</p> <p>(This vaccine is NOT RECOMMENDED by the World Small Animal Veterinary Association)</p>	<p>3 initial doses, 2 to 4 weeks apart, if indicated.</p>	<p>NOTE: initial vaccination can cause a False + FIV test result on ALL commercial FIV tests for several years. Kittens having nursed from a vaccinated cat may also have a False + test result if tested prior to 6 months of age.</p>
<p>Feline <i>Bordetella bronchiseptica</i></p> <p>Attenuated Live Intranasal (non-adjuvanted)</p>	<p>A single dose, administered intranasally, as early as 4 weeks of age, if indicated</p>	<p>Booster annually where the risk of exposure is present.</p> <p>Indications for use of this product are limited.</p>
<p>Feline <i>Chlamydomphila felis</i> (formerly: <i>Chlamydia psittaci</i>)</p> <p>(both non-adjuvanted and adjuvanted products are available)</p>	<p>2 initial doses 3 to 4 weeks apart, if indicated.</p>	<p>Booster annually where the risk of exposure is present.</p> <p>Indications for use of this product are limited.</p>
<p>Virulent Systemic (VS) Calicivirus</p> <p>Killed-adjuvanted</p>	<p>2 initial doses 2 to 4 weeks apart, if indicated</p>	<p>Disease prevalence is considered low, even within high-density housing environments (eg, shelters).</p>

NOTE: Unless specifically indicated for intranasal administration, all feline vaccines should be administered by the SQ route.

NOTE: The Feline Infectious Peritonitis (FIP) vaccine has been re-categorized as NON-Core, but is still not recommended by most authors. The World Small Animal Veterinary Vaccine does not recommend administration of this vaccine.

BOOSTER Recommendations for ADULT DOGS:

- After completing the initial series CORE vaccines (distemper+parvovirus+adenovirus-2) it is recommended to administer a single dose (combination vaccine) every 3 years or longer. *NOTE: substantial data exists to demonstrate that dogs derive protective immunity for several years following administration of MLV Core vaccines.*
- *RABIES boosters...In the US, all States currently recognize and accept the use of “3-year” rabies vaccine in dogs. NOTE: some local municipalities may mandate stricter requirements (annual booster) for rabies vaccination.*
- Non-CORE vaccines: administer annually where risk of exposure is sustained.

BOOSTER Recommendations for ADULT CATS

- **CORE Vaccines** (MLV panleukopenia+herpesvirus+calicivirus): administer a single dose every 3 years *following completion of the initial kitten series and the first booster.*
- **Recombinant (NON-adjuvanted) Rabies:** is currently available as a 1-year product; administer a single dose annually in accordance with State, local or Provincial law.
- **(Alternative) Killed (adjuvanted) Rabies:** administered in accordance with State, local or Provincial law.
- **Non-CORE Vaccines:** (FeLV) recommended every 1 (or 2) years if risk is sustained (ie, outdoor cats with reasonable risk of encounter with other cats). The parenteral recombinant FeLV (rFeLV) vaccine is not adjuvanted; all other FeLV vaccines contain adjuvant.

(NOTE: recommendations for booster intervals of FeLV vaccine in adult cats vary from “annually” to “every 3 years”...regardless of the product used. Discussions I’ve had with scientists involved with vaccine development support the recommendation that no FeLV vaccine should be administered at an interval of more than 2 years.)

- Other non-core vaccines are seldom administered and should be considered only after assessing and defining a clear risk of exposure. All other non-core vaccines are recommended for annual administration as long as the risk of exposure persists.

PART II
FREQUENTLY ASKED QUESTIONS: The FACTS vs. The FICTION

1. Selection and use of vaccines.

FICTION: All vaccines for the same disease are essentially the same; save cash and buy the cheapest product available.

FACT: From the standpoint of both safety and efficacy, the differences among the various vaccine types can be significant.

Vaccines can be divided into 3 types based on manufacturing technology: **Inactivated** (killed), **Attenuated** (modified live); and **Recombinant**. Knowledge of vaccine type is becoming increasingly important to veterinarians as more product enters the market, creating more choice for vaccinating against the same disease. (NOTE: the terms “infectious” vs. “non-infectious” are also being used to categorize vaccines on the basis of mechanism for inducing an immune response)

Inactivated Vaccines contain *killed* antigens (bacteria or virus). As such they are “non-infectious” and cannot replicate or revert to virulence post-injection. Because of that, they are often classified as “very safe” vaccines. However, inactivated vaccines tend to contain extraneous proteins (excipient), many also contain adjuvant, which can increase risk for development of acute vaccine reactions (facial edema, shock) and have been attributed to causing delayed onset adverse reactions, eg, “injection-site sarcoma” in cats.

In addition, inactivated vaccines tend to have the shortest durations of immunity (typically 1-year). Veterinarians should be alert to the package label, which must classify the immunizing antigen as “killed”.

When an alternative choice is available, it is generally preferable to use either an attenuated or recombinant product...the potential advantages being longer duration of immunity and reduced reaction risk.

NOTE: for some diseases, eg, leptospirosis, canine influenza, FIV, canine rabies, injectable *B. bronchiseptica* (the IN *B. bronchiseptica* vaccines are attenuated) the only current option available is a Killed vaccine.

Modified-Live (attenuated, or MLV) Vaccines contain either bacteria or virus capable of replicating in the patient following inoculation, hence they are also called “infectious” vaccines. Because vaccine virus/bacteria have been attenuated, the risk of causing clinical signs/illness post-inoculation is significantly low today.

Attenuated vaccines induce a sustained protective immune response lasting, typically, for several years following initial immunization. Unless combined with a killed antigen, attenuated vaccines do not contain adjuvant. The safety of MLV vaccines used today is excellent. For this reason, MLV vaccines are recommended over killed vaccines when the choice is available. Technically speaking, there is a slight risk that, in some patients, replicating virus/bacteria in the vaccine will cause clinical signs consistent with the disease the vaccine intends to prevent following inoculation. Occasional reports of illness have been linked to IN *Bordetella bronchiseptica* vaccines, MLV Distemper and Parvovirus (dog and cat) vaccines. True reversion of attenuated vaccine virus to a virulent virus is not likely today.

Recombinant Vaccines, and there are different kinds of recombinant vaccines, represent the latest technology available today for the immunization of animals. Recombinant vaccines are in widespread use in dogs, cats, and horses (and ferrets) throughout the world. A variety of technologies are used today to produce recombinant vaccines. However, one property they share is the ability to induce a protective immune response without the need for administering whole live, or killed, virus/bacteria. This technology takes advantage of the ability to isolate selective genetic sequences from pathogens and selectively ‘deliver’, in the form of a vaccine, sequences that subsequently express immunogenic protein...but only the protein needed to induce immunity. The greatest advantage to recombinant vaccine use is safety. Today, none of the recombinant vaccines sold in North America contain adjuvant.

REF: 2011 AAHA Canine Vaccination Guidelines, available at: www.aahanet.org

REF: Greene CE and Schultz RD. Immunoprophylaxis. Chpt 100, in CE Greene (ed): Infectious Diseases of the Dog and Cat. 3rd ed. pp. 1069-1119, 2006.

REF: Tizard IR. *Veterinary Immunology: An Introduction* (8th ed), Saunders-Elsevier, 2009.

2. Vaccines not recommended.

FICTION: If it's a licensed vaccine, I can use it with confidence in my practice.

FACT: Well...you *can*...administer any licensed vaccine to the species it approved for. After all, they are licensed. However, independent studies conducted on canine and feline vaccines since their original release (some of these vaccines have been on the market, unchanged, for over 25 years) have indicated that, while safe to use, there is limited to no immunologic value in administering the product. In the US and Canada, the canine coronavirus vaccine AND the Feline Infectious Peritonitis (FIP) virus vaccine are not recommended...in practice or even for use in higher risk environments, such as shelters.

REF: 2011 AAHA Canine Vaccination Guidelines; available at: www.aahanet.org

REF: AAFP Feline Vaccine Guidelines-2006; available at www.catvets.com.

3. Use of 'combination' (ie, multivalent) products.

FICTION: Giving too many vaccines at the same time to the same patient could "overwhelm" the immune system resulting in little or no immune response.

FACT: Immunologists will point out that the immune system of a healthy dog or cat is quite capable of responding to all of the combination antigens in vaccines on the market today. 3-in-1 and 4-in-1 products are commonly used...but even 5-in-1 and 6-in-1 products are considered to be efficacious.

4. Use of multiple vaccines in individual dogs at the same appointment.

FICTION: Size of the patient is *not* a consideration when there is a need to administer multiple vaccines at the same time.

FACT: Doing so may pose increased risk for an acute-onset reaction (hypersensitivity)...especially small breed dogs receiving multiple vaccines at the same appointment.

Giving multiple doses of vaccine at the same appointment (especially among small breed dogs) has been shown to be associated with increased risk of causing an acute vaccine adverse event. Today, it is recommended that, especially in small breed dogs, that veterinarians consider delaying administration of NON-core vaccine until 2 to 4 weeks after completion of the CORE vaccines. Then, administration of any NON-core vaccine should be limited to those patients having a reasonable risk of exposure to the pathogen.

REF: Moore GE, Guptill LF, Ward MP, et al. Adverse events diagnosed within three days of vaccine administration in dogs. *J Am Vet Med Assoc.* 227:1102-1108, 2005.

5. Splitting vaccine doses for "small" dogs.

FICTION: Vaccines are safe and effective when given at, for example, weekly intervals.

FACT: Vaccines can be "safely" administered at weekly intervals...HOWEVER, doing so poses the risk that the innate immune response to the first dose (cytokines, etc) will interfere with the second dose given a week later...it is currently recommended that vaccines be administered at a MINIMUM interval of 2 weeks...*regardless of the antigen.*

REF: 2011 AAHA Canine Vaccination Guidelines; available at: www.aahanet.org **REF:** Guidelines for the Vaccination of Dogs and Cats. WSAVA, published in *JSm Anim Pract.* 51:1-32, 2010. Available at: www.wsava.org.

6. Reducing the volume of a vaccine dose to reduce the risk of an adverse reaction.

FICTION: Giving half of a vaccine dose will reduce the risk of reactions in small dogs.

FACT: There are no data to support the practice of reducing the volume of vaccine in small breed dogs. In fact, it is possible that doing so may result in a sub-immunizing response...ie, not enough antigen to effectively protect the patient. Furthermore, there is no evidence that doing so *actually* reduces the risk of causing an adverse reaction...if the patient is truly hypersensitive to one of the constituent proteins, the patient could still react if given 10% (0.1 mL) of the dose.

REF: 2011 AAHA Canine Vaccination Guidelines; available at: www.aahanet.org

REF: Guidelines for the Vaccination of Dogs and Cats. WSAVA, published in JSm Anim Pract. 51:1-32, 2010. Available at: www.wsava.org.

7. Mixing vaccines from different manufacturers in the same syringe.

FICTION: As long as the vaccine is approved for use in that species, mixing vaccines from different manufacturers is OK.

FACT: This practice is NOT recommended. Because manufacturing processes vary among companies, mixing different vaccines from different manufacturers may result in pH or osmolality incompatibility that will render one or more immunizing antigen ineffective. PLUS...if a serious post-vaccinal reaction or injury resulted, the veterinarian could be deemed negligent.

ALSO...vaccines from different manufacturers can be administered to an individual patient at the same appointment...however, it is recommended that vaccines be administered in different sites using a separate syringe for each dose administered.

8. Effectiveness after re-constitution.

FICTION: Once re-constituted, MLV vaccines have a 'shelf-life' of several hours or, if kept in the refrigerator, several days.

FACT: Vaccines sold as a freeze-dried (lyophilized) product (typically MLV vaccines) should be used promptly...regardless of whether they are stored in the refrigerator. Especially important is the fact that once re-constituted (rehydrated with diluent), MLV vaccines are susceptible to degradation and may become completely inactive. In the case of canine distemper vaccines, for example, the re-constituted product can become inactive within 2 hours. *THEREFORE*...it is currently recommended to adhere to the following principle:

"1 HOUR...use it...or lose it!" ...regardless of how it's stored.

REF: 2011 AAHA Canine Vaccination Guidelines; available at: www.aahanet.org

9. Canine *Bordetella* vaccination: IN or SQ?

FICTION: When immunizing dogs against *B. bronchiseptica*, the appropriate protocol entails administering an IN vaccine first...then, administering parenteral (injectable) vaccine for all subsequent boosters.

FACT: Although that was advocated (10 years ago), current studies have challenged that practice. When feasible, studies have shown that it is preferable to inoculate dogs against *B. bronchiseptica* and parainfluenza virus via the IN route. Not only does this rapidly (within 3 days) reduce the risk of clinical illness following exposure, but prevents post-exposure shedding. For high-density populations at risk of

exposure to infectious respiratory disease, IN vaccination is recommended. Dogs that are deemed to be at risk of exposure, but aggressively resist IN vaccination, should be vaccinated parenterally.

REF: Davis R, Jayappa H, Abdelmagid OY, et al. Comparison of the mucosal immune response in dogs vaccinated with an intranasal avirulent live culture or a subcutaneous antigen extract vaccine of *Bordetella bronchiseptica*. *Vet Therap.* 8:32-40. 2007.

REF: Ford RB: *Bordetella bronchiseptica*: Beyond "Kennel Cough", J Bonagura and DC Twedt (eds). Kirk's Current Veterinary Therapy XIV. Saunders-Elsevier, St. Louis. 2009.

REF: Buonavoglia C and Martell V. Canine respiratory viruses. *Vet Clin N Am:Sm Anim Pract.* 38:355-273. 2007 (Review: 173 references)

REF: Keil DJ and Fenwick B: Canine respiratory bordetellosis: Keeping up with an evolving pathogen. In LE Charmichael (ed): *Recent Advances in Canine Infectious Diseases*. International Veterinary Information Service (www.ivis.org) Document No. A0104.0100) 13 January 2000.

10. Administration of an IN vaccine by the SQ route...eg, *Bordetella bronchiseptica*.

FICTION: A vaccine intended for IN use can also be administered by the SQ or oral routes.

FACT: This **MUST NOT** be done. Severe post-vaccination complications associated with replication of bacteria and release of toxic proteins that target the liver could cause acute hepatocellular injury and death following a single dose. **WARNING:** some products licensed for IN administration are packaged as though they are intended for parenteral administration. **ALL PERSONNEL AUTHORIZED TO ADMINISTER VACCINE MUST BE TRAINED ON PROPER ADMINISTRATION TECHNIQUES.**

Administering an IN vaccine orally will render the vaccine ineffective and will not immunize.

REF: Toshach K, et al. Hepatocellular necrosis associated with subcutaneous injection of in intranasal *Bordetella bronchiseptica*-canine parainfluenza vaccine. *JAAHA.* 33:126-128, 1997.

11. Leptospirosis vaccination.

FICTION: 2 points surface in discussions on leptospirosis vaccination: 1) I've never diagnosed a case in this practice, therefore, vaccination is not warranted...vs...2) leptospirosis is a zoonotic disease therefore vaccination should be considered CORE.

FACT: As of Fall 2010, all leptospirosis vaccines provide protection against the 4 serovars (*L. canicola*, *L. icterohaemorrhagiae*, *L. grippityphosa*, *L. pomona*) most often recognized to be pathogenic for dogs (living in the United States). The so-called "2-way" vaccines (*L. canicola* and *L. icterohaemorrhagiae*) are currently not recommended *in the event the practice recommends vaccination*.

Whether or not to recommend the vaccine remains a complex question. The fact that a practice has never diagnosed a case of leptospirosis is, obviously, no guarantee that it won't. The MAJOR limiting factor regarding leptospirosis diagnosis is the lack of a point-of-care diagnostic test (...that may be changing soon!). Current diagnostic tests (MAT and PCR) must be sent out to a qualified laboratory...the patient, on the other hand, has acute liver or renal failure. Quite likely, leptospirosis is "under" diagnosed in the US.

On the other hand, leptospirosis is a zoonotic disease...and vaccination is justified in areas where risk exists...the problem here is, considering the lack of testing conducted in practice, where is the risk? In addition, leptospirosis vaccines are among the most reactive vaccines in the inventory. The decision to vaccinate...or not to vaccinate...remains the discretion of the clinician and the owner. When the decision to vaccinate is made, there are some considerations worth noting:

All Leptospirosis vaccines are killed and contain adjuvant except one (Merial-Recombitek® 4 LEPTO). There are no attenuated or recombinant leptospirosis vaccines available today.

Because duration of immunity (DOI) information on the 2-way leptospirosis vaccines had never been defined, veterinarians and academicians have questioned the need to administer leptospirosis vaccine

every 6 months (or more often) to sustain a protective level of immunity. In 2010, the Recombitek® 4 Lepto vaccine (Merial) was released in the US; this product does carry a label claim of 15.5 months DOI for *L. grippityphosa*. Data is available that demonstrates a 12 month DOI for serovars *L. canicola* and *L. icterohemorrhagiae*. Challenge studies have shown that the Recombitek® 4 Lepto vaccine prevents infection as well as shedding of spirochetes.

It should be noted that other manufacturers of Leptospirosis vaccines are seeking, or have already obtained, a DOI label claim of 1 year. Some have also obtained labeling that supports the prevention of infection and shedding.

REF: Minke JM, et al. Onset and duration of protective immunity against clinical disease and renal carriage in dogs provided by a bi-valent inactivated leptospirosis vaccine. *Vet Microbiol.* 120:137-145, 2009.

REF: Greene CE, et al. Leptospirosis. Chpt 44, in CE Greene (ed): *Infectious Diseases of the Dog and Cat*. 3rd Edition. Saunders-Elsevier, St. Louis, 2006, pp. 402-417.

REF: Product Label/Package Insert: Recombitek® 4 Lepto

12. Vaccination against Lyme disease.

FICTION: Lyme disease is not even a disease, and the vaccine causes worse disease than the infection.

FACT: Canine Lyme borreliosis (aka, Lyme disease) is real. What's more, canine infections are occurring in regions of the US and Canada (especially Southern Ontario) that have not previously had the disease. Regionally speaking, infections are expanding.

The published data is clear on the fact that the commercial vaccines for Lyme disease do a relatively good job of protecting dogs...for about 12 months. It is not expected that 100% of the patients vaccinated will develop protective immunity to Lyme borreliosis. Two vaccine types are on the market: a killed, whole spirochete and a recombinant OspA (outer surface protein-A). All vaccines depend on the same antigen, OspA, to immunize. Killed, whole spirochete vaccines contain numerous excipient proteins + adjuvant and do seem to be associated with acute (1-3 days) vaccine adverse events.

None of the vaccines used in the US today cause a False '+' test result on the IDEXX 3Dx or 4Dx test for Lyme borreliosis.

Administration of a Lyme vaccine should NOT be used as part of the *treatment* for Lyme disease!

REF: Hebert D and Eschner A. Seroprevalence of *Borrelia burgdorferi*-specific C6 antibody in dogs before and after implementation of a nonadjuvanted recombinant outer surface protein A vaccine in a Rhode island small animal clinic. *Vet Therap.* 11:E1-E8, 2010.

REF: Wikle RE, et al. Canine Lyme disease: one-year duration of immunity elicited with a canine OspA monovalent lyme vaccine. *Intern J Appl Res Vet Med.* 4:23-30, 2006.

REF: Greene CE and Straubinger RK. Borreliosis. Chpt 45, in CE Greene (ed): *Infectious Diseases of the Dog and Cat*. 3rd Ed. Saunders-Elsevier, St. Louis. pp. 417-435, 2006.

13. Overdue for booster vaccination.

FICTION: A dog or cat that is overdue for CORE vaccines must re-start the initial 3-dose series to be immunized.

FACT: Regardless of the number of weeks, months, or years *overdue* a dog or cat may be, administration of a single dose (MLV or Recombinant CDV), is expected to rapidly induce a protective level of antibody. The reason: immunologic "memory".

Overdue for RABIES: In the event a dog or cat has exceeded the 3-year vaccination interval required by State or local statutes for RABIES, most States/municipalities consider a single dose to be all that is required to 'boost' the patient's immunity to rabies. *However*, rabies vaccination requirements do vary from State to State and even among different cities/counties within a State. It's important to check the

official position of your State/municipality by contacting the State Dept of Public Health or the State Public Health Veterinarian when making these types of vaccination decisions.

14. Vaccination during pregnancy.

FICTION: Vaccinating a pregnant dog/cat will assure good levels of maternally derived antibody in newborn puppies/kittens.

FACT: Vaccination with MLV (attenuated) and/or killed (inactivated) vaccines during pregnancy should be avoided, if possible, to avoid potential injury to the fetus. The only reasonable exception is in shelter-housed dogs/cats, where vaccination would be advised if the pregnant animal has never been vaccinated and there is risk of exposure to a highly pathogenic virus (e.g. CDV, CPV-2, FPV).

REF: AAHA Canine Vaccine Guidelines (2007-revised); available at: www.aahanet.org and AAHP Feline Vaccine Guidelines-2006; available at www.catvets.com.

15. Breed-specific vaccination recommendations.

FICTION: The initial vaccination series in Dobermans and Rottweilers should be continued until 20 or 24 weeks of age.

FACT: Today, most authors agree that these breeds do NOT have a uniquely higher risk of acquiring parvovirus following exposure nor are they more likely than any other breed to fail to be immunized following parvovirus vaccine administration. The high disease incidence and the frequency of vaccine failures recognized in the late 70's and early 80's is not considered to be a concern today.

16. Adjuvanted feline vaccines...friend...or...foe?

FICTION: Killed (adjuvanted) feline vaccines are as safe and efficacious as MLV feline vaccines.

FACT: Concern is over the role of adjuvant-containing vaccines (virtually all killed feline vaccines contain adjuvant) in causing fibrosarcoma. This continues to be a highly controversial issue. A few facts are worth considering: adjuvants, by their very nature, induce inflammation, typically...chronic inflammation lasting days to weeks (or longer). The cellular response associated with adjuvant-induced inflammation is still regarded by most oncologists and other academicians who work with vaccines to be responsible for the DNA injury (oxidative injury) associated with metaplasia in fibroblasts. In genetically pre-disposed cats (it appears), there is risk of neoplastic transformation of fibroblasts into fibrosarcoma (or other types of mesenchymal tumor). BE PRACTICAL...avoid adjuvanted vaccines in cats!

REF: AAHP Feline Vaccine Guidelines-2006; available at www.catvets.com.

REF: Martano M. et al. Feline Injection-site Sarcoma: Past, Present, and Future Perspectives. *Vet. J.* 2011 (188) 136-141.

REF: Woodward KN. Origins of Injection-Site Sarcomas in Cats: The Possible Role of Chronic Inflammation- A Review. *ISRN Vet. Sci.* 2011. Article ID 210982

17. Onset of immunity following vaccination.

FICTION: Post vaccinal onset of immunity is not predictable.

FACT: Consider the following:

- KILLED VACCINE-assuming no maternal antibody, 2 doses are required, 2 to 4 weeks apart, *then* about 10 days later (~ 24-25 days minimum)

- MODIFIED-LIVE-assuming no maternal antibody, about 5 to 7 days post vaccination (earlier for some infections such as distemper).

- RECOMBINANT Vectored-same as MODIFIED-LIVE. Exception: The recombinant canine distemper virus (rCDV) vaccine has been shown to immunize dogs in the presence of maternal antibodies. rCDV is indicated in high exposure risk environments.

- RABIES...the unique 'exception': In most locations in the world, onset of immunity to rabies following administration of the INITIAL vaccine is determined *by law...not by serological response (Ab)*. In most locations...a dog and cat will be considered (by law) to be immunized 28 days following the initial vaccination.

REF: Greene CE and Schultz RD. Immunoprophylaxis. Chpt 100, in CE Greene (ed): Infectious Diseases of the Dog and Cat. 3rd ed. pp. 1069-1119, 2006.

REF: Larson, L and Schultz, RD. Effect of vaccination with rCDV vaccine immediately before exposure under shelter-like conditions. *Vet Therap* 7(2):113-118, 2006.

REF; Pardo MC, Tanner P, Bauman J, et al: Immunization of puppies in the presence of maternally derived antibodies against canine distemper virus. *J Comp Path.* 137:S72-S75, 2007.

REF: Compendium of Animal Rabies Prevention and Control . MMWR Recomm Rep. 2011 Nov 4;60(RR-6):1-17.

18. Antibody titers as an assessment of immunity.

FICTION: Antibody titers can be used in place of annual vaccination boosters to assess immunity.

FACT: It depends! ...specific limitations apply to titers when assessing the immune status of an individual patient. Fact: titers for CDV, CPV, and feline parvovirus (panleukopenia) correlate extremely well with immunity...dogs/cats that have a "positive" titer are considered immune...quite likely for many years. Fact: a "negative" titer does not always correlate with susceptibility. Antibody is a glycoprotein and does dissipate over time. Animals that were previously vaccinated may lose Ab over time; however, immunologic "memory" (B-lymphocytes) is retained for many years for these 3 diseases. Exposure to virulent virus in a previously vaccinated, but antibody negative patient, typically results in a rapid anamnestic 'boost' of antibody titer and a protective immune response. Annual or triennial boosters are merely a form of immunologic insurance for these 3 diseases.

For other diseases, antibody titers are *not* good correlates of protective immunity. Feline herpesvirus-1 and feline calicivirus titers can be obtained, but are not recommended for the assessment of the individual patient's immunity to those diseases. FeLV titers are not valid at all because of the lack of a valid test method. Leptospirosis titers are routinely performed but generally are used to define exposure/infection...not immunity. See RABIES TITERS (next question).

REF: Greene CE and Schultz RD. Immunoprophylaxis. Chpt 100, in CE Greene (ed): Infectious Diseases of the Dog and Cat. 3rd ed. pp. 1069-1119, 2006.

Indications for the use of Antibody Titers in Clinical Practice

- To determine whether or not a puppy or kitten was immunized following administration of the initial vaccine series, a titer can be submitted 2 or more weeks following the last dose of the initial series.
- To assess whether an adult animal has maintained an antibody titer (CDV, CPV, Feline parvovirus) following previous vaccination (e.g., years earlier, with no recent revaccination).
- Veterinarians may elect to determine titers, rather than administer booster vaccines in patients with a history of having had a vaccine reaction -or- having been treated for and recovered from an immune-mediated disorder (e.g., hemolytic anemia or thrombocytopenia) can be tested.

REF: 2011 AAHA Canine Vaccination Guidelines; available at: www.aahanet.org

19. Rabies titers to assess immunity in a dog or cat

FICTION: Rabies titers can be used to assess immunity.

FACT: Titers can NOT be used to assess immunity. States/local municipalities generally do not accept FAVN (fluorescent antibody virus neutralization) rabies titer results as a replacement for vaccination or as an index of immunity in a dog/cat. FAVN test results (only provided in the US by Kansas State University and DoD [military members only]) are used to comply with requirements on the exportation of animals to designated Rabies-Free areas of the world.

COST: \$80 (October 2011 price); takes ~3 to 4 weeks.
1-2 mL serum (shipped on a cold-pack)

Attn: FAVN Rabies Laboratory
Kansas State Veterinary Diagnostic Laboratory
Mosier Hall O-245
1800 Denison Avenue
Kansas State University
Manhattan, KS, USA 66506-5601

Phone: 785-532-4483
Forms: www.vet.ksu.edu/rabies

REF: Compendium of Animal Rabies Prevention and Control . MMWR Recomm Rep. 2011 Nov 4;60(RR-6):1-17.

20. Legal Considerations when vaccinating cat/dogs.

FICTION: Because recommendations contained within the Canine (AAHA) and Feline (AAFP) Vaccination Guidelines *differ* from the manufacturers' recommendations listed on the package insert, I'm subject to legal liability if I choose to follow the Guidelines.

FACT: It is fact...the Guidelines do make recommendations that, in part, differ from the manufacturer's recommendations. Specific examples include: Boosters of CORE vaccines can be administered every 3 years (or longer) vs. (manufacturer) "annual booster recommended".

Guideline recommendations on the frequency of vaccination are based on several studies that substantiate these recommendations. In addition, each of the major vaccine manufacturers has reviewed these recommendations in advance of publication. As stated in the context of the Guidelines: "veterinarians have considerable latitude in the selection and use of veterinary biologic products licensed for dogs [and cats], with rabies vaccine being a noted exception, and that these Guidelines, although not intended to dictate an exclusive protocol or standard, do meet accepted standards of professional practice."

REF: 2011 AAHA Canine Vaccination Guidelines; available at: www.aahanet.org