2016 Canine Vaccination Protocols

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ach year, and despite the availability of published vaccination guidelines, veterinarians continue to be challenged with new, sometimes complex, even conflicting, information regarding the selection and use of companion animal vaccines. New products, new issues, and of course, new controversies seem to emerge regularly. It's all part of a dynamic, changing market that not only complicates the effort of publishing current and relevant vaccination guidelines but challenges practitioners to maintain a level of vaccine awareness that goes beyond price and the marketing brochures.

Part 1 of this manuscript summarizes current recommendations for the vaccination of dogs; this includes protocol-related information on the latest canine vaccines to be released in the United States (e.g., H3N2 canine influenza virus) since the last iteration of the AAHA Canine Vaccination Guidelines was published in 2011 (currently in revision).

Part 2 of this manuscript attempts to address some of the more common controversial questions raised by practicing veterinarians as they review/revise current vaccination protocols in practice; for example:

- REDUCING the dose when vaccinating small-breed dogs? Why **not** to do this?
- WHY VACCINATE at 8 weeks of age if maternal antibody interferes with vaccination?
- VACCINE TITERS—When are they indicated? And what do the results really mean?
- LEGAL LIABILITY—Published guidelines versus manufacturer recommendations?
- RABIES VACCINATION—Required (in most states) by law...are you really AWARE?
 And more...

It should be noted that this manuscript is written for and applicable to veterinarians practicing in the **United States** and **Canada**. Although a small number of vaccines are used in the United States that are not currently available in Canada, the recommendations outlined in this paper are applicable to veterinarians practicing in both countries. For veterinarians practicing outside of the United States and Canada, the World Small Animal Veterinary Association (WSAVA) has recently updated vaccination guidelines for dogs (2016).^a There is considerable consistency among the recommendations outlined by respective guidelines, highlighting the fact that vaccination guidelines are "going global."

Although veterinarians are encouraged to follow published guidelines, unique variables (e.g., age, chronic illness, exposure risk) exist that may require clinicians to modify a conventional vaccination protocol to meet specific needs of an individual patient/client.

Therefore, vaccination recommendations outlined in this paper are **not** intended to define a universal vaccination protocol or the "standard of care" for vaccination. Instead, they are intended to guide practitioner decisions on how to best implement a rational vaccination protocol that provides maximum levels of protection among the patient population seen in an individual practice.

NOTE: Vaccination recommendations for dogs 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 and ones that are may not fall within the manufacturers' label recommendations.



^aWorld Small Animal Veterinary Association's Vaccine Guidelines 2016: Soon to be available at www.wsava.org.

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Part I. Canine Vaccination Recommendations

TABLE 1. VACCINATION OF PUPPIES/DOGS		
CORE Vaccines	Administration	Booster Recommendations
Combination product administered as: MLV or recombinant canine distemper virus + MLV parvovirus + MLV adenovirus-2 OPTION: May include MLV canine parainfluenza virus.	3 doses are recommended between 6 and 16 weeks of age. Example: 8 weeks; and 12 weeks; and 16 weeks of age. NOTE: The last dose in the initial series should be administered between 14 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. NOTE: A minimum interval of 2 weeks between any 2 doses of vaccine is recommended. Administer subsequent boosters every 3 years (or longer).
Rabies (killed) 1-year and 3-year vaccines are available.	A single dose of rabies vaccine should be administered not earlier than 12 weeks of age. (In most practices, rabies vaccine is usually administered at 12 or 16 weeks of age.) (State/local/provincial law applies.)	Schedule a second dose to be administered not later than 1 year following administration of the first dose, regardless of the dog's age at the time the initial dose is given. Then every 3 years thereafter. (State/local/provincial law applies.)
NONCORE Vaccines	Administration	Booster Recommendations
Bordetella bronchiseptica + canine parainfluenza virus (intranasal only) Some intranasal products may also contain CAV-2 antigen.	Single intranasal (IN) dose at 12 or 16 weeks of age. (Optional: Some authors recommend 2 doses at 12 and 16 weeks of age.) Intranasal vaccine may be administered as early as 3 to 4 weeks of age.	Where risk of exposure is sustained, administer a single dose 1 year following the last dose administered, then every year thereafter.
Bordetella bronchiseptica only (monovalent) 3 options are available: • Parenteral (killed-bacterin) OR • Intranasal (avirulent live) OR • Intraoral (avirulent live)	 Parenteral (SQ): 2 doses are required, 2 to 4 weeks apart. Intranasal (IN): The manufacturer recommends a single initial dose. Intraoral: The manufacturer recommends a single initial dose. 	Where risk of exposure is sustained, administer a single dose 1 year following the last dose administered, then every year thereafter.
Leptospirosis (killed) 4-serovar NOTE: Routine use of a 2-serovar leptospirosis vaccine is not recommended.	 2 initial doses, 2 to 4 weeks apart, are required regardless of the dog's age. NOTE: It is not recommended to administer the first dose before 12 weeks of age. Small-breed dogs (<20 lb [9 kg]): Consider delaying initial doses until the CORE vaccine series has been completed. 	Where risk of exposure is sustained, administer a single dose 1 year following completion of the <i>initial</i> 2-dose series, then every year thereafter.
Lyme disease (recombinant OspA or killed whole-cell bacterin)	2 initial doses, 2 to 4 weeks apart, are required regardless of the dog's age. NOTE: For small-breed dogs (<20 lb [9 kg]): Consider delaying initial doses until the CORE vaccine series has been completed.	Where risk of exposure is sustained, administer a single dose 1 year following completion of the initial 2-dose series, then every year thereafter. OPTION: For dogs residing in endemic regions, administration of the first booster 6 months following completion of the initial 2-dose series is a reasonable alternative schedule. An additional booster is recommended at 1 year following completion of the initial series, with annual vaccination recommended thereafter.
Canine influenza virus—H3N8 (killed)	2 initial doses, 2 to 4 weeks apart, are required.	Where risk of exposure is sustained, administer a single dose 1 year following completion of the <i>initial</i> 2-dose series, then every year thereafter.
Canine influenza virus—H3N2 (killed)	2 initial doses, 2 to 4 weeks apart, are required.	Where risk of exposure is sustained, administer a single dose 1 year following completion of the initial 2-dose series, then every year thereafter.

NOTE: Canine coronavirus vaccination is not recommended. *Crotalus atrox* (Western Diamondback rattlesnake) vaccine should only be used in dogs with a defined risk for exposure. Follow the manufacturer's recommendations for dosing. CAV=canine adenovirus; MLV=modified-live virus; OspA=outer surface protein A; SQ=subcutaneous.

Overdue for Vaccination

Studies focused on dogs that are overdue for routine vaccination have not been published. The following recommendations represent expert opinion and are intended to provide a practical approach to immunizing dogs when conventional vaccination guidelines have not been followed.

Overdue during the initial vaccine series: While most practices administer the initial core vaccine series to young dogs at intervals of 3 to 4 weeks, dogs exceeding a 6-week interval between any of the initial doses should receive 2 additional doses, 3 to 4 weeks apart.

The same is true during the initial 2-dose series recommended for dogs receiving noncore vaccines. If the interval between doses exceeds 6 weeks, 2 additional doses, 3 to 4 weeks apart, should be administered.

Overdue for core vaccine booster: Administer a single dose of a combination core vaccine *regardless of the number of years that have lapsed.*

Overdue for rabies booster: Requirements for revaccination of dogs that are overdue for a rabies booster vary from state to state and may vary within an individual state. Many states follow recommendations published in the 2011 Rabies Compendium, which states: Administer a single dose, after which the dog will be considered *immediately* immunized.

Overdue for leptospirosis, Lyme, and/or parenteral Bordetella booster: Dogs that are within 2 years of a previous dose may receive a single dose. Dogs exceeding a 2-year interval should restart the initial 2-dose series.

Overdue for intranasal or intraoral Bordetella booster:

Administer a single dose regardless of the number of years that have lapsed.

Overdue for canine influenza virus booster: Dogs that are within 3 years of a previous dose may receive a single dose. Dogs exceeding a 3-year interval should restart the initial 2-dose series.

Part II. Questions on Vaccination Protocols

The following questions are among the most commonly asked questions I've received that address vaccination protocols and recommendations. The responses are based on our understanding of immunologic principles as they apply to vaccines and vaccination as well as the collective opinion of internists, immunologists, and virologists.

If you have a question that is not represented here, please contact me at **rbford@ncsu.edu**, and I'll get a response to you.

Should I reduce the 1.0 mL vaccine dose for small breeds? This seems to be a relatively common practice today...but it should **not** be. Generally, this is done for (at least) 2 reasons:

- Administering a 1.0 mL dose of vaccine to a 4 lb (~2 kg) dog seems excessive when the same dose is required for a 110 lb (50 kg) dog, and...
- Reducing the volume might reduce the risk of an adverse reaction (this is commonly done with leptospirosis and killed Lyme vaccines) when administering vaccine to small-breed dogs.

While all vaccine licensing studies are based on ~22 lb (~10 kg) beagles, arbitrarily reducing the administered volume of vaccine because the patient weighs 4 lb (2 kg) may induce an immune response that is below that required to induce (or sustain) protection...the fact is, you're experimenting. There are no published studies addressing the weight:vaccine dose. One might also argue that the 1.0 mL dose administered to a 50 kg (110 lb) Great Dane might be inadequate...that's not been studied either.

An immune response subsequent to administering a vaccine (*biologic product*) is far more complex (e.g., antigen processing and presentation; expression of epitopes, B-cell activation) and quite unlike that associated with administering an antibiotic (*pharmaceutical product*).

Additionally, if a dog is truly hypersensitive to one or more components of a vaccine, simply reducing the volume is certainly no guarantee that the risk of a reaction will be reduced.

Because inactivated (usually adjuvanted) vaccines tend to be associated with adverse reactions (although this is still argued), we (AAHA Guidelines Task Force) have recommended that veterinarians avoid administering multiple vaccine doses at a single appointment to small-breed (≤10 kg [22 lb] estimated adult body weight) dogs. It is also recommended to give the full dose, but to **delay** administration of noncore (optional, and usually killed) vaccines to small-breed dogs until at least 2 weeks after administering core (priority) vaccines. Informal surveys with veterinarians who practice this approach with small-breed dogs suggest that client compliance (additional vaccine appointments) is high…especially when it is explained that the reason for doing so is **safety**.

If maternal antibody is so likely to interfere with a dose of vaccine administered at 6 to 8 weeks of age, why even worry about this dose?

Over the past few years, vaccination guidelines for dogs have emphasized extending the initial vaccine series to 14 to 16 weeks (dog) to avoid vaccine interference with maternally derived antibody...so why even bother with giving a dose at 6 to 8 weeks of age?

In practice, there is really no practical means of measuring interfering levels of maternal antibody. Conventional recommendations to administer the first dose between 6 and 8 weeks of age is intended to provide protection in the event there is no maternal antibody present. If, in fact, maternal antibody is not present at 6 weeks of age (e.g., orphan pup), a single dose of a core vaccine will, quite likely, immunize. The goal is to "be there with vaccine when maternal antibody is not there." Hence, the recommendation for the initial vaccine series beginning at 6 to 8 weeks of age.

What should I know about vaccine "titers"?

The demand for assessing antibody levels induced by vaccines has increased substantially over the past 2 years. Titers can be measured by either sending serum to a commercial laboratory or documenting "protective" levels through use of test kits for point-of-care testing in practice (~25 minutes per test run).

IMPORTANT: There are some limitations to be aware of. A "positive" result does correlate with "protection" when assessing parvovirus (canine/feline) and canine distemper and adenovirus. But not all "titers" correlate with protection. For example, leptospirosis titers are measured in an attempt to diagnose infection, but the antibody levels do **not** correlate with protection. The same is true with rabies. A titer can be measured, but rabies antibody titers represent prior/recent exposure to vaccination; they are **not** a legal index of protection. **No state in the United States recognizes rabies antibody titers as** "**protective.**"

Indications for testing include:

- Assessing the antibody response following completion of the initial vaccine series (test 2 to 4 weeks following the last dose in the initial series). This is a valuable means of assessing maternal antibody interference **or** identifying a so-called genetic nonresponder (they still exist).
- Assessing antibody levels in a patient with a chronic illness (or history of immune-mediated disease) in which boosters might not be indicated. A "positive" test result indicates
 2 things: (1) the patient is protected, and (2) the patient has "memory" (the presence of antibody indicates B-cell activation and "memory," which for parvovirus, distemper virus, and adenovirus likely correlates with lifelong protection even though the antibody levels may decline in the future).
- Distinguishing "protected" from "susceptible" animals in the event of an infectious disease outbreak (e.g., shelterhoused dogs). Knowledge of the antibody level enables selective isolation/fostering and avoids the need to arbitrarily euthanize large numbers of animals.

What is my legal liability to administer core vaccines? Do I follow guidelines or manufacturer recommendations?

True malpractice litigation linked to vaccination is rare in veterinary medicine. Yet, veterinarians continue to challenge the "legality" of administering (core) vaccines triennially when the majority of vaccine labels (package inserts) recommend annual vaccination. We've looked at this issue carefully and from the legal perspective. Here's how it goes: The manufacturer cites recommendations for administering a vaccine...not requirements. **Fact**: With the exception of rabies (which is required by state or local statutes), veterinarians have considerable discretion in the selection and use of vaccine. There is nothing illegal about administering a vaccine every 3 years when the manufacturer recommends annual boosters. It's your choice.

How stable are vaccines in the vial?

Once a freeze-dried (lyophilized) vaccine is rehydrated (reconstituted to a liquid state), how long will the vaccine remain stable and immunogenic? Vaccines sold as a freeze-dried (lyophilized) product (typically modified-live virus [MLV] vaccines) should be used promptly following reconstitution, regardless of whether they are stored in the refrigerator. Especially important is the fact that once reconstituted, MLV vaccines are susceptible to degradation and may become inactive within hours. In the case of canine distemper vaccines, for example, the reconstituted product can become inactive within 2 hours. Therefore, we have recommended the following:

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

I gave the Bordetella vaccine SQ...oooops! What do I do? It happens. An intranasal or oral *Bordetella bronchiseptica* vaccine is inadvertently administered by the subcutaneous route. What action, if any, is appropriate?

IMPORTANT: Any vaccine specifically licensed for administration onto a mucosal surface (intranasal, conjunctival, or oral) is a live, attenuated bacteria or virus. (Killed vaccines administered onto a mucosal surface are not immunogenic.) Because some of the *Bordetella* vaccines (intended for intranasal or oral administration) are sold in vials that resemble parenteral products, they are occasionally injected into the patient, usually via the SQ route.

While anecdotal reports from veterinarians suggest that many dogs tolerate SQ injection of an intranasal or oral *Bordetella* vaccine with minimal consequences, some dogs will develop severe injection-site reactions, and a very small number are at risk of dying...from acute hepatic failure.

In the event this does happen, administer an antibiotic (preferably doxycycline or amoxicillin–clavulanic acid) at conventional doses for at least 5 to 7 days starting as soon as possible subsequent to the injection. If an abscess develops at the injection site, it should be opened, drained, and thoroughly lavaged. Although attenuated, the *B. bronchiseptica* in the vaccine is live and susceptible to antibiotics. Simply "diluting" the vaccine by injecting sterile saline into the injection site is not a reasonable treatment.

AND as a reminder...when administering an intranasal or oral vaccine to a patient, it would be wise to ensure that the patient is **not** also receiving concurrent antibiotic therapy, thereby avoiding the risk of "killing" the vaccine.

What is my legal requirement to administer the rabies vaccination? And what is the Rabies Awareness Initiative?

Rabies immunization is the **only** companion animal vaccine that is required (at least in most states) by law. And, in many states, only a licensed veterinarian is authorized to administer the vaccine. Although it's not the veterinarian's responsibility to ensure that animals are vaccinated, it is the veterinarian's responsibility to understand state (and local) rabies law and the implications of rabies regulations when, for example, a dog bites a human or when a pet that is overdue for a rabies booster is "exposed" to rabies (wildlife or an unvaccinated dog).

The application, interpretation, and enforcement of rabies vaccination laws are well known to vary significantly from state to state and can even vary within states. We have learned that practitioner awareness of complex and sometimes conflicting rabies laws can lead to considerable confusion, misinterpretation of state/local statutes, and inappropriate actions...some of which

have led to unnecessary euthanasia of dogs. Knowledge and application of state/local rabies law by veterinarians is further compounded in some states by outdated online resources, disparate distribution of rabies information, and the complexity of state/local government websites citing immunization law.

To address the most critical issues concerning rabies immunization and law, the Rabies Awareness Initiative has been created for veterinarians practicing in the United States (and Puerto Rico).

The **Rabies Awareness Initiative** is a national educational program that is supported by Merial Inc. Content is solely derived from the rabies control authorities in each state, generally the state public health veterinarian.

The goal of the Rabies Awareness Initiative is to raise veterinarians' awareness of (individual) state immunization

requirements for rabies, enhance clinical services to companion animal clientele, and promote rabies vaccination compliance among pet owners. Online resources will soon be available (2016) that will provide the most up-to-date information and the necessary tools to help educate pet owners on the importance of rabies vaccinations.

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