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Considerations In Designing Effective And Safe Vaccination Programs For Dogs

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Introduction

During the past 50 years many vaccines have been developed to prevent a variety of infectious diseases of dogs. Currently there are 16 canine vaccines licensed in the USA which are available commercially (Table 1). Although a few of the vaccines are available as monovalent products (e.g. rabies, canine parvovirus), most are available only as multi-component products that contain between 2 to 10 components. Some vaccines have had a profound effect by reducing, or eliminating, diseases characterized by moderate to high morbidity and/or mortality. However, other vaccines have had little or no recognized beneficial effect because they were designed to prevent infections that cause little or no morbidity and/or mortality. Some vaccines are so new that the potential benefits they provide are not known e.g., *Giardia*, *Leptospira (L.) grippotyphosa* and *L. pomona*.

Table 1. List of the Licensed Canine Vaccines Available Commercially in the United States¹.		
Viral	Bacterial	Paracite
Canine Distemper Virus (MLV) Canarypox-Distemper Virus (LRV) Canine Distemper Virus/Measles Virus (MLV) Canine Parvovirus-2 (MLV, K) Canine Adenovirus-1 (K) Canine Adenovirus-2 (MLV, K) Canine Parainfluenza Virus (MLV) Canine Coronavirus (MLV, K) Rabies Virus (K)	<i>Bordetella bronchiseptica</i> (MLV, K) <i>Borrelia burgdorferi</i> (Lyme) (K, KR) <i>Leptospira canicola</i> (K) <i>Leptospira grippotyphosa</i> (K) <i>Leptospira icterohaemorrhagiae</i> (K) <i>Leptospira pomona</i> (K)	<i>Giardia</i> (K)

MLV = Modified Live Vaccine; KR = Killed Recombinant Vaccine; K = Killed Vaccine; LRV = Live Recombinant Vaccine

1. Only a few of these vaccines are available as monovalent products. Almost all commercial products contain two or more of these vaccines. The most common multi-component product contain CDV, CPV-2, CAV-2, CPI, *Leptospira canicola*, *Leptospira icterohaemorrhagiae*. This product is often referred to as a "7-way vaccine" because it should protect against (CAV-2 and CAV-1) in addition to the other 5 components.

"Core" Vaccines

Canine vaccines which are considered essential, and should be given to every dog, are termed "core vaccines." All other vaccines are regarded as "non-core" and should be used in dogs considered at high risk on an as

needed basis. Core vaccines are considered essential because they are designed to prevent important diseases that pose serious health threats to susceptible dogs, irrespective of geographic location or the life style of a dog. Some "non-core" vaccines also may be considered "core" because they are designed to prevent a disease that is a potential public health threat.

Efficacy and safety of a product are critical in deciding whether a vaccine should be considered core. Diseases that pose a serious risk to susceptible dogs, or to public health, which are readily preventable by current vaccines include rabies, a major public health disease caused by the rabies virus (RV); canine parvovirus caused by canine parvovirus-2 (CPV-2); canine distemper caused by canine distemper virus (CDV), and infectious canine hepatitis (ICH) caused by canine adenovirus type-1 (CAV-1). ICH is effectively controlled by canine adenovirus-2 (CAV-2) vaccine which has replaced CAV-1 vaccines because it is much safer. As part of a minimum disease prevention program, every dog should receive CPV-2, CDV, CAV-2 and rabies vaccines at least one time at or after the age of 12 weeks (Table 2). If that were the only vaccination a dog ever received, and the products used were modified live CPV-2, CDV, CAV-2 and a 3-year killed rabies, the dog would have a >80% probability of developing immunity to those four viruses for 3 or more years.

Vaccination programs for highly contagious diseases are most effective when all, or the highest percentage possible, of animals in the population have been vaccinated. Therefore, every effort should be made to ensure that as many dogs as possible over the age of 12 weeks are vaccinated with at least one dose of the four core vaccines.

Table 2. Duration of Immunity and Efficacy for Canine Vaccines Commercially Available in the United States.		
Vaccine	Minimum Duration of Immunity	Estimate of Relative Efficacy (%)
Core		
Canine Distemper	$\geq 7 \text{ yr}^1$	>90
Canine Parvovirus-2	$\geq 7 \text{ yr}^1$	>90
Canine Adenovirus-2	$\geq 7 \text{ yr}^1$	>90
Rabies Virus	$\geq 3 \text{ yr}^1$	>85
Non-Core		
Canine Coronavirus	"lifetime" ^{3,5}	---
Canine Parainfluenza	$\geq 3 \text{ yr}^1$	>80
<i>Bordetella bronchiseptica</i>	$\leq 1 \text{ yr}^{1,2}$	< 70
<i>Leptospira canicola</i>	$\leq 1 \text{ yr}^2$	≤ 50
<i>Leptospira grippotyphosa</i>	$\leq 1 \text{ yr}^4$	---
<i>Leptospira icterohaemorrhagiae</i>	$\leq 1 \text{ yr}^2$	≤ 75
<i>Leptospira pomona</i>	$\leq 1 \text{ yr}^4$	---
<i>Borrelia burgdorferi</i> (Lyme disease)	$\geq 1 \text{ yr}^1$	≤ 75
<i>Giardia</i>	$\leq 1 \text{ yr}^4$	---

1. Experimental challenge studies and/or serologic studies have been performed. Field experience during outbreaks also confirm experimental challenge studies.
2. Based on field experience and observations from outbreak studies and clinical records. Reliable experimental or controlled studies often not available.
3. Not available; cannot be determined. CCV has not been shown to cause significant disease.
4. Vaccines recently licenced; information not available except from company data.
5. See text.

Minimum Disease Prevention

In the United States, which has the highest percentage of vaccinated dogs, I estimate that less than 60% of all dogs receive the minimum disease prevention vaccination program (Table 3). In many countries less than 30% of dogs receive this one time vaccination with the four core vaccines. Efforts to increase the percentage of vaccinated dogs will require a better understanding by veterinarians and dog owners of the importance, effectiveness and safety of this one time vaccination program. In contrast to a minimum disease prevention program, the vaccination programs for the majority of well cared for pets are vaccination practices considered to provide "maximum disease prevention". Thus, most pet dogs receiving routine veterinary care are given the core vaccines several times; in addition, they routinely receive several of the non-core vaccines. Based on a national survey that we have done during the past 2 years, a majority of veterinary practices began the puppy vaccination program at, or shortly after, 6 weeks of age. The product used most often was a multi-component vaccine containing CPV-2, CDV, CAV, canine parainfluenza (CPI) virus, and *L. canicola* plus *L. icterohemorrhagiae* bacterins. Approximately 50% of dogs received Canine Coronavirus (CCV) in combination or as a separate vaccine. The pups were then revaccinated 3 to 5 times with the same product at 2 to 4 week intervals until they reach an age of 14 to 18 weeks. One dose of rabies vaccine was given at 12 to 16 weeks of age. In approximately 25% of animals, two or more doses of an intranasal vaccine containing *Bordetella bronchiseptica* (*B. bronchiseptica*) and CPI-virus was given to pups before 18 weeks of age! Additionally, Lyme vaccine (*Borrelia burgdorferi*) is sometimes included in the puppy program. In the majority of practices, dogs would then be revaccinated with the vaccines noted above at least annually for the remainder of their lives. An exception to annual revaccination is rabies, which would be given at 1 year of age, and then once every 3 years thereafter, unless more frequent vaccination was required by law or believed necessary by the veterinarian.

Table 3. Vaccination Programs for Dogs.
"Core" Vaccines (Every Dog)
<p>Program A - Minimal Approach Primary Immunization at 12 weeks or older - Canine parvovirus-2 (CPV-2) - Canine Distemper Virus (CDV) - Canine Adenovirus (CAV-2) and Rabies Virus <u>Note:</u> Canine Parainfluenza (CPI) will have to be included since there are no products with CPV-2, CDV and CAV-2 without CPI. Revaccination Rabies - 1 year after primary, then once every 3 years. Other vaccines would not be given again.</p>
<p>Program B - Moderate Approach Primary Immunization - 6 to 9 weeks - CPV-2 + CDV - 12 to 15 weeks - Rabies, CPV-2 + CDV + CAV-2 + CPI* Revaccination - 1 Yr. later - Rabies, CPV-2 + CDV + CAV-2 + CPI*, then again every 3 years for rabies; every 3 -5 years for other vaccines. *See note under Program A</p>

Program C - Maximal Approach

Primary Immunization

- 6 to 8 weeks - CPV-2 +CDV - 9 to 11 weeks - CPV-2 + CDV + CAV-2 + CPI* - 12 to 14 weeks - Rabies, CPV-2 + CDV + CAV-2 +CPI*

Revaccination

- 1 Yr CPV-2 + CDV + CAV-2 + CPI* + Rabies. - 3 Yr CPV-2 + CDV + CAV-2 + CPI* + Rabies. *See note under Program A

"Non-Core" Vaccines

(Give only if the dog is at high risk and then only the vaccine that is needed)

Program D - Minimal Approach

- Give only "core" vaccines ("Non-core" vaccines are not given)

Program E - Moderate Approach

Primary Immunization

- 6 weeks of age, or older - 1 dose of intranasal *B. bronchiseptica* + CPI*
- 12 week and 14 to 15 weeks - 2 doses of *Leptospira* bacterin (2- or 4-serovars)

Revaccination

- Annually - *Leptospira* bacterin + intranasal *B. bronchiseptica* + CPI*

*See note under Program A

Program F - Maximal Approach

Primary Immunization - 6 to 14 weeks of age - 2 doses Intranasal *B. bronchiseptica* + CPI*

- 9 to 11 weeks and 12 to 14 weeks - *Leptospira* bacterin (2-serovars or 4-serovars)

- 9 to 11 and 12 to 14 weeks - 2 doses Lyme disease vaccine

- 6 to 8 weeks and 9 to 11 weeks - 2 doses *Giardia* vaccine

*See note under Program A

Revaccination

- Annually with intranasal *B. bronchiseptica* and CPI

- At least annually with *Leptospira* bacterin (2-serovars or 4-serovars)

- Lyme vaccine - annually, a few months prior to peak tick season

- Omit *Giardia* vaccine

Additional Recommendations

When Canine Parvovirus is a serious threat:

- CPV-2 monovalent MLV product starting at 5 weeks of age then giving the product every other week until 15 weeks of age. A more reliable program would be to determine antibody titers to CPV-2 and vaccinate pups when CPV-2 antibodies no longer interfere with immunization.

When Canine Distemper is a serious threat:

- Measles virus - CDV combination at 4 to 6 weeks of age; then a product containing CDV without MV at 12 weeks of age or older.

Program A, B, or C for "core" products can be matched with any of the "non-core" product programs D, E, or F. Therefore, Program A can be matched with D (no "non-core" product given) or with F, where any of the non-core vaccines needed could be given and given again annually for dogs at high risk. Vaccination more often than listed in C and F should rarely, if ever, be done.

Considering the difference between the minimum disease prevention program that protects >80% of dogs from the important canine diseases and the program described above, it is not surprising that neither the dog-owning public nor veterinarians appreciate the exceptional benefit derived from the "minimum disease prevention program".

Why are there significant differences in number of doses and components of vaccines routinely given in the maximum vs. minimum disease prevention programs? Those differences arise primarily from misperceptions about how vaccines work, which vaccines are necessary, and how often vaccines should be given during the life of the dog to provide protective immunity.

Common Questions Regarding Vaccines/Vaccination

- At what age should the vaccination program begin?
- How often does a dog need to be revaccinated? (What is the duration of immunity?)
- How does one determine the risk of disease, and therefore the necessity for one or more of the "non-core" vaccines?
- How effective are the vaccines?
- Do all current vaccines for a given disease provide similar protection?
- What are the risks of causing adverse reactions with certain vaccines or when giving vaccines too often?

Those questions are being asked more now than in the past since most vaccine experts, and many dog owners, believe that certain vaccines are given too often and some are unnecessary. Answers to the above questions are complex and depend on the needs of a particular animal as well as the expectations of the owner and veterinarian. [1,2,3,4,5].

At What Age and Which Vaccines to Use?

Unfortunately, simple and universally agreed on answers are not available. Most experts agree that puppy vaccination programs should begin at 6 to 9 weeks of age; the first puppy vaccination should begin prior to 6 weeks of age only in special situations, e.g., humane shelters. Vaccination at less than 6 weeks of age is often not effective due to interference of vaccinal immunity by passively acquired antibodies and, rarely (e.g. <2 weeks of age), inability of a pup's immune system to respond effectively to the vaccine. Ideally, pups should be kept in a clean environment prior to vaccination and have no, or minimal, contact with dogs other than the dam and littermates. The first and second doses of vaccine in a puppy series optimally includes only the CPV-2 and CDV components. Those are the most important vaccines for a pup less than 12 weeks of age because canine parvovirus and canine distemper are the two most serious infectious diseases of dogs. CPV-2 is now the most important vaccine in the USA since pups are most likely to encounter this virus because of its high prevalence and environmental stability. When CDV is a major threat to young pups, as in known distemper-infected kennels or humane shelters, the most effective product is the combined measles virus (MV)-CDV vaccine. This product can be used in pups as young as 4 weeks of age when necessary. When MV-CDV is used, revaccination should be done with a CDV product that does not contain MV. After 9 weeks of age, the vaccine regimen should include a rabies vaccine (12 weeks or older) and multi-component vaccines (CPV-2, CDV and CAV). All current commercial products also contain CPI virus, however, CPI is not needed in the parenteral vaccine since it is often given and is more effective when given intranasally in combination with *B. bronchiseptica*. Intranasal products are available which contain CAV-2 in addition to *B. bronchiseptica* and CPI. Use of the three-way intranasal product would eliminate the need to give CPI and CAV-2 parenterally.

Leptospira bacterins, if needed, should ideally be given at 9 weeks of age or older. *Leptospira* bacterins require two doses of vaccine which should be given at intervals of 2 to 4 weeks between doses. Multiple doses of modified live viral vaccines are generally required only in pups less than 12 weeks of age because after this age passively acquired antibodies from the dam have usually declined below levels which prevent successful immunization. When MLV vaccines are given to pups that have lost their passively acquired antibody (~12 weeks of age), a single dose of vaccine can immunize. Multiple doses are required for primary vaccination with certain killed vaccines (e.g. *Leptospira* spp., Lyme disease) but single doses are sufficient when revaccinating at a later time, usually at 1 year. Due to improvements in multi-component core vaccines, especially the CPV-2 component, and the lower antibody titers of dogs in vaccinated populations it is no longer necessary to administer vaccines through the age of 18 to 20 weeks. Previous recommendations for the last dose of vaccine at 18 or 20 weeks were made in the 1980's and early '90's because CPV-2 vaccines failed to immunize a high percentage of pups even when passively acquired antibody titers were well below the level of antibody that provided protection from infection with virulent virus. [3,6] Also at that time, a large proportion of dogs had antibodies recently engendered by virulent virus, rather than vaccines. The "window of vulnerability" ("critical period" - see Canine Parvovirus chapter; U. Truyen), was as long as several months when certain of the older CPV-2 vaccines were used! However, with the improved CPV-2 vaccines now available from the major vaccine manufacturers, the "window of vulnerability" has been reduced to 2 weeks, or less. It is, therefore, not necessary to vaccinate pups beyond 12 to 14 weeks of age. The other core vaccine

components also will immunize a majority of dogs when the last dose is given at 12 to 14 weeks of age. [6,7,8].

How Often to Vaccinate?

Repeated vaccinations with multi-component vaccines need not be repeated at intervals more often than every 2 to 4 weeks in a puppy program. Two to three doses of vaccine should be adequate to immunize when vaccination is started at 6 to 9 weeks. The most important aspect of a puppy vaccination program is to make certain that the last dose of vaccine in the series is given when the animal is at least 12 to 14 weeks of age. However, as mentioned above, pups often receive 4 to 6 doses of the same multi-component vaccine during the first 3 - 4 months of life. The higher number of doses may be justified for animals in humane shelters, commercial kennels, or other areas where animals are at high risk. However, pet dogs in a single or multi-dog household are at low risk of exposure to most diseases. Such animals would not need to be revaccinated every 2 weeks and they should never be vaccinated every week, as practiced in the USA by some breeders and veterinarians. Furthermore, if a dog is at high risk of exposure to an important disease like CPV-2, a monovalent CPV-2 vaccine is recommended, not a multi-component product. The risk of adverse reactions has been greater with multi-component vaccines.

Expected Immunization Success

Since passively acquired antibody declines below the level where it can interfere with the current core vaccines by 12 to 14 weeks of age, modified live CPV-2, CDV and CAV vaccines given at this age will immunize a very high percentage of pups (>90%) and the immunity from that single dose of vaccine will last for several years. Our research on duration of immunity for the CPV-2, CDV and CAV vaccines has demonstrated a minimum duration of immunity of 7 years; the maximum duration of immunity may be for the life of most (>80%) vaccinated animals. Many killed rabies vaccines have a minimum duration of immunity of 3 years. However, a small percentage of pups (<5%) fail to develop immunity to one or more of the core components and a much higher percentage of pups (>25%) fail to develop immunity to certain of the non-core vaccines for a variety of reasons. Reasons which have been given include: The presence of passively acquired antibody at time of last vaccination; delay in maturation of the immune system; poor vaccinal immunogenicity; vaccine not given often enough; genetic inability to respond to certain vaccine antigens; immunosuppression; too many components in a multi-component vaccine; or ineffective lots of vaccine. [9, 10].

To ensure that all pups become immune, one dose of rabies vaccine is given at 12 weeks of age or older, followed by a second dose 1 year later, or at 1 year of age. Revaccination is then done at 3 year intervals. Similarly the CPV-2, CDV and CAV vaccine could be given at 1 year and then every 3 to 5 years without concern about loss of immunity. There is no evidence, or reason, to believe that revaccination with the core vaccines more often than recommended above would provide more effective protection from the important diseases since the minimum duration of immunity from the core vaccines is at least 3 years. States in the USA which require annual revaccination for rabies should remove those requirements because annual revaccinations are unnecessary. Vaccinating the same animal less often also would reduce the risk of adverse reactions. In areas where there is a high risk of rabies, programs must be developed to immunize those dogs that have never been vaccinated or have not been vaccinated within the past 3 or more years. Unvaccinated dogs pose the greatest threat for the transmission of rabies virus, not dogs which have been previously vaccinated or, especially, those vaccinated within the past 3 years. In our studies, pups vaccinated annually with modified live CPV-2, CDV and CAV vaccines received no added benefit from annual revaccination throughout a period of 7 years when compared to dogs that were vaccinated as pups then challenged with virulent virus at 7 years of age. Both groups of dogs were protected from challenge infection with CPV-2, CDV and/or CAV. Therefore, for those vaccines that provide immunity for 3 or more years, I believe that annual revaccination is contraindicated - the increased risk of adverse reactions from revaccination provides no benefit. In contrast, use of those products which provide only a short duration of immunity (~1 year) requires annual, or even more frequent, vaccinations - but only with products that contain vaccine components that are needed in a particular region (e.g. Leptospira or Lyme disease bacterins), not with multi-component products containing unnecessary vaccines.

"Non-Core" Vaccines: Which are Needed and When?

Which "non-core" vaccines are really needed? This question is difficult to answer and depends on the animal

and its environment.

Leptospira bacterins - The most important "non-core" vaccine is for leptospirosis since this infection can cause mild to severe illness and it is a zoonosis. The question could be asked why leptospira bacterins are not included as "core" vaccines? The principal reason concerns vaccine efficacy - a high percentage of vaccinated dogs do not develop protective immunity, or they develop immunity for only a short duration of time. Until recently, bacterins contained only two serovars (*L. canicola* and *L. icterohaemorrhagiae*) and cross protection between leptospiral serovars does not occur. Furthermore, the *Leptospira* sp bacterins are among the more reactogenic components in multi-component vaccines. Clinically, immediate and/or chronic immune-mediated reactions have been observed and, experimentally, multiple types of immune mediated hypersensitivities have been induced with leptospiral antigens. Moreover, leptospira bacterins do not prevent infection or shedding of the organisms in the urine, even when they reduce or eliminate the clinical signs of disease. Thus, the public health threat from organisms being shed in the environment persists. Finally, leptospira bacterins are not considered "core vaccines" because leptospirosis is rare in many geographic regions of the USA and few or no clinical cases have occurred for many years. Very recently, new vaccines have been licensed in the USA that contain *L. grippityphosa* and *L. pomona*. The new vaccines should provide broader immunity and, hopefully, will prevent disease caused by those serovars. However, the new vaccine containing the four serovars requires evaluation in a large number of dogs before it is known whether it will reduce the incidence of canine leptospirosis in endemic areas and if adverse reactions are worse than those caused by current products which contain only 2 serovars.

According to our recent survey on vaccination programs, approximately 30% of veterinary practices do not vaccinate for leptospirosis. The responding practitioners either didn't believe that leptospirosis was a significant problem in their area or the vaccine containing *L. canicola* and *L. icterohaemorrhagiae* serovars failed to provide protection. Also, there were concerns about adverse reactions when the current products were used. Approximately 50% of the veterinarians completing the survey must have felt leptospirosis was a significant problem since they vaccinated >75% of the dogs with the products containing *L. canicola*+*icterohemorrhagiae*. According to our survey leptospira bacterins were used in more dogs than any of the other "non-core" vaccines except CPI.

Canine parainfluenza and *B. bronchiseptica* - CPI is included as a component of all current parenteral vaccines containing CDV, CPV-2 and CAV; therefore, it is given to every dog that receives the core vaccine. Approximately 80% of practices surveyed vaccinated less than 50% of dogs with *B. bronchiseptica*. The product used most often for kennel cough was an intranasal vaccine that contained both *B. bronchiseptica* and CPI. Many non-vaccinated dogs never develop "kennel cough" or they develop mild, self-limiting disease; however, other dogs, both vaccinated and non-vaccinated, developed severe, protracted kennel cough requiring treatment. Efficacy of the present kennel cough vaccines is controversial (see: Canine Respiratory Bordetellosis, Keil and Fenwick) and duration of immunity, if present, would be less than 1 year. Ventilation and hygiene are important in environments where kennel cough is prevalent. In certain kennels, improvement in ventilation has eliminated or reduced the need for kennel cough vaccines. Also, in some environments vaccination at intervals as frequent as every 3 to 6 months failed to significantly reduce respiratory disease.

Coronavirus vaccines - Although approximately 50% of practices routinely use coronavirus vaccine, most vaccine experts agree that this vaccine is not needed. Some experts consider CCV vaccines useless. Clinical disease rarely occurs with CCV infection and when disease does occur it is usually mild, self-limiting and most commonly seen in pups less than 8 weeks of age - an age which is earlier than vaccine would provide benefit. Based on our observations that the preponderance of clinical cases caused by CCV occur in young pups, any "protection" derived from vaccination of pups or from natural infection would, in the practical sense, last a lifetime. Furthermore, CCV alone has not been shown to experimentally cause significant disease in susceptible dogs. The demonstration that CCV can enhance the severity of disease caused by CPV-2, does not suggest a need for CCV vaccine since dogs vaccinated with CPV-2 vaccine only, are completely protected when co-infected with a combination of CCV and CPV-2. [6] CCV vaccine alone provided no protection for dogs challenged with a combination of CCV and CPV-2.

Lyme Disease Vaccine - This vaccine should be used only in areas where Lyme disease is known to occur, and where it may pose a serious threat to the health of the dog. Even in areas where Lyme disease has been shown to be endemic, and where infection with *Borrelia burgdorferi* is common, clinical illness is rare. When seen, it is often mild and readily treated with antibiotics. In certain highly endemic areas where infection of the natural vectors (mice and deer) is almost 100%, disease in dogs may be more common, and sometimes severe, but cases are responsive to antibiotic treatment.

After the release of the first human Lyme disease vaccine, a segment of the human population with a particular human leukocyte antigen type, determined by genetics, was found at increased risk to developing chronic arthritis after vaccination with the Lyme vaccine. This finding should signal caution in the over use of canine Lyme vaccine since a similar phenomenon may occur in dogs. Lyme disease vaccine, if used, should be given only to dogs that are truly at very high risk of infection/disease.

Giardia vaccine - This relatively new product may be valuable in a highly specialized market, mainly in larger breeding kennels which whelp and raise many puppies. It is unlikely to provide benefit as a routine vaccine. The effectiveness and safety of the *Giardia* vaccine in those special situations where it is used remains to be determined. Use of this vaccine would likely play an insignificant role in reducing the public health concerns of human *Giardia* infection.

Adverse Reactions

The risks of adverse reactions from vaccines are not well studied, nor are the adverse reactions rates well documented. Even where documented, the information is not readily available. The immune mediated hypersensitivities caused by vaccines are well known and occur in every species. [4, 10,11] The most commonly observed hypersensitivity is a type I (immediate) reaction which is most often caused by IgE antibody resulting in a local or generalized anaphylaxis. The most common signs of local reactions are facial edema, hives, itching and rarely sneezing; signs of a systemic reaction include urination, vomiting, diarrhea, which is sometimes bloody, dyspnea and collapse. According to a recent survey we have conducted, the most common vaccination reactions observed in dogs include pain, soreness, stiffness and/or lethargy at variable times after vaccination. Swelling, a persistent lump, irritation, hair loss and/or color change of hair at site of injection were also observed as common reactions. A change of behavior was reported in a small percentage of dogs after vaccination. Post-vaccinal neurologic disease (e.g. encephalitis) was rare. All of the reactions noted above generally occur within minutes, hours or days after vaccination; they were, therefore, likely to have been associated with a vaccination. More recently, it has been shown experimentally that dogs develop an autoimmune response after vaccination, something that was known to occur in other species [11]. Furthermore, a study of dogs in veterinary clinics showed a slight increase in cases of autoimmune hemolytic anemia within 30 days following vaccination with multi-component vaccines [12]. It is very difficult to document a "cause and effect" relationship between vaccination and disorders occurring weeks to months after vaccination, but it would not be unexpected for vaccines to trigger immune-mediated disease (including autoimmune disorders) in a small percentage of animals [4, 5, 11, 12]. Adverse reactions from vaccines should not be used as a reason not to vaccinate; instead, it is sensible not to use vaccines which are unnecessary, or to vaccinate more often than needed. In general, bacterial vaccines are more likely to cause immune-mediated reactions than do viral vaccines. Killed vaccines, especially those which contain adjuvants, are more likely to cause adverse reactions than do modified live vaccines. Because immune mediated reactions are genetically determined, some breeds, especially certain families of dogs, are at much greater risk of developing adverse reactions than the canine population as a whole [4].

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