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CANINE VACCINATION

Craig E. Greene, DVM, MS, Ronald D. Schultz, PhD,
and Richard B. Ford, DVM, MS

Despite the concerns over recommendations to reduce the frequency and number of vaccines administered annually to dogs and cats, the need for companion animal vaccines and vaccinations continues to be a fundamental part of health management programs in the twenty-first century. What is happening now, however, is an effort by academicians and practitioners to review companion animal vaccination standards in the United States. The American Association of Feline Practitioners and the Academy of Feline Medicine, in a consensus paper compiled by a panel of experts, have already published the latest vaccination recommendations for cats[27] (the reader is referred to the article on feline vaccination in this issue).

What constitutes the ideal vaccination protocol goes beyond a document of vaccine recommendations used at a veterinary teaching hospital or compiled by a panel of academicians. Instead, a vaccination protocol selected for use within a practice entails identifying preventable diseases that pose a serious risk to the individual animal, and vaccinating that animal at an early age, hopefully prior to exposure to the pathogen, with a product that provides long term immunity and has minimal risk of causing adverse reactions. There are currently a number of products that meet these requirements.

What follows is an objective and clinically relevant review of the canine vaccines licensed for use in North America today and a discus-

From the Department of Small Animal Medicine, College of Veterinary Medicine, University of Georgia, Athens, Georgia (CEG); Department of Pathobiological Sciences, School of Veterinary Medicine, University of Wisconsin–Madison, Madison, Wisconsin (RDS); and Department of Clinical Sciences, College of Veterinary Medicine, North Carolina State University, Raleigh, North Carolina (RBF)

sion of the facts that have compelled so many authors to challenge existing vaccination practices. This article is not intended to establish new vaccination standards for dogs, nor should it be used as a template for a national canine vaccination protocol. Nevertheless, change is in the wind, and revised recommendations for canine vaccination can be anticipated. The material presented in this article serves as a guide for clinicians willing to consider proposed canine vaccination recommendations as they apply to individual patients. Table 1 represents a summary of the information presented in this article.

WHY CHANGE?

Is it really necessary to revise vaccination recommendations for dogs? Many would challenge that premise. After all, vaccination practice over the last 20 years has, in fact, worked well; canine distemper, canine parvovirus, and canine rabies are virtually nonexistent among vaccinates. Yet, despite the obvious successes attributable to companion animal vaccination, veterinarians must be willing to at least review, if not revise, vaccination practice standards as new vaccines are introduced and new vaccine technologies are developed. The objective, quite simply, is to administer the most appropriate vaccine(s) at the most appropriate stage of life and to do so with the best product(s) available. What should not occur is complacency and regimentation with respect to selection and administration of vaccines. Yet, that does happen.

The demand among veterinarians that vaccines be simple to administer and timesaving has led to the long-term and widespread use of polyvalent vaccines. Twenty-five years ago, the most commonly used polyvalent products contained three vaccines (distemper-hepatitis-leptospirosis). Today, products containing eight or more vaccines per dose are routinely administered to dogs. Furthermore, polyvalent vaccines are routinely administered annually with seemingly little regard for the actual risk of infection. This is a disturbing trend. Annual administration of polyvalent vaccine implies that each vaccine antigen, whether of bacterial or viral origin, in each polyvalent product induces the same degree of immunity for the same duration in every patient. Immunologically, this is irrational. Depending on the vaccine and based on the results of controlled challenge studies, dogs derive protective immunity that persists for as little as a few months to as long as 7 or more years.[2, 4, 7, 14, 18, 20, 25, 29, 30] Convenience rather than science seems to be the driving force behind conventional recommendations listed on vaccine "labels" (product inserts). Even the 1995 ruling by US Department of Agriculture that manufacturers of new veterinary biologic agents must document the duration of immunity listed on the label (this ruling does not apply

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Table 1. RECOMMENDED GUIDELINES FOR THE ADMINISTRATION* OF VACCINES TO DOGS

Vaccine	Primary Vaccination (puppy)	Primary Vaccination (adult)	Booster†	Recommendation
Canine distemper virus (CDV) (MLV)	2, 3, and 4 months of age	One dose	Annual	*Highly recommended:* Despite annual booster recommendations, adult dogs challenged 7 years (Rockborn strain) and 5 years (Onderstepoort strain) after MLV vaccination were protected. A booster vaccination interval of every 3 years in adult dogs is reasonable.
Recombinant canine distemper virus (rCDV)	2, 3, and 4 months of age	Two doses, 3–4 weeks apart	Annual	*Highly recommended:* May be used interchangeably with MLV-CDV vaccine. Level of protection conferred by the rCDV vaccine is comparable to that provided by MLV vaccines. Duration of immunity for rCDV has not been established beyond 1 year.
Distemper–measles (MLV) (administer intramuscularly only)	One dose between 6 and 12 weeks of age only (one MLV-CDV or rCDV vaccine follows—distemper-measles vaccine at 14–16 weeks of age)	Not indicated for use in female dogs over 12 weeks of age	Not recommended	*Optional–not recommended for routine use:* Intended to provide temporary protection in young dogs only. Indicated for use in households/kennels where distemper is a recognized problem. Do not administer to female dogs over 12 weeks of age.
Canine adenovirus-1 (CAV-1) (MLV or killed)	Two doses every 3–4 weeks until 12 weeks of age	Two doses 3–4 weeks apart	Annual	*Not recommended:* Infectious canine hepatitis is uncommon in the United States. Considering the low (to absent) prevalence, the risk of "hepatitis blue-eye" reactions and the fact that CAV-2 cross-protects against CAV-1, use of vaccines containing this antigen is not recommended for use in routine vaccination protocols.
Canine adenovirus-2 (CAV-2) (MLV or killed)	2, 3, and 4 months of age	One dose (if using MLV) Two doses 3–4 weeks apart (if using killed)	Annual	*Recommended:* Demonstrated cross-protection against canine hepatitis (CAV-1) and CAV-2, one of the agents known to be associated with infectious tracheobronchitis. Usually combined with CDV and CPV vaccine. Currently, this product is not available as a monovalent vaccine. Adult dogs challenged 7 years after CAV-2 MLV vaccination were found to be protected against the more virulent CAV-1.

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Table 1. RECOMMENDED GUIDELINES FOR THE ADMINISTRATION* OF VACCINES TO DOGS *(Continued)*

Vaccine	Primary Vaccination (puppy)	Primary Vaccination (adult)	Booster†	Recommendation
Parainfluenza virus (CPiV) (MLV)	2, 3, and 4 months of age	One dose	Annual	*Recommended:* Usually combined with CDV and CAV vaccine. Currently, this product is not available as a monovalent vaccine.
Bordetella bronchiseptica (killed bacterin) (administer parenterally)	6–8 weeks of age, then 10–12 weeks of age	Two doses 2–4 weeks apart	Annual	*Optional:* The parenteral vaccine may be less efficacious than the topical *B. bronchiseptica* plus parainfluenza virus vaccines in their ability to stimulate a local immune response (upper respiratory tract).
Bordetella bronchiseptica (live avirulent bacterin) + parainfluenza virus (MLV) (topical [intranasal] use only)	Administer a single dose as early as 2 weeks of age (see product literature for specific age recommendations)	Not stipulated, although a single dose is recommended	Annual or 1 week before possible exposure	*Optional:* For use in dogs housed in kennels, shelters, or pounds, or before boarding in kennels. Transient (3–10 days) coughing, sneezing, or nasal discharge occurs in a small percentage of vaccinates. Antimicrobial therapy may be indicated (doxycycline or 5–7 days) to manage postvaccination upper respiratory signs (persistent cough and nasal discharge). Topically administered vaccines for canine infectious tracheobronchitis may provide a superior local immune response compared with parenterally administered vaccines.
Bordetella bronchiseptica (live avirulent bacterin) + parainfluenza virus (MLV) + canine adenovirus-2 (MLV) (topical [intranasal] use only)	Administer a single dose at not less than 8 weeks of age	A single dose is recommended	Annual	*Recommended:* For use in dogs considered to be at risk of exposure to any of the pathogens listed. Topically administered vaccines for canine infectious tracheobronchitis may provide a superior local immune response compared with parenterally administered vaccines.

Canine parvovirus (MLV)	2, 3, and 4 months of age	One dose	Annual	*Highly recommended:* Although annual boosters are recommended by vaccine manufacturers, studies have shown protection against challenge 7 years after vaccination with MLV vaccine. It has been suggested that adult dogs vaccinated against parvovirus with MLV vaccine remain immune for at least 3 years after vaccination. Adult dogs challenged 7 years after parvovirus MLV vaccination were found to be protected.
Canine parvovirus (killed)	2, 3, and 4 months of age	Two doses 3–4 weeks apart	Annual	*Recommended:* A suitable alternative to the MLV canine parvovirus vaccine. Killed parvovirus products are susceptible to maternal antibody interference in puppies as old as 16 weeks (or older?). Although annual boosters are recommended by vaccine manufacturers, studies have shown protection against challenge 16 months after vaccination with killed vaccine.
Borrelia burgdorferi; Lyme borreliosis (killed bacterin)	Initial dose may be given at 12 weeks of age and a required second dose 3–4 weeks later	Two doses 3–4 weeks apart	Annual	*Optional:* Lyme disease has limited regional prevalence. Recommendation for use is limited to dogs with a known high risk of exposure.
Borrelia burgdorferi; recombinant Lyme borreliosis outer surface protein A	Initial dose may be given at 9 weeks of age and a required second dose 2–3 weeks later	Two doses 2–3 weeks apart	Annual	*Optional:* Lyme disease has limited regional prevalence. Recommendation for use is strictly limited to dogs with a known high risk of exposure. Most authors recommend the recombinant Lyme vaccine over the killed bacterin for reasons of safety (fewer adverse reactions).

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Table 1. RECOMMENDED GUIDELINES FOR THE ADMINISTRATION* OF VACCINES TO DOGS *(Continued)*

Vaccine	Primary Vaccination (puppy)	Primary Vaccination (adult)	Booster†	Recommendation
Canine coronavirus (killed and MLV)	Every 2–4 weeks of age until 12 weeks of age (MLV); begin as early as 6 weeks of age and administer every 2–3 weeks, with the final dose at 12 weeks of age (killed)	One dose (if using MLV) Two doses 2–3 weeks apart (if using killed)	Annual	*Optional:* Prevalence of clinical cases of confirmed canine coronavirus infection does not justify routine inoculation of all dogs. Clinical infections are most likely to occur in puppies less than 6 weeks of age. Clinical signs are mild and typically resolve spontaneously. The authors currently recommend that animal shelters *not* use coronavirus vaccine in routine vaccination programs because of additional costs incurred by doing so and the lack of benefit. Experience has shown no additional increase in infectious enteritis among adults or puppies subsequent to discontinuing canine coronavirus vaccine in shelters.
Leptospira interrogans (*L. canicola* combined with *L. icterohaemorrhagiae*) (killed bacterin) (now available with serovars *grippotyphosa* and *pomona*)	12 and 16 weeks; do not administer to dogs less than 12 weeks of age	Two doses 2–4 weeks apart	Annual; some authors recommend a booster every 6 months in dogs considered to be at significant risk of exposure	*Optional:* Anecdotal reports from veterinarians and breeders suggest that the incidence of postvaccination reactions (acute anaphylaxis) in puppies (<12 weeks of age) and small-breed dogs is high.
Giardia (killed)	Initial dose may be given at 8 weeks of age; a second dose should be given 2–3 weeks later	Two doses 2–3 weeks apart	Annual	*Not recommended for routine use:* The vaccine prevents oocyst shedding but does not prevent infection. Although giardiasis is the most common intestinal parasite among people in the United States, the source of human infection is contaminated water. Infections in dogs and cats are not likely to be zoonotic.

Rabies 1-year (killed) (route of administration may not be optional—see product literature for details)	Administer one dose as early as 3 months of age	Administer a single dose	1-year rabies vaccine may be used as a booster vaccine when dogs are required to be vaccinated annually against rabies (local statutes apply)	*Required:* MLV vaccines are not available; state and local statutes govern the frequency of administration for products labeled as "1-year rabies." The rabies (1-year) vaccine is generally administered as an initial dose followed 1 year later by administration of the rabies (3-year) vaccine; state and local statutes may dictate otherwise.
Rabies 3-year (killed) (route of administration may not be optional—see product literature for details)	The 3-year rabies vaccine may be used as an alternative to the 1-year rabies vaccine for initial and subsequent doses (local statutes apply); administer one dose as early as 3 months of age	The 3-year rabies vaccine may be used as an alternative to the 1-year rabies vaccine for initial and subsequent dose (local statutes apply); administer a single dose	Second rabies vaccination is recommended 1 year after administration of the initial dose regardless of the animal's age at the time the first dose is administered; depending on local statutes, booster vaccines should be administered annually or every 3 years	*Required:* State and local statutes govern the frequency of administration for products labeled as rabies (3-year); these statutes vary throughout the United States. The rabies (1-year) vaccine is generally administered as an initial dose followed 1 year later by administration of the rabies (3-year) vaccine; state and local statutes may dictate otherwise.

*Route of administration is subcutaneous or intramuscular unless otherwise noted by the manufacturer.
†As recommended by the manufacturer.

to vaccines licensed before 1995) is not likely to change "annual booster" recommendations stipulated by manufacturers. It is important to understand that manufacturers are not mandated to establish the full duration of immunity but only to document what they claim. Studies to establish the *maximum* duration of immunity that would meet USDA guidelines are not economically feasible.

The recommendation that virtually all canine vaccines be administered annually to adult dogs has been embraced by the veterinary profession for many years. Interestingly, however, for most vaccines administered to dogs today, there are no scientific studies at all establishing a 12-month duration of immunity. Vaccine efficacy studies for most vaccines in use today challenged vaccinates just 3 to 4 weeks after the last inoculation. The paradigm that adult dogs and cats require annual boosters for all the commonly administered vaccines is being challenged. We simply cannot continue to arbitrarily administer vaccines without regard for the number and type of vaccine antigens in the product and without realistic consideration of the risk of infection facing the individual animal.[12, 15, 16, 22, 24]

CANINE DISTEMPER

Modified live virus (MLV) vaccines have been most effective in protecting dogs against canine distemper. Inactivated whole viral vaccines are not effective; however, a vectored recombinant vaccine is currently available. In puppies, distemper vaccination is performed at 3- to 4-week intervals, with the earliest inoculation being given when the puppy is 6 to 8 weeks of age. Most distemper vaccines used in North America today overcome maternal immunity by the time puppies are 12 weeks of age. Vaccination in puppies is usually continued until they reach 16 weeks of age. Dogs older than 12 weeks of age at the time they are presented for initial vaccination should receive at least two canine distemper virus (CDV) inoculations 2 to 3 weeks apart. The minimum duration of immunity, as determined by challenge, to attenuated (MLV) CDV is at least 7 years for vaccines using the Rockport strain of CDV, although that for vaccines using the Onderstepoort strain is at least 5 years.[2, 29]

The recombinant CDV vaccine is a canary pox–vectored vaccine that expresses distemper fusion and hemagglutinin glycoproteins.[23] Dogs receiving this vaccine must receive at least two doses initially. The reported duration of immunity is at least 12 months. Annual booster vaccination is recommended when using this product.

A combined distemper–measles vaccine is still available. At a stage of life when administration of MLV CDV vaccine is expected to fail, measles vaccine is capable of causing a heterotypic immune response in

the presence of high concentrations of maternally derived distemper antibody. Some veterinarians still recommend administration of a CDV–measles virus vaccine to puppies between 6 and 9 weeks of age. This product should not be used in female puppies over 12 weeks of age, because maternal antibodies to CDV and measles may develop. These antibodies would be transferred to subsequent offspring at a level that could interfere with both measles and CDV vaccination in the puppies. Therefore, antibodies would interfere with the protective effects of the MV-CDV vaccination and the heterotypic MV would not provide early protection from CDV. Administration of a combined MLV CDV–measles virus vaccine should be limited to those puppies in which the nursing status is unknown or that are likely to face CDV exposure as puppies. Measles vaccine is not indicated in dogs over 16 weeks of age.

INFECTIOUS CANINE HEPATITIS (CANINE ADENOVIRUS INFECTION)

Vaccination for canine adenovirus infection, the cause of infectious canine hepatitis (ICH), is usually done in combination with that for distemper and other diseases beginning when puppies are 6 to 8 weeks of age. Attenuated (MLV) adenovirus vaccines are generally used in the United States because of their ability to produce a superior immune response, but inactivated products are still available in the U.S. and marketed in many countries. Vaccination for ICH reduced the prevalence of a disease that was once widespread. Outbreaks or isolated cases still occur when vaccination of puppies is delayed or incomplete. Shedding of modified viruses and high stability outside the host have been responsible for inadvertent immunization of many dogs. Vaccines for ICH contain either a killed homologous canine adenovirus-1 (CAV-1) or a closely related respiratory isolate, MLV canine adenovirus-2 (CAV-2). The former is generally shed in the urine, and the latter is shed in upper respiratory secretions; however, the amount that is shed varies between individual products. Another side effect of attenuated CAV-1 vaccine is its ability to produce anterior uveitis and corneal edema with opacification ("blue eye") in a small percentage of dogs. It is not documented that CAV-2 vaccines cause uveitis. Although inactivated vaccines produce a lesser serologic response, they are not shed by the host, nor do they cause anterior uveitis. In the absence of exposure to virulent virus, periodic boosters of inactivated adenovirus vaccine might be required to sustain immunity.

The half-life of maternal antibody to ICH is similar to that of CDV: approximately 8.5 days. By the time a puppy reaches 14 to 16 weeks of age, maternal antibody is not usually detectable. Vaccination for ICH is

thus typically combined with that for CDV. The initial vaccines can be administered when puppies are 6 to 8 weeks of age and every 3 to 4 weeks until they reach 16 weeks of age. Although booster inoculation is recommended annually in adult dogs, challenge studies have demonstrated that the duration of immunity is at least 7 years when attenuated CAV-2 is used as the vaccine antigen.[29] The duration of immunity of killed CAV-2 vaccine and the MLV CAV-2 (intranasal) is not known.

MLV CAV-2 has been shown to immunize dogs against the respiratory (CAV-2) and hepatic (CAV-1) adenoviruses. Considering the risks associated with administration of CAV-1 to dogs, the use of the MLV CAV-1 vaccine is not recommended.

CANINE INFECTIOUS TRACHEOBRONCHITIS

Infectious tracheobronchitis (ITB), or kennel cough, is a complex clinical infection caused by a number of respiratory pathogens that can infect dogs alone or in combination. Causative viruses include distemper (CDV), adenovirus (CAV-2), parainfluenza virus, herpesvirus, and Reovirus. *Bordetella bronchiseptica* is a recognized bacterial pathogen.[4, 13] Secretory antibody (not that in serum) provides protection against infections of the upper respiratory mucosal surfaces. Parenteral and intranasal vaccines exist for CAV-2, parainfluenza virus, and *B. bronchiseptica*. Although protection against most agents develops after routine vaccination programs, vaccines against some agents such as herpesvirus or Reovirus are not available. The duration of immunity produced by many vaccines against respiratory pathogens has not been well established, but the labels of most products recommend annual boosters. It is unlikely that dogs derive significant immunity beyond 12 months subsequent to intranasal vaccination. For intranasal *B. bronchiseptica* vaccine, the duration of immunity may actually be less than 12 months.

The performance of parenterally administered infectious tracheobronchitis (ITB) vaccines is quite different from that of intranasally (topically) administered vaccine. Parenterally administered vaccine for ITB provides a duration of immunity of up to 7 months or longer depending on the antigen.[7, 29] It is not known whether parenteral administration of ITB antigens culminates in the development of an effective local (upper respiratory tract) immune response. Maternal antibody interferes with parenterally administered vaccine. On the other hand, vaccine labeled for intranasal (topical) administration can be administered in puppies as young as 3 weeks of age (depending on the product), seems to induce a local immune response that is not interfered with by maternal antibody, and has a relatively rapid onset (3–5 days). It should be noted that although pneumonia caused by virulent *B. bronchiseptica*

has been reported in immunocompromised human beings, inadvertent nasal or ocular exposure to avirulent live canine *B. bronchiseptica* vaccine is not known to have caused clinical illness or symptoms in human beings.

Vaccination with separate parenteral products usually begins in puppies at 6 weeks of age and is safe for pregnant animals. Animals should receive at least two doses 2 to 4 weeks apart, and complete protection is not expected until 2 to 3 weeks after the second vaccination. Intranasal parainfluenza and *Bordetella* vaccines may protect within 72 hours after their use; thus, they can be used to help prevent illness in an outbreak in a kennel or in pets before hospitalization or boarding.[17] Vaccination against respiratory pathogens does not induce sterile immunity. In other words, vaccinated animals that are challenged are expected to become infected and may exhibit a mild short clinical illness. Clinical signs of upper respiratory infection may develop subsequent to intranasal administration of vaccine. Signs are generally mild or unnoticeable.

CANINE PARVOVIRAL ENTERITIS

Canine parvovirus-2 (CPV-2) vaccines are available as inactivated or MLV products. Recombinant vaccines are not currently available but are being developed. MLV products offer faster, more effective protection against disease and shedding of virulent virus after challenge than inactivated vaccines. For this reason, older dogs that are housed with younger susceptible animals should be vaccinated with MLV vaccines. In case of an outbreak, MLV vaccines should always be used. MLV CPV-2 products are consistently shed in the feces of vaccinated dogs. Infected contact animals may develop weak positive reactions on fecal parvovirus enzyme-linked immunosorbent assay (ELISA) tests but will not develop disease. Maternal antibody blockade is the predominant reason that parvoviral vaccination is inconsistent in protecting pups during their primary vaccination series.[10, 16] Attenuated or inactivated vaccines do not break through maternal immunity as effectively as virulent canine parvovirus. To overcome the period of maternal antibody blockade, manufacturers have raised the titers or lowered their serial passage.[8, 28, 29] Recommendations for use of these potent parvoviral vaccines are a complete series beginning at 6 weeks of age. Repeat vaccines are given every 3 to 4 weeks until dogs are 16 weeks old despite the fact that some products have label claims of protection by 12 weeks of age. The last inoculation should be given at 16 weeks of age for breeds such as Doberman Pinschers and Rottweilers, which have been identified as being poorly responsive to CPV vaccination. In the absence of maternal immunity, where pups are presented after 16 weeks of age, one MLV

CPV-2 inoculation may be sufficient for protection against parvoviral infection. Vaccination with MLV CDV with concurrent CPV-2 vaccination does not cause immunosuppression as has been observed in coinfection with virulent CPV-2 virus. Alternating between distemper and parvoviral vaccines in young puppies on a weekly or longer interval is thus not needed or recommended.

If an animal recovers from a documented parvoviral infection, it is recommended to wait 4 weeks before vaccinating it so that the immune response is recovered. Immunity to parvoviral infection is probably lifelong; however, boosters are given because of the convenience afforded by combination products. Because of the great environmental resistance of parvoviruses, young pups should be kept away from parks, boarding facilities, and dog shows until the vaccination series is complete. Veterinarians should attempt to limit suspected parvovirus-infected dogs from coming into contact with susceptible puppies in their veterinary hospital waiting rooms and wards. Vaccination of cats against feline panleukopenia protects them against CPV-2b infection.

There has been a genetic and resultant antigenic shift of canine parvovirus since its initial evolution in 1978. Nevertheless, cross-protection still exists between the old CPV-2 strains in the vaccine and the new field isolates (CPV-2a and CPV-2b). Similarly, immunodiagnostic tests based on monoclonal antibodies to original isolates are still sensitive in detecting newer strains of virus. Newer field isolates can infect cats. There is limited evidence to suggest that vaccines based on 2b strains do not infect cats.

Duration of immunity of MLV CPV-2 vaccines is several years (at least 7 years based on challenge studies),[29] and overvaccination is a consideration. The duration of immunity subsequent to administration of inactivated (killed) CPV products has been shown to protect puppies from challenge for at least 16 months after vaccination.[25] Under field conditions, dogs may be partially protected by weaker MLV or inactivated products yet still boost their immunity when exposed to virulent virus.

CORONAVIRAL INFECTION

Most vaccines licensed for canine coronavirus (CCV) are inactivated canine coronaviral or feline coronaviral strains. One attenuated (MLV) canine coronaviral product exists. Manufacturers recommend that two doses of vaccine be given 2 to 3 weeks apart beginning in puppies at 6 to 8 weeks of age, with the last one being given at least after 12 weeks of age. The vaccines seem to be safe; however, allergic reactions may occur more commonly when inactivated coronaviral vaccines are com-

bined with leptospiral bacterins. To avoid potential interactions, CCV vaccine could be used in puppies between 6 and 9 weeks of age, and *Leptospira* vaccination could be instituted thereafter. Otherwise, the clinician may prefer to decide whether or not it is important or necessary that both products be administered.

CCV challenge studies are not indicative of "protection" since it is not possible to produce experimental disease in dogs over 12 weeks of age. Furthermore, manufacturer recommendations to administer CCV booster vaccines annually are difficult to justify based on the fact that CCV does not cause disease in adult dogs. CCV produces significantly less morbidity and minimal mortality compared with CPV-2. Experimentally, combined infections with CPV-2 and CCV have been shown to produce clinical disease that is more severe than with either infection alone.[1] Nevertheless, it has also been shown that vaccination with CPV can prevent clinical disease when both viruses are present.[19, 28]

The routine and frequent use of CCV vaccine in dogs is difficult to rationalize. Clinical infection typically occurs in puppies 6 weeks of age or younger. Some studies have suggested that the duration and quality of immunity derived from natural exposure and infection are actually preferred over attempts to immunize by way of vaccination.[28] In the absence of reliable commercial or in-hospital diagnostic assays for CCV, the prevalence of clinical disease associated with CCV infection in dogs is unknown but is considered to be extremely low, even in high-density shelter environments. Yet CCV, both killed and MLV, is commercially incorporated into several multivalent vaccines combined with distemper, adenovirus, parainfluenza virus, and parvovirus antigens. The fact that multivalent vaccines containing CCV outsell vaccines that do not contain CCV in the United States suggests that routine CCV inoculation of dogs throughout life is common. CCV vaccine is considered to be among the least important vaccine antigens given to dogs today, however, and has been identified by several authors as a vaccine that, quite simply, is not needed.[9, 28]

LEPTOSPIROSIS

Most leptospiral vaccines for dogs contain inactivated serovars of *canicola* and *icterohaemorrhagiae*. Vaccination with these products is not recommended in animals less than 9 weeks of age because of the allergenic nature of these products. *Leptospira* bacterin is usually used to reconstitute the lyophilized components in combination vaccines. *Leptospira* bacterins may not produce as high a level or as long a duration of immunity as other agents. Although postvaccination titers often decline to undetectable levels, unpublished challenge studies suggest that immu-

nity in some dogs is sustained for 1 year. Inactivated *Leptospira* vaccines may not, however, protect against the carrier state that may develop after exposure to virulent organisms. One vaccine manufacturer has employed a technology that involves separating surface proteins, or immunogens, of *Leptospira* from extraneous cellular debris, thereby avoiding the need to use whole-cell bacteria. It is not known whether or not this technology can reduce the incidence of adverse events in young dogs and toy breeds over that recognized with conventional whole-cell bacterins. Leptospiral vaccines have been considered optional by veterinarians in many areas because of the perceived low incidence of the disease, short duration of immunity, and risk of postvaccinal hypersensitivity. The use of *Leptospira* vaccine is probably responsible for the reduced prevalence of disease caused by *L. canicola* and *L. icterohaemorrhagiae.*

Recently, it has been shown that the incidence of confirmed cases of canine leptospirosis may be increasing in the United States.[5, 33] Furthermore, dogs are being diagnosed with infections by serovars of *L. interrogans* that we do not routinely vaccinate against. Serovars of *L. grippotyphosa, L. pomona, L. bratislava,* and others are reported throughout the United States and have been linked to acute renal failure.[6, 33] Another interesting point is that many of these reports are on dogs living exclusively in urban areas. The risk of infection is not limited to dogs living outdoors in rural environments. Vaccines containing conventionally used serovars of *L. canicola* and *L. icterohaemorrhagiae* do not cross-protect against other serovars known to infect dogs.[5]

Less than 2 years ago, *Leptospira* vaccines were introduced that are believed to protect against serovars *L. grippotyphosa* and *L. pomona.* Additional *Leptospira* serovars are likely to be introduced in the near future. Nevertheless, the incidence of acute anaphylaxis among young dogs (especially those under 12 weeks of age) and toy breeds (regardless of age) makes the decision to include routine vaccination of dogs with all available *Leptospira* serovars difficult. Without regional incidence data for canine leptospirosis, practitioners still have insufficient information at their disposal to make a reasonable risk:benefit analysis regarding use of leptospira vaccines.

LYME BORRELIOSIS

Commercial inactivated (killed) whole-cell bacterins and one recombinant outer surface protein A (OspA) vaccine is licensed in the United States.[14, 26] In Europe, the vaccines are of the whole-cell type. Vaccines have been shown by challenge studies conducted by the manufacturer of the recombinant outer surface protein A vaccine to provide a duration

of immunity for up to 1 year. Vaccination protected challenged dogs from spirochetemia and clinical limping episodes as compared with unvaccinated dogs. Lyme borreliosis vaccines are recommended by the manufacturer for use in dogs as young as 9 to 12 weeks of age, and primary vaccination consists of two inoculations 3 weeks apart. Immunization should be given early in life to high-risk dogs living in endemic regions. It should be noted that all vaccines stimulate antibody that produces a positive test result with the indirect fluorescent antibody serodiagnostic test. Dogs having a positive indirect fluorescent antibody test should be retested using either of two tests: the Western blot technique, which may discriminate between infection and vaccine-induced antibody, or the recently introduced in-hospital ELISA test (SNAP 3Dx Assay; IDEXX Laboratories, Westbrook, ME), which has been shown to react only to antibody from a unique C6 surface peptide.[21] The ELISA test does not cross-react to antibody produced by any of the commercially available vaccines on the market in the United States.

Claims of hypersensitivity induced by whole-cell Lyme vaccines have been reported. The most common observation is postvaccination lameness among dogs that did not show clinical or serologic evidence of infection. Unfortunately, the vaccines contain a limited number of strains, which may not cross-protect against the known isolates of *B. burgdorferi*. Routine testing of dogs using the in-hospital ELISA test in regions of the United States where Lyme borreliosis is suspected or is known to occur in human beings can provide new information pertaining to the regional incidence of infection among the canine population. Today, that information is largely extrapolated from human incidence data maintained by the Centers for Disease Control and Prevention. In the meantime, routine vaccination of dogs against *B. burgdorferi* is not indicated outside regions of known high disease prevalence.

GIARDIASIS

Infection with the protozoan *Giardia lamblia* is known to affect mammals and birds worldwide. Differences exist in the pathogenicity and host range of various strains. Colonization of the intestinal lumen results in intestinal villus shortening and malabsorptive diarrhea. Neonatal animals are most susceptible to infection.[3] Areas with impounded unfiltered surface water that is used for recreation or drinking are most often associated with infection. Unsanitary conditions can lead to endemic infections. An inactivated adjuvanted vaccine is available for vaccination of puppies and kittens. The first dose can be given in animals as young as 8 weeks of age. Neither routine or annual revaccination is indicated

Table 2. DOCUMENTED MINIMUM DURATION OF IMMUNITY* OF INDIVIDUAL VACCINE ANTIGENS USED IN DOGS

Vaccine	Duration of Immunity by Challenge	Duration of Immunity by Serology (antibody titer)	Correlation of Titer with Immunity	References
Canine distemper–MLV (Rockport strain)	7 years	15 years	SN Ab: strong	2, 29
Canine distemper–MLV (Orderstepoort strain)	5 years	9 years	SN Ab: strong	29
Canine distemper (Recombinant)	1 year	Not demonstrated	Not demonstrated	Merial, Ltd.
Canine parvovirus–MLV	7 years	7 years	HI AB: strong	2, 29
Canine parvovirus–killed	16 months	Not reported	HI or SN: strong	7, 25, 29
Canine coronavirus–MLV or killed	Can not be determined	Not reported	SN Ab: strong	
Canine adenovirus 2–MLV	7 years	9 years	SN Ab: strong	29
Canine adenovirus-1†	Not applicable	Not applicable		
Canine parainfluenza–MLV (topically administered)	Unpublished study demonstrated protection "in excess of 1 year" after vaccination	Unpublished study demonstrated minimal antibody detected after vaccination	Does not correlate	Unreleased research report
Canine parainfluenza–killed (parenterally administered)	Not reported	2 years	Neutralizing Ab	4
Bordetella bronchiseptica (parenterally administered	Only short-term (up to 3 weeks) studies are published	Not reported	Does not correlate	Unreleased research report

Bordetella bronchiseptica (topically administered)	Unpublished study demonstrated protection "in excess of 1 year" after vaccination	Unpublished study demonstrated significant "agglutinating antibody" titer persisted "in excess of 1 year" after vaccination	Does not correlate	Unreleased research report
Borrelia burgdorferi–whole bacterin	156 to 207 days	Not reported	Ab titer does not correlate with immunity	Package insert
Borrelia burgdorferi–recombinant outer surface protein A	1 year	Not reported	Ab titer does not correlate with immunity	Package insert
Leptospira interrogans canicola *L. icterohaemorrhagiae*	Up to 14 months	≥12 months with both serovars	Neutralizing IgG titers are protective	14
Leptospira interrogans *L. grippotyphosa* *L. pomona*	Not reported	Not reported	Unknown	
Giardiasis	Not reported	Not reported	Unknown	
Rabies–killed	39 months	7 years	Challenge studies required	

*The duration of immunity listed for individual antigens represents the length of time dogs were followed before challenge or before measuring antibody; it does represent the maximum possible duration of immunity.

Although a modified-live canine adenovirus-1 vaccine is still available at this writing, use of this product in clinical practice is not recommended.

MLV = modified live virus; SN = serum neutralizing (in reference to method of determining antibody titer); Ab = antibody; HI = hemagglutination inhibition.

with this product, except in the unusual situation where recurrent exposure and infection are documented and cannot be controlled using conventional hygienic methods. This vaccine has been shown to diminish fecal shedding of the infectious cysts for up to 1 year. The vaccine also reduces the rate and quantity of infection when given before exposure. If the prevalence of infection is high in a group of animals or in a specific area, this vaccine might be an adjunct to help control the disease. It is not recommended for administration to all dogs, and its use must be coupled with other management procedures. The current vaccine has been shown to cause granuloma-like masses at the inoculation site.

It is important to note that accurate identification of *Giardia* in dogs with diarrhea is not as straightforward as it may seem. As such, false-positive diagnoses of giardiasis are probably common. Conventional saline fecal flotation techniques are not adequate to diagnose *Giardia* cysts in feces. Furthermore, direct fecal examination is limited by the experience of the microscopist and by the fact that many other structures in the feces of dogs such as yeast bodies are easily confused with *Giardia* cysts. Feces should be subjected to centrifugal flotation in a 33% zinc sulfate solution. The slide should be scanned with a $\times 10$ objective magnification.

RABIES

Rabies vaccines have been extremely effective in reducing the prevalence of this disease in dogs. As a result, the prevalence of human disease has decreased substantially, although the relative prevalence of feline rabies has increased in the United States. In most countries, inactivated (killed) vaccines are used. Inactivated virus vaccines have been shown to provide a minimum duration and level of immunity comparable to those of MLV products. They often contain high viral content and potent adjuvants, however, which can sometimes produce acute or chronic hypersensitivity reactions. An avipoxvirus-vectored recombinant rabies vaccine that produces minimal inflammatory reactions has been licensed for use in cats.[31] A single rabies vaccine is generally administered in animals 3 to 4 months of age. A second dose should be administered 1 year after the first dose regardless of the dog's age. Subsequent boosters are required every 1 or 3 years thereafter as mandated by state law or local statutes.

CONCLUSIONS

New technologies for vaccine development[11, 32] and infectious disease diagnosis[21] are likely to be introduced in the near future. With this

new technology comes the opportunity to vaccinate companion animals against even more infectious agents than is currently practiced in the United States today. As we look forward, it becomes particularly important to review current vaccination standards applied to dogs with respect to current knowledge of duration of immunity (Table 2), awareness of the incidence and likelihood of injurious or even fatal adverse events associated with vaccination, and individual risk factors that dictate which vaccines are most appropriate at which stage of life.

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Address reprint requests to

Richard B. Ford, DVM, MS
Professor of Medicine
Department of Clinical Sciences
College of Veterinary Medicine
North Carolina State University
Raleigh, NC 27605

e-mail: richard_ford@ncsu.edu