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Duration of immunity for canine and feline vaccines: A review

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Abstract

In our studies aimed at assessing the minimum duration of vaccinal immunity (DOI), approximately 1000 dogs have been vaccinated with products from all the major US veterinary biological companies. The DOI for the various products is determined by antibody titers for all dogs and, by challenge studies in selected groups of dogs. Recently, all major companies that make canine vaccines for the U.S. market have completed their own studies; published data show a 3 years or longer minimum DOI for the canine core products, canine distemper virus (CDV), canine parvovirus type 2 (CPV-2), and canine adenovirus-2 (CAV-2). Studies with feline core vaccines – feline parvovirus (FPV), calicivirus (FCV) and herpes virus type I (FHV-1) have shown a minimum DOI of greater than 3 years. Based on these results, the current canine and feline guidelines (which recommend that the last dose of core vaccines be given to puppies and kittens $\geq$12 weeks of age or older, then revaccination again at 1 year, then not more often than every 3 years) should provide a level of protection equal to that achieved by annual revaccination. In contrast, the non-core canine and feline vaccines, perhaps with the exception of feline leukaemia vaccines, provide immunity for $\leq$1 year. In general the effectiveness of the non-core products is less than the core products. Thus, when required, non-core vaccines should be administered yearly, or even more frequently.

Keywords: Core vaccines; Duration of immunity; Revaccination; Antibody; Challenge

Work began in my laboratory in the mid-1970's to determine the duration of immunity (DOI) for canine and feline vaccines. My interest in vaccine DOI was stimulated by several factors: (1) the observation that dogs who had recovered from canine distemper and cats who had recovered from panleucopenia were completely resistant to experimental viral challenge many years later; (2) that my three children were receiving a series of vaccinations that would end about the time they entered school with most of the vaccines never being given again; (3) a veterinarian in the US Army Veterinary Corps asked me to design a vaccination program for dogs and cats that did not require yearly revaccinations; (4) it was not known if yearly vaccinations were necessary for dogs and cats, but most experts I consulted believed they probably were not needed. Based on our observations and existing knowledge of duration of immunity following natural infection and/or vaccination we published "An Ideal (But Not Proven) Immunization Schedule for Dogs and Cats" in 1978. We recommended a series of puppy/kitten vaccinations followed by revaccination at 1 year, then revaccination every 3 years. (Schultz and Scott,

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1978). Our early recommendations form the basis for the 1998 and 2000 Reports of the American Association of Feline Practitioners and Academy of Feline Medicine Advisory Panel on Feline Vaccines and the Report of the American Animal Hospital Association Canine Vaccine Task Force: 2003 Canine Vaccine Guidelines, Recommendations and Supporting Literature (Elston et al., 1988; Richards and Rodan, 2000; Paul et al., 2003, 2006). Field observations in those early years suggested that immunity after natural infection or vaccination for viral diseases was long lived in most species including cats and dogs, however, experimental studies demonstrating an extended DOI for canine and feline vaccines had not been undertaken. All vaccines, with the exception of rabies vaccines, were licensed by the United States Department of Agriculture (USDA) based on challenge studies performed from only a few weeks to a few months after vaccination. All the vaccine labels included the statement "Annual Revaccination Recommended" without the knowledge of whether the true DOI was a year or a life time. Therefore, I decided to perform a minimum DOI study with dogs that were being used for other long term studies. The dogs were administered modified live vaccines (MLV) from Norden Laboratories, Lincoln NE, that contained canine distemper virus (CDV), canine adenovirus-1 (CAV-1), and canine parainfluenza (CPI) virus. At the time this study began canine parvovirus type 2 (CPV-2) had not yet infected the canine species, thus a vaccine to prevent CPV-2 did not exist. However, some of the dogs included in the study prior to 1978 became naturally infected and subsequently antibody positive to CPV-2 and others that were added to the study were vaccinated with CPV-2 vaccine when the vaccine became available. The dogs used in the original study included 6 males and 13 females representing a variety of different breeds. Four of the dogs in addition to receiving the Norden vaccines had been vaccinated with unknown products prior to inclusion in the study, whereas the remaining dogs were vaccinated two to three times as puppies then never again. Dogs vaccinated after 1979 received a combination vaccine from Norden Laboratories, that contained CDV, CPI, canine adenovirus-2 (CAV-2) as well as CPV-2 vaccine. All the vaccines were administered intramuscularly. Antibody titers were done sporadically throughout the holding period and serum was collected just prior to challenge with CDV, CAV-1, and/or CPV-2. The results of this study showed that antibody titers were maintained for years without revaccination. It also showed that all challenged animals were protected from clinical disease. These observations came as no surprise to me or my colleagues studying the diseases prevented by the vaccines because we had observed long term immunity in the field (Carmichael, 1999; Schultz, 1980; Schultz et al., 1980). Seventeen of the 19 dogs vaccinated with CDV were challenged with CDV, 11 of the 11 dogs vaccinated with CPV-2 were challenged with CPV-2 and 2 of the 19 dogs vaccinated with either CAV-1 or CAV-2 were challenged with CAV-1. The challenges were performed sequentially when dogs received more than one virus. In this case the dogs were challenged first with CDV, followed by CAV-1 or CPV-2. None of the dogs were challenged with all three viruses and two of the dogs were only challenged with CPV-2. The period of time from the last vaccination to challenge ranged from 1 year (because at that time few 1 year DOI studies had been reported) to as long as 11 years. Sixteen of the dogs were 3 or more years from their most recent vaccination at time of challenge. Three years was the revaccination interval we had suggested in our 1978 paper (Schultz and Scott, 1978). None of the challenged dogs developed signs of disease irrespective of time since vaccination. Age, sex, and breed matched unvaccinated control dogs were not available, thus susceptible pups were used as challenge controls to ensure the virulence of challenge virus. The CDV used for challenge routinely caused 100% morbidity and at least 60% mortality in susceptible pups. The CPV-2a strain that we used caused 100% morbidity and at least 75% mortality. The CAV-1 isolate caused at least 50% morbidity and 25% mortality. The results from this limited group of dogs clearly demonstrated the Norden modified live vaccines provided immunity for at least 11 years against CDV and CPV-2. Although, only two dogs were challenged with CAV-1 it was the opinion of canine infectious disease experts that all these vaccines and especially the CAV-1 and CAV-2 vaccines provided many years of immunity (Schultz et al., 1977; Carmichael, 1999). Since completing that initial study on duration of immunity in the early 1990's we have performed seven additional DOI studies, and have further studies in progress. In total for all these studies approximately 1000 dogs have been vaccinated with products from all the major US veterinary biological companies. The DOI for the various products is

determined by antibody titers and in certain studies animals were challenged with CDV, CPV-2 and/or CAV-1 (Phillips and Schultz, 1992; Schultz, 1998, 1999a,b, 2000; Larson et al., 2002). Furthermore, during the last 2 years all the major veterinary biological companies that make canine vaccines in the US have completed their own studies, with some having been published, demonstrating a minimum 3 years DOI for their canine core products, CDV, CPV-2, and CAV-2 based on antibody titers and, in some cases, challenge studies (Abdelmagid et al., 2004; Gill et al., 2004; Mouzin et al., 2004a,b). At present, it should be understood that rabies vaccines are the only products for which the USDA require minimum DOI studies for licensing purposes. Currently, USDA approval is not required for the recommendation of extended DOI vaccination programs for any other vaccine. Thus, a veterinarian or animal owner can administer any vaccines other than rabies as often or as infrequently as needed or desired regardless of whether minimum DOI studies have been performed or recognised by the USDA. Therefore, all USDA licensed canine and feline vaccines can legally be used to meet the extended interval guidelines recommended by AAHA, AAFP, or suggested in any other reports (Green et al., 2001, 2005; Paul et al., 2003, 2006; Richards and Rodan, 2000; Schultz, 1998, 2000).

Duration of immunity following vaccination or natural infection is dependant on two major mechanisms: (1) the persistence of memory B and T cells stimulated at time of vaccination/infection and (2) the persistence of long lived plasma cells that I have termed ''memory effector B cells'', which continue to produce antibody for years after initial immune stimulation (Schultz, 1998, 1999a,b; Schultz and Conklin, 1998; Rimmelzwaan and Osterhaus, 1997; Janeway et al., 2001). Although, it remains controversial, DOI studies in both the cat and dog show ''memory effector B cells'' continue to produce antibody to the core vaccines in the absence of overt antigenic stimulation for many years. Thus, revaccination does not appear necessary to maintain these cells. The continued presence of antibody in animals in the absence of any 'booster' revaccination is a direct consequence of continued antibody production by ''memory effector B cells''. In contrast memory B and T cells can only become reactivated (i.e. they become effector cells) after reinfection or reimmunization. The ability to detect antibody, regardless of titer, in a previously vaccinated and actively immune animal demonstrates that ''memory effector B cells'' are present and functional (Phillips and Schultz, 1992; Schultz, 1998; Schultz and Conklin, 1998). The presence of antibody also suggests that memory B cells (not producing antibody) are very likely present. The memory B cell can be demonstrated by the difference in kinetics of the antibody response and the increased amount of antibody produced by immune versus naïve animals. Antibody is a primary mechanism of protective immunity for the canine core vaccines, CDV, CPV-2, CAV-1, and rabies. If antibody cannot be detected after vaccination with the core vaccines it should be assumed the animal may not be immune and should be revaccinated (Abdelmagid et al., 2004; Schultz, 1998) Antibody titer testing is performed by many diagnostic laboratories and a commercial in-office test, TiterChek™ is available from Synbiotics, San Diego, CA, that detects antibody to CDV and CPV-2. Such tests are useful in ensuring an animal has developed an immune response after its puppy vaccination series. If the animal has not developed antibody to CDV and CPV-2 two or more weeks after the last dose of vaccine the animal should be revaccinated and re-tested to ensure it is immune and is able to develop a response to these vaccines. The level of antibody or titer detected by a specific serologic test is not as important as the presence or absence of antibody after vaccination. Titers vary depending on the animal and the test used as well as the laboratory performing the test.

Results of our many vaccine DOI studies (Table 1) show that the modified live CDV vaccines containing

Table 1
Estimated minimum duration of immunity (DOI) of commercially available canine core vaccines based on challenge (C) and/or serology (S)

Vaccine	Estimated minimum DOI (years)	
Canine distemper virus		
Rockborn/snyder hill strains (MLV)	≥7 (C)	≥15 (S)
Onderstepoort strain (MLV)	≥5 (C)	≥9 (S)
rCainine distemper virus (R)	≥3 (C)	≥3 (S)
Canine adenovirus-2 (MLV)	≥7 (C)	≥9 (S)
Canine parvovirus-2 (MLV)	≥7 (C)	≥9 (S)
Rabies virus (K)	≥3 (C)	≥7 (S)

MLV, Modified live virus; R, Recombinant vectored virus; K, Killed. CAV-2 vaccinated dogs challenged with CAV-1, antibody titers to CAV-1.

the Rockborn or Snyder Hill strains have a minimum DOI of 7 years based on challenge and up to 15 years based on serology. The minimum DOI for the modified live CDV vaccines with the Onderstepoort strain is 5 years based on challenge and 9 years based on serology. For the recombinant canarypox vectored CDV vaccine the minimum DOI is 3 years based on challenge and serology. Based on serologic results it appears immunity may continue beyond 3 years (Schultz, 2004), thus it is possible that the DOI for the vectored vaccine will be the same as for MLV products. It is important to understand that these are minimum DOI's and longer studies have not been done with certain of the above products. It is possible that some or all of these products will provide lifelong immunity. The minimum DOI for CAV-2 vaccines against challenge with CAV-1 is 7 years and 9 years based on CAV-1 serology. The CPV-2 vaccine studies include all the current USA manufacturer's products with minimum DOI of 7 years based on challenge and a DOI of 9 years based on serology. There are some differences among the vaccines from different companies regarding their ability to immunize pups in the presence of passively acquired maternal antibody (Larson and Schultz, 1997). However, after the vaccines induce active immunity the minimum DOI appears to be similar for all products we have tested. This is not unexpected since all the CPV-2 products are modified live vaccines. There is no information available for the DOI of killed parvovirus vaccine and there is not likely to be information since the killed parvovirus vaccines are no longer available from the major US veterinary biological companies. Based on challenge studies the minimum DOI for rabies is 3 years and based on serologic studies killed rabies vaccines were shown to have a minimum DOI of 5–7 years.

Only a few studies are available on DOI for feline vaccines. A study with a killed combination feline parvovirus (FPV), feline calicivirus (FCV), and feline herpes virus (FVR) showed protection 7.5 years after two doses as kittens. In this study, the vaccinated cats were held in isolation along with unvaccinated age matched controls. They were then challenged sequentially with the three viruses. The cats challenged 7.5 years after vaccination had the same level of protection as cats challenged 1 year after vaccination with a similar combination vaccine (Scott and Geissinger, 1999). It should be recognized that the FPV vaccine is highly effective (estimated $\geq$99%), whereas the FCV and FVR vaccines, regardless of interval after vaccination, are not as effective (estimated $\leq$75%). A second study, based on serology has demonstrated a minimum DOI of 4 years for the feline core vaccines (Mouzin et al., 2004a,b).

Based on the results of studies which have demonstrated an extended DOI of more than 3 years to canine and feline core vaccines, the current canine and feline guidelines (which recommend that the last dose of core vaccines be given to puppies and kittens that are at least 12 weeks of age or older then revaccination again at 1 year, then not more often than every 3 years) should more than adequately provide a level of protection equal to that achieved by annual revaccination (Carmichael, 1999; Schultz, 1999a,b, 2000). It is very important to emphasize that in contrast to the canine and feline core vaccines that provide years of protection the non-core canine and feline vaccines, perhaps with the exception of feline leukaemia vaccines, provide immunity for 1 year or less. Thus, when required, non-core vaccines should be administered yearly, or even more frequently. Furthermore, unlike the canine core vaccines that are effective in a very high percentage ($\geq$99%) of dogs, some of the non-core products (e.g. leptosira bacterins) may provide protection for only 6–9 months and may only be effective in a low percentage ($\leq$50%) of the vaccinated dogs. In general, the DOI for viral vaccines is longer than for bacterial vaccines, the DOI from modified live vaccines is longer than for killed vaccines and the DOI for vaccines that prevent systemic disease is greater than the DOI for vaccines against mucosal diseases. Extending the revaccination intervals for canine and feline core vaccines does not place the animal at increased risk to developing vaccine preventable disease, but it does reduce the potential for adverse reactions (Phillips and Schultz, 1992). Vaccinating a larger percentage of dogs and cats at least once in their lifetime after the age of 3–4 months with the core vaccines would significantly enhance population (herd) immunity and also reduce the public health risks associated with rabies. Therefore, we encourage all practitioners to follow the new canine and feline vaccination guidelines and to

understand: ''Vaccination is a medical practice that requires the same considerations and reasoning skills required when selecting an appropriate medical treatment or specific surgical procedure. Vaccination should not be considered an innocuous procedure, since vaccines may have harmful consequences to patients as well as owners'', thus use those vaccines that are required, give them only as often as is necessary and vaccinate as many cats and dogs in the population as possible (Schultz, 1998).

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