Canine Parvovirus Infection, Canine Distemper and Infectious Canine Hepatitis: Inclination to vaccinate and Antibody Response in the Swedish Dog Population

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Olson, P., A. Hedhammar and B. Klingeborn: Canine parvovirus infection, canine distemper and infectious canine hepatitis: Inclination to vaccinate and antibody response in the Swedish dog population. Acta vet. scand. 1996, 37, 433-444. - The mclination of dog owners to vaccinate was investigated by sending a questionnaire to randomly selected Swedish dog-owning households. According to the owners (n = 538), 86.7% of the dogs had been vaccinated against CPV and 95.8% had been vaccinated against CD/ICH. The inclination to vaccinate mixed breeds was significantly lower than the inclination to vaccinate pure-bred dogs. In a second study titres of CPV, CD and CAV-1 virus antibodies were measured in 176 randomly selected dogs with known vaccination histories. CPV antibody titres ≥1:80 were detected in 70.9% of the CPV vaccinated dogs. There was a significant difference in the fraction of dogs with CPV titre ≥1.80 between the group last vaccinated with live attenuated vaccine and the group last vaccinated with inactivated vaccine. Titres of CD and CAV-1 virus antibodies ≥1:16 were found in 86.1% and 91.6% of the vaccinated dogs respectively. The fraction of dogs with CAV-1 antibody titres ≥1:16 was significantly greater in the group that received inactivated CAV-1 vaccine than in the group vaccinated with attenuated live CAV-2 vaccine. Approximately 50% of the dogs were booster vaccinated against all 3 diseases at one year of age.

adeno virus: vaccination.

Introduction

In Sweden dogs are regularly vaccinated against canine parvovirus (CPV) infection, canine distemper (CD) virus infection and canine adenovirus-1 (CAV-1) infection. CAV-1 being the cause of infectious canine hepatitis (ICH). The vaccines used against CPV infection are either live attenuated or killed. It is standard practice to vaccinate puppies against CPV at 7-8, 12, 16 and 20 weeks of age if using a killed vaccine, and at 7-8 and 12 weeks of age if using an attenuated live vaccine. In both cases a revaccination is recommended at 1 year of age

(Olson et al. 1987, Olson et al. 1988, Wierup et al. 1982). Boosters can then be given annually or every other year.

To protect against CD and ICH pups are either given 2 vaccinations at 7 and 12 weeks of age, or one vaccination at 12 weeks of age. A re-vaccination at 1 year of age is also recommended (Olson et al. 1987, Olson et al. 1988). Re-vaccinations of adult dogs are most commonly performed either every second year or every 4th year thereafter. All vaccines used in Sweden against CD and ICH are attenuated live canine distemper virus (CDV) vaccines combined with

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the vaccine against ICH. The latter component consists of either inactivated CAV-1 or modified live canine adenovirus-2 (CAV-2), the strain which causes respiratory disease in dogs. This study was undertaken to investigate the inclination to vaccinate dogs against CPV infections, CD and ICH among Swedish dog owners. We also related antibody titers against CPV, CDV and CAV-1 to the vaccination history in a selected group of dogs.

Materials and methods

The study consists of 2 parts. The first part (A) is a questionnaire in which dog owners are asked about their inclination to vaccinate. The second part (B) is an antibody titre study of dogs with known vaccination histories.

Questionnaire (part A)

Dog owners were recruited by telephone from a random sample of all Swedish households. Questionnaires were sent out to 700 dog-owning households, 538 (76.9%) of which were filled in and returned. The recruiting and sending out/receiving procedures were handled by a professional survey institute together with questions from a commercial dog food company. The owners were asked if and when their dogs had been vaccinated against CPV infection or CD/ICH, respectively; the choices being within the last year, within the last 2 years, more than 2 years earlier or never. Other information obtained was if the dog was pure-bred or mixed and the age of the dog.

Antibody study (part B)

Dogs from 6 breeds, i.e. Clumber spaniel, Finnish hound, Italian greyhound, Pointer, Tibetan terrier and West Highland white terrier, were originally selected from the stud book at the Swedish Kennel Club for a study of the genetic

relationship between individuals using a DNA-fingerprint technique. The individual dogs from these breeds were randomly selected from all dogs born between 1 January 1990 and December 31st 1990, except for the Clumber spaniel and Italian greyhound that were sampled from dogs born between 1 January 1988 and December 31st 1990 owing to a low number of individuals of these 2 breeds.

The owners were asked to participate by visiting a veterinary clinic, and a blood sample was taken from each dog and plasma was stored in -20 °C until analysed. Samples were obtained from 176 dogs. As collection of plasma was performed as a part of another study, the age of the dogs varies. The number of dogs in the different breeds and their age when sampled are presented in Table 1. The dogs' complete vaccination histories were obtained.

There was an equal sex ratio, with 49.4% male dogs and 50.6% females. Twenty-three dogs (13.1%) were younger than one year of age, and 153 dogs were older than one year of age. The mean age of the young dogs was 289 days, range 179–62 days, and the mean age of adult dogs was 721 days (1 year 11 months), range 365–569 days.

Antibodies to CPV were measured by ELISA in plasma and were then assigned haemagglutination-inhibition (HI) test values as previously described (Rimmelzwaan et al. 1990). Virus neutralisation test for detection of antibodies to CDV and CAV-1 were measured as described (Appel & Robson 1973).

Geometric mean titers (GMT) were calculated. Titers against CPV ≥1:5120 were designated as 1:5120, and titers against CDV and CAV-1 ≥1:256 were designated as 1:256.

Statistical analyses were performed using the JMP statistical software from SAS Institute Inc. 1989-1994. Comparison between proportions of dogs was performed by using chi-square or Fischer's exact test, and comparison between

Breed	No. of dogs	%	Mean age Days	Mın age Days	Max age Days
Clumber spaniel	32	18.2	978	302	1569
Finnish hound	27	15.3	703	371	915
Italian greyhound	25	14.2	698	225	1282
Pointer	33	18.8	574	262	980
Tibetan terrier white	29	16.5	515	188	809
West Highland terrier	30	17.0	526	179	904
Total	176	100	667	179	1569

Table 1. Numbers and ages of dogs of different breeds included in the antibody study.

Table 2. Dog owners' response to questionnaire (study A) on vaccination against CPV enteritis, CD and ICH.

Vaccinated latest	CPV	enteritis	CD and ICH		
	No.	%	No.	%	
Within 1 year	248	47.3	229	43.9	
Within 2 years	81	15.5	105	20.1	
> 2 years ago	125	23.9	166	31.8	
Never	44	8.3	15	2.9	
Do not know	26	5.0	7	1.3	
Total	524	100	522	100	

levels of titres was performed by using Student's T-test.

Results

Questionnaire (part A)

In total, answers were obtained from 524 owners regarding CPV vaccination and 522 regarding CD/ICH vaccination. The results of the questionnaire are presented in Table 2. According to the owners, 86.7% of the dogs had been vaccinated at some time against CPV, 62.8% within the last 2 years. The percentage of dogs that, to the knowledge of their owners, had never been vaccinated against CPV infection was 8.3%. The CPV vaccination status of the dogs in relation to their age were obtained from 479 owners and are presented in Fig. 1. In dogs younger than 6 months of age all but one had been vaccinated against CPV; the owner of the

remaining dog did not know its vaccination history. Out of all dogs less than 12 months of age, 88.3% had been vaccinated at least once against CPV. Out of dogs older than one year of age, 4.6% of the owners stated that their dogs had never been vaccinated against CPV, and 5.9% of the owners did not know their dogs' vaccination status.

A 95.8% proportion of the dogs had been vaccinated at some time against CD/ICH, with 64.0% vaccinated within the last 2 years. Only 2.9% of the dog owners responded that, to their knowledge, their dogs had never been vaccinated against CD and ICH. The relation between CD/ICH vaccination status and age for 488 dogs is presented in Fig. 2. In dogs younger than 6 months of age 70.6% had been vaccinated against CD/ICH. Out of all dogs less than 12 months of age, 80.5% had been vaccinated

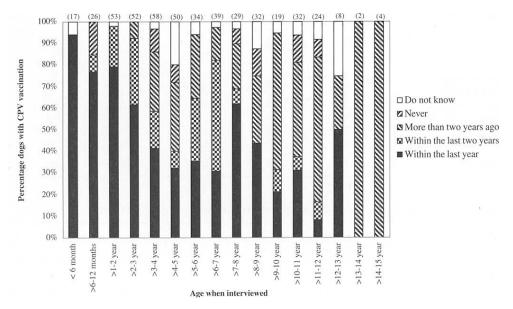


Figure 1. Percentage of dogs in various age classes that were vaccinated against CPV enteritis at different ages. Number of dogs in each age group in paranthesis.

at least once against CD/ICH. Out of dogs older than one year of age only 1.2% of the owners stated that their dogs had never been vaccinated against CD/ICH, and 3.7% of the owners did not know their dogs' vaccination status.

The proportions of dogs vaccinated at least once against CPV and CD/ICH were higher for pure-breds than for mixed. The percentage of dogs vaccinated against CPV infection was 89.9% in purebreds and 69.8% in mixed breeds (p<0.001). Corresponding figures for vaccination against CD/ICH are 97.6% in purebreds and 85.4% (p<0.001) in mixed breeds.

Antibody study (part B)

Vaccination against CPV had been performed in 165 dogs, of which it was possible to determine the type of vaccine for 157. Twenty dogs had been vaccinated with live attenuated CPV vaccine and 137 dogs with killed CPV vaccine as the most recent vaccine. Vaccinations against

CD/ICH had been performed in 166 dogs. The type of ICH vaccine could be determined in 159 dogs of which 34 were vaccinated with killed CAV-1 vaccine and 125 dogs with live attenuated CAV-2 vaccine.

Prior to 6 months of age 93.3% of all dogs had been vaccinated at least once against CPV, and 97.6% had been vaccinated at least once before 12 months of age. Corresponding figures for CD/ICH was 88.5% vaccinated prior to 6 months of age and 95.2% before 12 months of age. Of the dogs vaccinated before 12 months of age, 51.4% were booster vaccinated against CPV and 53.9% against CD/ICH between 1 and 2 years of age. On average, the dogs had been vaccinated 3.2 times (median 3 times) against CPV, and 1.5 times (median 2 times) against CD/ICH. The mean time for all dogs since the most recent vaccination against CPV was 315.7 days (median value of 277.0 days). The mean time for all dogs since the previous vaccination

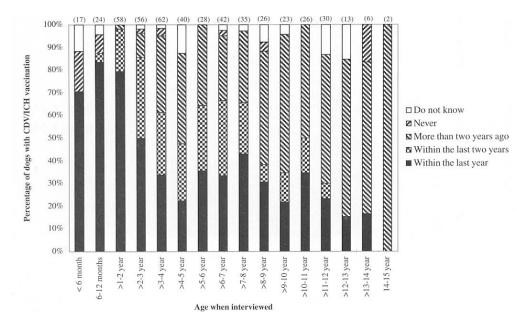


Figure 2. Percentage of dogs in various age classes that were vaccinated against CD/ICH at different ages. Number of dogs in each age group in paranthesis.

against CD/ICH was 355.3 days (median value of 309.5 days).

Breed differences were found in the age at which the first vaccination was performed. In dogs vaccinated before one year of age, the Finnish hound was on average vaccinated against CPV at 139 days of age, whereas the mean for all other breeds was 67 days, corresponding figures for CD/ICH was 151 days and 96 days respectively. These differences being statistically significant. There was also significant breed-related variation in the time since the most recent vaccinations, being longer for Clumber spaniels and Finnish hounds compared with some of the other breeds (Table 3). Among the dogs known to have been vaccinated against CPV, 70.9% had CPV titre ≥1:80. Out of 11 dogs without a documented CPV vaccination only 2 had antibody titers ≥1:80 (18.2%). The differences in the proportion of vaccinated and non-vaccinated dogs with CPV titre ≥1:80 was significant (p<0.001). Among the dogs documented to have been vaccinated against CD, 86.1% had a CD virus antibody titres ≥1:16. Of the 10 dogs not documented as having been CD vaccinated seven (70%) had antibody titers ≥1:16. For the dogs documented to have been vaccinated against ICH, 91.6% had ICH virus antibody levels ≥1:16. Of the 10 dogs without a documented ICH vaccination eighth (80%) had ICH virus antibody titers ≥1:16. The differences in the percentage of vaccinated and non-vaccinated dogs with CD/ICH virus titre ≥1:16 was not significant.

Among the dogs last vaccinated with attenuated CPV vaccine the proportion reaching ≥1:80 was 90.0% as compared with 68.6% among dogs last vaccinated with killed vaccine. This difference was statistically significant (p<0.05) (Fig. 3).

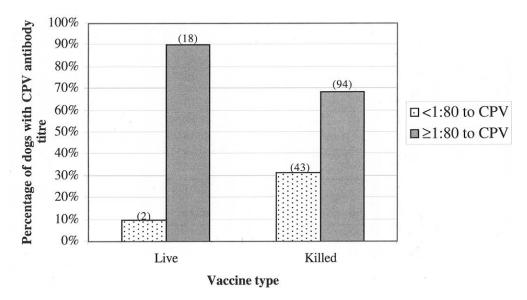


Figure 3. Percentage of dogs with CPV antibody titres ≥1:80 in groups vaccinated with live and killed vaccines.

Among the dogs that received the attenuated CAV-2 vaccine the percentage reaching ≥1:16 was 89.6%. The corresponding value for the group receiving the killed CAV-1 vaccine was 100%. This difference is statistically significant (p<0.05) (Fig. 4).

The overall GMT against CPV in vaccinated dogs was 1:99. It was 1:90 in dogs last vaccinated with killed vaccines and 1:187 in dogs last vaccinated with attenuated vaccines. This

difference was not statistically significant. The overall GMT to CD virus in vaccinated dogs was 1:60. The overall GMT to CAV-1 in vaccinated dogs was 1:84. There was a statistically significant difference (p<0.05) in GMT to CAV-1 between dogs vaccinated with killed CAV-1 at 1:126 and those receiving attenuated CAV-2 vaccine at 1:75.

There was no significant difference in the proportion of dogs with CPV antibody levels ≥1:80

Table 3. Mean time (days) since the last CPV and CD/ICH vaccination.

Breed	Mean time since last CPV vaccination (days) ¹	Mean time since last CD/ICH vaccination (days)		
Clumber spaniel	436.3 ^{cdef}	528.8 ^{bcdef}		
Finnish hound	369.9 ^b	400.6 ^b		
Italian greyhound	291.5°	355.6°		
Pointer	312.6 ^d	302.6 ^d		
Tibetan terrier	214.9eb	212.9ebc		
West Highland white terrier	259.8 ^f	310.2 ^f		

¹ Significant (p<0.05) breed differences are indicated by the same superscript letters.

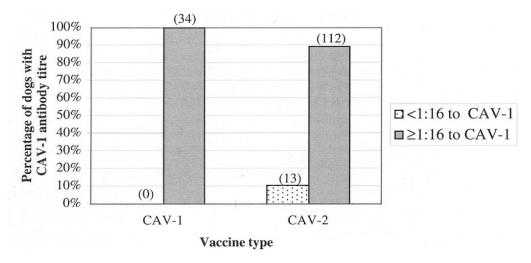


Figure 4. Percentage of dogs with antibody titres ≥1:16 to CAV-1 and vaccinated with different types of vaccine.

or antibody levels ≥1:16 against CD or ICH whether last vaccination was performed <1, 1-2 or ≥2 years earlier.

There was a significant difference in the proportion of dogs reaching titres ≥1:80 against CPV between dogs not vaccinated and those vaccinated twice or more (p<0.001). There was also a significant increase in the fraction of dogs with CD virus antibody levels ≥1:16 vaccinated twice or more (p<0.05). There was no statistical difference in the percentage of dogs with ICH virus antibody levels ≥1:16 among the groups vaccinated one, 2 or 3 times.

There was no statistical difference between vaccinated dogs less than one year of age and older dogs in the proportion reaching ≥1:80 against CPV, or ≥1:16 against CD or ICH.

Discussion

In Sweden, the disease situation regarding CPV, CDV and CAV-1 infections, as monitored by the Board of Agriculture, is good (Table 4), although there is some uncertainty regarding the

true number of CPV infected dogs. Numbers of dogs infected with CDV and CAV-1 are very low, and all cases refer to young dogs that had not been vaccinated or had an incomplete vaccination history. Except for the dramatic numbers of CPV infections registered in the early 1980's, the total numbers of dogs suffering from these 3 infectious diseases have been low in Sweden (Olson et al. 1988). The situation seems to be under control in most of the European countries (Grøndalen & Sjerve 1994) although epidemiological information on infectious diseases in dogs, with the exception of rabies, are not well documented. There are, however, exceptions such as the distemper epidemics that have occurred recently in Finland (Liisa Sihvonen, personal communication, 1995), in Denmark (Blixenkrone-Möller et al. 1993) and in France (Adelus-Neveu et al. 1991). Not much has previously been published about the inclination of owners to vaccinate their dogs (Robertson et al. 1991). The most important finding from the questionnaire is that so many dogs have been vaccinated against CPV and

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Table 4. Total primary laboratory-verified incidences of infections with CPV, CDV and CAV-1 as reported to)
the Board of Agriculture 1986-1992.	

Disease	Year									
	1986	1987	1988	1989	1990	1991	1992	1993	1994	Total
CPV infection	153	79	68	28	24	34	11	9	7	413
Canine distemper	1	1	3	6		3	5			19
Infectious canine hepatitis	1	4	1				3	6	4	19

that almost every dog in Sweden has been vaccinated at least once against CD and ICH. The figures on inclination to vaccinate dogs less than one year of age in the questionnaire are supported by the analysis on inclination to vaccinate in the antibody study. In a similar study from Australia, *Robertson et al.* (1991) reported that 90.8% of the dogs had been vaccinated at some time, with 72.7% vaccinated the preceding year. In a study on dogs from a Liverpool veterinary hospital population, 83% had been vaccinated against CPV and CD at least once, and of these animals 62% and 77% had been vaccinated as puppies against CPV and CD respectively (*Tennant et al.* 1991).

From the antibody study it is clear that a little more than 50% of all dogs are booster vaccinated between one to 2 years of age. This finding is also supported in the questionnaire. A booster vaccination at one year of age is a good practice to ensure that a dog is immunised in the absence of maternal antibodies.

The significant differences between owners of purebred dogs and owners of mixed breeds in their inclination to vaccinate, which was most pronounced for CPV vaccinations, could be explained by the fact that many of the mixed-breed dogs are not bred by experienced breeders, who have a strong influence on their puppy buyers on matters such as vaccinations. This is in accordance with the higher figures concerning inclination to vaccinate in the antibody study explained by the fact that this part of the study only contained purebred dogs.

A difference in vaccination pattern between breeds was found in the antibody study. For instance, Finnish hounds are considerably older when receiving their first CPV and CD/ICH vaccination compared with all other breeds. The Finnish hound and Pointer are the only breeds among those selected that are used exclusively as gun dogs. The difference between the breeds in time since last vaccination is partly due to the difference in age within the material, Clumber spaniels being older.

A titre of 1:80 to CPV was chosen since it is generally accepted that this titre protects dogs against the disease (*Pollock & Carmichael* 1982).

The overall numbers of vaccinated dogs reaching ≥1:80 in their CPV antibody titre in this study was 70.9% which is notably higher compared with the value obtained in the Swedish 1988 study (Olson et al. 1988). In 1988, the overall proportion of vaccinated dogs with an antibody ≥1:80 titre was below 40%, and at no time after vaccination did this proportion exceed 50%. The proportion of dogs with CPV titre ≥1:80 found in the current study is comparable to figures published from dogs in a Liverpool hospital population where 70% were positive at ≥1:80 (Tennant et al. 1991).

One reason for the higher proportion of vaccinated dogs with CPV antibody titres ≥1:80 in this study compared to the 1988 study, could be that a larger proportion of the puppies was vaccinated more than twice as a result of published recommendations on vaccinations (Olson et al. 1987). The proportions of dogs vaccinated 3

times (48.3%) and 4 times (28.4%) against CPV before one year of age in this study were much higher than in the 1988 study (13.1% and 2.4% respectively). It has earlier been shown that the chances of reaching protective levels can be improved by giving boosters of either killed or attenuated live CPV vaccines (O'Brien 1994, Olson et al. 1988, Wierup et al. 1982). In addition to this, introduction of attenuated live CPV vaccines on the Swedish market, and larger antigenic masses of the recent vaccines also contribute to the better results (Pollock & Coyne 1993).

The interval between the most recent vaccination and the time of sampling may also have influenced on the result, being longer in the 1988 study than in the present one. In the study of *Tennant et al.* (1991), the presence of CPV antibodies was not influenced by factors such as age, vaccination status, or rural/urban living. This result was attributed to the continuous boosting of antibody levels through natural challenge, thus masking any vaccine-derived immunity (*Tennant et al.* 1991).

Although, the GMT titre did not differ significantly between groups, the proportion of dogs reaching ≥1:80 was significantly higher in the group receiving attenuated CPV vaccine at last vaccination than in the group vaccinated with killed vaccine. This is in accordance with other studies where attenuated vaccines have been proved to be more efficient than killed vaccines in eliciting antibody titres in the absence of maternally derived antibodies (Buonavoglia et al. 1992, Burtonboy et al. 1991, Pollock &Coyne 1993).

A CDV/CAV-1 antibody level of $\geq 1:16$ was chosen as protective level as the titre $\leq 1:8$ in some samples was toxic to the cells and caused cell deaths in the virus neutralisation test. A titre of $\geq 1:16$ could thereby certify that the dogs had a specific antibody titre to these viruses. The overall frequency of vaccinated dogs with

CDV titers ≥1:16 in this study was 86.1%, whereas it was only around 70% in 1988 (Olson et al. 1988). This discrepancy can be explained by the age difference between the 2 sets of dogs involved: in the present study only dogs younger than 5 years of age were selected whereas in the 1988 study dogs were selected at random. The corresponding figure in the Liverpool study was 84% (Tennant et al. 1991). There was no difference in the proportion of dogs with CDV titres ≥1:16 between vaccinated and non-vaccinated groups. In contrast, Tennant et al. (1991) showed that both the presence of and level of antibody to CDV were influenced by vaccination status. Our findings that 70%-80% of the dogs not documented as having been vaccinated against CD/ICH showed elevated titres of the antibodies suggest that the current owners were in some cases mistaken; i.e. their dogs had in fact been vaccinated. It is doubtful that these dogs had been infected with wild virus since none of them had been ill. The risk that increased antibody titres were a reflection of a past subclinical infection rather than of vaccination induced immunity was probably low. This assumption is supported by official statistics as well as by the general impression that disease incidence is low. Consequently, the results of the comparison between vaccinated and non-vaccinated dogs should be interpreted with great caution.

The number of dogs with CAV-1 titres ≥1:16 was 91.6% in this study but only about 80% in the 1988 study. This difference is also reflected in the overall GMT which was 1:84 and 1:37 respectively. In the 1988 study it was not possible to compare dogs vaccinated with killed CAV-1 vaccine with those vaccinated with attenuated live CAV-1 vaccine. In the present study, however, significant differences were found between these 2 categories in the number of dogs with titre ≥1:16 and in GMT. A possible explanation for this could be that vaccination

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with the modified live CAV-2 virus vaccine results in lower concentration of heterotypic (CAV-1) antibody compared with the use of killed CAV-1 vaccines (Fischerman & Scarnell 1976).

The dogs in the antibody study could either have been vaccinated with a signal component vaccine or with a combination of one to 3 different vaccines at the same time. The combinations could have been a mix of attenuated live and inactivated vaccines. This study has not evaluated the possible interactions between the different vaccine components. There are reports in the literature on immunomodulative effects when using combination vaccines (Phillips et al. 1989, Miyamoto et al. 1992, Miyamoto et al. 1995), although without affecting the antibody titre levels (Phillips et al. 1989). A high inclination to vaccinate and the availability of effective vaccines are important prerequisites for keeping a population free from disease caused by CPV, CDV or CAV-1. The most significant findings of this study are that there was a high overall inclination to vaccinate. The highest inclination to vaccinate was found in owners of purebreds (90%), except for some breed of gun dogs, whereas the corresponding value for owners of mixed breed dogs was 10-20% lower. A higher proportion of the Swedish dog population was found to be protected against CPV when compared to the situation in 1988. The variation in the capacity of the different vaccines to elicit an antibody response is also an important finding. Live attenuated CPV vaccines and boostring increased the fraction of dogs protected against CPV. In contrast, the inactivated CAV-1 vaccine was superior to attenuated CAV-2 vaccines in evoking immunity.

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Sammanfattning

Parvovirusinfektion, valpsjuka och HCC – Benägenhet att vaccinera och antikroppssvar hos den svenska hundpopulationen.

Diurägares benägenhet att vaccinera sina hundar undersöktes hos slumpvis utvalda hundägande svenska hushåll. Enligt ägarna (n = 538) hade 87,7% av hundarna blivit vaccinerade någon gång mot CPV (canine parvo virus) och 95,8% hade blivit vaccinerade mot CD/ICH (canine distemper/infectious canine hepatitis). Benägenheten att vaccinera blandrashundar var signifikant lägre jämfört med rasrena hundar. I en andra del av studien analyserades antikroppshalten mot CPV CD och CAV-1 hos 176 slumpvis utvalda hundar med känd vaccinationsbakgrund. CPV antikroppshalter ≥1:80 uppmättes hos 70,9% av de vaccinerade hundarna. Andelen hundar som nådde ≥1:80 1 titer mot CPV var signifikant högre i den grupp som var vaccinerade med levande modifierat parvovirusvaccin jämfört med hundar vaccinerade med avdödat vaccın. Antıkroppstıtrar mot CD och CAV-1 ≥1:16 uppmättes hos 86,1% och 91,6% respektive. Andelen hundar med CAV-1 antikroppar ≥1:16 var signifikant högre 1 den grupp hundar som vaccinerats med inaktiverat CAV-1 vaccin jämfört med den grupp som vaccinerats med modifierat levande CAV-2 vaccin. Ungefär 50% av hundarna booster vaccinerades mot alla tre sjukdomarna vid cirka ett års ålder.

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