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AN OBSERVATIONAL STUDY OF CANINE KENNEL COUGH*

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SUMMARY : *A case-control study was conducted to determine vaccinal efficacy against canine kennel cough. Cases and controls were selected from the veterinarian using dog population of the United Kingdom by simple random sampling of small animal veterinary practitioners. Data were reported on postal questionnaires. A logistic model was constructed with vaccinal status against a variety of vaccines as the explanotory variables, and kennel cough as the response variable. This demonstrated that vaccination against Bordetella bronchiseptica and parainfluenza virus was efficacious when used in conjunction with the usual routine vaccinations.*

RESUME : *Une étude cas-témoins a été effectuée afin de déterminer l'efficacité vaccinale contre la toux de chenil. On a choisi des cas et des témoins parmi les chiens des clientèles de vétérinaires du Royaume Uni par simple échantillonnage aléatoire auprès de vétérinaires s'occupant de petits animaux. Les données ont été recueillies au moyen de questionnaires envoyés par la poste. On a construit un modèle logistique avec statut vaccinal vis-à-vis de divers vaccins comme variables d'explication, et la toux de chenil comme variable de réponse. Ceci a démontré que la vaccination contre Bordetella bronchiseptica et le virus para-influenza a été efficace lorsqu'elle a été utilisée en conjonction avec les vaccins canins habituels.*

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INTRODUCTION

Kennel cough is a world-wide, infectious, upper respiratory tract disease of dogs, usually characterised by a harsh, dry cough. The lesion generally is a tracheobronchitis. Infection frequently occurs when dogs are mixed in groups, such as when in kennels, which explains the name of the disease. Field outbreaks often are referred to practising veterinary surgeons who usually treat the condition with antibiotics, antitussives and, sometimes, steroids.

The cause of kennel cough appears to be multifactorial [Appel and Binn, 1987], with reports of bacterial and virus isolates (table 1). However, several bacterial isolates also may be found in healthy dogs [Brennan and Simkins, 1970 ; McKiernan et coll., 1982] ; and many kennel cough infections are mixed [e.g., Wagener et coll., 1984]. These characteristics complicate causal inference. Nevertheless, the two organisms considered to be major causes are *Bordetella bronchiseptica* and canine parainfluenza virus (CPIV).

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Table 1 : Agents implicated in canine kennel cough.

Bacteria :
Bordetella bronchiseptica
Pasteurella spp.
Streptococcus spp.
Mycoplasmata
Coliforms
Viruses :
Canine parainfluenza virus
Canine distemper virus
Reoviruses
Canine herpes virus
Influenzavirus

The disease has been experimentally induced by *B. bronchiseptica* [Thompson et coll., 1976] and this bacterium is known to persist in dogs [Bemis et coll., 1977]. Canine parainfluenza virus has been reported frequently in the United States [e.g., Appel and Percy, 1970]. However, the frequency of occurence of putatively causal organisms in national dog populations is not known because attempts to identifiy microbes are not made in the majority of cases.

Vaccines are available against *B. bronchiseptica* and CPIV ; an intranasal *B. bronchiseptica* and a subcutaneous CPIV vaccine are used in the United Kingdom. Additionally, routine vaccination against canine distemper virus (CDV) and canine adenovirus (types CAV-1 and CAV-2) may be relevant to the pathogenesis of kennel cough because both CDV and CAV-2 have been isolated from cases (table 1), and attenuated "live" CAV-1 (infectious hepatitis) vaccine will protect against CAV-2 infection [Cornwell et coll., 1982].

This paper presents the results of a case-control study to investigate the efficacy of a variety of vaccines for which there is *a priori* evidence of a protective role. This approach was used because of the impracticality of conventional microbiological techniques for determining causes in a widespread practitioner-based study and the problems associated with inferring cause when mixed infections may occur. This study was part of a larger one which also included investigation of the disease's incubation periode and clinical signs, and efficacy of treatment (to be reported later).

MATERIALS AND METHODS

Collection of data

A simple random sample of veterinary practitioners was selected from a list of members of the British Small Animal Veterinary Association. The sample size was determined according to the criteria of Schlesselman [1979], with the requirement of one of the sponsoring drug companies that breed-specific indications of vaccinal efficacy should be capable of identification. Statistical significance and test power were set at 5 % and 20 %, respectively, and the detectable odds ratio in favour of disease between non-vaccinated and vaccinated animals for the least-used vaccine set at 2.

The proportion of vaccinated animals in the "cared-for" dog population was estimated from records of vaccine sales. Information on vaccinal status for cases and controls was recorded on postal questionnaires, details of which are given by Trusfield et coll. [1989]. The study was run for two 4-month summer periods in 1986 and 1987.

Data analysis

The degree of association between kennel cough and vaccinal status for a particular vaccine was based on parameter estimates derived from a 2 x 2 contingency table (table 2) which can be generated by cohort, case-control or cross-sectional procedures [Thrusfield, 1986]. Two parameters are the "relative risk" and "odds ratio". The relative risk (RR) is the ratio of the incidence of disease in exposed animals to that in unexposed animals :

$$RR = \frac{\frac{a}{a+b}}{\frac{c}{c+d}}$$

Table 2 : The 2 x 2 contingency table constructed in observational studies to identify risk factors. The letters a, b, c, d and n refer to the number of animals in each of the four cells in the body of the table.

	Diseased animals	Non-diseased animals	Totals
Animals exposed to the risk factor	a	b	a + b
Animals not exposed to the risk factor	c	d	c + d
Totals	a + c	b + d	a + b + c + d = n

In cohort studies, (a + b) and (c + d) are predetermined.

In case-control studies, (a + c) and (b + d) are predetermined.

In cross-sectional studies, only n can be predetermined.

Although the RR can be calculated directly only in a cohort study, it is approximated by the odds ratio when disease is rare (which is the usual circumstance). The case-control design, used in this study, allows calculation of an "exposure odds ratio" (OR_e) : the odds of exposure to the factor in the diseased group relative to the odds of exposure in the control group :

$$OR_e = \frac{\frac{a}{c}}{\frac{b}{d}} = \frac{ad}{bc}$$

In this study, the factor is "not-vaccinated" against microbes for which there is evidence of a causal association with kennel cough. There are thus 6 relevant vaccines : against *B. bronchiseptica*, CPIV, CDV, CAV-1 (with either "live" or inactivated vaccine) and CAV-2 infection. In this circumstance, there may be estimability problems for the OR_e because of the possibility of small or zero values in cells in the various contingency tables. However, a model can be constructed which produces "smoothed" estimates of the risks for each category, using information from the other categories, allowing the risk of disease to be estimated for various combinations of vaccine. A linear logistic model [Breslow and Day, 1980] was used and was fitted using the GLIM (Generalised Linear Interactive Modelling) statistical package [Payne, 1986]. This is based on the "logit ("log odds" : Cox, 1970) transform" of the probability of developing disease. Since the RR usually is well approximated by the OR_e in case-control studies, the model is easily interpretable in terms of the relative risk.

The model, the full derivation of which is presented by Thrusfield et coll. [1989], was run to estimate the reduction in log RR associated with various combinations of the 6 vaccines. The best fit to the data was provided when some statistical interaction terms (based on a multiplicative scale) were included.

RESULTS

Questionnaires relating to 2456 dogs were returned over the 2 years study period. Removal of ambiguous and incomplete questionnaires left 1354 cases and 493 controls for use in the model. The model was constructed within the context of usual vaccinal strategies and therefore was fitted relative to dogs vaccinated against only CDV, because this vaccine is a basic requirement for dogs. The estimated changes in log odds (log RR) in this model, and their associated standard errors, are given in table 3. These must be considered in the context of concurrent vaccination with other vaccines. The values for the usual vaccinal combinations can be calculated from table 3. For instance, the reduction in log odds (log RR) for a dog vaccinated against CDV, *B. bronchiseptica* and CAV-2 is calculated thus :

$$- 0.3 - 0.2 - 1.5 = - 2.0$$

Calculation of the associated standard error shows that this is significant. This computation includes the main effects of the individual vaccines (the first two numbers) and the interaction (the third number).

DISCUSSION

The model shows the efficacy of various vaccines in combinations that are likely to occur in general veterinary practice in the United Kingdom. Efficacy is measured in terms of the reduction in the lof odds (log RR and, equivalently, the relative risk) in favour of disease in dogs that have been vaccinated with one or more relevant vaccines. Application of the figures in table 3, and calculation of associated standard errors, suggest that the two vaccines specifically designed to protect against kennel cough (those against *B. bronchiseptica* and CPIV infection) are effective when given to animals that are vaccinated against CDV and both types of adenovirus (with any of the three types of adenovirus vaccine).

Table 3 : Estimates and their associated standard errors of the changes* in the log odds (log relative risk [log RR]) in favour of a kennel cough case for each of five vaccines and their associated interactions for dogs which have already received canine distemper virus (CDV) vaccine.

Vaccine	Estimated change in log odds (log RR)	Standard error of estimated change in log odds (log RR)
B. br.	- 0.3	0.48
CPIV	- 2.0	0.53
CAV-1 (I)	- 0.7	0.21
CAV-1 (L)	- 2.8	0.84
CAV-2	- 0.2	0.26
B. br. + CPIV	1.3	0.42
B. br. + CAV-1 (I)	- 0.8	0.55
B. br. + CAV-1 (L)	- 2.2	0.78
CPIV + CAV-1 (I)	2.7	0.69
CPIV + CAV-1 (L)	3.8	0.99
B. br. + CAV-2	- 1.5	0.56
CPIV + CAV-2	1.1	0.57

* A reduction is indicated by a negative value, and an increase by a positive value.

B. br. = Bordetella bronchiseptica
CPIV = canine parainfluenza virus
CAV-1 (I) = Inactivated canine adenovirus Type 1
CAV-1 (L) = "Live" attenuated canine adenovirus Type 1
CAV-2 = "Live" attenuated canine adenovirus Type 2

CAV-1 and CAV-2 interaction is not included because it is unlikely to be of practical significance.

There is statistical interaction between *B. bronchiseptica* and CPIV vaccines when given with any of the adenovirus vaccines. However, this should not be interpreted as a biological interaction which implies that one vaccine antagonises the effects of the other [Rothman et coll., 1980]. Statistical interaction is a characteristic of the type of model : it may be present in one model but absent in another, and its value is often predictive (as in this study).

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