

Neutralising antibody titration in 25,000 sera of dogs and cats vaccinated against rabies in France, in the framework of the new regulations that offer an alternative to quarantine

F. Cliquet, Y. Verdier, L. Sagné, M. Aubert, J.L. Schereffer, M. Selve, M. Wasniewski & A. Servat

Agence Française de Sécurité Sanitaire des Aliments - Nancy, Laboratoire d'Études et de Recherches sur la Rage et la Pathologie des Animaux Sauvages, Domaine de Pixérécourt, B.P. 9, 54220 Malzéville, France

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Summary

Regulations governing international movements of domestic carnivores from rabies-infected to rabies-free countries have recently been loosened, with the adoption of a system that combines vaccination against rabies and serological surveillance (neutralising antibody titration test with a threshold of 0.5 IU/ml).

Since 1993, the Research Laboratory for Rabies and Wild Animal Pathology in Nancy, France, has analysed over 25,000 sera from dogs and cats using a viral seroneutralisation technique. The statistical analyses performed during this time show that cats respond better than dogs. Although no significant difference in titres was observed between primovaccinated and repeat-vaccinated cats, repeat-vaccinated dogs had titres above 0.5 IU/ml more frequently. In primovaccinated dogs, monovalent vaccines offered a better serological conversion rate than multivalent ones. Finally, the results of these analyses showed a strong correlation between antibody counts and the time that elapsed between the last vaccination and the blood sampling.

Keywords

Booster – International movements – Monovalent vaccine – Multivalent vaccine – Neutralising antibody – Primary vaccination – Rabies.

Introduction

Many countries impose strict controls on the importation of domestic carnivores to reduce the introduction of new diseases. Regarding rabies, world-wide movement of cats and dogs from infected countries to those countries or areas free of rabies meant that until recently, on arrival at their destination these animals were placed in quarantine for between four and six months in establishments approved and supervised by public Veterinary Services. The effects of this quarantine have been satisfactory: between 1971 and 1993 (20), for example, no case of rabies was detected during quarantine in Great Britain despite the importation of about 200,000 cats and dogs. The duration of the quarantine is justified by the incubation period of rabies, which can vary, but in general does not exceed six

months (33). This formality, however, represents a great expense for the owner of the animal, probably one of the reasons leading to fraud. In addition, the psychological and physical condition of an animal confined for six months can be severely modified.

Considering the intensification of international exchanges, the demand for the free circulation of people and property among Member States of the European Union (EU) and the improvement of scientific knowledge, regulations on the international transfer of animals have now been simplified.

In 1992, the 8th report of the Expert Committee on rabies of the World Health Organization (WHO) recommended an antibody titration for those countries unable to apply strict

quarantine measures (35). In the same year, an in-depth bibliographical review (4) showed that quantification of the antibodies neutralising the rabies virus in the serum of domestic carnivores (cats, dogs) properly vaccinated against the disease made it possible to predict the resistance of these animals to possible infection.

Since 1993, the OIE (World organisation for animal health) has recommended performing a test which consists in the titration of neutralising antibodies whenever cats and dogs are imported from countries infected with rabies (22).

Anti-rabies vaccination of domestic carnivores induces a humoral response, resulting in the production of antibodies which neutralise the rabies virus. Epidemiological studies on the effects of anti-rabies vaccination in animals are largely based on the determination of neutralising antibody levels. The synthesis of these antibodies able to neutralise the infectious rabies virus is triggered by glycoprotein G, anchored on the surface of the rabies virus (11).

In 1993, New Caledonia implemented a system relaxing quarantine laws for carnivores for which a valid anti-rabies vaccination certificate could be provided in addition to the results of a serological test mentioning the anti-rabies antibody titration and a certificate of good health.

Since then, similar measures have been taken by other countries, enabling the free circulation of cats and dogs from countries where canine rabies is absent or under control to countries exempt of rabies, namely, the United Kingdom (UK) (14), Sweden (21), Norway (21), Australia, New Zealand, New Caledonia, Hawaii (18), French Polynesia and the Island of Reunion.

Anti-rabies serological tests are conducted by laboratories having been approved by one of three competent authorities, i.e. the Brussels European Commission, the UK Veterinary Authorities or the Scandinavian Veterinary Authorities. The laboratory of the authors has been designated as the reference laboratory for these three authorities and is responsible for organising tests for the approval of laboratories willing to perform the serological tests and their annual evaluation. The laboratory is also one of twenty-two approved laboratories in Europe.

This study presents a retrospective analysis of the titration results obtained since 1993 on cats and dogs having undergone parenteral vaccination with approved inactivated anti-rabies vaccines. Several criteria were studied, in particular the frequency of titres above the positivity threshold (0.5 IU/ml), the effect of the vaccine type and the vaccination history of the animals.

Materials and methods

Techniques for the titration of seroneutralising antibodies

Two cell seroneutralisation techniques were used. The first was the rapid fluorescent focus inhibition test (RFFIT) described by Smith *et al.* (29) and Zalan *et al.* (36) with modifications according to Sureau *et al.* (30). The second method used was the fluorescent antibody virus neutralisation (FAVN) test (23). This technique presents the advantage of being more rapid and more precise, and perfectly correlates with the RFFIT (7, 9). Both tests consist in neutralising a constant dose of virus by antibodies present in the serum to be assayed. The titre of the serum corresponds to the dilution at which 50% of the constant viral dose is neutralised by the antibodies. Comparison of the results of the tested sera with those of the OIE reference serum of dog origin of known titre (23) (IU/ml) enables the definition of a titre for each serum.

A titre of 0.5 IU/ml is considered by the WHO (35) as the minimum protective antibody level, i.e. from this threshold up, the rabies virus is completely neutralised by rabies antibodies.

Anti-rabies vaccines and sera

The sera arrived at the laboratory with a certificate completed by the veterinary surgeon who took the blood sample, and which provided details of the animal species, the identification (tattoo and/or electronic chip), the vaccine used and the country of destination of the animal. On arrival, the sera were identified and the information was recorded in a computer database.

The anti-rabies vaccines used by the veterinary surgeons are all authorised in Europe and have all received marketing authorisations in their countries of origin. They are inactivated vaccines, with or without adjuvants, administered in monovalent or multivalent form and containing at least one international antigenic unit per millilitre. Multivalent vaccination consists in inoculating various elementary vaccines (i.e. leptospirosis, hepatitis, distemper, etc.), including the rabies valency. Inoculation can be performed in one day by injecting the different elementary vaccines in different parts of the body, or by injecting the associated vaccines in a single part of the body. In this study, the choice of inoculation was unknown.

Statistical analysis

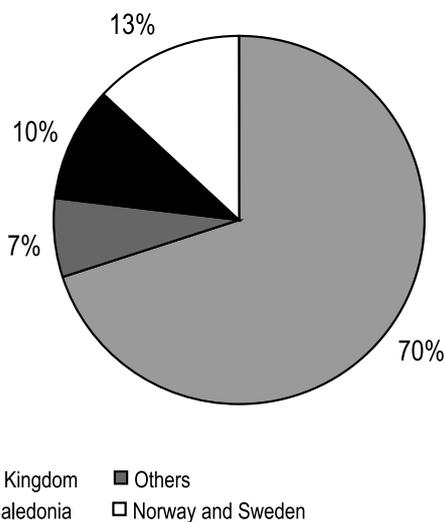
A questionnaire was sent to all veterinary surgeons requesting the date of birth and vaccination status of the animal, as well as the date of the blood sample so that as many parameters as possible which affect the immune response could be included in the analysis. Thus, all the names of the vaccines given to the animal since birth were provided. Statistical analyses were

performed according to the square chi (χ^2) test and variance analysis for one factor. The minimum probability retained after statistical analysis was $p = 0.95$.

Results

Origin and destination of the cats and dogs

Figure 1 shows in detail (in percentage) the countries of destination of the cats and dogs from which blood samples were analysed between July 1993 and December 2002. The sera received came mainly from Europe and principally from France (72%) with the most popular destinations being the UK (70%), Norway or Sweden (13%) and New Caledonia (10%).



Others: Australia, New Zealand, Reunion, Hawaii

Fig. 1
Destination of dogs and cats from which blood samples were analysed

Vaccines used

The vaccines used came from several different French producers but most came from two particular manufacturers. The first of these companies provided the vaccines in the vast majority of cases (66% of the cats and dogs) and the other company provided the vaccines for 20% of the animals. Of this 66%, a monovalent vaccine was administered in 65% of cases, a pentavalent vaccine (canine distemper, viral hepatitis, parvovirus infection, leptospirosis and rabies) in 15% and a bivalent vaccine (leptospirosis and rabies) in 8% of cases. Of the 20% of animals that received the vaccine from the other manufacturer, 40% received a monovalent vaccine.

Neutralising antibody titre values

Large individual variations were observed in the response levels of anti-rabies antibodies (from 0 IU/ml to more than 100 IU/ml), both in cats and in dogs. Figure 2 shows the

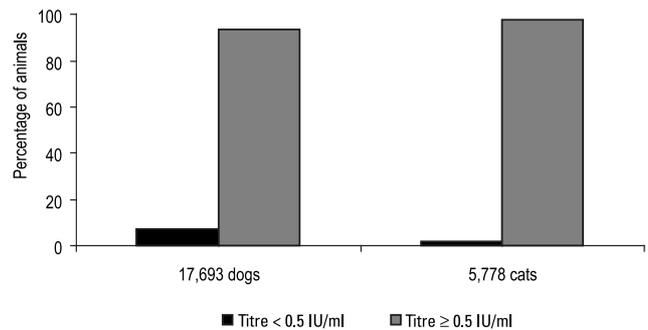


Fig. 2
Rabies neutralising antibody titres (IU/ml) in vaccinated dogs and cats

results obtained, irrespective of vaccination status in terms of percentage of animals presenting titres lower or higher than the threshold value of 0.5 IU/ml.

Of a total of 17,693 dog and 5,778 cat sera analysed, respectively 1,301 (7.4%) and 109 (1.9%) samples showed an antibody titre of less than 0.5 IU/ml. The difference between the two percentages is highly significant ($\chi^2 = 209 > \chi^2 = 10.83$, $p < 0.001$).

Distribution of titres according to vaccination status

Based on the answers to the questionnaire, the cats and dogs were classified as primo-vaccinated, i.e. animals vaccinated against rabies for the first time or multi-vaccinated, i.e. animals having received several annual anti-rabies injections over the past years. Figure 3 presents the distribution in antibodies according to the number of vaccine injections. Of the primo-vaccinated dogs, 14.5% presented titres lower than the minimum threshold as opposed to 2.6% of primo-vaccinated cats ($p < 0.001$). Dogs who had been vaccinated twice or more (with an interval of one year) had titres significantly higher than primo-vaccinated dogs ($p < 0.001$). No significant difference was observed in the percentage of dogs with titres equal to or higher than 0.5 IU/ml after two injections.

For cats, no significant difference was observed between the primo-vaccinated and the multi-vaccinated groups (Fig. 3).

The marked difference in seroconversion levels observed in dogs vaccinated for the first time and in those vaccinated twice a year apart cannot be explained by a difference in age. The average age in both groups was statistically similar ($p = 0.16$). Furthermore, the average age of non-seroconverted primo-vaccinated dogs was not statistically different from that of primo-vaccinated dogs with seroconversion ($p = 0.14$) (data not shown).

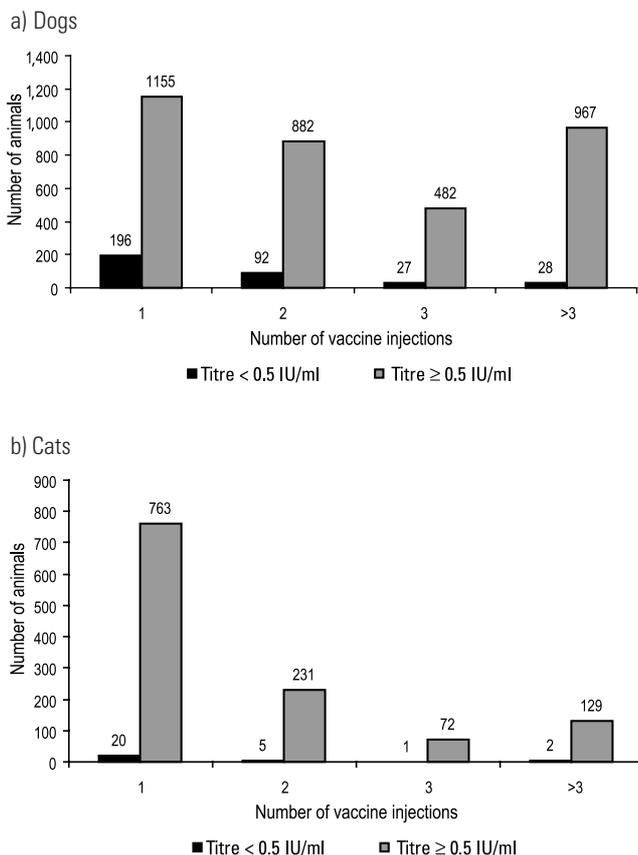


Fig. 3
Rabies neutralising antibody titres according to the number of vaccine injections

Comparative analysis of the titres determined in cats and dogs irrespective of the number of vaccines received shows (Fig. 4) that canine sera anti-rabies antibody titres are weaker than those of cats ($\chi^2 = 318$, $p < 0.001$). Titres lower than 5 IU/ml were observed in 50% of primo-vaccinated dogs and 6% of multi-vaccinated dogs against 15% of primo-vaccinated cats and 7% of multi-vaccinated cats.

Comparison of titres according to vaccine type (monovalent or associated from the same manufacturer)

This analysis was conducted on dogs. Figure 5 illustrates the seropositivity rate in primo-vaccinated and multi-vaccinated animals according to the vaccine formulation. Multivalent vaccines administered in primo-vaccination appear to induce a titre considered protective (equal to or higher than 0.5 IU/ml) less frequently than monovalent rabies vaccines ($p < 0.001$ for primo-vaccinated dogs).

Effect on antibody titres of the interval between the last injection and the blood test

For cats and dogs that have been vaccinated several times against rabies, antibody titres do not depend on the time

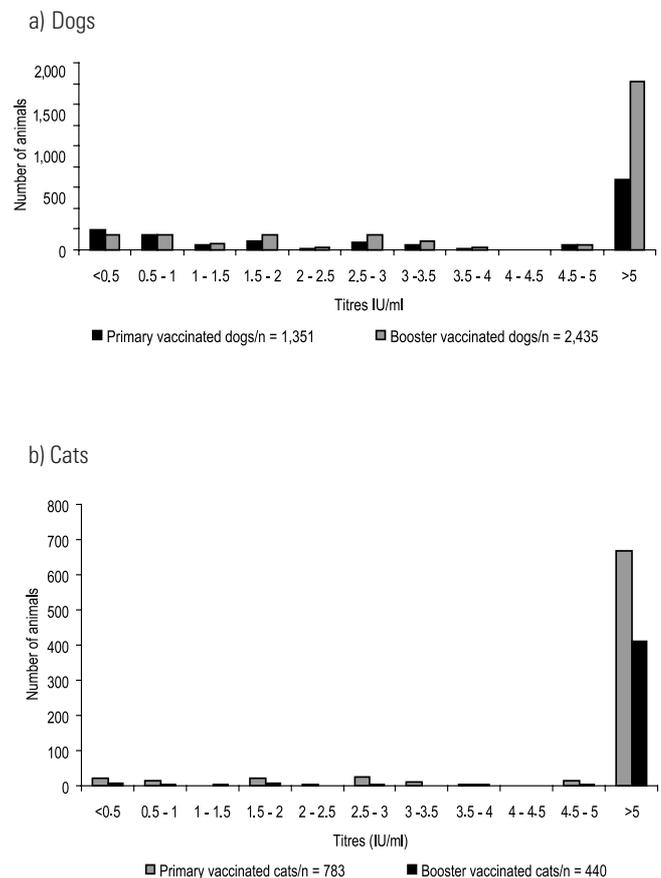


Fig. 4
Comparison of rabies neutralising antibody titres (IU/ml) in primary and booster vaccinated dogs and cats

elapsed since the last vaccination (data not shown). On the other hand, humoral response becomes significantly weaker in primo-vaccinated dogs five months after vaccination (Fig. 6) ($0.01 < p < 0.05$). The percentage of dogs with a titre less than 0.5 IU/ml was 7.8% two months after primo-vaccination, 19.1% between two and four months, 25% four to six months and 22% more than six months after the vaccination.

Discussion

Context of alternative measures to quarantine

The WHO made the first concrete recommendations relaxing quarantine conditions in 1992 by proposing an alternative measure for those countries or zones not applying strict quarantine rules (35). A minimum of two anti-rabies vaccinations is required, one after the age of three months and the second at least six months later. The departure of the animal can only take place between three and six months after the last vaccination. On arrival, two serological tests are performed at least four weeks apart with the animal being kept in quarantine

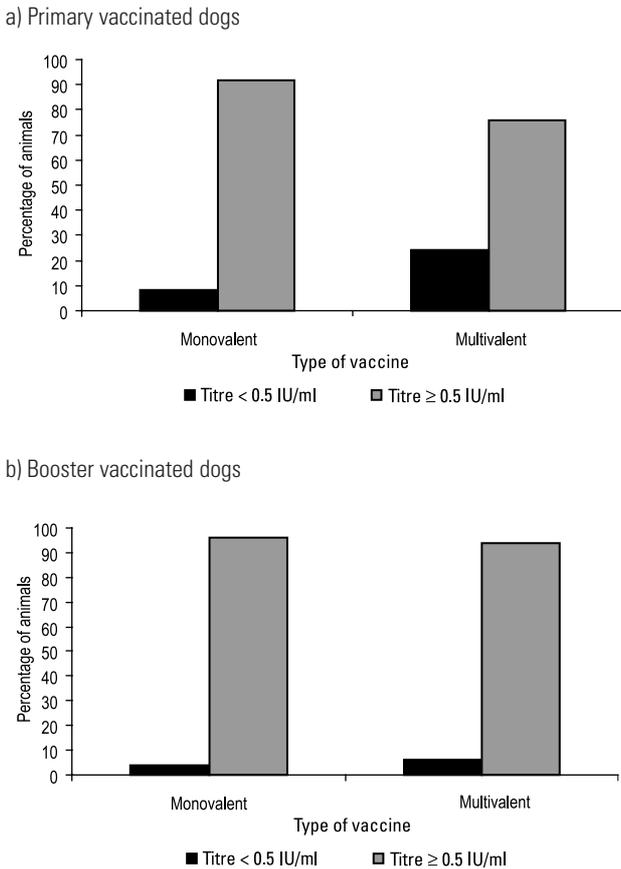


Fig. 5
Rabies neutralising antibody titres (IU/ml) according to the type of vaccine (mono or multivalent)

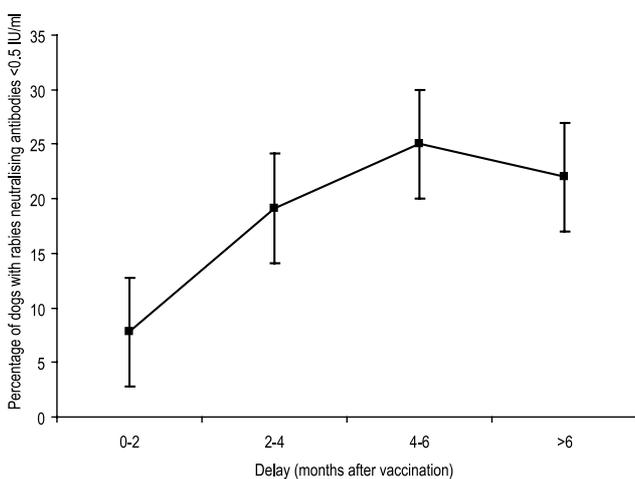


Fig. 6
Effect of time on the percentage of seroconversion in primary vaccinated dogs between the last vaccination and blood sampling

during this time. Animals presenting two positive tests are then exempt from further quarantine, but are required to stay indoors for ten weeks. In the same context, in 1993, the OIE recommended a serological test between three and twenty-four months before the trip (22).

In 1992, an in-depth review listed in detail the scientific knowledge accumulated on the significance of neutralising antibodies in domestic carnivores vaccinated against rabies (4). This analysis of many experimental results led to the conclusion that cats and dogs producing neutralising antibodies at levels above 0.5 IU/ml after an anti-rabies vaccination, irrespective of the period of time elapsed since the injection have a very high probability of survival after a later rabies infection, even if on the day of the challenge the serum contained no detectable anti-rabies antibodies. The humoral response to parenteral anti-rabies vaccination shows a classic profile: a latent phase followed by an exponential phase and a plateau, then a decrease in the antibody levels. The peak is generally reached between four and six weeks (5) after vaccination if the antigenic response is stimulated for the first time. However, specific antibodies may appear in vaccinated subjects that are in a rabies incubation phase, whether they were contaminated before or after vaccination. At the present time, titration techniques do not differentiate between the antibodies induced by vaccination and those that appear after contamination by the rabies virus. The incubation period of rabies is extremely variable and depends on several factors, such as the dose of virus inoculated, the route and place of inoculation and the strain, but generally ranges from seven to 125 days after contamination (13). National authorities seeking to implement an alternative system to quarantine are thus faced with two questions on the choice of the date of the blood test and the date of departure, as follows:

a) a blood test performed thirty days after vaccination shows whether a cat or dog has responded to vaccination and thus has a better chance of being protected. A period of delay before the departure makes it possible to ensure that the animal presents no clinical signs of rabies and that the antibodies measured were only the result of vaccination and not of rabies infection. This blood test also reveals whether the vaccinated animal is immunocompetent so that if a few days before departure the cat or dog comes into contact with a rabid animal, it will be able to resist. This is the system adopted by the Authorities in Great Britain, where a waiting period of six months is imposed between the blood test and the departure. This corresponds to a quarantine period of six months in an infected country where the animal is protected by vaccination. Australia has implemented an original system based on a flexible waiting period of six months after vaccination either at home or in quarantine, leaving free the choice of the date of the blood test (but at least thirty days after vaccination) and of the departure

b) a blood test performed at least three or four months after vaccination, depending on the country, enables the selection of cats and dogs with a good response to primo-vaccination. An

additional waiting period of three months after the blood test is often required before departure (this is the case in New Caledonia, New Zealand and French Polynesia, although the date of the blood test is not imposed in French Polynesia). Sweden and Norway require a blood test at least four months after vaccination and departure can take place as soon as the results are known.

Standardisation of the conditions to be applied in all rabies-free areas is highly desirable since regulations are based on well-controlled scientific data.

The result of serological analysis is the criterion enabling animals to travel. Only standardised titration techniques that have been validated and recognised by the OIE are considered reliable and may be used (4). However, when inter-laboratory tests are conducted to decide whether a laboratory can be granted approval for anti-rabies serological testing in Europe, considerable differences may be observed in the antibody titres measured on identical sera (results not published).

Limits of this study

The veterinarians provided very little data on the animals from which the serum samples were taken. A questionnaire was therefore sent together with the titration results. A significant part of this analysis is based on information provided by the veterinary surgeons that could not be verified. However, several veterinarians reported that they vaccinated twice (without noting this in the vaccination book) to achieve higher titres in the blood test. In the strict sense of the regulations, the blood test should be made after a certain period of time (which varies according to the different countries) after the last vaccine injection. The practice reported here enables the veterinarians to gain several months before departure. The different results presented in this study do not systematically come from the same animals as information on certain analysis criteria was sometimes missing in certain records. In all cases, any incorrectly filled-in questionnaires were discarded.

Finally, in the study on multi-vaccinated cats and dogs, only the last vaccine was taken into account.

Antibody titres

As far as the authors are aware, this study is the first report of the serological response developed in a large number of domestic carnivores vaccinated against rabies in field conditions in all parts of France. Similar studies have already been published (6, 12, 27), but only on the canine species, with a limited number of dogs (156, 47 and 66, respectively) and vaccines used. The fact that some data provided by the veterinary surgeons may not be reliable is true for all the animals and is probably compensated for by the large number of samples analysed (17,693 dog sera and 5,578 cat sera).

The individual variations observed in both cats and dogs, including those in laboratory dogs kept in highly standardised conditions, have been widely described (4).

Study on dogs

Of the primo-vaccinated dogs, 14.5% showed antibody titres lower than the required minimum. However, absence of antibodies or the presence of antibody levels lower than the minimum requirement at time *t*, does not necessarily mean that the animal is not protected: the animal may have presented a seroconversion before the date of the blood test. Furthermore, cell mediated immunity plays an important part in protection.

A more detailed analysis of these percentages of seroconversion in primo-vaccinated dogs, which focused on the time elapsed between vaccination and the blood test, revealed that two months after vaccination, 93% of dogs showed levels equal to or greater than 0.5 IU/ml. This percentage dropped to 81% between two and four months, and finally to about 75% more than four months after primo-vaccination. This rapid decrease of rabies antibodies in primo-vaccinated dogs following parenteral vaccination has already been described in pet dogs (31). On the other hand, for multi-vaccinated dogs, including those vaccinated twice just twelve months apart, no evidence of a significant drop in antibody levels was observed, irrespective of the date of the blood test.

The data in this paper correspond to those quoted in the literature, even if the vaccines and the administration routes are different (the administration route was not requested in the questionnaire). Thus, Sage *et al.* (24) report 73% of positive responses in the Alaskan dog two months after vaccination and 76% six months after vaccination. A study performed in Dakar (1) on primo-vaccinated dogs shows similar percentages, i.e. 74% one month after vaccination, with this value dropping sharply to 31% six months after vaccination. One year after vaccination, most studies reveal very low levels of antibodies ranging from 6.6% to 6.7%, depending on the authors (1, 17, 24, 31). A follow-up study conducted in Europe (27) on forty pet dogs vaccinated subcutaneously showed higher levels one month and one year after primo-vaccination (97% and 83%, respectively). In contrast, the results of this study are different from those obtained by Sikes *et al.* in 1971 on laboratory dogs with less potent vaccines than the ones used currently (28). In this latter study, no dogs were without antibody four weeks after vaccination. However, laboratory dogs are known to respond better to vaccination than pet dogs (4).

Antibody titres were found to be higher in dogs that had received several vaccinations, confirming data already published (25).

In the context of international exchange, certain regulatory protocols require a blood test three to four months after

vaccination. This time limit coincides with a decrease in antibody levels, which means dogs that have been vaccinated only once run a high risk of having a titre lower than 0.5 IU/ml. In this case, the animal must be vaccinated again and after the regulatory waiting period of four months must have another blood test.

The results reported in this study in no way question the immunogenicity of authorised vaccines. Veterinary anti-rabies vaccines must have a marketing authorisation before being commercialised and are severely controlled (for more than ten years, the laboratory of the authors has controlled all the batches produced in France or which are imported). The manufacturers must follow the recommendations of the European Pharmacopoeia which demand that vaccine efficacy be tested in primo-vaccinated animals one year later (at the end of the validity) by severe virulent challenge that should kill at least 80% of the unvaccinated reference dogs (2).

In conclusion, most of the studies conducted on primo-vaccinated dogs suggest giving two primo-vaccination injections (16, 17, 24, 27, 34), which is confirmed by this study. This practice would yield higher antibody titres three or four months after the second injection. Moreover, even if this was not studied here, intramuscular injection should be preferred to the subcutaneous route (24).

Study on cats

The analyses on cats showed considerable individual variations (titres of more than 500 IU/ml were found in some cats). Cats vaccinated just once or several times showed statistically similar antibody levels. Furthermore, only 2.5% of primo-vaccinated cats failed to reach the threshold level of 0.5 IU/ml. Antibody kinetics after vaccination were the same in primo and multi-vaccinated animals. Several studies, among which that of Sharpee *et al.* (26), show antibody kinetics comparable to those observed in dogs. Finally, antibody levels are significantly higher ($p < 0.001$) than in the dog. The higher humoral response obtained after parenteral vaccination of cats is generally related to the antigenic mass/weight ratio (15).

The application of regulatory protocols in cats presents no difficulty: even if three or four months after primo-vaccination there is a drop in antibody levels, this value still remains considerably higher than that of the dog and continues to be above the minimum requirement.

Effect of the vaccine presentation on the serological response

This criterion was studied in dogs. The results show that monovalent vaccines induce a better immune response (in

terms of response lower or higher than the minimum threshold) in primary vaccinated dogs. These data do not comply with those found in the literature (10, 32). The study published by Terré (32) on primary vaccinated laboratory dogs compares the humoral response of a monovalent anti-rabies vaccine, of this same vaccine associated with two leptospirosis valencies and finally this vaccine associated with leptospirosis components, distemper and contagious canine hepatitis. Under experimental conditions different from those of the studies reported in this paper, no significant differences between the serological responses of the three dog groups were observed. In the latter protocol the rabies valency had no additives contrary to the vaccines in the studies in this paper. Thus, one or two extra valencies could inhibit the development of the immune response to rabies. This hypothesis must be verified on a large number of field dog groups vaccinated according to the protocols provided by the vaccine manufacturers, each group receiving a different vaccine.

Conclusion

Since 1993, no vaccine failure has been observed in any of the 15,000 cats and dogs entering Norway and Sweden each year. In France, about 4,250,000 cats and dogs are vaccinated every year against rabies. The probability of these animals developing rabies was estimated at 0.014/100,000 (4) in 1992. This probability is lower today, with the country being free from rabies for over a year. Based on current regulations, the results in this paper would suggest primo-vaccinating dogs with a monovalent vaccine, followed by a booster one month later and a blood test as soon as possible, while at the same time respecting regulations. The authors are in favour of harmonising the very diverse regulations, at least in the EU. The relaxing of quarantine measures in the UK (where conditions to be met differ from those of other countries in the EU) in February 2000 supports this (19). Since obtaining the rabies-free status in April 2001 (8), France has in turn adopted a regulation of a vaccination followed thirty days later by serological titration, with the animal not being allowed to enter the country until four months after inoculation (3). This regulation, half-way between that of countries in Scandinavia and that in Great Britain, would appear to be an alternative to the excessively long six-month waiting period and also limits the risk of obtaining a titre below the minimum requirement when the blood test is performed four months after vaccination.

Furthermore, the question of whether the threshold value of 0.5 IU/ml, determined at the Centre for Disease Control and arbitrarily adopted by the WHO and the OIE, is too severe, may be raised. However, even if this were the case, this value constitutes an extra guarantee for importing countries.

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Recherche d'anticorps neutralisants conduite sur 25 000 sérums de chiens et de chats vaccinés contre la rage en France dans le cadre de la nouvelle réglementation alternative à la quarantaine

F. Cliquet, Y. Verdier, L. Sagné, M. Aubert, J.L. Schereffer, M. Selve, M. Wasniewski & A. Servat

Résumé

Les réglementations régissant les mouvements internationaux des carnivores domestiques de pays infectés vers des territoires libres de rage ont récemment été allégées, avec l'adoption d'un système alliant la vaccination antirabique de l'animal et le contrôle sérologique (recherche d'un titre d'anticorps neutralisants supérieur au seuil de 0,5 UI/ml).

Depuis 1993, le Laboratoire d'Études et de Recherches sur la Rage et la Pathologie des Animaux Sauvages (Nancy, France), a analysé plus de 25 000 sérums de chiens et chats par une technique de séroneutralisation virale. Les analyses statistiques conduites dans cette étude montrent que les chats sont meilleurs répondeurs que les chiens. Alors qu'aucune différence statistique sur les titres n'a été observée entre chats primovaccinés et plurivaccinés, les chiens plurivaccinés montrent plus fréquemment des titres supérieurs au seuil de 0,5 UI/ml. Chez les chiens primovaccinés, les vaccins monovalents offrent un meilleur taux de conversion sérologique que les vaccins multivalents. Enfin, les analyses montrent une forte corrélation entre le taux en anticorps et le délai écoulé entre la dernière vaccination et la prise sanguine.

Mots-clés

Anticorps neutralisant – Mouvement international – Primo-vaccination – Rage – Vaccin monovalent – Vaccin multivalent – Vaccin de rappel.

Búsqueda de anticuerpos neutralizantes en 25.000 sueros de perros y gatos vacunados contra la rabia en Francia, en el marco de una nueva reglamentación alternativa a la cuarentena

F. Cliquet, Y. Verdier, L. Sagné, M. Aubert, J.L. Schereffer, M. Selve, M. Wasniewski & A. Servat

Resumen

En los últimos tiempos se han flexibilizado las reglamentaciones sobre el movimiento internacional de carnívoros domésticos de países infectados a países libres de rabia, con la adopción de un sistema que combina la vacunación antirrábica del animal y el control serológico (determinación de un título de anticuerpos superior a un valor umbral de 0,5 UI/ml).

Desde 1993, el Laboratorio de investigación de rabia y de patología de animales silvestres (Nancy, Francia) ha sometido más de 25.000 sueros de perro y gato a una prueba de seroneutralización viral. Los análisis estadísticos realizados en ese estudio ponen de relieve que los gatos responden mejor que los perros. Mientras que no se observa ninguna diferencia estadística entre los títulos de gatos primovacunados y los de gatos plurivacunados, los de perros plurivacunados superan con más frecuencia el valor umbral de 0,5 UI/ml. En perros primovacunados, las vacunas monovalentes ofrecen un mejor índice de conversión serológica que las vacunas multivalentes. Por último, los análisis ponen de manifiesto una estrecha correlación entre la tasa de anticuerpos y el tiempo transcurrido entre la última vacunación y la extracción de la muestra sanguínea.

Palabras clave

Anticuerpo neutralizante – Movimiento internacional – Primovacunación – Rabia – Revacunación – Vacuna monovalente – Vacuna multivalente.



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