

Persistence of vaccine immunity against canine parvovirus and canine distemper virus for determination of vaccine protocol in dogs: impacts and challenges in Brazil

Persistência da imunidade vacinal contra parvovírus canino e vírus da cinomose canina para determinação de protocolo vacinal em cães: impactos e desafios no Brasil

Persistencia de la inmunidad de la vacuna contra el parvovirus canino y el virus del moquillo canino para la determinación del protocolo de vacunación en perros: impactos y desafíos en Brasil

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Abstract

Vaccine protocols were established for dogs and cats, considering the circulating period of maternal antibodies from the puppies, the type of antigen used to make the vaccines and the vaccine immunity duration. This study aimed to approach the duration of vaccine immunity against the canine parvovirus (CPV-2) and the canine distemper virus (CDV), as determining factor to choose the adequate vaccine protocol, besides to stand out the main implications found in Brazil that difficult the application of these current protocols, as the technical challenges to use them. For that, this article described some information about the types of current vaccines, the immunity duration against the CPV-2 and CDV, as well the respective vaccine protocols that were applied. The searches were done in the database of PubMed, SciELO, Google Scholar, Capes Journals and academic books, by the following keywords: vaccination guidelines; humoral immune response; vaccination strategy; distemper; parvovirus infection; and duration of vaccine immunity. Considering the facts, it is understood that the annual revaccination against the CPV-2 and CDV for dogs must be individually assessed, because the vaccine immunity has an average duration of three years, that is, the best alternative for the animal would be the application of routine serological tests, aiming to assess if the antibodies titration remains protective. Another alternative is the use of divalent or trivalent vaccines.

Keywords: Antigen; CDV; CPV-2; Vaccines.

Resumo

Protocolos vacinais são estabelecidos para cães e gatos, considerando o tempo de circulação dos anticorpos maternos dos filhotes, o tipo de antígeno utilizado para fazer as vacinas e o tempo de imunidade vacinal. Este estudo teve como objetivo abordar a duração da imunidade vacinal contra o parvovírus canino (CPV-2) e o vírus da cinomose canina (CDV), como fator determinante para a escolha do protocolo vacinal adequado, além de destacar as principais implicações encontradas no Brasil que dificultam a aplicação desses protocolos atuais, como os desafios técnicos para utilizá-los. Para tanto, este artigo descreveu algumas informações sobre os tipos de vacinas atuais, a duração da imunidade contra o CPV-2 e o CDV, bem como os respectivos protocolos vacinais que foram aplicados. As buscas foram feitas nas bases de dados PubMed, SciELO, Google Scholar, Periódicos Capes e livros acadêmicos, por meio dos seguintes descritores: diretrizes de vacinação; resposta imune humoral; estratégia de vacinação; cinomose; infecção por parvovírus; e duração da imunidade à vacina. Diante dos fatos, entende-se que a revacinação anual contra o CPV-2 e CDV para cães deve ser avaliada individualmente, pois a imunidade vacinal tem duração média de três anos, ou seja, a melhor alternativa para o animal seria a aplicação de testes sorológicos de rotina, com o objetivo de avaliar se a titulação dos anticorpos permanece protetora. Outra alternativa é o uso de vacinas bivalentes ou trivalentes.

Palavras-chave: Antígeno; CDV; CPV-2; Vacinas.

Resumen

Se establecieron protocolos de vacunación para perros y gatos, considerando el período de circulación de los anticuerpos maternos de los cachorros, el tipo de antígeno utilizado para elaborar las vacunas y la duración de la inmunidad de las mismas. Este estudio tuvo como objetivo enfocar la duración de la inmunidad de la vacuna contra el parvovirus canino (CPV-2) y el virus del moquillo canino (CDV), como factor determinante para elegir el protocolo de vacunación adecuado, además de resaltar las principales implicaciones encontradas en el Brasil con dificultad de aplicación de estos protocolos actuales, como los desafíos técnicos para utilizarlos. Por eso, este artículo describió cierta información sobre los tipos de vacunas actuales, la duración de la inmunidad frente al CPV-2 y CDV, así como los respectivos protocolos vacunales que se aplicaron. Las búsquedas se realizaron en la base de datos de PubMed, SciELO, Google Scholar, Capes Journals y libros académicos, por las siguientes palabras clave: pautas de vacunación; respuesta inmune humoral; estrategia de vacunación; moquillo; infección por parvovirus; y duración de la inmunidad a la vacuna. Teniendo en cuenta los hechos, se entiende que la revacunación anual contra el CPV-2 y el CDV para perros debe evaluarse individualmente, pues la inmunidad vacunal tiene una duración promedio de tres años, es decir, la mejor alternativa para el animal sería la aplicación de las pruebas serológicas de rutina, con el objetivo de evaluar si la titulación de anticuerpos sigue siendo protectora. Otra alternativa es el uso de vacunas bivalentes o trivalentes.

Palabras clave: Antígeno; CDV; CPV-2; Vacunas.

1. Introduction

Animal healthcare has become more and more frequent, mainly regarding the prevention of infectious diseases. Beyond the sanitary protocols to control and prevent some infectious diseases in dogs, immune-prophylaxis also has an important role. Although there are many questions about the harmlessness of the vaccination process, the necessity of immunization remains an element of great importance for animal and public health.

In Brazil, vaccines against the canine parvovirus (CPV-2), reclassified in the genus *Protoparvovirus* and the canine distemper virus (CDV) are considered core viral vaccines, once the infections by these viruses cause higher morbidity and mortality ratios. Besides that, they are largely disseminated around the country with a great prevalence (Dezengrini et al., 2007; Alves et al., 2018; Headley et al., 2018; Costa et al., 2019).

Currently, a great part of CPV-2 and CDV vaccines, commercialized in Brazil, are multi-antigens and contain other ones beyond these antigens, such as canine adenovirus (CAV-2), canine parainfluenza virus (CPIV), *Leptospira interrogans* (serovars Canicola, Icterohaemorrhagiae, Pomona and Grippotyphosa), and some vaccines contain the rabies antigen, and all these ones are core. Moreover, other vaccines bring the canine coronavirus with itself, which is not recommended according to the Vaccine Guidelines Group (VGG) from the World Small Animal Veterinary Association (WSAVA) (Day et al, 2020).

The use of multivalent vaccines is considered, by many veterinaries, a practical and safe way to reach the animals' immunity, and indeed these vaccines efficiently act in the initial protocols. However, there are scientific pieces of evidence that the use of vaccines with multiple antigens at the revaccination phase, which often is annual, may harm animal health. Thereby, precautions regarding their use of the vaccine reinforce have been expressive, due to the difference of the immunity duration

face to the different types of immunogens (Greene et al., 2001).

Although some vaccines are very durable regarding their protection, such as the immunogens against CPV-2, CVD and CAV-2, others persist in lower levels into the organism and do not allow an adequate immunization for the animal, not beyond one year. Because of that, the ideal decision would be the optimization of an individual vaccine protocol that considers the risk of each infectious disease and the immunization time of each vaccine (Banerji et al., 2007).

For that will be possible, it is necessary to know the prevalence and distribution of these infectious diseases, besides a joint awareness process for the establishment of more elaborate vaccination systems, according to the individuality of each animal (Vilela, 2016). Nevertheless, many limiting factors were appointed about the implementation of these protocols, such as the lack of actualization and capacitation of the veterinary doctor, besides the market interests.

On this context, this study aimed to approach the duration of vaccine immunity against the canine parvovirus (CPV-2) and the canine distemper virus (CDV), as determining factor to choose the adequate vaccine protocol, besides to stand out the main implications found in the country that difficult the application of these current protocols, as the technical challenges to use them.

2. Methodology

This methodology is about an integrative literature review, which systematic researches were developed and ordained based on scientific indexers such as PubMed, SciELO, Google Scholar, Capes Journals, besides academic books about the theme, consolidating from the theme identification, literature search, data collection, and review presentation, according to Pereira et al. (2018). Current documents, which worked on the topic approached in a didactic and technical way, thinking about the training of veterinary doctors and professional practical application, were included in this article.

3. Core Vaccines: Protocols and Challenges in Brazil

3.1 Types of vaccine

Vaccines applied to dogs and cats were classified as 'core', 'non-core', or 'not recommended'. Core vaccines are those that regardless of the circumstances or locations, all dogs must receive, while the non-core vaccines must be regularly applied only in some individuals from a population. In this sense, possible risk factors related to geographic localization, environment, or lifestyle must be assessed. Conversely, those ones considered as 'not recommended' are not efficient or safe for the target-species, or prevent only diseases without clinical or epidemiological importance (Scavone, 2014).

Moreover, the vaccines were characterized regarding their origin, that is, 'infectious' or 'not infectious'. Infectious vaccines have the advantage to induce effectively both cell-immune and humoral responses, through intact and attenuated organisms, modified live virus (MLV), and recombining vectors. The non-infectious vaccines contain inactivated microorganisms, DNA or subunits, and often require an association with one adjuvant to increase the immune response. In these cases, they have a shorter immunity duration (ID) compared to those ones of the infectious vaccines (Day et al., 2016).

According to the vaccination schedule of FIAVAC-COLOVAC (2016) in Brazil, the core vaccines for dogs are those ones that have immunogens against CDV (attenuated-live or recombining), CPV-2 (attenuated-live), CAV-2 (attenuated-live) and rabies virus (inactivated) (Labarthe et al., 2016). Following the recommendations about vaccination for veterinary doctors of small animals from Latin America of VGG, the *Leptospira interrogans* vaccine (inactivated) is classified as a non-core one (Vilela, 2016).

Non-core vaccines for dogs in Brazil are those ones that have antigens against CPIV (attenuated-live) and *Bordetella bronchiseptica* (inactivated and attenuated-live), while the not recommended vaccines are those ones against the immunogens CCoV (inactivated) and *Giardia lamblia* (inactivated) (Day et al., 2016; Day et al., 2020).

3.2 Duration of vaccine immunity against CPV-2 and CDV

Many projects of scientific research have been carried out in recent decades, aiming to explain the persistence period of protection by vaccine antibodies for dogs face to the CPV-2 and CDV. Twark and Dodds (2002) measured the titration of serum antibodies for CPV and CDV in 1,441 and 1,379 dogs, respectively, with intervals between one and seven years from the last vaccination, and without association regarding age, gender and breed. For the CPV, 95.1% of the dogs showed adequate responses of antibodies, with a titration greater than 1:5, or equal, while only 4.9% presented inadequate responses. For the CDV, 97.6% of the dogs obtained congruent responses and 3.4% were incongruent. One of the sampled animals aged 17 years-old and presented a titration lower than 1:5 regarding the two viral antigens and the last vaccine reinforcement must have occurred two years ago.

Bohm et al. (2004) evaluated antibodies against the CPV-2 in 143 adult dogs with vaccination intervals of three years or more, of which 94.4% showed adequate protection, only 5.6% presented limiting titer and no one presented non-protection levels of antibodies. About the CDV analysis, 71.5% of the dogs showed protection titer, 18.1% had limited titers and 10.4% showed very low or undetectable titers. Abdelmagid et al. (2004) started an experimental assay with 10 immunized dogs by a multivalent vaccine against CDV, CPV-2, CAV-2 and CPIV. The authors observed that at 57 months after the first vaccinations, all animals demonstrated protection, without clinical condition regarding the parvovirus disease and canine hepatitis. However, 90% of the dogs positively responded to the challenge against the CDV, but there are no deaths.

Gore et al. (2005) did another analysis like these ones mentioned above, that time through a challenge of immunity against the CDV, CPV-2, and CAV-1 antigens, after three years from the second dose of the initial vaccination. In this research, 23 serum-negative puppies, aged from seven to eleven-week-old, were immunized with multivalent vaccines, and after three years of isolation, they were challenged. No one of the animals showed clinical conditions of canine distemper, parvovirus, or adenovirus diseases.

Larson and Schultz (2007) evaluated the duration of immunity against CDV using a recombinant vaccine (rCDV) that was vectored by the canarypox virus and against CPV-2, CAV-1, CPIV, and *Leptospira* sp. after multivalent vaccination. The authors observed three-year security with the use of this protocol.

Ford (2008) described that the vaccination against canine distemper, canine parvovirus disease, canine infectious hepatitis, and the “kennel cough” should occur every three years, however, the annual revaccination continues as one of the most relevant paradigms for the publication of vaccination guidelines, and that the recommendation of a triennial reinforcement did not accept by all professionals. Lappin (2010, p. 1309) comments: “Vaccinated dogs must receive a reinforcement after one year, and then, every three years or more [...] many products containing CDV, including the rCDV vaccine, present a three-year protection”.

Vila Nova et al. (2018) verified the serum-reversion of CDV and CPV, in seven adult dogs differently aged, and observed an average serum-reversion ratio of 2.86 years for CDV, and 7.63 years for CPV. The authors suggested that the high indexes of serum-prevalence of CPV occur because of the virus' high resistance to the environment, a fact that raises the chances of exposition by the animal and a consequent increase of antibody production. Conversely, the CDV is easily inactivated in the environment, a fact that reduces the exposition of the animal to this virus, and generates a humoral immune response that is capable to create protection. However, the author concluded that these results should be interpreted with precaution, considering that the vaccine response is specific for each individual and depends on many factors.

In parallel, the vaccines against *Leptospira* spp. does not provide prolonged protection compared to those ones against the canine distemper virus and parvovirus. The circling antibodies against these bacteria remain only for few months, and the immune memory presents a relatively short deadline, about only one year (Day et al., 2016).

Immunity duration acquired by the vaccines depends on many factors, such as the composition of the specifics antigens, the nature of the vaccine, the protection efficiency (Chart 1), and the administration way (Scavone, 2014).

Chart 1 – Estimation of the minimum immunity duration (ID) of antigens of Marketed Canine Vaccines.

CORE VACCINES	ESTIMATED MINIMUM ID	ESTIMATED RELATIVE EFFICIENCY (%)
CDV (VVM)	> 7 years	> 90
CDV (Recombining)	> 1 year	> 90
CPV-2 (VVM)	> 7 years	> 90
CAV-2 (VVM)	> 7 years	> 90
Rabies virus (Inactivated)	> 3 years	> 85

Fonte: Adapted from Paul et al. (2003).

3.3 Protocols of core vaccines in Brazil

Vaccination schedules for pets (dogs and cats) from the Latin-American Committee of Pets' Vaccinology – LACPV owned to the Ibero-American of Veterinary Association of Pets – IAVAP, which was disclosed in 2016, suggest very important recommendations about the vaccination of dogs and cats at the Latin America, considering the scenario and necessities from each region (Labarthe et al., 2016). Thereby, in Brazil, the vaccination schedule against the core immunogens are available in Chart 2.

Chart 2 - Vaccination schedule for pets: dogs and cats.

VACCINE ANTIGEN	INITIAL VACCINATION (<16-week)	INITIAL VACCINATION (>16-week)	REVACCINATION
CDV (attenuated or recombining)	Start between 6-8 weeks, with repetitions at each 3-4 weeks, and last dose after 16 weeks	2 doses with an interval of 3-4 weeks	With 1-year-old, and then at each 2 years
CPV-2 (attenuated)			
CAV-2 (attenuated)			
<i>Leptospira interrogans</i> (inactivated)	Start between 10-12 weeks, with repetitions at each 3-4 weeks, and last dose after 16 weeks	2 doses with an interval of 3-4 weeks	With 1-year-old, and then yearly
Rabies virus (inactivated)	Start from 12 week-old, with an unique-dose	Unique-dose	With 1-year-old, and then at each 1-3 years 1-3, according to the current legislation

* In Brazil, only annual vaccines are available. Source: Adapted from LACPV-IAVAP (Labarthe et al., 2016)

The VGG from WSAVA done a regional project from 2016 to 2019, aiming to analyze the particularities of the vaccination process in pets from Latin America, and developed a document recognizing that the availability of products does not allow the veterinary doctors, from this region to vaccinate these pets according to the published guidelines from 2016. In

face of that, this new document pointing out some recommendations that can be currently done, called by “pragmatics”, and other ones desired for the future, called by “ambitious”.

Regarding the pragmatic schedule of core vaccines, it is recommended to select a product with great quality containing VVM that allows the administration of the minimum combination of core antigens for dogs (CDV, CAV, CPV-2). Besides that, it is prudent to use a diluent instead to reconstruct the vaccine with a non-core vaccine, if this vaccine is not necessary for the animal. The VGG classifies the vaccination against the *Leptospira* spp. as a non-core one, however, recommends discussing with the owner, if necessary, about the animal’s lifestyle and the risk of exposition, to choose a quality product that contains only the needed antigen in the least possible combination related to other non-core compounds (Chart 3).

Chart 3 - Pragmatic vaccination schedule for dogs.

VACCINE ANTIGEN	INITIAL VACCINATION (<16-week)	INITIAL VACCINATION (>16-week)	REVACCINATION
CDV (attenuated or recombining)	Start between 6-8 weeks, with repetitions at each 2-4 weeks, and last dose after 16 weeks	2 doses with an interval of 2-4 weeks, but one dose containing VVM or rCDV is considered protective	According to the new global approach for core revaccination, if allowed by the tutor, the administration of core vaccines with guaranteed quality containing VVM must not be more frequently than every 3 years
CPV-2 (attenuated)			
CAV-2 (attenuated)			
<i>Leptospira interrogans</i> * (inactivated)	Administration according to pharmaceutical’s recommendations: often 2 doses with 2-4 weeks interval.	2 doses with 2-4 weeks interval.	Non-core vaccines are generally administered annually, unless the medicine leaflet specifically recommends otherwise.
Rabies virus (inactivated)	Start from 12 week-old. In high-risk areas (that is, NOT the major ones from Latin America), an eventually second dose may be administrated 2-4 weeks after the first one.	A second vaccine must be administrated 12 months after the first one or with 12 months old, even in areas without higher risks	With 1-year-old**

**L. interrogans* considered non-core by VGG-WSAVA, but it is core in Brazil.

** VGG recommends pressuring the associations and governments to allow the triennial revaccination using products with guaranteed quality and three-year ID. The VGG also recommends pressuring the industry sector to register these products with some years ID in their countries.

Source: Adapted from Day et al. (2016) e Day et al. (2020)

The VGG advises veterinary doctors from Latin America to adopt ambitious vaccine protocols, based on the global guidelines of WSAVA from 2016 (Day et al., 2016). For that, the VGG encourages the national and local regulatory agencies to allow that the veterinary doctors use core vaccines containing VVM with guaranteed quality, according to the guidelines from WSAVA, as “product used out of the indication of the leaflet”, with the client’s permission (Chart 4). Despite that, the leaflets of these vaccines with three years of ID are not currently accepted by the Latin-American countries.

The VGG also reinforces that “this approach has been successfully used by other countries that wait by the acceptance of international vaccines leaflets with quality guaranteed by national and local authorities” (Day et al., 2020, p. 11).

Chart - 4 Ambitious vaccination schedule for dogs.

VACCINE ANTIGEN	INITIAL VACCINATION (<16-week)	INITIAL VACCINATION (>16-week)	REVACCINATION
CDV (attenuated or recombining)	Start between 6-8 weeks, with repetitions at each 2-4 weeks, and last dose after 16 weeks	2 doses with an interval of 2-4 weeks, but one dose containing VVM or rCDV is considered protective	Revaccination with core vaccines with guaranteed quality, containing VVM, must not be more frequent than every 3 years. Serology can be used to monitor protective immunity and assist in making decisions about revaccination intervals.
CPV-2 (attenuated)			
CAV-2 (attenuated)			
<i>Leptospira interrogans</i> * (inactivated)	Administration according to pharmaceutical's recommendations: often 2 doses with 2-4 weeks interval	2 doses with 2-4 weeks interval.	Non-core vaccines are generally administered annually, unless the medicine leaflet specifically recommends otherwise
Rabies virus (inactivated)	Start from 12 week-old. In high-risk areas (that is, NOT the major ones from Latin America), an eventually second dose may be administrated 2-4 weeks after the first one.	A second vaccine must be administrated 12 months after the first one or with 12 months old, even in areas without higher risks	All canine rabies vaccines with guaranteed quality have a three-year license DI, in several countries outside of Latin America

**L. interrogans* considered non-core by VGG-WSAVA, but it is core in Brazil.
Source: Adapted from Day et al. (2016) e Day et al. (2020)

3.4 Adverse vaccine effects

Although vaccination is an excellent resource for the prevention of diseases, this procedure may be not innocuous (Munday et al., 2003, Strasser et al., 2003, Rashid et al., 2009, Roth; Spickler, 2010, Scavone, 2014),

Hypersensitive reactions of type I, II, III or IV, facial edema, pruritus, fever, transient lethargy, allergic reactions, injection site sarcoma, cutaneous vasculitis, and development of autoimmune diseases are some examples of the most reported adverse effects (Wolf, 2010). These conditions can be increased depending on the amount of applied immunogen in a short time interval. (Moore; Hogenesch, 2010).

Strasser et al. (2003) identified a transitory change in the balance of cellular and humoral immunity (Th1/Th2), in immunized dogs that received multivalent vaccines. However, the authors pointed out that this reaction seems to be only an alteration in the homeostasis, caused by the immunization. Thereby, they concluded that the vaccination is a stressful procedure, even when done in healthy animals and according to the correct protocol describe on the medicine leaflet. For that reason, unnecessary vaccination must be avoided.

3.5 Challenges in the implementation of new protocols

Administration of many vaccines jointly and indiscriminately is yet common conduct in Brazil, even many scientific results showing that some vaccines promote lasting protection. Dogs immunized with core vaccines of VVM, and that obtain protective responses, maintain a satisfactory immunologic memory and revaccinations are not necessary for a long period (Mitchell et al. 2012).

Day et al. (2016) described that the minimum DI recommended in the vaccine packages was 12 months, for a long time, and because of that, the annual reinforcement was induced. However, the same companies recently have pointed out a minimum DI of three years for core vaccines, or even more, for all life of the animal. Nevertheless, in Brazil, many companies advocate annual reinforcement through medicine leaflets.

Many laboratories marketed multivalent vaccines because they follow the current regulation from Brazil, and this harms the adoption of new protocols. According to Day et al. (2016), how lower the number of present agents into the vaccines, how better is for the WSAVA guidelines adoption by the veterinary doctors. The ideal procedure would be the use of multivalent vaccines only against CDV, CAV-2 and CPV-2, besides the use of immunogens that have DI of 12 months, or either for non-core vaccines as that one against *Leptospira* spp., the use of monovalent vaccines that can be administrated only when the result of the risk/benefit analysis will benefit.

Moreover, there is another commercial factor in this scenario. Many owners of veterinary clinics, hospitals and agricultural stores do not consider the current protocols as economically feasible, because they worry about an eventual decrease in revenue, mainly if the vaccination intervals will be extended (Vilela, 2016).

The lack of updating and training of the veterinary doctor is another restrictive factor, once that to elaborate individual protocols instead of a pragmatic one, the professional must consider the distribution and prevalence of infectious diseases according to the habitat and animal's lifestyle, besides if they are zoonosis and even the current legislation. Moreover, it is necessary to guide the owners regarding the recommendations about sanitary control. The vaccination guide for dogs and cats must not be a fixed protocol by all animals, but an instrument that helps veterinary doctors to elaborate an adequate protocol for each animal, individually (Ford, 2008, Day et al., 2016).

Ford (2008) described that the initial protocol for dogs' core vaccines must be the same in all conditions, regardless of the risks. Nevertheless, the revaccination protocol will be necessary only when the animal aged 4 years old, and after at 7 years old, that is, considering an ID of three years about the core vaccines. For animals classified with high or moderate risk, serologic tests may be done annually to verify an eventual revaccination necessity.

Availability of kits of quick serologic tests has been increased at the veterinary clinics, since 2010. These tests individually verify the presence of specific antibodies for CPV and CDV, but they are complementary to laboratory technics such as hemagglutination inhibition and virus neutralization test, which are considered as the gold standard for serology, yet. These kits were developed in order to provide a three-year interval for core vaccines, as an alternative to revaccination. However, unfortunately, they have a high economic cost compared to a vaccine dose (Day et al. 2016).

4. Conclusion

Antibody titration after primary vaccination is influenced by some factors, such as the amount of maternal antibodies acquired via colostrum; level of exposure to disease (environmental factors); age at the beginning and end of the first doses, as well as the interval among them; and the type of used vaccine. Thereby, the initial protocol for core vaccines follows a standard. However, regarding the dogs' revaccination protocols, the procedures applied in most parts of Brazil diverge from the current guidelines, yet. There are many challenges, such as the lack of knowledge about the immunity duration against CDV and CPV-2, the lack of assessment related to the habitat and the animal's lifestyle, and the lack of analysis about what may interfere, or not, in the quality of the animal's immunologic response, besides the used vaccine and other accidental diseases. Moreover, another challenge is related to the market, because many vaccines marketed in Brazil are multivalent, a factor that limits the adequacy of protocols. Vaccination guides aiming to help the veterinary doctors' conduct, therefore, they

do not need to follow pragmatically these guides. The ideal procedure would be to institute an individual vaccine protocol for each animal, considering factors as exposition risks, besides the type and nature of the used vaccines.

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