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Vaccine use and disease prevalence in dogs and cats

Marian C. Horzinek*

Haydnlaan 15, 3723KE Bilthoven, The Netherlands

Abstract

A yearly revaccination of adult pets against distemper, the adenoviral and parvoviral diseases is scientifically unwarranted, professionally obsolete and ethically questionable; other vaccinal antigens, however, may need yearly or even more frequent injections. Base immunisation is redefined: it is complete only after the multivalent booster in the second year of life. A yearly revaccination interview, not necessarily an injection, should become the new standard. This interview is a professional service that must be taught, expertly performed and invoiced. Adult animals should be "vaccinated to measure", taking age, breed, lifestyle, the epidemiologic situation, etc. into account. Post-vaccination serology should become a guide in revaccination decisions. For a solid herd immunity, more animals of the population must be vaccinated. The profession should issue regular updates of the 'code of vaccination practice'. To counteract vaccination antagonism, a concerted action of academia, the veterinary profession and industry is required.

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1. Introduction

When lecturing about pet vaccination and vaccine use in the last decade, I used to confront veterinary audiences with the following scenario:

'A pediatrician client presents her cat to a vet and asks:

"Doctor, why do I need to pay you a yearly visit for revaccination of my cat? I see my children patients no more than twice in their lifetimes!"

What do you suggest as an answer? Can you perhaps be more creative than

- ... this is what we always did.
- ... this is in the product documentation.
- ... this is what most clients want.

... this is what representatives of our profession want us to do.

... this does not hurt.

... this is because the immunity conferred by veterinary vaccines is short-lived.

... this is scientifically correct ...'.

The ensuing hilarity was somewhat laboured. The difference between the medical approach and the veterinary lore of immunisation against infectious diseases is striking. This is the current schedule for routine childhood vaccination in the Netherlands:

^{*} Tel.: +31 30 2287029; fax: +31 30 2252857. *E-mail address:* horzinek@planet.nl.

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 $6 \times$ (4 of which in the first year)—diphtheria, tetanus and polio (all inactivated).

 $5 \times$ (4 of which in the first year)—pertussis, Haemophilus influenzae B.

 $2\times$ —mumps, measles, rubella: at 14 months and 9 years (all live).

1×—Meningococcus C: at 14 months.

Due to the different living and hygienic conditions, human babies can take their first live virus immunisations relatively late in life, at 14 months, when they are immunologically mature and maternal antibody interference is no longer a concern. While about one-half of 6-month-old infants still have detectable levels of maternal antibodies to measles virus, none of the 12-month-olds show this. Among those without passive immunity to measles, only about one-third of the 6-month-olds mustered enough antibodies upon vaccination to resist an infection, compared with 100% of the 9- and 12-month-olds. Consequently, the human immune system continues to develop postnatally, acquiring key abilities past the age of 6 months. The development of the canine immune system shares many similarities with that of the human. In both species immune competence, also of the mucosal immune system, is fully developed before birth although further maturation of the responses may continue into the postnatal period (Felsburg, 2002).

Thus, in man, a single booster at 9 years of age is accepted as being sufficient for lifelong protection. This practice is based on epidemiologic evidence only, since challenge based duration of immunity (DOI) studies are out of the question. Amongst the live virus vaccines are those against measles—the human counterpart of canine distemper. Dogs, however, may be treated to a dozen or more boosters during their lifetimes. The question arises whether this is rational.

2. The yearly revaccination

Why has veterinary medicine adopted a practice that causes raised eyebrows in the biomedical environment, e.g. when talking to immunologists? The reason is largely historic: in the first years of vaccine development, the objective of maximum protection was thought to be achieved by maximum antigenic stimulation. At the time this seemed to be the right thing to do, with the newly developed, attenuated distemper and canine infectious hepatitis virus preparations. It became common practice in subsequent vaccine developments, including the parvovirus preparations, without asking why.

In recent decades, however, the frequency of vaccination has become a matter of debate-first in the USA, more recently in Europe. The scenario in Germany (2003) turned grim, when a well-informed journalist issued a declaration of war in a nation-wide newspaper. The lay public was activated, the foe included vets and the biologicals industry. In England (2004), a similar initiative of several newspapers based on information contained in a letter from more than 30 British vets, contained quotes like: "unnecessary, potentially dangerous, fraud by misrepresentation, fraud by silence, theft by deception, complete overkill" and the like. The scenario world-wide, including the medical scene is not different, and websites abound advertising pamphlets with titles like "Vaccination, Social Violence and Criminality", "The Hidden Truth", "Vaccines Represent a Medical Assault on the Immune System", "What Doctors Don't Tell You", to quote a few. Whereas yearly revaccination is a veterinary specialty, indiscriminate vaccination antagonism with traits of paranoia, persecution mania and all kinds of conspiracy theories is not-it is also prominent in the medical environment. Actually, the first cartoons depicting a "vaccination monster', appeared in the 18th century, short after Edward Jenner's seminal discovery.

From the immunologist's viewpoint, the veterinary profession should weigh the perceived risks of side effects due to overvaccination together with vaccination failures against the true risks of a decreased herd immunity with the re-emergence of epidemics as a consequence. Statistically, these are minor problems, when weighing the significance of the sporadic cases of immune-mediated pathology with that of sweeping epidemics. The real and serious threat to veterinary medicine (and of course to the canine and feline populations) is the vaccination antagonism in the public with its aggressive undertones. The professional organizations should be even more concerned about their loss of credibility.

The term 'overvaccination' is suggestive in that it evokes the picture of an organism swamped with antigens, its immune system paralysed by too many components in one shot. This is an erroneous conception, in view of the fact that any organism is bombarded with antigenic molecules during its lifetime. In both veterinary and human medicine, this issue has received much attention, also from manufacturers, and the consensus is that carefully selected, tested and registered combinations are neither inferior in immunogenicity nor in safety.

In veterinary medicine, overvaccination rather refers to vaccinating with excessive frequency, which has been controversial for more that a decade ("Are we vaccinating too much?" (Smith, 1995). After a period of indifference, the profession is now faced with organised militant campaigning combined with scaremonging. The reported side effects fulfill the criteria of selective observations, and although some have achieved prominence in the scientific literature like the injection site fibrosarcoma in cats - they are comparatively rare. However, also some infections have become rare, and it must be anticipated that vaccination will be discontinued when the disease to protect against is no longer around. The scenario is similar to that during the final phase of smallpox vaccination, when the rare side effects (less than 1 in a million vaccinees) exceeded the number of natural disease cases.

In line with the romantic idea that natural infections are superior to vaccines, "infection parties" (measles and parvo) are being organized, e.g. in Germany. This is both irrational and irresponsible. Infections with wild viruses are always more serious than those with their attenuated laboratory counterparts – this is why field strains were attenuated in the first place. Voltaire said: "People who believe in absurdities will inevitably commit atrocities."

The scientific arguments in favour of less frequent revaccinations are traditionally based on antibody titers. Protection against most viral diseases is indeed antibody-mediated, and antibodies are easily measured. In dogs these have been found to persist for more than 7 years, the study did not look later. The high prevalence of adequate antibody responses (CPV, 95.1%; CDV, 97.6%) in a large population (>1500 animals) "suggests that annual revaccinations against CPV and CDV may not be necessary" was the authors' conclusion (Twark and Dodds, 2000). In the cat, antibodies to FPV, FCV and FHV were detected for more than four years (Mouzin et al., 2004). The question whether the titers found are protective or not against a field virus challenge is irrelevant for this discussion. It is not the residual serum antibody that determines survival to challenge but the population of memory cells that can quickly expand. The question about the longevity of memory cells has now been answered experimentally; the question was not, if lifelong immunity exists (which is common knowledge), but whether its mechanism relies on a lifelong presence of the antigen in the animal's organism or of the cells' longevity. The latter was not found to be the case "Memory B-cell persistence is independent of persisting immunising antigen"; (Maruyama et al., 2000). However, it is not an individual memory B-cell, rather a population of slowly dividing clones that persists during the life of the organism. Like in neurobiology, a paradigm has been shattered: neurons and memory cells can indeed divide.

Finally, duration of immunity (DOI) experiments in dogs have now proven beyond reasonable doubt that 3 years protection is achieved against challenge with distemper, adenovirus-1 and parvovirus (Gore et al., 2005). While this is a timely – though by no means surprising – finding, it has been achieved at a considerable cost. It is this financial aspect (statistically sufficiently large group sizes, isolation facilities, quarantine conditions) that will preclude any further study of DOI, I am afraid. Underpinned by the conservatism of the veterinary profession this study will become a monument in veterinary vaccinology and determine the periodicity of revaccination. Few will dare to do otherwise, i.e. to vaccinate even less frequently.

3. The interview

Though it has been the financial mainstay of many a companion animal practice, vaccination is not exciting. An injection is technically not as demanding as repairing a fracture, and the client does not see much – if she does, it is the failures: the side effects and vaccination breaks. Neither can the vet impress her client – she vaccinates, but cannot (and for time reasons does not want to) explain the basic principles of immunology and epidemiology to the client. Nor can any effect of the immunisation be shown. What is commonplace in surgery and internal medicine is lacking here: vaccination is probably the only veterinary measure without a follow-up. It is what I called the "Shoot-and-Trust Principle". Post-vaccination serology (PVS) would introduce evidence, and serve the industry and the profession alike, but it meets with considerable opposition.

A yearly vaccination interview, sensibly part of a yearly health check, but not necessarily followed by an injection, should become the standard. Why yearly, why an interview, what should it be about, how should it be performed—these are the obvious questions.

Why yearly? Because many owners are used to that routine, to contact their vets for the yearly shot, for a dental appointment or other health reasons. Decisions about holiday travels are taken on a yearly basis, with possible vaccinological consequences (stay in a boarding kennel, cattery, visit to foreign countries with new pathogens). The vet can schedule these visits, to entertain the relationship with the client and show responsibility for the animal family member.

Why an interview? Because it provides the practitioner with informations necessary to take vaccinological decisions and to explain them to the client. If she fails to do this, the client will obtain them from sources of doubtful reliability. However, a conversation not only informs about the measures to be taken, it also prepares, encourages, warns, reassures and comforts. Its first purpose is to build a vet-client relationship of trust, which needs to be established and developed. "Customer loyalty" is the term in commercial publications, and a practice is a business enterprise after all. This relationship is in need of improvement - only about 70% of the clientele return for follow-up vaccinations; the last visit to the vet obviously did not leave a lasting impression. This is hardly unexpected: an injection given in passing, to minimise the time investment, cannot achieve customer loyalty. This myopia has done much damage to the profession. After all, the client has prepared her visit to the veterinary clinic, comes with expectations, opinions (and prejudices), which need to be taken seriously. To reject the client's views as an irrelevant lay opinion is no basis for a dialogue. Emotional and social intelligence will eventually be decisive factors for forging a lasting relationship with the owner.

The vaccination interview will be different for each year, and a catalogue of questions and answers must be developed. For the first year it might look as follows: The owner is informed about

• The preventable diseases.

- The advantages of vaccination versus treatment.
- Possible side effects and complications.
- Possible lack of protection.
- Risk/benefit considerations.
- How to handle the vaccinee after the shot.
- The basic vaccination program (with the boosters in the second year).
- The onset and duration of protection.

The veterinarian is informed about

- The origin of the animal.
- The responsibilities within the family.
- Other animals in the household.
- Vacations and travel plans (abroad).
- Medical (vaccination) history, previous treatments, etc.

The interested dialogue is of paramount importance (professionals like to hold monologues); questions for self-assessment include:

- Did I practice active listening?
- Did I show empathy?
- Did I choose the right place, time, situation, climate?
- Did I feel pressed for time?
- Did I take in all messages?
- Did I use the correct query technique?
- Did I stimulate the client to ask questions?
- Did I properly structure the interview (introduction, aim, course, conclusion)?
- Did I respect the listener's need for pauses?
- Did I use killer phrases?
- Did I use diversion strategies (stray, digress, evade, deviate, disparage, patronize, condescend)?
- Did I ask too much from the client?
- Did I ignore (or even induce) worries in the client?
- Was my client's reality the same as mine?

The vet is the authoritative source of healthrelevant information and sells her knowledge (expertise) to the client. As long as this context is ignored, the prestige of the profession remains at stake.

4. The vaccination

The interview with its considerations of the patient history, of explanations of risks and contra-indications, of the reaching of agreements, and of an informed consent, will be followed by a clinical examination: only healthy animals are vaccinated. Whereas the "one-size-fits-all" shot has been practiced as a routine in the past, "vaccination to measure" will have to come in its place in the future. Any ad hoc vaccination must address the individual risk of infection and disease of the vaccinee—a pampered Devon Rex has a lifestyle different from a stray cat, when considering the risk of exposure; the former may leave the home only for a visit to the vet. Customtailored vaccination schedules will differ

- For the free-roaming animal.
- For the hunting and utility dog.
- For the lap cat and dog.
- For the travel companion.
- For pets in border countries.
- For the show cat and dog.
- For the breeding cat and dog.
- For the pedigree animal (breed).
- For the old animal.

The client's companion is not just a dog or cat – it is a dear family member, has been given a name, is an individual and requires individual attention. Neither is the client just a time-consuming nuisance – she is a partner in a conversation and deserves interest, sometimes empathy.

Vaccines protect against infectious disease, and a precondition for their use is a risk of infection. In most cases this hazard is an assumption, an impression not based on epidemiological data. The prevalence of e.g. distemper virus in Europe amongst domestic dogs and in feral carnivores is unknown. From yearly endemics amongst unvaccinated pups, however, it can be inferred that the virus is still around. Infectious canine hepatitis, on the other hand, has been seen here by clinicians and pathologist only rarely, nor has it been evidenced by PCR analysis in dogs with respiratory signs in the UK (Erles et al., 2004), in contrast to e.g. the USA, Canada, Mexico and Australia. It is present in wild carnivores though. Parvovirus, however, is ubiquitous, both its canine and feline varieties. Herpes-, calici- and coronaviruses abound amongst cats, with high prevalences in crowded communities. FeLV infections are phasing out in several countries in Western Europe, thanks to testing and vaccination, while the prevalence of FIV has hardly changed.

This is an oversimplified global view of canine and feline viral epidemiology—the vaccinating veterinarian must positively know about the local situation in her area. There is no dedicated information service available, and contacts with the regional veterinary schools and diagnostic institutions will be left to personal initiatives. ProMED-mail – the Program for Monitoring Emerging Diseases – is an Internet-based reporting system dedicated to rapid global dissemination of information on outbreaks of infectious diseases and can be queried (http://www.promedmail.org). The veterinarian is the designated expert to provide competent advice to the client concerning epidemic risk factors and their vaccinological consequences.

5. Objective assessment of immunisation

As stated above, vaccination is about the only veterinary measure whose result is not routinely evaluated. Post-vaccinal serology, however, is not new to companion animal medicine: evidence of antibodies to rabies virus decides whether a dog may travel. An assessment of the animal's immune status would provide the vet with information about the success rate of her measures, and reassure the client. The proposal is to assess the result of vaccination by asking the question: did the vaccinee's immune system recognise the antigen? No assertion of protection, only a probability can be given - similar to the results of many assays in clinical chemistry. The first serum samples should be tested in the 3rd year of life, to see whether the pup vaccination (first year) plus boost (second year) have resulted in immunological memory; later tests can be done if so desired by the client, e.g. before the 3-yearly interval, as an aid in the decision about revaccination.

When the vaccination history of an animal is unknown, a prime-boost regime will usually be preferred, unless requested otherwise by the client. Interpretation of the serology data will be an element of the vaccination interview.

The purpose of PVS should be to show antibody against the core vaccine components distemper, hepatitis and parvovirus (dog and cat). If antibody is present, the animal has been immunised (which is not synonymous with immune or protected). Forget about titers (titres) - the bad experience with FIP serology is still on everybody's mind. Titer values have been attributed a biological significance they intrinsically lack, and high coronavirus antibody titers have been the veterinary death sentence for many a healthy cat. There are many reasons for rejecting titers: values differ per laboratory, because of technical variations in the tests, "40" and "80" are not different titers ("1:40" and "1:80" are no titers at all but the serum dilutions tested), the difference is just two-fold. Virologists start to think about specificity when the titer difference is four-fold.

Only yes/no-data should be communicated by the laboratory – which leave no room for doubt (no uncertainly of interpretation). Ideally, the vaccine industry should be involved in PVS, which could corroborate their claims of the potent antigenicity of their products.

In a nutshell: the laboratory (or an in-practice test) should give a robust yes/no answer with a threshold value safely in the positive range. If the potential vaccinee tests negative (false or true) vaccination is recommended. A false-negative test will result in vaccination (in spite of antibodies) – which is similar to the present situation in many cases. If an animal tests positive (false or true) vaccination is not recommended. A false-positive test is unlikely in view of the high prevalence of antibodies in the population.

6. We vaccinate the same animal too often, but too few animals of the population ...

Most animals in an area, a province, a country should be vaccinated—rather than revaccinating the same dog or cat time and again, which neither improves its own immune status nor contributes to herd immunity. Herd immunity is defined as the indirect protection of susceptible members of a population brought about by the presence of immune individuals. To prevent serious losses from epidemics (like during the distemper epidemic in Finland 1994– 1995, where >5000 dogs were infected, of which $\sim 30\%$ succumbed; (Ek-Kommonen et al., 1997), active campaigning for vaccination should be targeted at achieving about 70% immune coverage. This figure has been obtained by mathematical modelling of epidemics and confirmed by observations from natural outbreaks (like the Finnish epidemic), but may not be universal, i.e. for all infectious agents. In such a situation, the effective reproduction rate R would be reduced to <1, which means that there will be less than one new case per infected individual, and (if Rcontinues to be <1) the infection will locally die out. These considerations play a role in the eradication strategy for measles. Distemper cannot be eradicated because of spill-over infections from feral carnivore reservoirs and re-introduction of the agent into the domestic populations, but the spread of infection can be contained.

A milkmaid's calculation can show that we are far from that 70% goal. Thus, in Germany (2002)

- there are \sim 5 Mio. registered dogs;
- there are ~2.4 Mio. vaccine doses reaching the market (SHPPiLT & SHPLT);
- there are ~1.1 Mio. purebred dogs (most of which will be immunised);
- the remaining 1.3 Mio. vaccine doses thus are applied to 3.9 Mio. dogs = 30% (data kindly provided by Dr. Uwe Schultheiss, Nice/France; source: GFK Nürnberg).

Estimates made by intuitive assessments vary widely and may reflect selective observation or wishful thinking. It is of course more arduous to solicit new clients than to summon old ones, but it needs to be done.

7. Outlook

This opening article of a Special Issue dedicated entirely to pet vaccination is intended to set the scene for the various aspects of immunisation of the dog and cat. The discussions to follow will hopefully result in a new degree of awareness amongst veterinary practitioners. If the profession wants to play a leading role in the public discussion, if the vet (and not the internet) is to stay the animal health authority for pet owners – if microbiological, immunological and vaccinological knowledge is to be conveyed to (and rewarded by) the clientele, the profession must change its attitude. Vaccinological knowledge must be acquired, entertained and kept current, which should start at the university and be perpetuated by continued education.

Without further discussion, and as food for thought, these are my ten commandments of pet vaccinology:

- 1. The puppy schedule should be extended to include a vaccination at 16 week of age.
- 2. Base immunisation is complete only after the booster in the second year of life.
- 3. The routine of yearly revaccinations from the third year onward is questionable.
- 4. A yearly revaccination interview, not necessarily an injection, should become the standard.
- 5. The yearly revaccination interview is a professional service that must be taught, expertly performed and invoiced.
- 6. Adult animals should be "vaccinated to measure", taking age, breed, lifestyle, the epidemiologic situation, etc., into account.
- 7. Post-vaccination serology should become a guide in revaccination decisions.
- 8. For a solid herd immunity, more animals of the population must be vaccinated.

- 9. The profession should issue regular updates of the 'code of vaccination practice'.
- 10. To counteract vaccinophobia, a concerted action of academia, the veterinary profession and industry is of paramount importance.

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