CHANGING VACCINE PROTOCOLS

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The challenge to produce effective and safe vaccines for the prevalent infectious diseases of humans and animals has become increasingly difficult. In veterinary medicine, evidence implicating vaccines in triggering immune-mediated and other chronic disorders (vaccinosis) is compelling. While some of these problems have been traced to contaminated or poorly attenuated batches of vaccine that revert to virulence, others apparently reflect the host=s genetic predisposition to react adversely upon receiving the single (monovalent) or multiple antigen "combo" (polyvalent) products given routinely to animals. Animals of certain susceptible breeds or families appear to be at increased risk for severe and lingering adverse reactions to vaccines.

The onset of adverse reactions to conventional vaccinations (or other inciting drugs, chemicals, or infectious agents) can be an immediate hypersensitivity or anaphylactic reaction, or can occur acutely (24-48 hours afterwards), or later on (10-45 days) in a delayed type immune response often caused by immune-complex formation. Typical signs of adverse immune reactions include fever, stiffness, sore joints and abdominal tenderness, susceptibility to infections, central and peripheral nervous system disorders or inflammation, collapse with autoagglutinated red blood cells and jaundice, or generalized pinpoint hemorrhages or bruises. Liver enzymes may be markedly elevated, and liver or kidney failure may accompany bone marrow suppression. Furthermore, recent vaccination of genetically susceptible breeds has been associated with transient seizures in puppies and adult dogs, as well as a variety of autoimmune diseases including those affecting the blood, endocrine organs, joints, skin and mucosa, central nervous system, eyes, muscles, liver, kidneys, and bowel. It is postulated that an underlying genetic predisposition to these conditions places other littermates and close relatives at increased risk.

In cats, while adverse vaccine reactions may be less common, aggressive tumors (fibrosarcomas) can occasionally arise at the site of vaccination. A recent study from Italy reported finding similar tumors in dogs at the injection sites of vaccinations (Vascellari et al, 2003). These investigators stated that their "study identified distinct similarities between canine fibrosarcomas from presumed injection sites and feline post-vaccinal fibrosarcomas, suggesting the possibility of the development of post-injection sarcomas not only in cats, but also in dogs".

Additionally, vaccination of pet and research dogs with polyvalent vaccines containing rabies virus or rabies vaccine alone was shown to induce production of antithyroglobulin autoantibodies, a provocative and important finding with implications for the subsequent development of hypothyroidism (Scott-Moncrieff et al, 2002).

Vaccination also can overwhelm the immunocompromised or even healthy host that is repeatedly challenged with other environmental stimuli and is genetically predisposed to react

adversely upon viral exposure. The recently weaned young puppy or kitten entering a new environment is at greater risk here, as its relatively immature immune system can be temporarily or more permanently harmed. Consequences in later life may be the increased susceptibility to chronic debilitating diseases.

As combination vaccines contain antigens other than those of the clinically important infectious disease agents, some may be unnecessary; and their use may increase the risk of adverse reactions. With the exception of recently introduced mutivalent Leptospira spp. vaccines, the other leptospirosis vaccines afford little protection against the clinically important fields strains of leptospirosis, and the antibodies they elicit typically last only a few months. Other vaccines, such as for Lyme disease, may be advisable only in those geographical areas where the risk of exposure to *Borrelia burgdorferi* is significant. Annual or biannual revaccination for rabies is required by some states even though most USDA licensed rabies vaccine have a 3-year duration. Thus, the overall risk-benefit ratio of using certain vaccines or multiple antigen vaccines given simultaneously and repeatedly should be reexamined. It must be recognized, however, that we have the luxury of asking such questions today only because the risk of disease has been effectively reduced by the widespread use of vaccination programs.

Given this troublesome situation, what are the experts saying about these issues? In 1995, a landmark review commentary focused the attention of the veterinary profession on the advisability of current vaccine practices. Are we overvaccinating companion animals, and if so, what is the appropriate periodicity of booster vaccines ? Discussion of this provocative topic has generally lead to other questions about the duration of immunity conferred by the currently licensed vaccine components.

In response to questions posed in the first part of this article, veterinary vaccinologists have recommended new protocols for dogs and cats. These include: 1) giving the puppy or kitten vaccine series followed by a booster at one year of age; 2) administering further boosters in a combination vaccine every three years or as split components alternating every other year until; 3) the pet reaches geriatric age, at which time booster vaccination is likely to be unnecessary and may be unadvisable for those with aging or immunologic disorders. In the intervening years between booster vaccinations, and in the case of geriatric pets, circulating humoral immunity can be evaluated by measuring serum vaccine antibody titers as an indication of the presence of immune memory. Titers do not distinguish between immunity generated by vaccination and/or exposure to the disease, although the magnitude of immunity produced just by vaccination is usually lower (see Tables).

Vaccine Titer Testing: Alternative to Annual Booster Vaccination

Reasons for Vaccine Titer Testing *

- To determine that animal is protected (suggested by a positive test result).
- To identify a susceptible animal (suggested by a negative test result).
- To determine whether an individual animal has responded to a vaccine.
- To determine whether an individual vaccine is effectively immunizing animals.

* from: Schultz RD, Ford RB, Olsen J, Scott F. Vet Med, 97: 1-13, 2002 (insert).

Other Alternatives to Current Vaccine Practices

- avoid unnecessary vaccines or over-vaccinating.
- caution in vaccinating sick or febrile animals.
- tailor specific minimal vaccine protocol for dogs/cats breeds or families at risk for adverse reactions.
- start vaccination series later (9-10 wks, dog; 8 wks cat) , despite breeder and pet owner concern for infectious disease risk, especially for parvovirus.
- alert caregiver to watch puppy'/kitten behavior and health after boosters.
- avoid revaccination of those with prior adverse event.

Except where vaccination is required by law, all animals, but especially those dogs or close relatives that previously experienced an adverse reaction to vaccination can have serum antibody titers measured annually instead of revaccination. If adequate titers are found, the animal should not need revaccination until some future date. Rechecking antibody titers can be performed annually, thereafter, or can be offered as an alternative to pet owners who prefer not to follow the conventional practice of annual boosters. Reliable serologic vaccine titering is available from several university and commercial laboratories and the cost is reasonable (Twark and Dodds, 2000; Lappin et al, 2002; Paul et al, 2003; Moore and Glickman, 2004).

Relatively little has been published about the duration of immunity following vaccination, although new data are beginning to appear for both dogs and cats.

Our study (Twark and Dodds, 2000), evaluated 1441 dogs for CPV antibody titer and 1379 dogs for CDV antibody titer. Of these, 95.1 % were judged to have adequate CPV titers, and nearly all (97.6 %) had adequate CDV titers. Vaccine histories were available for 444 dogs (CPV) and 433 dogs (CDV). Only 43 dogs had been vaccinated within the previous year, with the majority of dogs (268 or 60%) having received a booster vaccination 1-2 years beforehand. On the basis of our data, we concluded that annual revaccination is unnecessary. Similar findings and conclusions have been published recently for dogs in New Zealand (Kyle et al, 2002), and cats (Scott and Geissinger, 1999; Lappin et al, 2002). Comprehensive studies of the duration of serologic response to five viral vaccine antigens in dogs and three viral vaccine antigens in cats were published by researchers at Pfizer Animal Health (Mouzin et al, 2004).

When an adequate immune memory has already been established, there is little reason to introduce unnecessary antigen, adjuvant, and preservatives by administering booster vaccines. By titering tiennially or more often, as needed, one can assess whether a given animal's humoral immune response has fallen below levels of adequate immune memory. In that event, an appropriate vaccine booster should be considered.

But, some veterinarians have challenged the validity of using vaccine titer testing to assess the immunologic status of animals against the common, clinically important infectious diseases.

With all due respect, this represents a misunderstanding of what has been called the "fallacy of titer testing", because research has shown that once an animal's titer stabilizes it is likely to remain constant for many years. Properly immunized animals have sterilizing immunity that not only prevents clinical disease but also prevents infection, and only the presence of antibody can prevent infection. As stated by eminent expert Dr. Ronald Schultz in discussing the value of vaccine titer testing, these tests "show that an animal with a positive test has sterilizing immunity

and should be protected from infection. If that animal were vaccinated it would not respond with a significant increase in antibody titer, but may develop a hypersensitivity to vaccine components (e.g. fetal bovine serum). Furthermore, the animal doesn't need to be revaccinated and should not be revaccinated since the vaccine could cause an adverse reaction (hypersensitivity disorder). You should avoid vaccinating animals that are already protected. It is often said that the antibody level detected is “only a snapshot in time". That's simply not true; it is more a “motion picture that plays for years".

Therefore, interpreting titers correctly depends upon the disease in question. Some titers must reach a certain level to indicate immunity, but with other agents like those that produce sterile immunity, the presence of any measurable antibody shows protection. The positive titer test result is fairly straightforward, but a negative titer test result is more difficult to interpret, because a negative titer is not the same thing as a zero titer and it doesn't necessarily mean that animal is unprotected. A negative result usually means the titer has failed to reach the threshold of providing sterile immunity. In sterile immunity, that means a zero titer, not just a low titer. This is an important distinction, because for the clinically important distemper and parvovirus diseases of dogs, and panleukopenia of cats, a negative or zero antibody titer indicates that the animal is not protected against canine parvovirus and may not be protected against canine distemper virus or feline panleukopenia virus. Whereas a low titer may still mean that the animal is protected.

Finally, what does more than a decade of experience with vaccine titer testing reveal ? Published studies in refereed journals show that 90-98% of dogs and cats that have been properly vaccinated develop good measurable antibody titers to the infectious agent measured. In general, serum antibody titers to the “core” vaccines along with any natural exposures last a minimum of 7-9 years, and likely are present for life. This corresponds with what we see clinically as the number of cases and deaths due to these diseases has decreased in the vaccinated population. So, in contrast to the concerns of some practitioners, using vaccine titer testing as a means to assess vaccine-induced protection will likely result in the animal avoiding needless and unwise booster vaccinations.

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Table 1. "Core" Vaccines *

Dog	Cat
Distemper	Feline Parvovirus
Adenovirus	Herpesvirus
Parvovirus	Calicivirus
Rabies	Rabies

* Vaccines that every dog and cat should have.

Table 2. Adverse Reaction Risks for Vaccines *

"There is less risk associated with taking a blood sample for a titer test than giving an unnecessary vaccination."

* Veterinary Medicine, February, 2002.

Table 3. Titer Testing and Vaccination *

"While difficult to prove, risks associated with overvaccination are an increasing concern among veterinarians. These experts say antibody titer testing may prove to be a valuable tool in determining your patients' vaccination needs."

* Veterinary Medicine, February, 2002.

Table 4. Vaccine Titer Testing *

"Research shows that once an animal's titer stabilizes, it is likely to remain constant for many years."

* Veterinary Medicine, February, 2002.

Table 5. Canine Vaccine Adverse Events *

- retrospective cohort study; 1.25 million dogs vaccinated at 360 veterinary hospitals
- 38 adverse events per 10,000 dogs vaccinated
- inversely related to dog weight
- vaccines prescribed on a 1-dose-fits-all basis, rather than by body weight.
- increased for dogs up to 2 yr of age, then declined
- greater for neutered versus sexually intact dogs
- increased as number of vaccines given together increased
- increased after the 3rd or 4 th vaccination
- genetic predisposition to adverse events documented

***** from Moore et al, JAVMA 227:1102–1108, 2005.

Table 6. Vaccine Conclusions For Canines *

Factors that increase risk of adverse events 3 days after vaccination:

- young adult age
- small-breed size
- neutering
- multiple vaccines given per visit

These risks should be communicated to clients

***** from Moore et al, JAVMA 227:1102–1108, 2005.

Table 7. Feline Vaccine Adverse Events *

- retrospective cohort study; 0.5 million cats vaccinated at 329 veterinary hospitals
- 51.6 adverse events per 10,000 cats vaccinated
- inversely related to cat weight
- increased for cats about 1 yr of age
- greater for neutered versus sexually intact cats
- increased as number of vaccines given together increased
- Lethargy with or without fever was most common sign

***** from Moore et al, JAVMA 231:94-100, 2007.

Table 8. Vaccine Conclusions For Felines *

Factors that increase risk of adverse events 30 days after vaccination:

- young adult age
- neutering
- multiple vaccines given per visit

These risks should be communicated to clients, and the number of vaccines administered concurrently limited

***** from Moore et al, JAVMA 231:94-100, 2007.