UPDATE ON VACCINE ISSUES & VACCINE TITER TESTING

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Introduction
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.

Adverse Vaccine Reactions
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. Vaccination of pet and research dogs with polyvalent vaccines containing rabies virus or rabies vaccine alone was recently shown to induce production of antithyroglobulin autoantibodies, a provocative and important finding with implications for the subsequent development of hypothyroidism. 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. Giardia and ringworm vaccines are not recommended, except in special circumstances. With the exception of a recently introduced multivalent Leptospira spp. vaccine, the other leptospirosis vaccines may afford little protection against the clinically important fields strains of leptospirosis, and the antibodies they elicit may be detectable for only a few months. Other vaccines, such as for Lyme disease, may not be needed, because the disease is limited to certain geographical areas. Annual revaccination for rabies is required by some states even though there are USDA licensed rabies vaccine with 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.
Changing Vaccine Protocols
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 led 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 Aimmune 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.

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.

Duration of Immunity
Relatively little has been published about the duration of immunity following vaccination, although new data are beginning to appear for both dogs and cats. Challenge studies in the cat from Cornell University following just two doses of trivalent killed vaccine given at 8 and 12 weeks of age showed complete protection from feline panleukopenia virus for more than 6 years, and good protection against feline calicivirus and herpes virus for 4 and 3 years, respectively. Colorado State University recently reported longterm vaccinal immunity in a large number of pet and laboratory cats. The 2003 report of the AAHA Canine Vaccine Task Force indicated that the duration of immunity following challenge studies in dogs was equal to or greater than 7 years for the three canine core vaccines against distemper virus (CDV), parvovirus (CPV) and adenovirus (hepatitis).

Vaccine Titer Testing
Use of serologic antibody testing to assess the need for booster vaccination has been controversial, as individuals may not understand its significance. Serologic testing for most non-core vaccines is not indicated because these are administered annually (presumably in order to sustain immunity), and rabies vaccination frequency is determined by law and so titer testing is not appropriate (except in selected cases of significant adverse reaction risk). In contrast, the utility of serologic testing for CDV and CPV has been scientifically proven in peer-reviewed publications, and a recently licensed in-office test kit publication. Admittedly, there is clearly a need to standardize methodology to permit easy consistent interpretations between or among laboratories. However, as long as each laboratory validates its methodology against an accepted standard, determines the reference ranges for healthy individuals, and offers a specific interpretive comment, it is not necessary that each method be standardized between or among laboratories. Validation of titer methodology should preferably be made using test method(s) known to correlate with immunity by challenge studies. Such methods are readily available at reasonable cost.

Humoral immunity as measured by antibody levels plays the principle role in protective immunity for CDV and CPV in the vaccinated animal. With both viruses, antibody prevents infection (sterilizing immunity). As stated in the 2003 AAHA Report, antibody titers can be helpful in clinical practice to monitor vaccine immunity: namely, to determine if there has been an immune response following vaccination; to
determine the duration of immunity; to ensure the vaccine is immunogenic; to know precisely when to vaccinate a puppy; and to determine whether the animal is a “low or non-responder” to certain vaccines.

Our 2000 publication, 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 these data, we concluded that annual revaccination is unnecessary.

Similar findings and conclusions have been reported recently for cats at Colorado State University and dogs in New Zealand. When an adequate immune memory has already been established, there is little reason to introduce unnecessary antigen, adjuvant, and preservatives by administering booster vaccines. Titering assures whether or not the animal has immunity whereas vaccination does not. By titering annually or biannually, one can assess whether a given animal’s humoral immune response has fallen below acceptable levels. In that event, an appropriate vaccine booster can be administered.

References

Kyle AHM, Squires RA, Davies PR. Serologic status and response to vaccination against canine distemper (CDV) and canine parvovirus (CPV) of dogs vaccinated at different intervals. J Sm An Pract, June 2002.
Table 1. “Core” Vaccines *

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<thead>
<tr>
<th>Dog</th>
<th>Cat</th>
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<tbody>
<tr>
<td>Distemper</td>
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<td>Parvovirus</td>
<td>Calicivirus</td>
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* 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, insert, February, 2002.

Table 3. Titer Testing and Vaccination *

“While difficult to prove, risks associated with over vaccination 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, insert, 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, insert, February, 2002.
Sample: Vaccine Antibody Titer Testing Consent Form

Please read and sign

Vaccine antibody titer testing analyzes or measures antibodies to certain diseases to determine whether your pet’s immune system has responded to previous vaccinations. This blood test helps us determine whether or not your pet will be protected from the infectious disease if your pet were to be exposed.

Vaccinations may last longer than one year. Vaccine antibody titer testing will help us assess your pet’s need for another vaccine. Vaccinations can cause adverse reactions. To reduce the risk of adverse reactions and to avoid unnecessary vaccinations, we recommend that your pet have a titer test done.

Prior to immunizing ___________________________ (Name of Patient), the caregiver, _________________________________ (Name of Client), has been informed about contemporary veterinary practice protocol, which recommends, but does not require, that vaccinations [except rabies vaccine which is required by the State] be given as a puppy/kitten series, with booster vaccinations given annually or at longer intervals, when applicable.

Please understand that vaccine antibody titer testing, as well as vaccinating annually, do not 100% guarantee that your pet will be protected against the above infectious diseases. It may, however, greatly reduce the risk of adverse reactions and/or complications and avoid unnecessary vaccinations to your pet.

□ Please perform the recommended titer test/s for my pet to determine whether or not revaccination is necessary.

□ I would like to discuss vaccine antibody titer testing further with my veterinarian.

□ I decline the recommended vaccine titer test/s at this time and request for you to proceed with annual vaccinations.

__________________________________________  ________________
Signature of Pet Caregiver                     Date