

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 multivalent *Leptospira* spp. vaccines, the other leptospirosis vaccines afford little protection against the clinically important field 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 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 inadvisable 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).

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 recent 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 recently 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 annually, 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 can be administered.

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Table 1. “Core” Vaccines *

<u>Dog</u>	<u>Cat</u>
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.