

## ADVERSE VACCINE REACTIONS

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Viral disease and recent vaccination with single or combination modified live-virus (MLV) vaccines, especially those containing distemper virus, adenovirus 1 or 2, and parvovirus are increasingly recognized contributors to immune-mediated blood disease, bone marrow failure, and organ dysfunction.<sup>1-11</sup> Potent adjuvanted killed vaccines like those for rabies virus also can trigger immediate and delayed (vaccinosis) adverse vaccine reactions.<sup>7-10</sup> Genetic predisposition to these disorders in humans has been linked to the leucocyte antigen D-related gene locus of the major histocompatibility complex, and is likely to have parallel associations in domestic animals.<sup>5, 7</sup>

Beyond immediate hypersensitivity reactions, other acute events tend to occur 24-72 hours afterwards, or 7-45 days later in a delayed type immunological response.<sup>1-4, 6-10</sup> Even more delayed adverse effects include mortality from high-titered measles vaccine in infants, canine distemper antibodies in joint diseases of dogs, and feline injection-site fibrosarcomas.<sup>5,7</sup> The increasing antigenic load presented to the host individual by modified-live virus (MLV) vaccines during the period of viremia is presumed to be responsible for the immunological challenge that can result in a delayed hypersensitivity reaction.<sup>2, 3, 6, 7</sup>

The clinical signs associated with vaccine reactions typically include fever, stiffness, sore joints and abdominal tenderness, susceptibility to infections, neurological disorders and encephalitis, collapse with autoagglutinated red blood cells and icterus (autoimmune hemolytic anemia) (AIHA), or generalized petechiae and ecchymotic hemorrhages (immune-mediated thrombocytopenia)(ITP).<sup>1, 2, 4, 7, 8, 12, 13</sup> Hepatic enzymes may be markedly elevated, and liver or kidney failure may occur by itself or accompany bone marrow suppression. Furthermore, MLV vaccination has been associated with the development of transient seizures in puppies and adult dogs of breeds or cross-breeds susceptible to immune-mediated diseases especially those involving hematologic or endocrine tissues (e.g. AIHA, ITP, autoimmune thyroiditis).<sup>1,7,10</sup> Post-vaccinal polyneuropathy is a recognized entity associated occasionally with the use of distemper, parvovirus, rabies and presumably other vaccines.<sup>2, 3, 7</sup> This can result in various clinical signs including muscular atrophy, inhibition or interruption of neuronal control of tissue and organ function, muscular excitation, incoordination and weakness, as well as seizures.<sup>7</sup> Certain breeds or families of dogs appear to be more susceptible to adverse vaccine reactions, particularly post-vaccinal seizures, high fevers, and painful episodes of hypertrophic osteodystrophy (HOD).<sup>7, 9</sup> Therefore, we have the responsibility to advise companion animal breeders and caregivers of the potential for genetically susceptible littermates and relatives to be at increased risk for similar adverse vaccine reactions.<sup>1, 4, 6-9, 14-17</sup> In popular (or rare) inbred and linebred animals, the breed in general can be at increased risk as illustrated in the examples below.

Commercial vaccines can on rare occasion be contaminated with other adventitious viral agents,<sup>3, 15</sup> which can produce significant untoward effects such as occurred when a commercial canine parvovirus vaccine was contaminated by blue tongue virus. It produced

abortion and death when given to pregnant dogs,<sup>15</sup> and was linked causally to the ill-advised but all too common practice of vaccinating pregnant animals. The potential for side-effects such as promotion of chronic disease states in male and non-pregnant female dogs receiving this lot of vaccine remains in question, although there have been anecdotal reports of reduced stamina and renal dysfunction in performance sled dogs.<sup>17</sup> Recently, a vaccine manufacturer had to recall all biologic products containing a distemper component, because they were associated with a higher than expected rate of central nervous system postvaccinal reactions 1-2 weeks following administration.<sup>17</sup> 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.<sup>10</sup>

Other issues arise from overvaccination, as the increased cost in time and dollars spent needs to be considered, despite the well-intentioned solicitation of clients to encourage annual booster vaccinations so that pets also can receive a wellness examination.<sup>6</sup> Giving annual boosters when they are not necessary has the client paying for a service which is likely to be of little benefit to the pet's existing level of protection against these infectious diseases. It also increases the risk of adverse reactions from the repeated exposure to foreign substances.

Polyvalent MLV vaccines which multiply in the host elicit a stronger antigenic challenge to the animal and should mount a more effective and sustained immune response.<sup>2, 3, 6</sup> However, this can overwhelm the immunocompromised or even a healthy host that has ongoing exposure to other environmental stimuli as well as a genetic predisposition that promotes adverse response to viral challenge.<sup>1, 2, 7, 14, 16, 17</sup> The recently weaned young puppy or kitten being placed in a new environment may be at particular risk. Furthermore, while the frequency of vaccinations is usually spaced 2-3 weeks apart, some veterinarians have advocated vaccination once a week in stressful situations, a practice makes little sense scientifically or medically.<sup>6</sup>

An augmented immune response to vaccination is seen in dogs with pre-existing inhalant allergies (atopy) to pollens.<sup>7</sup> Furthermore, the increasing current problems with allergic and immunological diseases has been linked to the introduction of MLV vaccines more than 20 years ago.<sup>3</sup> While other environmental factors no doubt have a contributing role, the introduction of these vaccine antigens and their environmental shedding may provide the final insult that exceeds the immunological tolerance threshold of some individuals in the pet population. The accumulated evidence indicates that vaccination protocols should no longer be considered as a "one size fits all" program.<sup>9</sup>

For these special cases, appropriate alternatives to current vaccine practices include: measuring serum antibody titers; avoidance of unnecessary vaccines or overvaccinating; caution in vaccinating sick or febrile individuals; and tailoring a specific minimal vaccination protocol for dogs of breeds or families known to be at increased risk for adverse reactions.<sup>6, 7, 18-21</sup> Considerations include starting the vaccination series later, such as at nine or ten weeks of age when the immune system is more able to handle antigenic challenge; alerting the caregiver to pay particular attention to the puppy's behavior and overall health after the second or subsequent boosters; and avoiding revaccination of individuals already experiencing a significant adverse event. Littermates of affected puppies should be closely monitored after receiving additional vaccines in a puppy series, as they too are at higher risk.

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