Adverse Reactions to Vaccination

From Anaphylaxis to Autoimmunity

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KEYWORDS

• Vaccine reactions • IgE • Anaphylaxis • Autoimmunity • Arthus reaction

KEY POINTS

- Vaccines are important for protection of individual animals and for creation of herd immunity against infectious diseases.
- Induction of immune responses to nontarget antigens present in most vaccines can lead to allergic sensitization, particularly in breeds with genetic predisposition.
- Reactions to vaccines can vary from allergic events (face swelling) to anaphylactic shock. Although uncommon, such responses can occur.
- Autoimmune diseases have a variety of causes and generally have a genetic predisposition. Overvaccination in a patient with a predisposition to autoimmune disease may enhance the likelihood for development of an autoimmune response.

Prevention of infectious disease by the use of vaccination is one of the most important procedures performed by veterinarians and human health professionals. In some instances, disease has been completely eradicated or greatly reduced through elicitation of herd immunity. Yet, vaccination is not without risk. A risk of vaccination is associated with misuse, overvaccination, and in a small proportion of the vaccinated population the potential for a potentially fatal allergic reaction exists.

HYPERSENSITIVITY TO VACCINE COMPONENTS

In large and small animal patients administration of a viral vaccine, particularly an inactivated and adjuvanted viral vaccine, can elicit an IgE response to proteins present in the vaccine that are nontarget antigens. These are proteins that are present in the cell culture medium used to grow the virus to be used in the vaccine preparation. If the virus is grown on mammalian cells, the most common nontarget antigens are bovine serum proteins, because of the use of fetal bovine serum in cell growth

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medium. Proteins shed from the cells used to grow the virus are another source of antigen. The actual virus that is the target immunogen is rarely the source of the misdirected immune response. When virus is grown in eggs, some of the egg protein can become a nontarget antigen. In addition, stabilizers, such as gelatin, can occasionally become a target of an unwanted immune response. The process of vaccine production varies with the manufacturer and the type of adjuvant used, but in general it is impossible for the viral antigens to be completely purified so that the tissue culture products are completely eliminated from the final product. For most patients, this is not a problem. Even if a small amount of IgG is made against fetal bovine serum proteins, it is usually harmless. However, in the population of patients with atopy (those that readily make IgE responses and are often allergic) elicitation of an IgE response by these nontarget antigens presents a potential problem.

The presence of the nontarget antigens in multiple viral vaccines means that each time a patient receives a vaccine containing the nontarget antigens those same nontarget antigens are available to restimulate the immune response.

Patients with atopy (dogs, horses) respond to nontarget antigens by making not only IgG but also IgE antibodies. These IgE antibodies have a high affinity for receptors on mast cells in the skin and nearby mucous membranes of the intestinal tract and the respiratory tract. IgE stays on these mast cells for months, even after serum IgE levels have waned. When the patient receives an injection of vaccine containing more nontarget antigens they bind to the IgE on mast cells and cause degranulation. This is a typical type I hypersensitivity response, with liberation of preformed mediators, such as histamine, and stimulation of production of arachidonic acid metabolites by the lipoxygenase and cyclooxygenase pathways. The leukotrienes thereby created along with the released histamine cause vasoactive responses, increased capillary permeability, and even smooth muscle contraction (**Fig. 1**). In the horse and the dog these responses have been shown to be associated with adverse clinical responses. In the horse, one may see signs of colic and in severe instances, respiratory distress and circulatory collapse (anaphylactic shock). In the dog, a common early sign is swelling and urticaria of the muzzle area, with systemic anaphylaxis occurring usually after one or more such episodes of vaccine responses.

These reactions can be startling to owners and veterinarians and can create a dilemma, particularly when giving the required rabies vaccine.

In 1983, Frick and Brooks[1] hypothesized that immunization of dogs with atopy for canine distemper and parvoviruse would alter immunoregulation of the IgE response. An inbred atopic dog colony was used to test this hypothesis. Vaccination of puppies before sensitization with grass and weed pollen extracts seemed to enhance production of IgE antibodies to the pollen allergens.[1]

HogenEsch and colleagues[2] studied a group of Beagles to evaluate the effect of vaccination on serum concentrations of total and antigen-specific IgE. A multivalent vaccine (without adjuvant) failed to alter IgE levels but addition of the rabies vaccine or rabies vaccine alone (containing alum adjuvant) caused there to be an increase in IgE reactive with vaccine antigens. The reactivity of the IgE included the nontarget proteins in the tissue culture fluid: bovine serum albumin and fibronectin.

The possibility that immunization with vaccines containing alum adjuvants would increase IgE antibody levels reactive with allergens to which the patient had already been sensitized was examined by Tater and colleagues.[3] Using a colony of Maltese-Beagle crossbred dogs known to be allergic to corn and soy, the investigators monitored IgE levels specific to these allergens before and after immunization with commonly used vaccines (canine distemper/adenovirus/measles, parvovirus, parainfluenza virus and rabies). In a second experiment the effect of aluminum