

# THE IMPORTANT ROLE OF VACCINE ADJUVANTS

A scientific paper published in the May-June 2003 edition of the *Journal of Veterinary Internal Medicine* offers a broad perspective on adjuvants and their central role in improving the safety and efficacy of animal vaccines.

Authored by Anna R. Spickler and James A. Roth of Iowa State University's College of Veterinary Medicine, the paper explores the history and development of adjuvants, as well as the materials used to make them and their mechanisms of action.

Adjuvants are agents designed to stimulate the immune response to vaccine antigens. Along with vaccine administration, adjuvants have been the subject of growing scrutiny in recent years due to the emergence of so-called injection-site sarcomas. The tumors are primarily associated with felines and are extremely rare. What role, if any, adjuvants or vaccine antigens may play in the development of the sarcomas is unknown.

The authors, however, assert that the benefits of adjuvants and vaccine administration outweigh whatever risks may be associated with them. Indeed, foregoing all vaccinations in order to avoid the possibility of an injection-site sarcoma creates a greater danger than the sarcoma risk itself.

Spickler and Roth suggest that going forward, it likely will be increasingly possible to design and select adjuvants tailored to the specific needs of the antigen, species and situation.

The first adjuvants were developed in the 1920's to boost immunity and immune responses to administered antigens. Materials employed in adjuvants include chemicals, microbial components and mammalian proteins.

The use of adjuvants has become prevalent in animal health as a way of reducing dependence on modified live antigens, which have the potential in immuno-compromised animals of inducing the disease they're designed to prevent. Used in conjunction with killed antigens, adjuvants can boost the efficacy of vaccines by providing artificial signals that stimulate the immune system.

This is particularly important in immuno-compromised animals, specifically the very young or the very old. Adjuvants can also decrease the amount of antigen needed, which can make the vaccine more cost-effective, and also lengthen its shelf-life. Finally, adjuvanted vaccines have been demonstrated to provide immunity for one year.

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Although their mechanisms of action are not completely understood, adjuvants appear to enhance antigen presentation, improve antigen stability and/or act as immunomodulators. A single adjuvant may have more than one mechanism of action, including preserving the structure of the antigen as well as increasing cell migration to the lymph nodes. Some adjuvants appear to trap the antigen at the injection site and thus provide a continuing supply to local antigen presenting cells (APCs).

Primary types of adjuvants include aluminum and calcium salts; oil emulsions, such as shark liver oil; liposomes and archeosomes, as well as nanoparticles and microparticles made from biodegradable polymers. Saponins, or complex chemical compounds extracted from plants and trees, also are used.

Attempts have been made recently to fit adjuvant mechanisms into more general hypotheses of immune function. According to some current theories, all APCs must first be activated for antigen presentation before they can initiate immune response. In one model, this activation is thought to occur when pattern recognition receptors on the APC bind to conserved motifs in bacterial lipopolysaccharides, sugars and other moieties.

If this idea is correct, adjuvants may act by mimicking these primitive bacterial signals. In fact, many adjuvants are derivatives of bacteria or resemble the motifs in bacterial proteins, carbohydrates or DNA. However, this model may not explain adjuvants such as oil emulsions, saponins or aluminum salts.

Adverse side effects associated with adjuvants can include fever, arthritis, anorexia, soreness and lethargy. Aluminum adjuvants can cause inflammation, and some authors suggest that they should be avoided in cats. This recommendation, however, is controversial. Not only have adjuvants other than aluminum been used in cases that result in injection-site sarcomas, but tumors also have occurred when vaccines without adjuvants are used.

At present, no one specific brand of vaccine seems to be associated with sarcomas. In general, it can be difficult to establish the incidence of rare adverse effects for any particular vaccine. Although these potential hazards must be understood and appreciated, in most instances the adverse effects of adjuvants are mild, and in general, their benefits outweigh the hazards of their use.

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