

What Everyone Needs to Know About Canine Vaccines and Vaccination Programs

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The three most important things to give a puppy, Dr. Ron Schultz said, are training, love, and vaccines.

The oldest and most common vaccine is the modified live vaccine (MLV). It is made by taking a disease-causing virus and altering, or attenuating, it to a non-disease-causing virus that is still capable of immunizing. Because natural infection or recovery from disease is the best kind of immunity, these vaccines most resemble natural immunization, Dr. Schultz said. MLV is highly effective and generally very safe for the species for which it was developed.

Vector vaccine (VV) is similar to MLV, but produced by genetic engineering that usually incorporates DNA from more than one species of organism—recombinant DNA technology. In the case of canary pox virus, two genes from the canine distemper virus (CDV) are genetically engineered into a viral vector—canary pox—that protects against distemper.

“Genetically engineered vaccines are the wave of the future,” Dr. Schultz said. “[They] are the way most new vaccines will be developed, because we can better control what we do to the particular virus or bacteria, and we can make a very effective vaccine.”

To make MLV most effective, it must become more like the virulent form of the virus, and is then more likely to cause disease. Genetically engineered vaccines, on the other hand, have no such inverse relationship between efficacy and safety. Both MLV and VV are infectious vaccines, Dr. Schultz said. If the vaccines do not infect, they do not immunize.

The second most common form of vaccine is the so-called noninfectious variety. Inactivated or killed vaccines are this type. They are made by treating a disease-causing virus with a chemical or radiation to kill it. The organism should retain its important antigens, and, its ability to induce an immune response. Dr. Schultz said that sometimes the addition of an adjuvant, a substance that will enhance the immune response, is needed.

Another form of noninfectious vaccine is recombinant subunit vaccine. Recombinant vaccines are produced through conventional technology: grow the organism, inactivate it with a chemical, and then concentrate or separate out that portion of the bacteria that is most immunogenic.

The immune system is actually two systems in one, Dr. Schultz said. The innate immune system, also called natural or unspecific, is present from birth, protects against any substance, is nonspecific, and is not enhanced by prior exposure. Stomach acid, cough reflex, fevers, gut microflora, and even age are all examples of the innate immune system.

In contrast, the acquired—also known as adaptive or specific—immune system is highly specific or tailored to a specific organism, and enhanced by prior exposure. It involves a variety of organs, most especially the bone marrow where many immune cells are made, and the thymus. Dr. Schultz said the acquired immune system can be further subdivided into the humeral, or antibody mediated system, and cellular, or cell mediated system. In the humeral system, bone marrow cells contact antigens in the spleen, which produces antibodies. The cells of the thymus become differentiated into a variety of T cells with a variety of purposes.

Immunologic memory allows the immune system to remember the antigens or organisms to which it has previously been exposed. For example, following exposure to CDV, a dog's immune system remembers for a lifetime that it has been exposed to the virus. A dog's immunologic memory of CDV, canine parvovirus (CPV), and canine adenovirus (CAV) guarantees long-term immunity against these diseases, similar to the long-term immunity afforded humans who have developed measles, mumps, or rubella.

"The number of cells and the kinds of networking that has to go on to produce that immune response is incredible," Dr. Schultz said. "Fortunately, we don't need to know much about this for the vaccine to work. The body itself knows what to do."

In general, vaccines are designed to stimulate the acquired, or adaptive, immune system. At times they also can enhance nonspecific immunity. For example, intranasal kennel cough vaccine contains bordetella and canine influenza virus (CIV), with or without canine adenovirus-2 (CAV-2). The bordetella activates the nonspecific immune system within minutes of the dog receiving the vaccine, he said. Although it is not initially protecting the dog from bordetella, it is providing some nonspecific defense against various viruses.

Disease is dependent on the dose, the route of exposure, the virulence of the particular organism, and the host immune response. Dr. Schultz said innate immune response likely prevents infection with about 90% of organisms capable of causing infection. The other 10% are handled by the adaptive immune response, which typically is more efficient at battling viruses than the innate system.

All canine vaccines will stimulate both aspects of adaptive immunity—humeral and cellular. As is the case for the measles, mumps, and rubella vaccination, Dr. Schultz said, the most important factor for CDV, CPV, and CAV in dogs is the antibody. In a vaccinated individual, the antibody either prevents infection or limits it so the disease will not develop.

Duration of immunity comes through the immunologic memory cells, but the only way these cells respond is if the individual becomes infected. Dr. Schultz said it is now known that some of the cell-producing antibodies called plasma cells are long-lived. Instead of being present in the peripheral lymphoid organs like the spleen and lymph nodes, they are present in the bone marrow, and are programmed to continue to produce antibodies. If a particular cell dies, it makes a new cell also capable of making that antibody. This explains why dogs vaccinated against CDV, CPV, and CAV, and isolated to prevent any chance of getting infected with these diseases, still have the antibodies five to seven years later.

In general, Dr. Schultz said, duration of immunity is much longer for viruses than bacteria, and longer against a systemic disease than a local mucosal disease. Since CDV, CPV, and CAV are all systemic, viral diseases, the vaccine offers long-term immunity. On the other hand, bordetella's contribution to kennel cough is more of a mucosal disease and a bacteria, so the immunity is short. MLV and recombinant VV provide a longer duration of immunity than any of the killed subunit vaccines.

Dr. Schultz described the role vaccines played in reducing the number of deaths associated with two diseases that have afflicted the canine species for hundreds, if not thousands of years, before a vaccine was made. The first vaccines were made in the late 1950s and early 1960s, he said.

The introduction of canine distemper vaccine led to significant reductions in the disease, though it has not been completely eliminated. The original vaccine for canine adenovirus was discontinued, after one in 500–700 dogs developed allergic reactions. However, the second-generation vaccine confers protection with no adverse reactions.

As a result, the United States has seen no cases of infectious canine hepatitis in domesticated animals in 15 years, except for three dogs in a San Diego shelter that had recently arrived from Mexico. The disease is still prevalent in countries and regions with lower vaccination rates.

Canine parvovirus first appeared in the late 1970s and “caused very, very high mortality before we really got a vaccine that worked,” Dr. Schultz said. Although the disease is far from being eliminated, immunization has led to a marked reduction in the number of parvovirus cases and resulting deaths.

Meanwhile, the past few years have seen a change in veterinary medicine's philosophy of vaccination. Until recently, the predominant view was that every pet should receive every licensed vaccine multiple times at an early age, then at least annually through adulthood. Dr. Schultz said most vaccines were combined in a single syringe for the owner's convenience, “not to worry about the animal itself being blown out of the water with 12-way, 14-way mombo combos.”

Practitioners assumed that even a vaccine that did not help would not hurt and, to this day, the labels on all USDA-approved vaccines specify annual boosters, regardless of the

immunity they actually provide. “It is an arbitrary and capricious statement,” Dr. Schultz said, but the requirement is a part of the Federal Code and can only be changed by Congress.

Historically, vaccine recommendations came from a committee of the American Veterinary Medical Association (AVMA). However, after the American Association of Feline Practitioners published its first set of vaccine guidelines in 1998, AVMA left it up to specialty groups to do the same for other species. A group of clinicians and practitioners published the first canine recommendations in 2003, with administrative support from the American Animal Hospital Association (AAHA).

The guidelines were updated in 2006, and are available at www.aahanet.org. For the first time, the document lists the core vaccines—distemper, adeno, parvo, and rabies—that should be administered to every dog. “And we did mean ‘every,’” Dr. Schultz said. Although the United States probably vaccinates more dogs than any other country, its coverage is only about 50%. With another 20–25% “we could, for all practical purposes, eliminate these diseases, because we would have so much better herd immunity.”

The main difference in 2006 was the recommended interval. The latest guidelines call for a last dose of core vaccine at 14–16 weeks, then at one year of age, then no more often than every three years. The exception is the rabies vaccine, which must be administered every three years. Optional vaccines for conditions like leptospirosis and bordetella are only recommended if an animal is at risk, but none of them provide more than a year of immunity. Dr. Schultz advised that if a dog requires one of the optional vaccines, “make sure it’s getting it often enough to get the protection you think it needs.”

For rabies, dogs require the first dose of vaccine at 12–16 weeks, then a year later, then every three years. A handful of states still require annual revaccination for rabies, but “that’s absolutely absurd. The law should be changed. There’s no immunologic or public health benefit,” and “you as a dog owner can help make that change.”

Since the minimum duration of immunity for the core vaccines is seven to 10 years, revaccinating every three years adds no benefit and increases the risk of adverse reactions. Those reactions are rare, but “it is not acceptable if an animal gets an injectable that is not needed and develops disease or dies.”

To determine the duration of immunity, the gold standard is to challenge with virulent agents. For an upcoming rabies vaccine study with which Dr. Schultz is involved, “the only way the results will be considered by the USDA and validated is by having a control group of dogs that will be challenged, and 80% of them must die from rabies for it to be a valid challenge. And then we will have to show the efficacy in the vaccinated group.”

He recalled a recent three-year study of a recombinant feline rabies vaccine that reported 100% protection in the vaccinated group, but only 79.3% mortality in the control. “That

was unacceptable according to the Federal Code, so they've had to start the study all over again."

Recent vaccine trials have shown long-term immunity of more than seven years for distemper and parvovirus, more than three years with a canary pox-vectored distemper vaccine, and more than seven years for canine adenovirus with the second-generation vaccine product. Where studies demonstrate three years of immunity, the next steps will be to test for five, then seven.

Dr. Schultz said it is critical for veterinary biological companies to endorse the three-year immunization schedule, as they have since 2004. "The practitioner really relies heavily on the company that supplies the vaccine. If anything goes wrong, they want to be backed up. If they need diagnostics, the company will generally pay for them."

For the optional vaccines, it is critical to balance the odds of infection and disease against the risk of adverse reactions, while recognizing that treatment must be repeated annually and efficacy cannot approach the core vaccines. He emphasized that *leptospirosis vaccines should never be combined with treatments for viruses, and should never be administered before 12 weeks of age, because of the more immediate need for viral immunity and the impact of the leptospirosis treatment on a puppy's immune system.*

Similarly, practitioners should *avoid mixing viral immunizations with the vaccine for bordetella bronchiseptica. The treatments should be administered on opposite sides of the animal, so that they affect different lymph nodes.*

Canine influenza virus jumped from horses to dogs in 2004, but Dr. Schultz said there was never any risk that influenza would become the next canine parvovirus epidemic. "Parvo is extremely environmentally stable, it's impossible to get rid of, it lives in the soil for at least a year or more, and remains infectious. Canine influenza is dead about the moment it comes out of the dog," so it seems to be most prevalent at Greyhound tracks, in shelters, and in some canine day cares or kennels.

AAHA specialists recommend against vaccinating for canine coronavirus or giardia. If coronavirus eventually emerges as a significant canine disease, most of the available countermeasures will not work, since killed vaccines do not induce mucosal immunity.

The issue of antibody titres has generated a great deal of confusion, Dr. Schultz said. Titres are often seen as a snapshot in time, but "what I want to tell you is that it doesn't matter with regard to distemper, parvovirus, and adenovirus. If there is any antibody that has been actively produced as a result of natural or artificial immunity, then the animal has immunologic memory and is immune." Younger animals should not be tested when there is any possibility of confusion due to passive immunity. Otherwise, the interpretation of test results showing low levels of immunity depends on which commercial test is used. For leptospirosis, antibody titres are indeed a snapshot in time.

It would be useful if puppies could be tested two or more weeks after their last dose of core vaccine to confirm immunity to distemper and parvovirus, Dr. Schultz said.

Animals with no immunity could then be revaccinated and tested again after two weeks. That will not be possible without a more user-friendly, cost-effective, rapid test that could be used in veterinary offices.

Apart from revaccination, dogs often receive natural immunity through exposure to the core diseases. Dr. Schultz said he worries most about a lap dog that spends its life in its owner's apartment, before being placed in a kennel without being revaccinated. "That dog is likely to be in a pretty risky situation of coming down with severe kennel cough."

Although adverse reactions are rare, they are bound to happen. "When you inject something into yourself or your dog, there is always the chance of adverse reaction," he said. Reactions are considered rare if they occur in less than one in 10,000 animals, uncommon at a rate of one per 1,000 to 10,000, and common if they are more frequent than one in 1,000.

The biggest "rude awakening" on adverse reactions in veterinary medicine occurred in the late 1980s and early 1990s, with reports of injection-site sarcomas in cats. "No one ever suspected that a vaccine given to a normal, healthy kitten would end up causing lethal cancer, and if you don't know, it can't be, right?" Dr. Schultz said. "You're convinced that a vaccine couldn't cause cancer, but it did." It turned out that felines lack the tumor suppression genes that would act on an injection site that became neoplastic through inflammation. The research in this area helped shift the philosophy that vaccines cannot hurt, even if they do not help.

Anaphylaxis is a much more common adverse reaction, but it has been known for 1000 years and veterinarians are trained to watch for it. Dr. Schultz listed a series of other adverse reactions—hives and facial edema, arthritis and polyarthritis, autoimmune hemolytic anemia, post-vaccination encephalitis or polyneuritis, seizures, abortion, congenital anomalies, embryonic or fetal death, failure to conceive, and transient immune suppression—in the five to seven days following a combined vaccination for distemper and adenovirus. He urged participants to report adverse reactions to veterinarians and vaccine manufacturers as a way of generating more reliable data on their occurrence.

Discussion

A participant asked whether a 15-month-old puppy should be immunized for leptospirosis along with its third dose of core vaccinations. Dr. Schultz said he would recommend administering the viral vaccines separately, following with the four-way leptospirosis vaccine at 17 and 20 weeks, then revaccinating six and 12 months later. If the dog is really at risk for leptospirosis, it should receive boosters every nine to 12 months.

The participant said she had never had her dogs vaccinated for leptospirosis in the past. "We're going through a period of leptospirosis," Dr. Schultz replied, "but lepto is no more a risk today than it was 20 years ago." He said the disease is a concern in the

participant's home region of northern Illinois, at an incidence of one case per thousand or two thousand dogs.

A participant said mixed messages about titres have led to confusion for breeders and veterinarians. Dr. Schultz said it is more important to test a puppy two weeks after its last dose of core vaccine, rather than waiting until it reaches one year of age. However, for veterinarians in search of a practice management tool to ensure client compliance, his advice is "by all means do titres. Do not vaccinate. I have never seen an animal harmed from taking a blood sample. I have seen harm brought to animals by giving them vaccines that they do not need."

With immunization as a management tool, "we have gotten the client to come in annually or more often, because everyone knew these vaccinations had to be given annually. We don't want to take away that annual visit, because it's critically important. So maybe the titre or the dental exam will do that."

In reply to a question about parvovirus vaccines, Dr. Schultz traced the development of different parvovirus variants from the mid-1980s through 2005. Vaccines produced by the five major manufacturers are effective against all variants. However, there is a "window of susceptibility" when a puppy's maternally derived antibody is insufficient to protect against infection, but still high enough to interfere with active immunity from the vaccine. Generally, that window has been reduced from 12 weeks to two, but it is still a factor.

"If you're in an environment where parvo is a real threat, like a shelter, we'll still see a few cases, even though we vaccinate every two weeks," he said. "The virulent virus gets in before the vaccine can prevent the infection."

He recommended against relying on some of the more obscure products available through catalogs.

A participant described her successful effort to eliminate giardia in her kennel, using a vaccine that veterinarians are hesitant to use. Dr. Schultz said the treatment is not needed for the majority of dogs, but that it makes sense in chronic cases where the benefit can be demonstrated. "If it works, by all means use it," he said; the treatment might eventually find its way to his optional list if enough breeders can demonstrate its value. The participant said it is unfortunate that veterinarians are hesitant to use the vaccine where it is needed.

Another participant asked whether there is correlation between dogs being vaccinated at eight weeks and developing puppy stranglers. Dr. Schultz said he has seen reports to that effect, and that a vaccine can contribute to the disease it is designed to prevent.

A participant asked whether bitches should be vaccinated prior to breeding. Dr. Schultz said revaccination is not generally needed. If it is, it should take place prior to estrus.

Responding to a series of questions about vaccinations for toy breeds, he said body size is less important with biologics than it is with pharmaceuticals. For a vaccine, a Toy Poodle is as likely to need a full dose as a Saint Bernard. He said most of the smaller toy breeds have difficulty with the leptospirosis vaccine.

A participant said she had heard conflicting reports on the efficacy of rattlesnake vaccine. Dr. Schultz cited a veterinarian in Colorado who had found the vaccine effective, based on considerable experience with night rescues. He emphasized that the vaccine buys time, not immunity: according to one emergency veterinarian, dogs have died because their owners assumed their dogs were protected from rattlesnake bites and only sought treatment after it was too late.

A participant cited her veterinarian's advice that parvovirus vaccine was unnecessary for a new litter of puppies born on a property that had recently been infected, as long as the puppies were dewormed. Dr. Schultz said an animal without intestinal parasites could still develop parvovirus, though dogs with both are more likely to get severe disease and die.

A participant asked whether the core vaccines could lead to a high incidence of autoimmune disease in specific breeds. Dr. Schultz said vaccines may trigger autoimmune disease, but they do not cause it. If dogs do not receive their core vaccines, he said, "They won't go on to develop thyroiditis. They'll die from distemper or parvo."

A participant who is a veterinarian challenged Dr. Schultz's statement that the rabies vaccine can be the most immunologically devastating for dogs. Dr. Schultz said the statement reflected practical experience. "Rabies is the most likely to cause an adverse reaction," he said. "That's what the quote is. And the reason is that it's a killed adjuvant vaccine."