Current Concepts

Are we vaccinating too much?

Concerns about vaccine reactions have left veterinarians and pet owners wondering about the best vaccination schedules for dogs and cats. There is little scientific documentation that backs up label claims for annual administration of most vaccines. Although it is possible that some vaccines work best when given annually, others need to be given more often, and many others may last for years. The only vaccine routinely tested for minimum duration of immunity is the rabies vaccine.

"There has been no study that compares all the FeLV vaccines on an equal footing. . . . It may be that those causing the greatest reaction are those that are most efficacious."
Dr. Dennis W. Macy

Duration of Immunity

It is known that some vaccines provoke short-lived immunity and should be given annually to dogs at risk. These include canine parainfluenza, bordetella, and leptospirosis vaccines. Questions arise about the need for annual boosters of almost all other vaccines.

"I kept a litter of dogs in isolation for over 5 years, and they still had antibody to parvovirus and distemper after being vaccinated as pups," said Dr. Leland E. Carmichael, professor of virology at Cornell University's Baker Institute for Animal Health.

"Canine distemper and adenovirus-2 vaccines both provide lifelong immunity," said Dr. Ronald D. Schultz, professor and chair of the Department of Pathobiological Sciences at the University of Wisconsin. "These need not be given annually."

"We see good titers to calicivirus and panleukopenia virus for 3 to 4 years in cats that are vaccinated when they're at least 12 weeks of age," said Dr. Fred W. Scott, professor of virology and director of the Cornell Feline Health Center. "I believe that immunity to herpesvirus is also long-lived, but antibody titers don't correlate with immunity and we have not yet done challenge studies."

Efficacy of the feline leukemia virus (FeLV) and feline infectious peritonitis (FIP) vaccines is controversial, and little is known about the duration of immunity following their use.

In the past, it was believed that annual vaccination would not hurt and probably would help most animals. However, concerns about side effects have begun to change this attitude. The incidence of anaphylaxis and other adverse reactions appear to be increasing.

First, Do No Harm

"One disadvantage to overvaccinating is the cost," Dr. Schultz said. "The client is paying for something with no effect or with the potential for an adverse reaction. I believe that adverse effects are increasing, because we are putting more and more components into these animals."

"Veterinarians need to be better prepared to deal with anaphylaxis," Dr. Scott said. "It is essential that epinephrine be given, since antihistamines and corticosteroids are not adequate to treat severe reactions."

"After a dog experiences anaphylaxis, annual measurement of distemper and parvovirus antibody titers would reveal if revaccination is necessary," Dr. Carmichael said.

Another side effect of vaccination is that it may lead to false-positive test results, especially in cats.

Prepared by Carin A. Smith, DVM, a relief veterinarian and writer who lives in Leavenworth, Wash.

"Some companies are producing live-virus vaccines that don't immunize as well as did the seed virus, because nonimmunizing mutants arise during passage in cell culture. . . . With vaccines that contain high amounts of nonimmunizing virus, you can't get enough virus in a vaccine vial to alter immune responses, since only virus that replicates in the dog will provoke immunity."
Dr. Leland E. Carmichael

"Bovine serum and other proteins can cause reactions that give false-positive ELISA results," Dr. Scott said. "We may see false-positive results on toxoplasmosis, FIP, or FIV tests after routine herpesvirus, calici, and panleukopenia vaccination."

Administration of the canine cell-cultured distemper vaccines may cause encephalitis in a minority of pups. According to Dr. Carmichael, vaccine batches that contain a high titer of distemper virus are more likely to cause encephalitis, especially when the vaccine is given to pups under 6 weeks old. In the past, encephalitis was more common when the distemper vaccine was given at the same time as the canine adenovirus-1 vaccine.

Sarcoma Formation

Rabies and FeLV vaccines have been associated with development of fibrosarcomas and other tumors in cats. The dramatic increase in these tumors since the mid-1980s closely paralleled several other events. First, there was a change from use of a modified-live rabies vaccine to use of a killed, adjuvanted product. Feline rabies vaccination increased because of the threat of disease in some areas of the country. At the same time, the first FeLV vaccines were introduced.

"I estimate there are about 22,000 cases of vaccine-associated tumors per year," said Dr. Dennis W. Macy, professor of medicine and oncology at Colorado State University. "Since surgery is usually unsuccessful, radiation treatment is necessary. Treating all these cats would cost $66 million per year."

Sarcomas found in vaccine sites are histologically identical to those observed in previously traumatized areas. Since inflammation is an antecedent to tumor formation, Dr. Macy's group believed they could potentially evaluate whether certain vaccines would be more likely to cause tumors by looking at their ability to cause chronic inflammation. In a study funded by the American Animal Hospital Association and the American Feline Practitioners Association, they evaluated 3 rabies and 3 feline leukemia vaccines, and found that all the rabies vaccines, and some of the feline leukemia vaccines, caused reactions.

"All products that contained aluminum hydroxide adjuvant caused inflammation, but products without that ingredient did also," Dr. Macy said. "The nonadjuvanted leukemia products did not cause inflammation. Because adjuvant ingredients are proprietary information, we don't know what other ingredients may predispose to inflammation. These reactions are not unique to the cat, but the cat is unique in its response and activation of oncogenes."

Although rabies vaccines caused more inflammation than did feline leukemia vaccines, retrospective studies revealed that leukemia vaccination leads to a slightly higher incidence of sarcoma development. There have been sporadic reports of tumors following other types of vaccines in cats, but Dr. Macy feels these are no more common than the rare tumor that develops in a previously traumatized area.

"Tumor development may depend on the type of antigenic stimulation associated with inflammation," Dr. Macy said. "The type of cytokines released are probably more important than the inflammation itself. Also, it is likely that the more vaccines given in a particular site, and the more vaccines given over time, the higher the chance of sarcoma development."

Immune-mediated Disease

Concerns about immune-mediated disease following vaccination are controversial. There are no data that directly connect autoimmune disease in pets to vaccination.

"There is a real concern that vaccines may predispose certain genetically susceptible individuals to immune-mediated disease," Dr. Schultz said. "The more antigens we administer, the higher the potential for hypersensitivity. Type 1 is IgE mediated; type 2, cytotoxic-antibody mediated; type 3, immune-complex mediated; and type 4, cellular mediated. All of these hypersensitivities are natural parts of the immune response, but they cause a certain amount of tissue damage. That damage may occur in the kidney, liver, or as was the case with canine adenovirus 1, in the eye. In many cases it is impos-

sible to show a direct connection between the damage and a vaccine, since it is the accumulation of many antigens over many years that results in clinically evident disease."

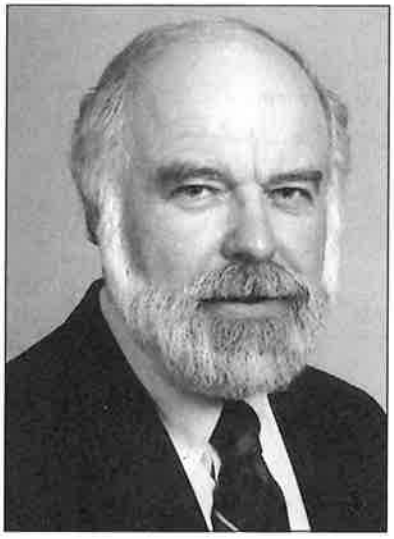
"Immune-mediated disease has developed in human beings following vaccination, as was seen with cases of Guillain-Barre syndrome following swine flu vaccinations, and rheumatoid arthritis following influenza vaccination," Dr. Schultz said. "However, we must evaluate the risk-benefit ratio of every vaccine. In the case of canine parvovirus, for instance, the risk of death from disease is extremely high compared with the minimal and as yet unproven risk of immune-mediated disease from the vaccine."

Vaccine Failure

Failure of protection is a perplexing problem that might lead some to believe that undervaccination, not overvaccination, is the main concern. Canine parvovirus continues to take its toll despite vaccination. The problem may be that of vaccine failure, interference by maternal antibody, or overwhelming exposure from which no vaccine could protect. Some veterinarians and breeders have resorted to weekly vaccination of pups in an effort to ward off disease.

"Weekly vaccination is unnecessary and could be harmful," Dr. Schultz said. "The antibody half-life is more than 1 week, so it will tie up any antigen presented by repeated vaccination and there won't be an adequate immune response. Also, if you ever want to experimentally reproduce hypersensitivity, all you have to do is give multiple small doses over a short period and give a challenge dose later."

"The window of vulnerability for parvovirus is greater than that of any other virus," Dr. Schultz said. "This is the time when there is enough maternal antibody to interfere with vaccines, but not enough to ward off infection. At the Infectious Gastroenteritis Symposium of the North American Veterinary Conference, we reported on a study where we evaluated 6 parvovirus vaccines that were administered 2 times, 3 weeks apart. We found that only 2 vaccines provided 100% protection against challenge with CPV-2a and -2b. One vaccine provided partial protection, and 3 did not protect at all.



"I am a strong advocate of vaccine use. . . . We need to strike a balance between those who feel that no vaccines should be given, and those who are vaccinating every week. We have come a long way in reducing disease through vaccination, but perhaps we have gone too far."
Dr. Ronald D. Schultz

"We recommend that one of the best vaccines be given at 6, 9, and 12 weeks," Dr. Schultz continued. "Even those pups with very high maternal antibody would be protected when vaccinated up to 14 weeks. In contrast, the least effective vaccine would have to be given up to 21 weeks of age. I don't think there is a need to vaccinate adult dogs, since early vaccination will be sufficient to stimulate memory cells. Dogs that developed parvo at 1 year of age were probably never immunized properly. They may have received insufficient doses of one of the less effective vaccines. There are also families of dogs, notably in the Doberman and Rottweiler breed, but probably in every breed, that do not respond to vaccination."

"I don't agree with one manufacturer's claim that all dogs will respond to their parvo vaccine by 12 weeks of age," Dr. Carmichael said. "Reported studies were done in kennels where bitches had low antibody titers, so the pups were susceptible at 6 to 12 weeks. For such a claim, studies would have to be done in a normal dog population. It is difficult and expensive to gather data about what percentage of dogs respond at a particular age. We have studied more than 20 litters of Rottweilers and Dobermans and have not encountered a pup that did not respond to an efficacious vaccine, but such instances may occur."

Other reasons for vaccine failure include interference and attenuation of vaccine virus.

"The more components we combine into a single dose of vaccine, the more likely they are to interfere with each other," Dr. Schultz said. "When multiple vaccines are given, there is competition at the antigen-presenting cell level. That will prevent the animal from responding normally to each antigen."

"Some companies are producing live-virus vaccines that don't immunize as well as the seed virus, because nonimmunizing mutants arise during passage in cell culture," Dr. Carmichael said. "With vaccines that contain high amounts of nonimmunizing virus, you can't get enough virus in a vaccine vial to alter immune responses, since only virus that replicates in the dog will provoke immunity. Some companies say they improved their vaccine by raising the titer of virus, but that has little effect unless the minimal immunizing dose is known."

"Parvovirus strains are more

virulent now than the virus that first appeared in the dog population, and antigenic changes have been demonstrated with monoclonal antibodies," Dr. Carmichael continued. "Nevertheless, claims that vaccines prepared with the 'newer types' (CPV-2a or -2b) provide better protection are misleading, since protection against one strain protects against them all."

Veterinarians may be tempted to administer a partial dose of vaccine to very small pups or kittens. Their good intentions may be inappropriately placed.

"We should assume that each vaccine dose contains only the minimal amount of antigen needed to stimulate immunity," Dr. Schultz said. "There is little difference in the number of the vaccine's target cells in a teacup Poodle compared with a Great Dane."

Room for Improvement

There is room for improvement in the efficacy and safety of most vaccines.

"Some vaccines are not performing optimally," Dr. Carmichael said. "Annual testing of all live vaccines in a few dogs should be required to show that they still immunize as expected. Without that, neither the vaccine company nor the veterinarian know what the vaccine is doing. In some countries, tests of each lot are required."

"Vaccine companies have no legal obligation to demonstrate duration of immunity," Dr. Schultz said. "The USDA may change that requirement, but will only ask for demonstration of the minimum, not the maximum duration of immunity. Although it is more expensive to test animals for several years, I hope that competition pushes the industry into doing so."

"The first company that gets a 3-year label on their FVRCP vaccine will have a corner on the market," Dr. Scott said. "That should prompt the others to follow suit."

The efficacy of vaccines against FIP and FeLV are often questioned.

"We can rotate vaccines so that the pet isn't getting all of them every year. Another option is to perform an annual physical exam and antibody titer screen to determine which vaccines need be administered. However, we need better tests for this to be feasible."
Dr. Fred W. Scott

Veterinarians may wonder whether they should use a vaccine of questionable efficacy in the face of potential reactions.

"There has been no study that compares all the FeLV vaccines on an equal footing," Dr. Macy said. "It may be that those causing the greatest reaction are those that are most efficacious."

What to Do

Veterinarians are now left wondering what course of action to take.

"Although this information is hard for veterinarians to hear, they want to know what's best for their patients," Dr. Macy said. "Whether they act on it is another story. Giving a vaccine less frequently than the label directs is taking a risk. My answer for now is to follow the label and to put pressure on the company or the USDA to act."

"It is my understanding that one should provide the current practice or art of medicine," Dr. Schultz said. "If I or one of my colleagues were asked, we would have to say that there is no scientific justification for annual vaccinations. However, a veterinarian is in a tough situation if all the others in the community are vaccinating annually, despite the scientific evidence. The medically correct approach is to understand which of those vaccines need to be used annually, and which last longer. We should examine what is needed at what ages, and give the appropriate vaccines at the appropriate time."

"There is a mistaken assumption that if we recommend annual vaccination, a greater percentage of animals will be vaccinated," Dr. Macy said. "But it doesn't do any good to overvaccinate one segment of the population and not vaccinate the rest. Your good clients' pets will have a higher risk of adverse reactions."

"I take a minimalist approach to vaccination," Dr. Carmichael said. "The main emphasis, especially in breeding kennels or where there are young pups, should be on stringent hygiene and preventing contact with infected animals. I vaccinate my own dogs once every 3 to 4 years, using only modified-live vaccines. Because immunity to killed vaccines takes 2 doses, takes about 3 weeks to develop, and doesn't last long, I don't recommend their use, especially in shelters or kennels."

"I don't see a need for coronavirus vaccines, since only 1 to 2 cases have been diagnosed at Cornell's Diagnostic Laboratory during the past 5 years," Dr. Carmichael continued. "The argument that corona- and parvovirus combined infections are more serious doesn't justify the corona vaccine, since we found parvovirus was just as severe in dogs vaccinated against coronavirus as in those that were not."

"I see no justification for the use of canine coronavirus or Lyme disease vaccines," Dr. Schultz said.

"The Lyme vaccine is purchased in inordinate amounts in states where the disease is rarely, if ever, diagnosed. We are about to see a new vaccine launched for canine rotavirus. I don't even know the disease it's supposed to prevent."

"I cannot support laws requiring annual rabies vaccination when the 3-year vaccine is available and is efficacious, especially in areas without endemic terrestrial rabies," Dr. Macy said. "I think that a 3-year cycle for FVRCP and rabies makes sense for most cats. After kittens receive their initial immunizations, I would booster at 1 year, and then go to every 3 years."

Experts agree that FIP and FeLV vaccines should be reserved for cats at high risk of exposure. However, it is unknown how often revaccination is necessary.

"The incidence of leukemia is so high," Dr. Scott said, "that I don't know how to determine which cats are not at risk. Even the indoor cat may be exposed when its owner brings home a stray."

"We now recommend that FeLV and rabies vaccines be separated, giving each SC on a limb," Dr. Macy said. "Giving vaccines IM will not protect from tumor development, but may retard diagnosis and make treatment difficult. Vaccination should not be given more frequently than is necessary."

Veterinarians may argue that annual vaccinations bring pets in for physical examination that would otherwise not be performed.

"We have to change our focus from a yearly vaccination to that of a yearly physical," Dr. Scott said. "We can also rotate vaccines so that the pet isn't getting all of them every year. Another option is to perform an annual physical examination and antibody titer screen to determine which vaccines need be administered. However, we need better tests for this to be feasible."

Risk versus Benefit

Experts urge balancing risks and benefits, and tailoring vaccination schedules to the individual patient.

"We should not allow politics, tradition, or greed to enter the decision," Dr. Macy said. "Changing vaccination schedules doesn't have to mean less profit, but that you'll have more income from some clients and less from others. Veterinarians and the industry need to have the guts to be honest with ourselves and assess risk, and not be trapped in tradition."

"We need better documentation in patient records as to the brand and type of vaccines administered," Dr. Scott said. "I am part of a feline biologics committee that is trying to set up a central reporting facility whereby we can document adverse reaction rates."

"I am a strong advocate of vaccine use," Dr. Schultz said. "We need to strike a balance between those who feel that no vaccines should be given, and those who are vaccinating every week. Annual vaccination has become a knee-jerk response that, for the most part, is unnecessary. We have come a long way in reducing disease through vaccination, but perhaps we have gone too far."

Urethral pressure response to smooth and skeletal muscle relaxants in anesthetized adult male cats with naturally acquired urethral obstruction

Administration of muscle relaxants to male cats with obstructive lower urinary tract disease was evaluated to determine whether relaxation of intraurethral skeletal and smooth musculature would affect removal of the urethral obstruction. Dantrolene sodium alone (n = 3) or in combination with prazosin (n = 3) was given to 6 obstructed male cats, and the urethral pressure profile was measured in the 3 segments of the urethra of each cat. After IV administration of dantrolene alone, only the postprostatic/penile segment had significantly decreased urethral pressure. The combination of dantrolene and prazosin caused a 20% decrease in pressure in the prostatic segment. Although the 2 drugs may be effective in relaxing urethral musculature in cats with obstructive urinary tract disease, it was not determined whether administration of the drugs would facilitate urethral catheterization and removal of the obstruction. Results further suggested that urethral muscle spasm had a minor role in the obstruction in these cats.—*I. M. Straeter-Knowlen, S. L. Marks, M. Rishniw, et al in Am J Vet Res 56 (July 1995).*