BRINGING VACCINE GUIDELINES TO LIFE

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IMMUNOLOGY

The immune system consists of primary and secondary lymphoid organs concerned with the body's ability to recognize and dispose of substances that it interprets to be foreign. The foreign substance, usually a protein, is called an antigen. The immune system in animals can be divided into two major divisions: innate (nonspecific) immunity, and adaptive (specific) immunity. Innate immunity consists of physical and chemical barriers such as skin and stomach acid. All antigens are treated similarly. The body responds the same no matter how often a particular agent is presented. There is no memory or changes to the body's response as innate immunity is nonspecific.

Adaptive (specific) immunity differs from innate immunity in that when the body is exposed to an antigen, an actual change is put into motion to adapt to the infection. The response is divided into two broad categories: humoral and cell-mediated (cellular) immunity.

Humoral immunity refers to the process in which antigens stimulate B lymphocytes to produce antibodies (immunoglobulins) specific to that antigen. The primary response begins immediately after initial contact with the antigen; IgM appears 48 to 72 hours after contact. This is a relatively weak and short-lived response. A secondary response occurs with a repeat contact of the same antigen. This reaction produces large quantities of IgG, which persists for a longer time, and generally, a high, longer-lasting titer can be measured.

Cell-mediated immunity is the second category of adaptive immunity and depends upon T lymphocytes' sensitization by initial exposure to a specific antigen. Subsequent exposure stimulates the release of lymphokines (which influence the behavior of lymphocytes), interleukins (which carry signals between immune system cells), and cytotoxic T lymphocytes. Immunity is designed to destroy or contain cells the body recognizes as expressing foreign antigens on their cell surface.

The immune system uses adaptive immunity via a combination of humoral and cell-mediated immunity to respond to an attack by an organism. This results in a balanced offense against infection. This prevents the further spread of the virus and destroys virus-infected cells. Levels of both antigens and antibodies can be measured in the laboratory sample.

Acquired immunity can come from natural exposure to disease or antigens in a vaccine. Passive immunity refers to the transfer of antibodies from a donor to a recipient. This occurs in domestic mammals via colostrum. Maternal antibodies prevent the initial disease in the young but also interfere with the first immunization's effectiveness by blocking the vaccine antigens.

VACCINATION

Vaccination has been used in companion animal species for over 50 years and has proven effective in controlling a range of major infectious diseases within the pet population. The goal of vaccination is to create adequate protective immunity to infectious diseases. For a vaccine to be effective, it should mimic the immune system's natural response. In young animals, vaccination is vital as they are generally more susceptible to infection and develop more significant disease. Maternal antibody interference is why serial vaccinations are required for animals under 16 weeks of age. Interference occurs because the vaccine does not reach the appropriate cells to stimulate an immune response. The maternal antibodies need to fall below a certain level before vaccination is effective. This level is variable and typically occurs anywhere between 8 and 16 weeks – depending on the vaccination history of the mother and the successful transfer of maternal antibodies via colostrum. When a vaccine against a specific disease is started for the first time, even in an adult animal, giving two vaccinations for most vaccine types is recommended. The second vaccination will produce a much more significant (logarithmically greater) response if it follows a vaccine given 2 to 4 weeks prior.

When developing vaccination protocols, remember that the veterinarian will need to evaluate patient needs individually and assess patient risk. There is no one-size-fits-all vaccine protocol. Vaccines have been broken up into two groups, called core and non-core. Core vaccines, some of which are required by law, protect against diseases that have public health significance, are highly infectious, and pose a risk of severe disease. These vaccines are considered high-benefit and low-risk to the patient population. The administration of non-core vaccines, which protect against diseases of less frequency and risk, should be based on the risk associated with vaccine administration vs. the individual's risk of contracting the disease. Some vaccines are not generally recommended in the pet population because they have been found to have little or no clinical indication, either because they do not produce a meaningful immune response or they have been associated with adverse events.

Canine core vaccines include canine parvovirus (CPV), canine adenovirus-2 (AV-2), canine distemper virus (CDV), and rabies. Canine non-core vaccines include *Bordetella bronchiseptica*, canine parainfluenza virus, leptospira, *Borrelia burgdorferi*, canine influenza virus (H3N8 and H3N2), and *Cortalus atrox*. The administration of non-core vaccines should be considered on an individual basis based on the risk of exposure, geographic location, and pet lifestyle. Canine conronavirus (CCV) vaccination is generally not recommended for dogs because it causes mild or subclinical disease, is most common in dogs under six weeks of age, and usually is self-limiting.

Feline core vaccines include feline parvovirus (FPV), feline herpesvirus-1 (FHV-1), feline calicivirus (FCV), and rabies. Non-core vaccines that are only administered to cats in specific risk categories include feline leukemia virus (FeLV), feline immunodeficiency virus (FIV), *Chlamydophilia felis*, *Bordetella bronchiseptica*, feline infectious peritonitis (FIP), and dermatophyte vaccines. The American Association of Feline Practitioners (AAFP) Feline Vaccination Advisory Panel recommends that all cats up to and including one year of age receive a FeLV vaccination. Kittens are more susceptible to FeLV and their future adult environment is often unpredictable. Adult cats determined to be at risk should continue to be vaccinated against FeLV.

Immunological memory may persist for decades in humans without re-exposure to antigens. Although memory is also likely to persist for extended periods in companion animals, there is considerable

individual variation in the potency of memory response. However, there is good evidence that protection conferred in adult dogs by both canine distemper and canine parvovirus vaccine exceeds five years. Based on this observation, these vaccines are administered triennially rather than annually.

TYPES OF VACCINES

Killed vaccines are either whole organisms or may contain genetically produced specific antigens. Both products require adjuvants to produce a good immune response as killed vaccines are considered less potent. An adjuvant is a substance added to a vaccine that increases the body's immune response. Adjuvants are necessary to develop strong immune responses to relatively poor immunogenic antigens. They promote a better immune response through inflammation and retain the antigen at the injection site for a longer time. The use of adjuvants results in high antibody titers with fewer doses of vaccine and smaller amounts of antigen, but boosters are often required to achieve the desired effect. Killed vaccines are stable and safer to use in immunocompromised animals.

Modified live virus (MLV) vaccines have been made non-pathogenic, but retain their ability to induce protective immunity. They do not require adjuvants to illicit a strong cell-mediated and humoral immune response, and multiple dosing is usually unnecessary. MLV vaccines are the most effective and produce the longest-lasting immunity. However, there is the rare possibility that they could revert back to their pathogenic form and cause significant disease in the patient. They also have a greater possibility of contamination during production and lower overall stability. Modified live virus vaccines must have careful attention paid to proper temperature and storage conditions.

A recombinant vaccine contains a pathogen in which the genetic material has been artificially modified. This alteration usually involves deleting all or part of a gene or inserting one or more genes from another organism. There are three different kinds of recombinant vaccines. A small portion of the protein can be removed and act as the antigen (subunit vaccine), the part of the pathogen that causes the disease can be removed or rendered inactive (gene-deleted vaccines), or the genes that produce an immune response are removed from the pathogen and inserted into a non-pathogenic vector vaccine (vectored vaccine). The advantage of recombinant vaccines is that they only contain pieces of the wild-type virus and cannot revert to a pathogenic virus. Also, testing can often distinguish between animals that have been vaccinated and those infected naturally. Recombinant technology has allowed these vaccines to prompt a robust immune response and be manufactured without adjuvants.

ADVERSE REACTIONS

Possible adverse vaccination events include mild reactions such as local inflammation, swelling, pain, irritation, hair loss, abscess formation, or simply a failure to immunize. More severe reactions include anaphylaxis, immunosuppression, autoimmune disorders, transient infections, the development of long-term carrier states, and local development of tumors. After vaccination, patients commonly experience mild fever, decreased appetite, or lethargy lasting one or two days. Rare vaccine-related outcomes include hypertrophic osteodystrophy, juvenile cellulitis associated with the modified-live virus distemper vaccine, and feline injection-site sarcoma.

Anaphylaxis is a rare, life-threatening, immediate allergic reaction to something ingested or injected that can result in shock, respiratory and cardiac failure, coma, and death. An anaphylactic reaction to a vaccine usually occurs within minutes to hours of the vaccination. The sudden onset of diarrhea, vomiting, seizures, facial swelling, hives, and signs of shock such as pale mucous membranes, prolonged capillary refill time, tachycardia, and hypotension may characterize it. Treatment of anaphylaxis may include administration of an antihistamine, corticosteroid, and epinephrine, IV fluid therapy, and continued monitoring and observation.

Feline injection-site sarcoma (FISS) is a rare but serious adverse reaction in cats. Adjuvanted vaccines have been implicated in FISS formation because they trigger a more significant inflammatory response, but this is controversial. Administering vaccines at the recommended sites assists in identifying the likely causative agent for local reactions and neoplasia and aids in management after a sarcoma has formed. The American Association of Feline Practitioners (AAFP) recommends that subcutaneous administration of FPV, FHV-1, and FCV vaccines be limited to the right forelimb below the elbow joint, rabies to the right rear limb below the stifle, and FeLV or FIV to be limited to the left rear limb below the stifle. This recommendation to administer vaccines in the distal limbs of cats has reduced the presence of sarcomas in the scapular area. Although the recommended administration sites have aided in identifying sarcomas, an unintended result of these changed vaccine sites is that there may be an increase in sarcomas found in the flank area. When a cat crouches during vaccine administration, the cat's skin is loose, and the vaccine may inadvertently be given in the lateral abdomen instead of the limb. This indicates a need for increased precision during vaccination. Following injectable vaccine site recommendations is an essential factor in reporting the number of cases of FISS and aids in research.

If a pet has any type of vaccine reaction, record the event in the medical record so that certain vaccines are no longer administered in the future or preventive measures can be taken. The American Veterinary Medical Association (AVMA) and World Small Animal Veterinary Association (WSAVA) encourage the reporting of any adverse events to the vaccine manufacturer and regional/governmental oversight committees such as the U.S. Department of Agriculture's Center for Veterinary Biologics (CVB). Reporting all adverse events will aid in monitoring and recognizing trends in the adverse effects of vaccination.

TITERS

Many veterinary diagnostic laboratories offer serum titers as an alternative to routine vaccination. Depending on the individual lab and the interpretation of various levels, the results may come back "protective" (high antibody titer), "not protective" (low or zero titer), or sometimes "low normal" or "borderline". Due to variations in lab assays, different reference ranges, and other factors, titers should not be compared between different laboratories. Diagnostic tests are available to assess antibody titers against canine distemper (CDV) and canine parvovirus (CPV). A high titer confirms protection against infection, but even if a titer is considered low, exposure to the same antigen may produce a rapid immune response with new antibodies produced within days or even hours. These animals might be susceptible to infection but, more commonly, are fully protected due to the memory capacity of the immune system and cell-mediated immunity. One must also consider that titers are only a snapshot in time. If titers are consistent with protective immunity, how rapidly they may fall to unprotective levels

is unknown. Also, it should be noted that titers only measure humoral immunity and do not measure cell-mediated immunity or the protection that the innate immune system provides.

RESOURCES

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