Update on Prevention of Select Infectious Diseases in Dogs and Cats

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Abstract. In these 2 lectures, the most important recommendations concerning prevention of infectious diseases, including the importance of flea and tick control, how to easily do strategic deworming, and how to optimize vaccine use and minimize vaccine side effects will be reviewed. The objectives of the lectures are:

1.   To understand the importance of preventative health visits.
2.   To review optimal vaccination protocol for dogs.
4.   To review optimal vaccination protocols for cats.
5.   To learn the new information about vaccine sarcomas in cats.
6.   To discuss vaccine side effects in dogs and cats

Keywords.   Tick, flea, vaccine, deworming.

Infectious diseases are a very common part of companion animal veterinary medicine. Some of the infectious agents can result in severe clinical disease, including death; canine parvovirus, leptospirosis, and feline panleukopenia are notable examples. Other infections have less severe manifestations during the acute phase, but can have long term sequelae of clinical significance; examples include Lyme polyarthritis and chronic upper respiratory infections induced by FHV-1 and FCV.

Of even more importance are infections that are shared between animal and man; the zoonoses. Rabies virus and *Bartonella henselae*, the cat scratch disease agent, are common examples. Use of vaccines and parasite control products in comprehensive wellness programs can lessen risk of infectious diseases in dogs and cats. However, some pet owners and veterinarians are still worried about vaccine associated side-effects which may limit clinic visits and compliance to veterinarian recommendations.

Preventing infections is always preferred over treating infections. Deworming guidelines and information concerning vector borne disease agent control is available from the Companion Animal Parasite Council (www.capcvet.org). Avoiding exposure is the most effective way to prevent infections. All puppies and kittens should be dewormed for roundworms and hookworms. Flea and tick control is indicated for most dogs and cats, year round for optimal preventative effects.

Most infectious agents of dogs and cats are transmitted in fecal material, respiratory secretions, reproductive tract secretions, or urine; by bites or scratches; or by contact with vectors or reservoirs. Some infectious agents such as FHV-1, *Bordetella bronchiseptica*, and canine influenza viruses can be transmitted by direct contact with clinically normal, infected animals. Many infectious agents are environmentally resistant and can be transmitted by contact with a

contaminated environment (fomites).

The avoidance of zoonotic transfer of infectious agents is extremely important because some zoonotic diseases, such as plague and rabies, are life threatening. Recognition of risk factors associated with infectious agents is the initial step in the prevention of infectious diseases. Veterinarians should strive to understand the biology of each infectious agent so they can counsel clients and staff on the best strategies for prevention.

Vaccines available for some infectious agents can prevent infection or lessen clinical illness when infection occurs. However, vaccines are not uniformly effective, are not available for all pathogens, and sometimes induce serious adverse effects. Therefore the development of sound biosecurity procedures is paramount to avoid exposure to infectious agents when developing a preventive medicine program.

Vaccines are available for some infectious agents of dogs and cats and can be administered to prevent infection or limit disease depending on the agent. Vaccination stimulates humoral, mucosal, or cell-mediated immune responses. Humoral immune responses are characterized by the production of immunoglobulin M (IgM), IgG, IgA, and IgE class antibodies, which are produced by B-lymphocytes and plasma cells after being presented an antigen by macrophages. Binding of antibodies to an infectious agent or its toxins helps prevent infection or disease by facilitating agglutination (viruses), improving phagocytosis (opsonization), neutralizing toxins, blocking attachment to cell surfaces, initiating the complement cascade, and inducing antibody-dependent cell-mediated cytotoxicity. Antibody responses are most effective in controlling infectious agents during extracellular replication or toxin production. Cell-mediated immune responses are mediated principally by T-lymphocytes. Antigen-specific T-lymphocytes either destroy the infectious agent or mediate destruction of the agent by producing cytokines that stimulate other white blood cells, including macrophages, neutrophils, and natural killer cells. Cell-mediated immunity is required for the control of most cell-associated infections. Currently available vaccines are either infectious (attenuated [modified-live] organisms or live virus–vectored recombinant vaccines) or noninfectious (killed virus, killed bacteria [bacterins], and subunit vaccines).

Attenuated vaccines replicate in the host to effectively stimulate an immune response and therefore generally have low antigen mass and do not require adjuvants. Different products are administered locally (e.g., modified-live *Bordetella bronchiseptica* oral vaccine or intranasal FHV-1 and FCV vaccines) or parenterally (e.g., modified-live canine distemper vaccine). In live virus–vectored recombinant vaccines, the specific DNA that codes for the immunogenic components of the infectious agent is inserted into the genome of a nonpathogenic organism (vector) that will replicate in the species being vaccinated. As the vector replicates in the host, it expresses the immunogenic components of the infectious agent, resulting in the induction of specific immune responses. Because the virus-vectored vaccine is live and replicates in the host, adjuvants and high-antigen mass are not required. Because only DNA from the infectious agent is incorporated into the vaccine, no risk of reverting to the virulent parent strain exists, as occasionally occurs with attenuated vaccines. Only vectors that do not induce disease in the animal being vaccinated are used. Another advantage to vaccines of this type is the potential ability to overcome inactivation by maternal antibodies.

Killed virus, killed bacteria (bacterins), and subunit vaccines are noninfectious and therefore usually require higher antigen mass than infectious vaccines to stimulate immune responses because they do not replicate in the host. Some noninfectious vaccines may stimulate immune responses of lesser magnitude and shorter duration than infectious vaccines unless adjuvants are added. Adjuvants improve immune responses in part by stimulating uptake of antigens by macrophages that present the antigens to lymphocytes. Although adjuvants have historically been associated with vaccine adverse effects, most newer generation adjuvants induce less inflammation. Subunit vaccines can be superior to killed vaccines that use the entire organism because only the immunogenic parts of the organism are used, which may decrease the potential for vaccine reactions. However, for some infections use of only one antigen does not adequate induce adequate protection (e.g. feline calicivirus vaccines). Native DNA vaccines and gene-deleted vaccines are currently being evaluated for several infectious diseases.

VACCINE SELECTION

Selection of optimal vaccines for use in dogs and cats is complicated. Multiple products for most infectious agents are available, but efficacy studies that directly compare different products are often lacking. The veterinarian may need to choose from infectious and noninfectious options for the same vaccine antigen. Some vaccine antigens are for intranasal or oral administration and others are for parenteral administration. Not all vaccines for a given infectious disease are comparable in every situation. Long-term duration of immunity studies and studies evaluating a vaccine's ability to block infection by multiple field strains are not available for all individual products. When making decisions about which products to use or when evaluating a new vaccine, the practitioner should request information concerning efficacy, challenge studies, duration of immunity studies, adverse reactions, and cross-protection capability. Vaccine issues are commonly debated in veterinary journals and continuing education meetings; these are excellent sources of current information.

Not all dogs and cats need all available vaccines. Vaccines are not innocuous and should only be given if indicated. The type of vaccine and route of administration for the disease in question should also be considered. A benefit, risk, and cost assessment should be discussed with the owner of each individual animal before determining the optimal vaccination protocol. For example, FeLV only lives outside the host for minutes; it is highly unlikely that an owner would bring the virus into the household. Therefore cats housed indoors are not likely to come in contact with the virus.

Before administering vaccines, the animal should be evaluated for factors that may influence the ability to respond to the vaccine or that may affect whether vaccination could be detrimental. Hypothermic animals have poor T-lymphocyte and macrophage function and are unlikely to respond appropriately to vaccination. Dogs with body temperature above 39.7° C respond poorly to canine distemper virus vaccines; this may be true for other vaccines as well. Immunosuppressed animals, including those with FeLV infection, FIV infection, canine parvovirus infection, *Ehrlichia canis* infection, and debilitating diseases, may not respond appropriately to vaccination; modified-live vaccines occasionally induce the disease in these animals.

If high levels of specific antibodies are present, vaccine efficacy is diminished. This is a particularly important consideration when vaccinating puppies or kittens from well-vaccinated dams. Disease may also develop in vaccinated puppies and kittens because infection had already occurred and was incubating when the animal was vaccinated. Vaccines can be rendered ineffective from mishandling. Vaccines should not be administered while the animal is under anesthesia because efficacy can be diminished; if a vaccine reaction occurs, it may be masked by the anesthesia.

Adverse reactions can potentially occur with any vaccine. However, they are relatively uncommon in dogs and cats. In a study of more than 1.2 million dogs, the overall rate of adverse reactions was 38.2/10,000 dogs that had received vaccines within the previous 3 days (Moore et al., 2005). In a study of 496,189 cats, the overall rate of adverse reactions was 51.6/10,000 cats that had received vaccines within the previous 30 days (Moore et al., 2007). Vaccination has been associated with injection site sarcomas in some cats and can be life threatening. These tumors can occur after administration of infectious or noninfectious vaccines (Dyer et al, 2008), but to date studies attempting to link different vaccine types or individual products to tumor formation have had variable results (Kass et al, 2003; Srivastav et al, 2012). Injection site sarcomas have developed after administration of other substances including parasiticides, long lasting glucocorticoids, meloxicam, cisplatin, antibiotics, and microchips. It is apparent that tumor development may relate to a genetic predisposition but P53 gene testing has not provided definitive results in all cases (Banerji et al, 2007; Muncha et al, 2012). Currently, the optimal way to avoid injection site sarcomas is to administer only products absolutely indicated by this route, including using the longest vaccination interval that is acceptable for the vaccine used. Intranasal products can result in transient sneezing and coughing. Vaccine side effects and vaccination associated sarcomas in cats have recently been reviewed (Kass, 2018; Gershwin 2018).

Feline vaccines for which the viruses were grown on cell cultures induce antibodies that cross-react with feline renal tissues (Lappin et al., 2005), and some hypersensitized cats have developed lymphocytic-plasmacytic interstitial nephritis (Lappin et al., 2006b). The immunodominant cell line antigen recognized by parenterally vaccinated cats is alpha enolase which is present in all mammalian cells (Whittemore et al, 2010). In people, anti-enolase antibodies are markers for immune-mediated disease, including nephritis. It is unclear whether post-vaccination or naturally occurring anti-enolase antibodies are associated with nephritis in cats. However, it appears that FVRCP vaccines should not be given annual as they are not needed and may be associated with a significant side effects. In a recent paper, the major findings that associated with CKD in cats were severity of dental disease and frequency of vaccination (Finch et al, 2016).

Suspected adverse reactions to vaccination should be reported. Administration of any vaccine to animals with proven vaccine-associated sarcoma or immune-mediated diseases, such as immune-mediated polyarthritis, immune-mediated hemolytic anemia, immune-mediated thrombocytopenia, glomerulonephritis, or polyradiculoneuritis, is questionable because immune stimulation may exacerbate these conditions. However, the potential legal ramifications of waiving vaccination in these patients should be discussed with the owners. This is primarily of

importance for rabies vaccination.

For some infectious agents, including canine distemper virus, canine parvovirus, feline panleukopenia virus (FPV), feline calicivirus (FCV), and FHV-1, serologic test results have been shown to correlate to resistance to disease after challenge in some studies. The advantages and disadvantages of the use of serologic testing have been reviewed (Moore et al., 2006). If validated laboratories or kits are used, results can be used accurately to make vaccination decisions for some dogs and cats (Lappin et al., 2002). For example, previously vaccinated animals that were presumed to have had a vaccine reaction and are still at risk of exposure to infectious agents could be assessed by serologic testing in lieu of arbitrary vaccination. In general, the positive predictive value of these tests is good (i.e., a positive test result usually predicts resistance on challenge).

INFECTIOUS DISEASE PREVENTION GUIDELINES FOR CATS

A physical examination, fecal parasite screen, and assessment of vaccine needs should be performed at least yearly for all cats. The American Association of Feline Practitioners (AAFP) Feline Vaccine Advisory Panel produces vaccine recommendations for cats (*http://www.catvets.com*). These guidelines are an excellent source of information for veterinarians when individualizing vaccination protocols. Vaccine antigens were divided into those that were considered core (FPV, FCV, FHV-1), noncore (rabies, FeLV, FIV, *Bordetella bronchiseptica*, *Chlamydia felis*, and feline infectious peritonitis [FIP]). In contrast to previous AAFP Panel Reports, rabies vaccines are no longer considered core as the guidelines are meant to be suitable for cats living worldwide and rabies is not endemic in all countries. Other sources for feline vaccine administration recommendations include the ABCD guidelines in Europe (Truyen et al 2009; http://abcd-vets.org/Pages/guidelines.aspx) and the WSAVA guidelines (Day et al, 2007; http://www.wsava.org/VGG1.htm). Cats should be administered flea control and periodic deworming, year round (www.capcvet.org). Heartworm preventatives that control hookworms, roundworms, and *C. felis* are great choices for routine parasite prevention. Advantage Multi and Seresto collars (Bayer Animal Health) has been shown to block the transmission of *Bartonella henselae* (cat scratch disease agent) amongst cats.

Core Vaccines

Feline Panleukopenia Virus, Feline Calicivirus, Feline Herpesvirus-1. All healthy kittens and adult cats without a known vaccination history should be routinely vaccinated with an intranasal or parenteral vaccine that contains FPV, FCV, and FHV-1 (FVRCP). Multiple modified-live products and one inactivated product are available, but they vary by country. In general, modified-live FVRCP vaccines are recommended for kittens housed in environments at high risk for exposure to FPV, as this type of vaccine is least likely to be inactivated by antibodies transferred to the kitten as part of maternally derived immunity. Inactivated FVRCP vaccines have the advantage of not replicating in the host and so are safe for administration to pregnant queens and do not colonize the host. Modified-live FVRCP vaccines for intranasal administration can induce protection against FHV-1 as soon as 4 days after administration, so this route may be preferred for kittens housed in environments at high risk for exposure to FHV-1 (Lappin et al., 2006a). The inactivated FVRCP vaccine induced faster serological responses to

FHV-1 than a modified live product in one study (Lappin et al, 2012). In a recent challenge study, we showed the inactivated FHV-1 vaccine to work as quickly as a MLV vaccine for protection against FHV-1. Modified-live products should not be administered to clinically ill, debilitated, or pregnant animals. Owners should be informed that the administration of intranasal FVRCP vaccines can induce transient, mild sneezing or coughing.

For kittens believed to have no more than routine risk of exposure to FPV, FCV, or FHV-1, administration of FVRCP vaccines is recommended starting no sooner than 6 weeks of age, with boosters every 3 to 4 weeks until 16 weeks of age. Older kittens and adult cats with unknown vaccination history should receive two killed or two modified-live FVRCP doses 3 to 4 weeks apart.

For kittens believed to have high risk of exposure to FPV, such as those housed in animal shelters or pet stores, modified-live FPV-containing vaccines can be administered as early as 4 weeks of age, particularly during an outbreak. However, intranasal administration of modified-live FVRCP vaccines instead of or in addition to parenteral administration of modified-live FVRCP vaccines may be superior for protection against FCV and FHV-1 in these environments. The current AAFP/ISFM Advisory Panel recommends a booster FVRCP vaccine 1 year later. According to several challenge studies, administration of FVRCP vaccines does not appear to be needed more frequently than every third year after the 1-year booster vaccine; the duration of immunity may be much longer, particularly for FPV. As previously discussed, serologic test results for antibodies against FPV, FCV, and FHV-1 can be used to help determine vaccine needs (Lappin et al., 2002).

Some variants of FCV induce systemic vasculitis in cats (virulent systemic calicivirus; VS-FCV), and clinical signs can be severe in some cats even if previously vaccinated with FVRCP vaccines (Hurley et al., 2004). Products containing two FCV strains, including a VS-FCV strain, are now available in the United States. Serum from cats vaccinated with this product has been shown to cross neutralize more FCV field strains than serum from cats vaccinated with products containing only one FCV strain (Huang et al, 2010). Similar results have been seen with a different FCV vaccine containing two strains that is marketed in Europe.

Optional Vaccines

Bordetella bronchiseptica. The currently available *Bordetella bronchiseptica* vaccine for intranasal administration can be administered as early as 4 weeks of age, has an onset of immunity as early as 72 hours, and has a minimal duration of immunity of 1 year. Many cats have antibodies against *B. bronchiseptica,* the organism is commonly cultured from cats in crowded environments, and sporadic reports have been made of severe lower respiratory disease caused by bordetellosis in kittens and cats in crowded environments or other stressful situations. However, the significance of infection in otherwise healthy pet cats appears to be minimal. For example, in client-owned cats in north-central Colorado, the organism was rarely cultured from cats with rhinitis or lower respiratory disease (approximately 3%). In addition, because the vaccine is administered by the intranasal route, mild sneezing and coughing can result. *Bordetella* vaccination should be considered primarily for use in cats at high risk for exposure and disease, such as those with a history of respiratory problems and living in shelters with

culture-proven outbreaks. Because the disease is apparently not life threatening in adult cats, is uncommon in pet cats, and responds to a variety of antibiotics, routine use of this vaccine in client-owned cats seems unnecessary.

Chlamydia felis. Killed and modified-live *Chlamydia felis*–containing vaccines are available. Infection of cats by *C. felis* generally results in only mild conjunctivitis, is easily treated with antibiotics, has variable prevalence rates, and the organism is of minimal zoonotic risk to people. In addition, use of FVRCP vaccines that also contained *C. felis* was associated with more vaccine reactions in cats when compared with other products (Moore et al., 2007). Thus whether *C. felis* vaccination is ever necessary is controversial. The use of this vaccine should be reserved for cats with a high risk of exposure to other cats and in catteries with endemic disease. Duration of immunity for *Chlamydia* vaccines may be short-lived, so high-risk cats should be immunized before a potential exposure.

Feline Leukemia Virus. Multiple FeLV-containing vaccines are currently available. Some contain killed FeLV with and without adjuvants, and one contains recombinant antigens of FeLV without adjuvant. . Because of difficulties in assessing efficacy studies that are performed with different experiment designs, which FeLV vaccine is optimal is unclear. In several studies, the preventative fraction was 100% for cats administered FeLV vaccines then undergoing a heterogenous FeLV challenge one year after the last booster. In the United States, one FeLV vaccine was granted a 2 year label. At the 2 year challenge in one study, 83% of the vaccinated cats remained FeLV negative (Jirjis et al, 2011). Recently, the canarypox-vectored FeLV was show to be inferior to a whole virus vaccine. The AAFP/ISFM panel recommended vaccinating kittens for FeLV because they are more susceptible than adult cats, and their housing status may not have been determined at that time. Although administration of FeLV vaccines does not block proviral integration, FeLV-associated disease was lessened (Hofman-Lehmann et al., 2007). FeLV vaccines are most indicated in cats allowed to go outdoors or those who are exposed to cats of unknown FeLV status. Vaccinated cats should receive two vaccinations initially. FeLV vaccines should be administered subcutaneously in the distal left rear limb to aid in identification and management of injection site disease. Although the products without adjuvants are known to induce less inflammation, whether they are safer than the products containing adjuvants is currently unknown. FeLV vaccines are not effective in cats with progressive viremia and are therefore not indicated. However, administration of the vaccine to viremic or latently infected cats does not pose an increased risk of vaccine reaction. FeLV testing should be performed before vaccination because the retrovirus serologic status of all cats should be known so appropriate husbandry can be maintained.

Feline Infectious Peritonitis. A relatively safe coronavirus vaccine that may protect some cats from developing FIP is currently available for administration after 16 weeks of age. The vaccine may result in mild, transient sneezing because it is administered intranasally. Antibody-dependent enhancement of infectivity has not been detected in field studies. Results of the vaccine in field studies have been variable. If cats have previously been exposed to coronaviruses, the vaccine is unlikely to be effective. Because the incidence of disease is low, cats are commonly exposed to coronaviruses before vaccination and the efficacy is questionable. The AAFP/ISFM panel considered this vaccine as non-core. The vaccine may be indicated for seronegative cats entering a known FIP-infected household or cattery.

Rabies. All cats in endemic countries, including the United States, should be vaccinated against rabies. Rabies vaccine should be administered subcutaneously in the distal right rear limb at the age recommended by the vaccine manufacturer (as early as 8 weeks depending on brand) in accordance with state and local statutes. Cats should be vaccinated one year later and then either annually or triennially according to state and local statutes and the vaccine product used for the initial immunization. A live virus–vectored rabies vaccine with a one-year label is available in some countries. This product induces less inflammation than inactivated rabies vaccines that contain adjuvants, but whether this vaccine is less likely to be associated with injection site sarcomas is currently unknown. A good website showing state by state rabies information is available (http://www.rabiesaware.org/).

VACCINATION PROTOCOLS FOR DOGS

A physical examination, fecal parasite screen, and vaccine needs assessment should be performed at least yearly for all dogs. The American Animal Hospital Association recently published the revised version of vaccination guidelines for dogs (www.aaha.org) that also included recommendations for use of canine vaccines in shelters. These guidelines are an excellent source of information for veterinarians to use when individualizing a vaccination protocol for dogs. Different forms of vaccine antigens were divided into those that were considered core, noncore, and not recommended. For the *Crotalus atrox* toxoid, the Task Force chose to take no position because of a lack of experience and paucity of field validation of efficacy. The WSAVA guidelines are another excellent source for canine vaccine administration recommendations (http://www.wsava.org). Dogs should be administered flea and tick control products and periodic deworming, year round (www.capcvet.org).

Core Vaccines

Canine Parvovirus, Canine Adenovirus, and Canine Distemper Virus. Because canine parvovirus (CPV-2), canine adenovirus 1 (CAV-1; infectious canine hepatitis), and canine distemper virus (CDV) can be life-threatening diseases, all dogs should be vaccinated. For CPV-2, only modified-live products should be used because of increased risk of maternal antibody interference with killed products. Both modified-live CDV and recombinant CDV (rCDV)-containing vaccines are considered adequate by the AAHA Task Force. Because of adverse effects associated with CAV-1 vaccines and poor immune responses associated with killed CAV-2 or modified-live topical CAV-2 vaccines, only modified-live CAV-2 vaccines for parenteral administration should be used. These vaccines cross-protect against canine infectious hepatitis induced by CAV-1 and the kennel cough syndrome induced by CAV-2. All puppies should receive at least three CPV-2, CAV-2, and CDV-containing vaccines, every 3 to 4 weeks, between 6 and 16 weeks of age, with the last booster being administered at 14 to 16 weeks of age. There is no documented breed predisposition to vaccine failure and so no indication for administering the final CPV-2, CAV-2, and CDV-containing vaccine booster after 16 weeks of age. Adult dogs with an unknown vaccination history can be given one dose of MLV CPV-2, CAV-2, and CDV-containing vaccines.. Puppies housed in shelters should be vaccinated on admission and then every 2 weeks while housed at the shelter or until 16 weeks of age. Vaccinated dogs should receive a booster vaccine 1 year later and then boosters at intervals of 3

years or longer. Several CDV-containing products, including the rCDV vaccine, were recently shown to protect for at least 3 years (Abdelmagid et al., 2004; Larson et al., 2007).

Dogs should be evaluated at least yearly for risk of infection by CPV, CDV, and CAV during the physical examination, checked for enteric parasites, and evaluated for *D. immitis* infection in appropriate regions. Positive serologic tests for CDV and CPV are predictive of resistance after challenge and can be used in lieu of arbitrary vaccine intervals if performed with validated assays. Dogs should complete the puppy series and be boosted at 1 year of age before using titers to help predict vaccine need. If the vaccination status of an adult dog is unknown, the dog should be vaccinated appropriately and then serologic assessment considered in subsequent years.

Rabies. All dogs should be given a one-year or three-year rabies vaccine following the manufacturer's recommendations as early as 12 weeks of age and based on state, provincial, and or local requirements. Both puppies and adult dogs with unknown vaccination history should receive one dose and return for a booster vaccination 1 year later. Intervals and product after that booster should be based on state and local statutes.

Optional Vaccines

Bordetella bronchiseptica. In general, *B. bronchiseptica* rarely causes life-threatening disease in otherwise healthy animals and is not the only cause of kennel cough syndrome. It is therefore considered a noncore vaccine. In addition, genetic information suggests that field strains of the bacterium vary considerably from vaccine strains, which may affect vaccine efficacy. Although parenteral products induce strong serum antibody responses, in one study intranasal administration was associated with superior protection on challenge (Davis et al., 2007). A product that can be given orally is now available in the United States and is very effective and was shown to be superior to parenteral vaccination in one study (Bronchi-Shield-Oral®; Boehringer-Ingelheim). Booster vaccines should optimally be administered 7 days before potential exposure. No more than two boosters are needed per year.

Borrelia burgdorferi. The pros and cons of administering *B. burgdorferi* vaccines were discussed in depth in a recent American College of Veterinary Internal Medicine Consensus Statement (Littman et al., 2006; *http://www.acvim.org*). The AAHA Task Force suggested that *B. burgdorferi* vaccination only be considered in dogs with a known high risk of exposure (Wellborn et al, 2011). The American College of Veterinary Internal Medicine also has a Lyme Consensus Statement (Littman et al, 2018). Depending on the product used, vaccination can start at 9 or 12 weeks of age and a second dose is recommended 2 to 4 weeks later, with annual boosters. Vaccination will not likely benefit a dog positive for antibody against the C6 peptide because most C6 antibody–positive dogs have already been infected. Whether vaccination protects against or is associated with Lyme nephropathy is unknown; the syndrome has been detected both in vaccinated and nonvaccinated dogs. Maintaining tick control is an important part of prevention of this disease.

Canine influenza. Canine influenza vaccine (killed virus; either H3N8 or H3N2 or combination) should be administered no earlier than 6 weeks of age, with a second dose dose 2–4 weeks later. A single dose will not immunize a seronegative dog. Not all areas are considered

endemic for these viruses and United States practitioners should contact their state veterinarian or state diagnostic laboratory to inquire about documented cases. Use in high risk dogs in endemic states should be considered, particularly those kenneled frequently and those is stressful situations like racing greyhounds. In a recent ACVIM abstract, our research showed that 1 dose of H3N2 vaccine (Zoetis) gave partial protection against clinical signs as early as 7 days after vaccination.

Distemper-Measles Virus. This modified live product was used previously between 4 and 12 weeks of age to attempt to breakthrough maternal immunity to CDV. The need for this product is now in question because the rCDV vaccine immunizes puppies in the presence of maternal immunity.

Leptospira interrogans. Vaccines containing multiple *Leptospira interrogans* serovars (canicola, icterohaemorrhagiae, grippotyphosa, and pomona) are generally recommended for dogs with high risk in known endemic areas. However, some serovars in the environment are not in any vaccine, and minimal cross-protection exists between serovars. Thus clients should realize that even though their dog has been given a *Leptospira* vaccine, 100% protection cannot be guaranteed. Newer generation vaccines have fewer adverse effects than previous vaccines. If the vaccines are to be used, puppies should receive the first dose at 12 weeks of age with a booster 2 to 4 weeks later. Adults should receive two doses 2 to 4 weeks apart. Annual revaccination is recommended for vaccines containing the four serovars. MAT titers generally do not last 12 months, but protection is usually present from cell mediated immune responses for at least 12 months with some vaccines.   Protection was documented to 15 months in dogs vaccinated in one study (Grosenbaugh et al, 2018).   Side-effects with current Leptospira spp. vaccines are unusual.

Parainfluenza virus. Multiple products that contain CPV-2, CDV, and CAV-2 also contain modified-live parainfluenza, so they are commonly administered at the same schedule of those core vaccine antigens. Considered alone, parainfluenza is noncore because it is not life threatening, is not zoonotic, and is a self-limited cause of kennel cough syndrome. A modified-live strain for intranasal administration combined with a live avirulent strain of *B. bronchiseptica* and with canine adenovirus 2 are also available. If used, the intranasal vaccine can be administered as early as 3 weeks of age; transient sneezing and coughing can occur. Booster vaccines are administered following the same schedule as the antigens in which parainfluenza is combined.

Rattlesnake Vaccine. The *Crotalus atrox* toxoid vaccine was designed to protect dogs against the venom of the Western Diamondback Rattlesnake. Some cross-protection may exist against the Eastern Diamondback Rattlesnake but not the Mojave Rattlesnake. Local reactions to this toxoid are common. The AAHA Task Force stated the vaccine should only be used in dogs with a defined risk of exposure. If used, practitioners should follow the manufacturer's label.

Not Recommended. As previously discussed, killed CPV-2 vaccines, MLV or killed CAV-1 vaccines, killed CAV-2 vaccines, modified-live CAV-2 vaccines for topical administration, Leptospire vaccines that contain 2 serovars, and canine coronavirus vaccines are currently not recommended.

Suggested Readings

Abdelmagid OY et al: Evaluation of the efficacy and duration of immunity of a canine combination vaccine against virulent parvovirus, infectious canine hepatitis virus, and distemper virus experimental challenges, *Vet Ther* 5:173, 2004.

Appel MJ: Forty years of canine vaccination, *Adv Vet Med* 41:309, 1999.

Banerji N, Kanjilal S. Somatic alterations of p53 tumor suppressor gene in vaccine-associated feline sarcoma. *Am J Vet Res* 2006;67:1766–1772.

Banerji N, Kapur V, Kanjilal S. Association of germ-line polymorphisms in the feline p53 gene with genetic predisposition to vaccine-associated feline sarcoma. *J Hered* 2007;98:421–427.

Carminato A, Vascellari M, Marchioro W, et al. Microchip-associated fibrosarcoma in a cat. *Vet Dermatol* 2011;doi: 10.1111/j.1365-3164.2011.00975.x.

Daly MK, Saba CF, Crochik SS, et al. Fibrosarcoma adjacent to the site of microchip implantation in a cat. *J Feline Med Surg* 2008;10:202–205.

Davis R et al: Comparison of the mucosal immune response in dogs vaccinated with either an intranasal avirulent live culture or a subcutaneous antigen extract vaccine of *Bordetella bronchiseptica*, *Vet Therapeutics* 8:1, 2007.

Day MJ. Vaccine side effects: fact and fiction. *Vet Microbiol* 2006;117:51–58.

Day MJ, Horzinek MC, Schultz RD, et al. Guidelines for the vaccination of dogs and cats. Compiled by the Vaccination Guidelines Group (VGG) of the World Small Animal Veterinary Association (WSAVA). *J Small Anim Pract* 2007;48:528–541.

Dodds WJ: Vaccination protocols for dogs predisposed to vaccine reactions, *J Am Anim Hosp Assoc* 37:211, 2001.

Duval D et al: Vaccine-associated immune mediated hemolytic anemia in the dog, *J Vet Intern Med* 10:290, 1996.

Dyer F, Spagnuolo-Weaver M, Cooles S, Tait A. Suspected adverse reactions, 2007. Veterinary Record, July 19, 2008, pp 69-72.

Fehr D et al: Placebo-controlled evaluation of a modified live virus-vaccine against feline infectious peritonitis-safety and efficacy under field conditions, *Vaccine* 15:1101, 1997.

Finch NC, Syme HM, Elliott J. Risk factors for development of chronic kidney disease in cats. J Vet Intern Med. 2016;30:602-610.

Gershwin LJ. Adverse Reactions to Vaccination: From Anaphylaxis to Autoimmunity. Vet Clin North Am Small Anim Pract. 2018;48:279-290.

Gore TC et al: Three-year duration of immunity in cats following vaccination against feline rhinotracheitis virus, feline calicivirus, and feline panleukopenia virus, *Vet Therapeutics* 7:213, 2006.

Greene CE et al: Canine vaccination, *Vet Clin North Am Small Anim Pract* 31:473, 2001.

Grosenbaugh DA, Pardo MC. Fifteen-month duration of immunity for the serovar Grippotyphosa fraction of a tetravalent canine leptospirosis vaccine. Vet Rec. 2018;182:665.

Hofmann-Lehmann R et al: Vaccination against the feline leukaemia virus: outcome and response categories and long-term follow-up, *Vaccine* 25:5531, 2007.

Horzinek MC: Vaccine use and disease prevalence in dogs and cats, *Vet Microbiol* 117:2, 2006.

Huang C, Hess J, Gill M, et al. A dual-strain feline calicivirus vaccine stimulates braoder cross-neutralisation antibodies than a single-strain vaccine and lessens clinical signs in vaccinated cats when challenged with a homologous feline calicivirus strain associated with virulent systemic disease. *J Feline Med Surg* 2010;12:129–137.

Hurley KE et al: An outbreak of virulent systemic feline calicivirus disease, *J Am Vet Med Assoc* 224:241, 2004.

Jirjis F, Davis T, Lane J, Carritt K, Sweeney D, Williams J, Wasmoen T. Protection against feline leukemia virus challenge for at least 2 years after vaccination with an inactivated feline leukemia virus vaccine. Vet Ther. 2010;11:E1-6.

Kass PH et al: Epidemiologic evidence for a causal relationship between vaccination and fibrosarcoma tumorigenesis in cats, *J Am Vet Med Assoc* 203:396, 1993.

Kass PH, et al. Multicenter case-control study of risk factors associated with development of vaccine-associated sarcomas in cats. J Am Vet Med Assoc 2003;223:1283–1292.

Kass PH. Prevention of feline injection-site sarcomas: is there a scientific foundation for vaccine recommendations at this time? Vet Clin North Am Small Anim Pract. 2018 Mar;48:301-306.

Lappin MR. Feline panleukopenia virus, feline herpesvirus-1 and feline calicivirus antibody responses in seronegative specific pathogen-free kittens after parenteral administration of an inactivated FVRCP vaccine or a modified live FVRCP vaccine. *J Fel Med Surg* 2012;14:161–164.

Lappin MR et al: Use of serologic tests to predict resistance to feline herpesvirus 1, feline calicivirus, and feline parvovirus infection in cats, *J Am Vet Med Assoc* 220:38, 2002.

Lappin MR et al: Investigation of the induction of antibodies against Crandall Rees feline kidney cell lysates and feline renal cell lysates after parenteral administration of vaccines against feline viral rhinotracheitis, calicivirus, and panleukopenia in cats, *Am J Vet Res* 66:506, 2005.

Lappin MR et al: Effects of a single dose of an intranasal feline herpesvirus 1, calicivirus, and panleukopenia vaccine on clinical signs and virus shedding after challenge with virulent feline herpesvirus 1, *J Fel Med Surg* 8:158, 2006a.

Lappin MR et al: Interstitial nephritis in cats inoculated with Crandall Rees feline kidney cell lysates, *J Feline Med Surg* 8:353, 2006b.

Lappin MR, Veir J, Hawley JR. Feline panleukopenia virus, feline herpesvirus-1, and feline calicivirus antibody responses in seronegative specific pathogen-free cats after a single administration of two different modified live FVRCP vaccines. *J Fel Med Surg* 2009 11:159.

Larson LJ et al: Effect of vaccination with recombinant canine distemper virus vaccine immediately before exposure under shelter-like conditions, *Vet Ther* 7:113, 2006.

Larson LJ et al: Three-year duration of immunity in dogs vaccinated with a canarypox-vectored recombinant canine distemper virus vaccine, *Vet Therapeutics* 8:101, 2007.

Larson LJ, et al: A comparative study of protective immunity provided by oral, intranasal and parenteral canine *Bordetella bronchiseptica* vaccines. *Intern J Appl Res Vet Med* 2013;11:153.

Levy J, Crawford C, Hartmann K, Hofmann-Lehmann R, Little S, Sundahl E.2008 American Association of Feline Practitioners' feline retrovirus management guidelines. *J Fel Med Surg* 2008;10:300-316.

Littman MP et al: ACVIM small animal consensus statement on Lyme disease in dogs: diagnosis, treatment, and prevention, *J Vet Intern Med* 20:422, 2006.

Littman MP, Gerber B, Goldstein RE, Labato MA, Lappin MR, Moore GE. ACVIM consensus update on Lyme borreliosis in dogs and cats. J Vet Intern Med. 2018;32:887-903.

Martano M, Morello E, Iussich S, Buracco P. A case of feline injection-site sarcoma at the site of cisplatin injections. *J Feline Med Surg.* 2012 May 24. [Epub ahead of print]

Moon A, Veir J. Vaccination and associated adverse events in dogs previously treated for primary immune-mediated hemolytic anemia. J Am Anim Hosp Assoc. 2019;55:29-34.

Moore GE et al: Adverse events diagnosed within 3 days of vaccine administration in pet dogs, *J Am Vet Med Assoc* 227:1102, 2005.

Moore GE et al: A perspective on vaccine guidelines and titer tests for dogs, *J Am Vet Med Assoc* 224:200, 2004.

Moore GE et al: Adverse events after vaccine administration in cats: 2,560 cases (2002-2005), *J Am Vet Med Assoc* 231:94, 2007.

Munday JS, Banyay K, Aberdein D, French AF. Development of an injection site sarcoma shortly after meloxicam injection in an unvaccinated cat. J Feline Med Surg. 2011 Dec;13(12):988-91. Epub 2011 Aug 31.

Mucha D, Laberke S, Meyer S, Hirschberger J. Lack of association between p53 SNP and FISS in a cat population from Germany. Vet Comp Oncol. 2012 Aug 10;9999(9999).

Scott FW et al: Duration of immunity in cats vaccinated with an inactivated feline panleukopenia, herpesvirus, and calicivirus vaccine, *Fel Pract* 25:12, 1997.

Scott FW et al: Long term immunity in cats vaccinated with an inactivated trivalent vaccine, *Am J Vet Res* 60:652, 1999.

Srivastav A, Kass PH, McGill LD, Farver TB, Kent MS. Comparative vaccine-specific and other injectable-specific risks of injection-site sarcomas in cats. J Am Vet Med Assoc 2012;241:595–602.

Tizard I et al: Use of serologic testing to assess immune status of companion animals, *J Am Vet Med Assoc* 213:54, 1998.

Torres AN, O'Halloran KP, Larson LJ, et al. Feline leukemia virus immunity induced by whole inactivated virus vaccination. *Vet Immunol Immunopathol* 2010;134:122–131.

Twark L et al: Clinical use of serum parvovirus and distemper virus antibody titers for determining revaccination strategies in healthy dogs, *J Am Vet Med Assoc* 217:1021, 2000.

Vaccine-Associated Feline Sarcoma Task Force: The current understanding and management of vaccine-associated sarcomas in cats, *J Am Vet Med Assoc* 226:1821, 2005.

Whittemore JC, Hawley JR, Jensen WA, et al. Antibodies against Crandell Rees feline kidney (CRFK) cell line antigens, α-enolase, and annexin A2 in vaccinated and CRFK hyperinoculated cats. *J Vet Intern Med* 2010;24:306–313.

Yao PJ, Stephenson N, Foley JE, Toussieng CR, Farver TB, Sykes JE, Fleer KA. Incidence rates and risk factors for owner-reported adverse events following vaccination of dogs that did or did not receive a *Leptospira* vaccine. J Am Vet Med Assoc. 2015;247:1139-1145.