2013 Update on Current Vaccination Strategies in Puppies and Kittens

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KEYWORDS

• Vaccination • Guidelines • Risk assessment • Puppies • Kittens

KEY POINTS

- Vaccines are perhaps one of the practitioner's greatest tools in preventing disease and maintaining individual and population health.
- Vaccines are to be used with forethought based on the risk of disease to the population and the individual, balanced with assessment of the risks associated with individual vaccines.
- It is the practitioner's role to educate pet owners regarding actual risks associated with both undervaccination and overvaccination.
- The goal is to reach the highest level of overall animal health with the minimum number of adverse events, based on scientific and epidemiologic merit.

This article is an update to "Current Vaccination Strategies in Puppies and Kittens" published in *Veterinary Clinics of North America, Small Animal Practitioner*, in May 2006. During her recent literature review as preparation for this update, the author has noted a significant increase in both interest and literature on this topic. There are now comprehensive guidelines readily available for small animal practitioners regarding canine and feline pediatric (and adult) vaccination recommendations. Perhaps more importantly, there is an increased dialogue regarding all aspects of preventive medicine, of which vaccination is only a small, yet significant portion; and an increased drive to provide scientific evidence for developing vaccination recommendations. The reader is strongly encouraged to read (and keep close at hand) the 2011 American Animal Hospital Canine Vaccination Guidelines and the 2013 American Associate of Feline Practitioners Feline Vaccination Advisory Panel Report (both readily available) for a sweeping review of vaccine types, indications,

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recommendations, and adverse events; as such, a comprehensive discussion is not possible here. As veterinarians we should look forward to the ongoing growth of this area of interest within clinical practice and within the research community, to eventually provide practitioners with answers currently sought by pet owners and veterinarians alike.

It is far better to prevent than experience disease. This tenet should be the philosophy and goal of every veterinarian and every pet owner. For decades the veterinary profession has diligently educated pet owners about the benefits of preventing infectious disease, so well that there has been a significant decline in many of these diseases, in large part attributable to the development and use of effective vaccines. Veterinary practice staff members have done remarkable jobs sending reminder cards to ensure that canine and feline patients are current on their vaccinations. In fact, vaccines have become such a priority that many pet owners are inclined to forfeit other, indicated medical care in lieu of vaccines lest their beloved pets fall behind on their vaccine schedule. Veterinarians should commend themselves on a job well done, and commend pet owners for such conscientious stewardship of their pets. Now, however, the veterinary community must reflect on what has been accomplished, and make decisions for current and future patient care based on scientific, rational merit.

With the advent of knowledge on demand (ie, the Internet), pet owners have access to information regarding all issues of animal care. However, such information may not be accurate. It is our duty to educate pet owners; in fact, it should be seen as an opportunity. Who better to disseminate knowledge about veterinary medicine to the general public than veterinarians? No other group of individuals is as equipped with knowledge, skills, and insight as the veterinary community.

BASIC IMMUNOLOGY

To adequately discuss and understand how to make appropriate choices regarding pediatric vaccinations, a brief review and discussion of terms relative to basic immunology are warranted. Passive transfer of immunity occurs when maternal antibody is transferred by the dam or queen to the fetus via the placenta, which occurs minimally in dogs and cats. It also occurs during initial suckling through the ingestion of colostrum, which has more significant effects in these species.[1] This maternal immunity does provide initial protection against many pathogens, but of course depends on the health and immune status of the mother and the health of the fetus and neonate. Although this may result in temporary protection for the neonate, in the long term it may be deleterious to that individual's health by essentially keeping the animal naïve to different antigens (eg, maternal antibody interference with vaccination of the neonate). Maternal or passive immunization is effective in protecting neonates for the first several weeks of life, but begins to decline and lose the ability to protect against diseases rapidly as the maternal antibodies are degraded through natural catabolic processes. Between the ages of 6 and 16 weeks, depending on multiple factors (including species, amount of maternal antibody produced, transferred, and absorbed, and the individual health status of the neonate), most puppies and kittens have maternal antibody levels below protective levels. However, if present at high enough levels, maternal antibodies can interfere with the neonate's ability to respond to vaccination, as the circulating maternal antibody within the puppy or kitten may effectively respond to and neutralize the vaccine antigen, or render it ineffective by preventing recognition of the antigen by the immune system.[1] This is one reason why multiple, sequential vaccines are recommended in kittens and puppies until

they are at least 14 to 16 weeks of age.[2,3] Of importance is that maternal antibodies can interfere with immunization, although the level of maternal antibody present may not be protective against pathogens.

A functioning immune system is composed of multiple parts. Innate immunity is the oldest (evolutionarily), least specific, and most immediate (in terms of response to potential invaders/pathogens) form of immunity. Macrophages, neutrophils, dendritic cells, and natural killer (NK) cells combined with numerous products produced by these cells comprise the innate immune system. Examples of some of the chemical components produced and released by these cells in response to microbial invasion include lysozyme, complement, various cytokines such as tumor necrosis factor α and interleukins, and various vasoactive molecules such as histamine.[4]

Active immunization is the process of the individual responding to an antigenic stimulus appropriately, by either natural infection or vaccination. Active immunization is processed through the acquired immune system. The 2 main types of acquired immunity are cell-mediated immunity and antibody, or humoral, immunity. Cell-mediated immunity is predominantly directed against pathogens that typically are obligate, intracellular organisms. Examples include viruses, some obligate intracellular bacteria, some fungi, and protozoa. T lymphocytes are the predominant effector cells, and depend on foreign protein (antigen) being presented to them before they can take effect against the pathogens; thus, multiple cell types are involved in forming cell-mediated immunity. Antibody or humoral immunity is predominantly directed against pathogens that can survive outside the host, or at least survive extracellularly. Examples include most bacteria, fungi, protozoa, and helminths. Multiple cells act in concert to confer humoral immunity as well, but the primary effector cell is the B lymphocyte.[5] Having stated this, in actuality humoral immunity is extremely important in protection against viral infections, and is intricately and definitively dependent on competent cell-mediated immunity.

Kittens and puppies will have varying degrees of ability to respond to antigens, whether resulting from natural or vaccine exposure, based on antigen load, route of exposure, antigenic virulence, genetics of the individual animal, and levels of persistent maternal immunity. In naïve animals whose maternal immunity has declined sufficiently so as not to interfere with an immune response; the first vaccine should stimulate a primary immune response (priming of the immune system). This initial exposure and recognition process and the ability to produce antibody to respond to the antigen typically takes 10 to 14 days; however, the maximum response takes up to 3 weeks. This primary response must not be confused with the animal having been immunized. A subsequent dose of vaccine (exposure) will lead to immunologic memory. Subsequent exposures to the same antigen elicit a stronger response: a greater amount of antibody is produced and the subsequent response is more rapid. This process is known as the secondary or anamnestic immune response, which results in immunity. Although multiple cell lines are involved in this response, subsets of T and B lymphocytes known as memory cells preserve the host's ability to recognize and respond to antigens to which the animal had previously been exposed.[4]

DEVELOPING VACCINE GUIDELINES USING RISK ASSESSMENT

To design, recommend, and actuate an effective plan for each patient, a practitioner must have familiarity with multiple variables. Those variables include duration of protection conferred on the neonate by the mother; the typical length of time maternal antibody may persist and pose interference with the young animal's ability to respond fully to a vaccine; and the length of time needed for an appropriate response. In

addition, knowledge of the various diseases that pose risks to pediatric patients and knowledge of available safe, efficacious vaccines is critical. In essence, each patient must be assessed as an individual within the population to provide optimal wellness over the lifetime of each individual, as well as the population. This rationale has led to the concepts of core and noncore vaccines, 2 terms commonly used when discussing vaccination within the veterinary field. Criteria for assigning vaccines into these categories, and a third category, "generally not recommended," are based on: (1) morbidity and mortality associated with the specific disease (does the organism cause serious illness or does it cause a mild, transient disease that may pose only minimal risk to the individual or population?); (2) the prevalence and/or incidence rate of the disease (although a specific disease may not commonly be seen, the organism is ubiquitous in the environment and therefore poses risk to the individual or population); (3) the risk of the individual for exposure to the disease (indoor-only animal vs free-roaming individual, regional variations of occurrence); (4) the efficacy of the vaccine (does the vaccine prevent infection or simply ameliorate some signs or length of disease?); (5) the risks associated with administering the vaccine (are the risks associated with that vaccine greater than the risk of the disease?); (6) the potential for zoonotic disease; (7) the route of infection or transmissibility.[2,3,6–8] When these criteria are assessed, general guidelines may be generated for the individual practitioner and the veterinary community at large. Again, guidelines are not to be thought of as absolutes, nor are they to be used to establish standard of care. Simply stated, they are tools for each of us to use to promote optimal wellness for our patients when considering all factors affecting the individual's health (environmental, organismal [both pathogen and host], owner concerns, and current vaccine technologies).[2,3,6–8]

TYPES OF VACCINES

Multiple vaccines are available for canine and feline patients, although most fall within 3 basic categories. Assignment of vaccine products (which are considered biological agents, not drugs, and are therefore assessed and approved under the United States Department of Agriculture [USDA] Animal and Plant Health Inspection Service rather than the Food and Drug Administration) into these categories is based on how the product is created. Simply stated, modified live virus (MLV) vaccines are vaccines created by altering (attenuating) the pathogen in some way so that it is no longer able to cause serious or clinical disease in the targeted species. Killed vaccines are vaccines produced by inactivating the pathogen completely, rendering it incapable of reproducing and thereby unable to cause disease. The third category of vaccines consists of recombinant vaccines, of which there are multiple types, and this category itself has 3 subcategories. These vaccines use genetic technologies to either introduce genetic material directly into the host (no vector, eg, purified subunit vaccines or type I recombinant, is used), alter the genetic material to change its virulence (gene deletion, type II recombinant), or incorporate genetic material from the desired pathogen into an attenuated vector organism (eg, feline rRabies [r = recombinant], type III recombinant).[9,10] Within the near future, multiple new technologies are likely to provide even more choices, potentially providing patients with better protection against disease with minimal vaccine-associated risks. A more recent discussion for categorizing vaccines has evolved, and assigns vaccines to 1 of 2 groups: infectious or noninfectious. Simply stated, infectious vaccines include those biologics that have the ability to enter host cells and undergo replication within the host (ML, rCanary poxvectored vaccines). Noninfectious vaccines do not have the ability to undergo replication within the host.[3] For a comparison between vaccine types, the reader is referred to **Table 1**.

GENERAL RECOMMENDATIONS

Vaccines are available in single-dose and multiple-dose (tank) vials. The use of single-dose vial vaccines is highly recommended in these species. Conversely, the use of multiple-dose vials is discouraged because of the increased risk of contamination and the inability to assure consistent levels of antigen and adjuvant in individual doses from a single vial.[2,3] Multivalent vaccines are not recommended in cats other than the core feline vaccine designed to protect against feline panleukopenia, feline herpesvirus I, and feline calicivirus. Owing to increased inflammation at the site of multivalent vaccines, all other vaccines should be given as a separate vaccine, at the indicated site (see later discussion on feline core and noncore vaccines).[2,6] Allowing vaccines to acclimatize to room temperature before administration, particularly in cats, is recommended, as the administration of cold vaccines was found to have an increased association for tumorigenesis in cats.[11]

Use of sterile, single-use syringes is also recommended, as vaccines may become inactivated and/or ineffective with exposure to various products used to clean and sterilize syringes. Mixing of more than 1 vaccine within a syringe should not be performed because of the potential for inactivation of vaccine material, in addition to increasing the amount of antigen deposited within a single site. Moreover, administration of reconstituted vaccines (MLV r) should be done within 1 hour of reconstitution or otherwise discarded, owing to the potential inactivation of product and loss of efficacy.[3]

The practitioner is advised to always follow the manufacturer's directions for dose and route of administration. Using a topical product parenterally or splitting doses should never be done. A full dose is required to stimulate the immune system; there is no medical basis for giving a smaller dose to a toy breed dog, and this practice could lead to vaccine failure in that animal. If done with a rabies vaccine the practitioner is not following federal requirements, which carries potential legal implications.[3,12]

The interval between various vaccines, whether using the same product serially in the initial series or whether using different products in an adult animal, should never less than 2 to 3 weeks. Interference between the first product administered and a second vaccine product may lead to failure to optimally respond to the second vaccine. The exact mechanism of this interference is unknown, but may be associated with interferon produced by cells processing an MLV agent, or by transient immunosuppression by an MLV agent. Multiple vaccines administered at the same time do not appear to elicit this interference and is therefore an acceptable practice.[7,9] The reader is referred to **Tables 2** and **3** for comparison between pediatric canine and feline core, noncore, and generally not recommended vaccines.

CORE CANINE PEDIATRIC VACCINES

The diseases that fall within this category carry high rates of morbidity and/or mortality, are of public health concern, or are readily transmissible or may be ubiquitous in the environment. In addition, safe, efficacious vaccines are available and either provide sterile immunity (prevent infection) or confer a high degree of protection (do not prevent infection, but may confer protection such that the animal will not develop clinical signs of disease).[3,6] Essentially, the vaccines that fall within this category are recommended for each individual within the population regardless of the animal's lifestyle or locale.

Distemper

Canine distemper virus (CDV), an enveloped morbillivirus, has been well controlled because of the widespread vaccination programs over the last several decades. However, the disease still persists and, in addition to high virulence, it is readily

Table 1
Vaccine types, benefits, and associated concerns

Vaccine Type	Manufacturing Process, Method of Action	Associated Benefits and Recommendations	Associated Precautions and Contraindications
Modified live (attenuated)	Virus or bacteria made less virulent via cell or tissue passage. Attenuated viruses able to enter host's cells and replicate. Stimulates cell-mediated and humoral immunity	Mimics natural infection Rapid response by host's immune system Many products able to stimulate adequate immune response with a single dose Does not require use of adjuvant Vaccination of a single individual will lead to viral shedding, which may be useful in a herd-health situation when rapid exposure of multiple animals with an attenuated organism is desired	Potential to cause disease in some individuals (should not use in immune-compromised animals) Potential of organism to revert to more virulent form and cause disease even in healthy animals Special handling of vaccines required (temperature sensitive, shorter shelf life than killed products) Vaccinates shedding the modified live vaccinal organisms may lead to disease outbreaks in certain environments Parenteral administration of topical ML bacterin products may lead to serious disease (focal abscess at vaccine site, sepsis)
Killed (inactivated)	Virus or bacteria chemically or heat inactivated Organism unable to actively enter host's cells, unable to replicate Stimulates both cell-mediated and humoral immunity	No potential to revert to virulence Vaccinates do not shed the pathogen, therefore no potential to spread through population Indicated for use in immune-compromised animals (eg, FIV+ and FeLV+ cats) Organism does not cause disease in vaccinates Longer shelf life and less sensitive to temperature/handling requirements	Increased lag time of exposure to immune system leading to increased interval from vaccination to protection Because less immunogenic, these products require adjuvants (vaccine virus unable to actively enter host's immunocytes and replicate). Products containing adjuvants should be avoided in cats when alternative products with equal efficacy are available

			Most killed products require a minimum of 2 doses to stimulate protective response Greater potential for contamination and adverse reactions (require higher antigen load and adjuvants may cause adverse effects)
Recombinant (subunit, gene deleted, vectored)	Genetic material from pathogen altered in some way; 3 categories of recombinant vaccine technology use various techniques Subunit vaccines are created by inserting specific genomic regions from the desired pathogen into nonpathogenic bacteria. The bacteria then produce protein as coded by the inserted genome. The desired protein is then harvested, purified, and used as a vaccine Vectored virus vaccines incorporate immunogenic genomic regions from pathogen into an attenuated nonpathogenic virus	Vector able to penetrate host's cells, delivering genetic material from pathogen into the cell, therefore, no need for adjuvant Rapid onset of immunity Stimulates cell-mediated and humoral immunity No potential for reversion to virulence May be able to overcome maternal antibody interference earlier than modified live or killed products Does not cause disease in healthy or immune compromised animals (appropriate for use in FIV+ and FeLV+) Vaccinates do not shed virus	Requires handling similar to modified live products (shorter shelf life, temperature sensitive) Increased cost in manufacturing and therefore increased cost to consumer
New (Alternative) Terminology/Categorization			
Infectious vaccine	Modified live/attenuated and canary pox-vectored recombinant vaccines	As stated above	As stated above
Noninfectious vaccine	Killed/inactivated (whole organism or particle), subunit vaccines	As stated above	As stated above

Abbreviations: FeLV, feline leukemia virus; FIV, feline immunodeficiency virus.

Table 2
Canine pediatric vaccines: core, noncore, and generally not recommended

Canine	Core	Noncore	Not Recommended
Distemper virus	MLV or recombinant beginning at 6–9 wk, given every 3–4 wk until ~16 wk old		
Adenovirus type 2 (CAV-II)	MLV, frequency as for CDV		
Parvovirus	MLV, frequency as for CDV		
Rabies	Killed, single dose, minimum age dependent on state and local regulations (12 or 16 wk)		
Leptospirosis		Killed bacterin, or purified subunit product, beginning at 12 wk, 2–3 doses given at 4-wk intervals	
Bordetella bronchiseptica		Attenuated bacterin, a single dose of an intranasal vaccine given 1 wk before potential exposure (minimum of 4 wk old)	
Parainfluenza		MLV, either use topical product combined with *B bronchiseptica* or parenteral vaccine contained in multivalent DAPP products	
Lyme disease (*Borrelia burgdorferi*)		Recombinant subunit vaccine (OspA) before exposure to ticks, 2 doses given 4 wk apart, beginning at 9 wk old	
Canine influenza		Killed-virus vaccine, typically not recommended but may be indicated in outbreak or kennel situations 2 initial doses 2–4 wk apart with first dose no earlier than 6 wk old	

Canine	Core	Noncore	Not Recommended
Table 2 **(continued)**			
Measles		Typically not recommended, use recombinant distemper vaccine for high-risk puppies instead of measles	
Coronavirus			Not recommended
Rattlesnake vaccine			Insufficient data to evaluate efficacy. Prevention of exposure, aversion training, and immediate veterinary attention postexposure highly recommended
Adenovirus type I (CAV-I)			Not recommended. CAV-II to prevent CAV-I infection is highly recommended

Abbreviations: CDV, canine distemper virus; DAPP, distemper, adenovirus 2, parvovirus, and parainfluenza; MLV, modified live virus; OspA, outer surface protein A.

transmissible. Infection with the virus causes respiratory, gastrointestinal, and neurologic signs, and is often fatal.[13] The distemper vaccine is commonly administered as part of a multivalent product. The general recommendation is to use a modified live or recombinant, multivalent product (CDV, canine adenovirus type II [CAV-II], canine parvovirus [CPV]) beginning at 6 to 9 weeks, and to give serial vaccines every 3 to 4 weeks until the puppy has reached 14 to 16 weeks of age.[3,9,14] Many studies support the improved ability of recombinant vaccines to overcome maternal antibody interference in comparison with modified live virus vaccines.[15,16] Most puppies will receive 2 or 3 distemper vaccinations, depending on the age at which they are first presented to the veterinarian. However, it is the interval between or the timing of the vaccinations, rather than the number, that is important. Serial vaccinations help to increase the likelihood of a complete response of the patient and thereby decrease the risk of vaccine failure that may occur when only 1 vaccine is administered. In addition, by eliciting a secondary immune response, they may help to increase the level of circulating antibody and decrease the lag time between exposure to an antigen and achievement of maximal antibody level.[4] Potential causes for vaccine failure include: a modified live vaccine that was improperly stored and therefore has lost its efficacy; the vaccine was improperly administered (wrong route or accidental loss of vaccine onto the skin of the patient); the patient's immune system did not respond (the immune system may have been responding to another antigenic challenge or the vaccine may have been given too soon after a previous vaccine); or maternal interference.[9] In theory, if a puppy were kept sequestered from exposure to this virus, 1 modified live distemper vaccine administered after 16 weeks of age would confer protection for at least 1 year.[1,3] However, in reality most pet owners are not inclined to isolate their puppies for the first 4 months of life, nor should they. Early socialization is an important part of families bonding with their puppies. Exposure to various people, other dogs, and new places helps decrease behavioral problems in the young adult and mature dog.[17] As long as the last distemper vaccine is administered after 16 weeks of age, the puppy should be able to mount a strong active response and fully overcome any residual maternal antibody. The current recommendation is to have the puppy return 1 year later (when approximately 16 months

Table 3
Feline pediatric vaccines: core, noncore, and generally not recommended

Feline	Core	Noncore	Not Recommended
Feline herpesvirus (feline viral rhinotracheitis)	MLV, give 2–3 doses of parenteral product beginning at 6–9 wk old, every 3–4 wk until ~12 wk old (or killed)		
Calicivirus	MLV, frequency as for FVR (or killed)		
Panleukopenia	MLV, frequency as for FVR		
Rabies	Recombinant canarypox-vectored product, single dose at minimum age of 12 wk but varies dependent on state and local regulations (or killed)		
Feline leukemia virus[a]	After viral screening confirming negative viral FeLV status, recombinant canarypox-vectored or killed product, 2 doses given 4 wk apart, as early as 8 wk old		
Chlamydiosis (*Chlamydophila felis*)			In high-risk environments, use parenteral attenuated bacterin product, 2 doses given 4 wk apart beginning at 9 wk old
Bordetella bronchiseptica			In high-risk environments, topical attenuated bacterin product designed for use in this species, single dose as early as 4 wk old
Feline immunodeficiency virus			Not generally recommended in kittens. Viral testing in kittens younger than 6 mo may yield false-positive results because of PMA. Vaccination causes positive Ab test
Feline infectious peritonitis			Not recommended. Vaccination causes positive Ab test

Abbreviations: Ab, antibody; FeLV, feline leukemia virus; FVR, feline viral rhinotracheitis; MLV, modified live virus; PMA, persistent maternal antibodies.
[a] Owing to increased susceptibility for infection in kittens, vaccination against feline leukemia virus is strongly recommended for all kittens. In single-cat households, households with known, negative viral status of all cats, and indoor-only cats, the practitioner may elect to consider this a noncore vaccine.

old) for another distemper vaccine. After the first annual vaccination, triennial immunization is recommended, regardless of vaccine type used.[2,3,9]

Canine Adenovirus

There are 2 types of adenovirus that cause disease in canine patients. Canine adenovirus type I (CAV-I), a nonenveloped virus in the family Adenoviridae, causes the potentially fatal disease infectious canine hepatitis. Clinical signs include fever, depression, vomiting and diarrhea, and potential petechiation and ecchymotic hemorrhage secondary to hepatic dysfunction. In addition, uveitis and renal disease are associated with infection with this virus. CAV-II causes respiratory tract disease. CAV-I is associated with severe, potentially fatal disease, and protection against this disease is recommended. Transmission is via the oronasal route and exposure to infected secretions. CAV-II infection typically results in mild self-limiting disease and is therefore considered to be a noncore disease; however, the modified live vaccine designed for prevention of CAV-I has been associated with adverse effects such as uveitis and corneal edema (an Arthus reaction, similar to effects caused by natural infection).[9,13] The current recommendation is to use the CAV-II modified live virus product, as it stimulates the immune system to protect against both CAV-I and CAV-II, without the associated adverse reaction caused by the type I vaccine.[3,14,18] The modified live adeno-type II virus is typically included in a multivalent injection (as mentioned earlier) and is therefore usually administered at intervals of 3 to 4 weeks, beginning between 6 and 9 weeks of age and ending between 14 and 16 weeks old. A vaccination 1 year later is recommended before instituting triennial vaccinations.

Canine Parvovirus

CPV is a nonenveloped type 2 parvovirus. The predominant form currently causing infection in the United States is type 2b, but other subtypes exist and cause disease elsewhere.[13] Because the virus is nonenveloped, it may exist (outside of a host) under certain environmental conditions, and is somewhat resistant to many disinfectants. Transmission is via the fecal-oral route, and clinical signs include lethargy, anorexia, pyrexia, vomiting, and diarrhea (typically hemorrhagic). Young animals appear to be at highest risk for developing severe, life-threatening disease. The current recommendation for vaccination is to use a multivalent MLV vaccine beginning at 6 to 9 weeks and to repeat the vaccine at intervals as already stated (every 3–4 weeks, until the puppy is 14–16 weeks old). In the past there was concern that certain breeds may have been at increased risk for contracting and developing severe parvoviral disease (Doberman Pinschers, Rottweilers), but it is generally agreed that these breeds will mount an appropriate response to a quality product if the last vaccine is given between 14 and 16 weeks of age.[3,13,19] There is, however, a small population of dogs that is genetically unable to respond to vaccination against CPV2, regardless of the number of vaccinations (nonresponders). One benefit of having a well-vaccinated population is that even those nonresponders are at decreased risk of exposure and subsequent infection by parvovirus, based on strong herd immunity. Studies using MLV CPV2b strains showed a higher antibody response to CPV2 and CPV2b, and were better able to overcome maternal antibody interference than the CPV2-strain vaccines used[20,21]; however, all CPV2 vaccines currently available should produce strong immunity in immunocompetent dogs. Immunization 1 year after completing the initial puppy series is recommended, with subsequent triennial vaccinations.[3,22,23]

There is also emerging evidence that Weimaraner puppies are at increased risk of developing a severe form of hypertrophic osteodystrophy (HOD) in association with vaccination with MLV distemper, adenoviral, and parvoviral products. The exact

mechanism is unknown, but the current recommendation is to use killed products in this breed for their pediatric vaccinations, and consider starting vaccinations when they are slightly older.[12]

Rabies

Rabies virus, an enveloped virus in the rhabdoviridae family, is capable of infecting all mammals.[13] Because it is an enveloped virus, it is not stable in the environment and is readily inactivated by most common disinfectants. The virus is transmitted through infected saliva, most commonly from a bite by an infected animal. Clinical signs range from anxiety or other vague behavioral changes to pica, dysphagia, photophobia, and paralysis. Because of the zoonotic potential and implications regarding public health, canine vaccination programs are strongly regulated and enforced. The current recommendation is to vaccinate puppies using a killed-virus vaccine at a minimum of 12 or 16 weeks of age. State regulations vary as to the minimum age for canine rabies vaccination: in California the legal minimum age of canine vaccination against rabies is 16 weeks. A second rabies vaccine (killed product) is administered 1 year later and then annually or triennially thereafter, depending on local regulations.[3,6] It is the practitioner's professional responsibility for knowledge of and adherence to regional laws regarding rabies vaccination frequency.[24]

NONCORE CANINE PEDIATRIC VACCINES

Vaccines in the noncore category may have limited efficacy, or the organism causing disease is not readily transmissible or may have limited geographic distribution or prevalence. In addition, the diseases these vaccines are designed to prevent may be so mild or self-limiting that the risks associated with administering the vaccines may be greater than the actual disease. Lastly, some vaccines may interfere with common screening methods for disease detection, and are therefore not recommended unless absolutely warranted for a specific individual. It is the burden of the practitioner, along with the pet owner, to make decisions regarding which, if any, of the noncore vaccines should be administered to a puppy.[3,6–8]

Leptospirosis

A bacterial pathogen that causes acute hepatic and renal disease, leptospirosis is typically transmitted through urine of infected animals (reservoir hosts include dogs, rats, wildlife, and livestock), and in contaminated water. There are at least 2 different species (*Leptospira interrogans* and *Leptospira kirschneri*) that can infect dogs, with multiple serovars (variants of the same species) of *L interrogans* causing disease in dogs.[25] Although these organisms have the potential to cause serious disease, dogs are not likely to be at risk in a mostly urban, controlled environment (housed in a fenced yard with no exposure to wildlife or livestock). However, a dog that frequents rural environments or has exposure to waterways or livestock is definitely at risk of infection and should therefore be protected against the disease. Again, the initial puppy appointments should involve a through history and include the owner's plans for the dog's future use. If an owner brings a Labrador retriever puppy to the veterinarian for "whatever vaccines he needs," it is up to the practitioner to ask "will he be a hunting dog, will he be used in field trials, will he be exposed to wildlife and waterways?" The Border Collie who lives on a working sheep ranch surely should be vaccinated appropriately against leptospirosis. Conversely, a long-haired miniature Dachshund who will spend her days on her owner's lap in an urban setting will be at minimal risk of exposure and, therefore, vaccination is most likely not warranted.

In essence, regional distribution, seasonality (increased prevalence during and immediately following the rainy season), and lifestyle of the puppy will be factored into the decision as to whether the puppy should be vaccinated. If the decision is made to vaccinate against leptospirosis, the general recommendation is to wait until the puppy is at least 12 weeks old, at which time a killed or purified subunit vaccine is administered. Infection is serovar specific, and no cross-protection is seen between different serovars; therefore, vaccination with as many serovars known to cause disease in a given region is recommended. An initial series of 2 vaccinations should be administered 3 to 4 weeks apart and repeated at least annually thereafter, as long as the risk of exposure to the agent exists.[26] The recommendation to wait until the puppy is at least 12 weeks old before administering the leptospirosis vaccine is based on the increased potential for adverse events associated with killed vaccines, and to increase the likelihood of a complete immune response.[3,27]

Bordetella

Bordetella bronchiseptica is a bacterial agent that causes infectious tracheobronchitis. Infection with this agent may occur in concert with other agents infecting the respiratory tract (canine parainfluenza virus [CPiV], CAV-II). Transmission occurs via direct contact or through aerosolized microdroplets from infected dogs, and is most likely to occur under crowded conditions such as boarding and grooming facilities and dog-show venues. The current recommendation is to vaccinate puppies at risk a minimum of 1 week before potential exposure with a combination vaccine containing both an avirulent live bacterin for *B bronchiseptica* and a modified live CPiV. The vaccine can be administered to puppies as young as 3 to 4 weeks of age, but is generally not indicated unless the puppy is in a kennel environment.[27] Many organized puppy socialization and obedience classes commonly require proof of vaccination against *Bordetella* at the time of enrollment or before beginning the course. The general consensus is that intranasal vaccines are superior to parenteral vaccines, as they stimulate rapid local immunity (which is not affected by persistent maternally derived antibody).[6,9] Intranasal vaccines should never be given subcutaneously, owing to the potential for severe (in some cases fatal) reactions (Fig. 1). If the puppy will be intermittently exposed throughout the year (traveling to shows, boarding or grooming facilities) the vaccine should be repeated every 6 months to annually.

Parainfluenza

As already stated, CPiV may occur in concert with other respiratory tract agents. The vaccine recommendations are as stated for *B bronchiseptica* if indicated. There are
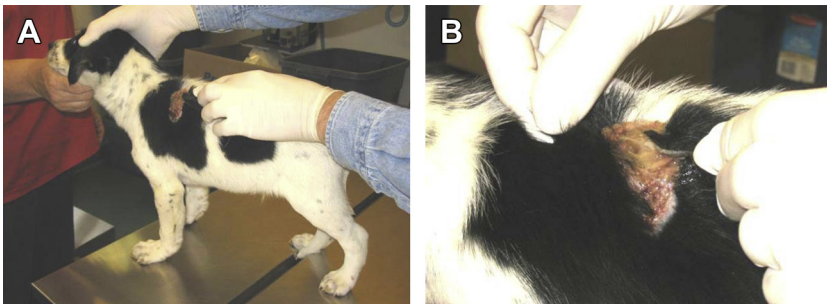
Fig. 1. (*A, B*) Local reaction with abscessation secondary to subcutaneous administration of a modified live bronchiseptica intranasal vaccine. (*Courtesy of* Dr Richard Ford, DVM, MS, DACVIM, Raleigh, NC.)

multiple products available, but the product currently recommended is the combination of intranasal vaccine containing a modified live parainfluenza virus with an attenuated *B bronchiseptica* bacterin. Intranasal vaccines can be used in puppies aged 3 to 4 weeks for individuals at high risk of exposure (depending on vaccine manufacturer label restrictions). For optimal protection, the vaccine should be administered every 6 months to annually if indicated. Alternatively many multivalent, parental products containing modified live CDV, CAV-II, CPV, and parainfluenza are available and appropriate for use.[3,9]

Borreliosis

Borrelia burgdorferi is a vector-borne, spirochete bacterium responsible for Lyme disease (borreliosis). Transmission occurs when an infected tick (various species within the *Ixodes* genera, also referred to as hard ticks) bites and remains attached to a host, in this case a puppy. Direct, horizontal transmission is not likely to occur, so the risk to humans and other pets is thought to be minimal. If a puppy has a significant burden with infected ticks, it of course increases the exposure to others in the household but, as ticks typically do not reattach once they have taken a complete meal, the risk is considered to be fairly small unless appropriate tick control is not instituted.[28] Vaccination to protect against Lyme disease is controversial, as the duration of immunity and degree of protection provided by vaccination is unknown, and vaccination with some vaccines interferes with standard screening diagnostics.[29] Therefore, vaccination against Lyme disease is warranted only if a puppy will be expected to be at high risk for tick exposure, and only if it lives in a *Borrelia*-endemic area. There are killed and recombinant (OspA subunit) vaccines available for use against *B burgdorferi*, and if vaccination is deemed warranted, the current recommendation is to use one of the subunit vaccines before exposure to ticks. The vaccine can be given as early as 9 weeks and should be repeated 3 to 4 weeks later.[27] The best prophylaxis is likely achieved by using appropriate tick prevention, such as fipronil with methoprene spray or spot-on products (eg, Frontline Top Spot; Merial Ltd, Iselin, NJ), amitraz collars (eg, Preventic collar; Virbac Animal Health, Fort Worth, TX), or an imidacloprid/permethrin topical product (eg, Canine Advantix; Bayer Animal Health, Shawnee Mission, KS).[29,30] These products should be chosen and recommended carefully by the veterinarian based on household situations, owner concerns, and the age of the puppy.

Measles

This virus, also a morbillivirus, can stimulate an immune response that is cross-protective against CDV. The indication for using this vaccine is for puppies that may have maternal antibody to distemper virus sufficient to cause interference with distemper vaccination but inadequate to protect against infection. If indicated (see later discussion on special circumstances), a single vaccination with a modified live vaccine should be given intramuscularly as early as 6 weeks of age. Subsequent immunizations with MLV CDV vaccines should be given serially as recommended (see CDV section).[1,3,31] Canine measles vaccines should never be administered to female puppies older than 12 weeks, as they may develop an acquired immune response to the virus, which could be problematic if a female puppy vaccinated against measles at 14 weeks of age later became pregnant. If she developed antibodies to the measles virus and maintained immunologic memory, she would confer measles antibody to her puppies via passive transfer, thus rendering measles vaccination in those puppies ineffective. A more appropriate alternative to administering a measles vaccine to a young puppy thought to be at risk for infection but too young to receive an MLV CDV vaccine would

be to use a recombinant CDV vaccine, thereby decreasing the likelihood of maternal antibody interference.[3,32]

Canine Influenza Virus

Canine influenza virus has been seen in various countries, most notably in enzootic outbreaks. This virus is typically seen in puppies and dogs in shelter, boarding, and day-care facilities, and often occurs as a coinfection in canine infectious respiratory disease (CIRD) with bacterial pathogens. There is a commercially available inactivated vaccine available for use in puppies as young as 6 weeks. Vaccination with this product should be used only in puppies with a high risk of exposure, such as to shelters and areas known to be dealing with current/recent outbreaks (typically not in client-owned puppies). In addition, some countries now require an initial vaccination series (2 doses, given 2–4 weeks apart) before importation.[3,33]

Rattlesnake Vaccine

A vaccine designed to protect against envenomation by *Crotalus atrox*, the Western Diamondback rattlesnake, was released onto the market several years ago. The original provisional licensure was granted to provide possible protection against this single species of snake, and was granted for use only in California. The company was later granted extended licensure for multiple states, and has extended its claim for potential protection against multiple species of members of the Crotalidae (pit vipers). To date, no challenge studies have been performed in the canine species to validate efficacy claims. All claims are based on antibody titer to the venom component included in the vaccine, to murid challenge studies, and to field reports of protection of naturally occurring envenomation.[34] No controlled, independent studies exist concerning the impact of prior vaccination on therapeutics after envenomation. The manufacturer does not claim that vaccination with this product will completely protect against effects of envenomation; rather, they claim it may slow the onset of clinical signs and decrease the severity of signs. Immediate veterinary care is still the gold standard for any snake bite. Because of the great potential for variability in envenomation (site of bite on animal, size and age of snake, amount of venom injected into animal, and species of snake), field observations and anecdotal reports of protection are difficult to substantiate. Challenge studies conducted under controlled conditions will likely be necessary to validate the efficacy of this product. At present, owing to the preceding statements, this vaccine is not recommended for general use. Aversion training and keeping dogs out of areas known to favor rattlesnake habitation, and immediate veterinary evaluation and care are still the standard recommendations for preventing and treating disease associated with rattlesnake envenomation. If an owner is extremely concerned about the potential for exposure and envenomation by a Western Diamondback rattlesnake, the decision to vaccinate should be made after a discussion between the veterinarian and owner, with full disclosure of vaccine efficacy and a risk/benefit analysis, understanding the potential for adverse events from vaccination. This vaccine has been shown to be safe for use in puppies as young as 4 months.

CANINE, GENERALLY NOT RECOMMENDED
Canine Corona Virus

An enveloped virus belonging to the family Coronaviridae, this virus is transmitted via the fecal-oral route. Vaccination against this disease is generally not recommended because the vaccines provide questionable protection, and the actual prevalence

and severity of the disease are unknown. Those most likely to be infected and develop clinical disease are neonates younger than 6 weeks. Clinical signs may include diarrhea, possibly hemorrhagic, but typically self-limiting. The general recommendation is to vaccinate puppies against CPV (as recommended in the section on CPV), as this practice appears to confer protection against coronavirus in addition to preventing infection with CPV2.[3,14]

Canine Adenovirus Type I

As stated in the canine core vaccine section, CAV-I causes serious disease in dogs; however use of the CAV-I is associated with a high incidence of adverse events. Vaccination with CAV-II induces an immune response that is protective against both CAV-I and CAV-II without the adverse effects. The recommendation is to use CAV-II as part of the canine core vaccination program; CAV-I should not be used.[3]

CORE FELINE PEDIATRIC VACCINES
Feline Panleukopenia Virus

Feline panleukopenia, a nonenveloped parvovirus closely related to canine parvovirus, causes serious, often fatal disease in kittens. Transmission typically occurs from direct contact with infected animals, although in utero infection and fomite transmission also occurs. Clinical signs typically include pyrexia, anorexia, lethargy, vomiting, and diarrhea. Kittens may be immunosuppressed subsequent to pancytopenia associated with this viral infection. Kittens infected in utero may exhibit cerebellar disease. Prevention is achieved by using modified live virus vaccines beginning between 6 and 9 weeks of age. The standard recommendation is to use a parenteral product (as opposed to intranasal products, which have higher incidences of postvaccinal viral shedding and potential for clinical disease induced by the more virulent viruses in these vaccines).[2,6,9] As is the case for canine distemper, adenovirus, and parvovirus, the core feline diseases, with the exception of rabies, are typically administered in a multivalent product in series. There are numerous vaccine products containing feline panleukopenia virus, herpesvirus I, and calicivirus (see later discussion). The current recommendation is to choose an MLV or killed product from a reputable manufacturer. Vaccines are administered subcutaneously in the distal aspect of the right thoracic limb (elbow or distally) and given every 3 to 4 weeks until the kitten is at least 16 to 20 weeks old. Repeat administration is recommended 1 year later before instituting a triennial schedule.[2,35]

Feline Herpesvirus I

Feline herpesvirus I (FHV-I), also known as feline viral rhinotracheitis virus, is an enveloped virus causing respiratory tract disease in cats. Clinical signs include sneezing, nasal congestion and discharge, conjunctivitis, and ocular discharge. In addition, kittens may exhibit pyrexia, anorexia, and lethargy along with oral/lingual ulcerations and associated hypersalivation. In some cases ulcerative, crusting dermatitis occurs, which may mimic other dermatologic disease.[36] The virus typically causes upper respiratory disease but the lower respiratory tract may become involved, especially in neonates or debilitated animals. Infection with this virus is lifelong, although many cats will "recover" and not show clinical signs. However, cats infected with FHV-I may have recurrent outbreaks, especially under times of stress or if their immunity is otherwise compromised. Cats may persistently shed the virus and act as a source of infection in shelters, catteries, and multiple-cat households. Therefore, prevention before exposure is key to controlling this disease.[36,37] Vaccination with a modified live virus (or killed product) beginning as early as 6 to 9 weeks is recommended, this being commonly administered

as part of a multivalent product, given subcutaneously, in the right thoracic limb. The current recommendation is for kittens to receive a second vaccination 4 weeks later. The last vaccine in the series should be given when kittens are 16 to 20 weeks of age. A vaccine should be given 1 year later before beginning the triennial schedule.[2]

Feline Calicivirus

Feline calicivirus causes respiratory tract disease in kittens and cats. Because it is a nonenveloped virus, it is more resistant to disinfectants and may therefore persist in the environment. Signs are similar to those associated with FHV-I, but lameness and stomatitis are also commonly seen. Transmission of both FHV-I and calicivirus is through direct contact, exposure to contaminated secretions, aerosolization, and fomites.[36,37] Another, highly virulent, strain of feline calicivirus was identified several years ago and carries a higher incidence of mortality. Transmission is through either direct contact or via fomites. Prior vaccination against feline calicivirus does not appear to be protective against this strain, and adult cats appear to be more severely affected than kittens.[38,39] The current recommendation is as for panleukopenia and FHV-I: administering a modified live virus inactivated-virus parenteral vaccine beginning at 6 or 9 weeks with a subsequent vaccine 4 weeks later (the last vaccination should be when the kitten is at least 16 to 20 weeks old). A booster vaccine should be administered 1 year later, and then every 3 years.[2]

Rabies

As stated earlier, rabies virus affects all mammals and in the United States, with most documented cases of rabies in pet animals occurring in cats.[40] Because of the significant risk to pets, wildlife, and humans, vaccination against rabies virus is highly recommended for all kittens and cats, even those kept inside.[2,6] Local requirements vary, but the general recommendation is that all kittens should be vaccinated beginning at 12 weeks of age with either the recombinant rabies vaccine (preferable) or a killed rabies virus vaccine.[2,6,41] The recombinant product uses gene-splicing technology: reverse transcriptase is applied to rabies viral RNA to create complementary DNA. The segment of rabies virus DNA that codes (a codon) for the immunogenic protein associated with the virus (glycoprotein G) is then spliced from the rabies DNA and inserted into a canarypox virus. The canarypox virus, which is attenuated, is nonpathogenic to mammalian cells and therefore carries no potential to cause disease in this species. Because the vaccine is essentially a modified live product, the canarypox virus can enter cells, delivering the codon for rabies virus glycoprotein G to its targeted site. Once inside the cell the canarypox virus is unable to replicate, but the rabies glycoprotein G codon is preserved, leading the host cell to express the glycoprotein on its surface; this stimulates both cell-mediated and humoral immune responses. Besides the benefit of stimulating both types of immunity, because this product is adjuvant-free there may be a decreased risk of local inflammation associated with vaccination, thereby potentially decreasing the risk of subsequent vaccine reactions and tumorigenesis. The current recommendation is to use either the rRabies virus vaccine (preferred when possible) or a killed-virus vaccine in a case where increased duration of immunity is required (not pertinent to kittens because all pediatric/initial rabies vaccinations provide only 12 months of protection, regardless of label claims).[2,6] Rabies vaccines should be administered subcutaneously in the right pelvic limb, as distally as is reasonably possible: the level of the stifle is acceptable and areas distal to the tarsus are difficult to inject, and therefore not really feasible or appropriate. Administering vaccines (or any injections for that matter) in the tail should be avoided. Giving injections in the tail is difficult because of the scant amounts of loose skin and subcutaneous tissue, which is

likely to cause more discomfort in patients during vaccination. More importantly, if a tumor does arise proximally on the tail, the potential for complete resection and cure are decreased because of the potential for tumor infiltration into the vertebral column. At present there is only one recombinant rabies vaccine approved for use in cats (PURE-VAX Feline Rabies vaccine'; Merial Ltd, Duluth, GA). The current USDA approval/label states that this product should be administered annually. There are multiple killed-virus rabies vaccines approved for use in cats, with initial vaccination occurring at 12 weeks of age with a subsequent vaccination 1 year later. Because regulations vary depending on state or region, the veterinary practitioner must be familiar with local laws regarding rabies vaccination in this species.[24]

Feline Leukemia Virus

Feline leukemia virus (FeLV) is a retrovirus primarily affecting cats of any age, but kittens and juvenile cats appear to be most susceptible to infection.[42] Clinical signs are numerous and nonspecific, and include pyrexia, failure to thrive, chronic or recurrent respiratory tract, and gastrointestinal disease. Infection in kittens occurs via vertical transmission from the queen to the fetus, but may also spread horizontally from queen to kitten during lactation and grooming. Transmission also occurs through direct and usually prolonged contact with other infected cats from behaviors such as grooming and sharing food, and water bowls, and litter boxes. Viral screening using an enzyme-linked immunosorbent assay (ELISA) test designed to detect antigenemia should be performed on all kittens, even if their owners plan to house them strictly indoors. Because the ELISA test detects antigen, maternal antibody and vaccination do not interfere with test results. Therefore kittens of any age may be tested, and the current recommendation is to test every kitten (and adult cats with an unknown viral status) prior to FeLV vaccination.[43] If a kitten is antigen negative, the current recommendation is to administer either a killed or a recombinant vaccine on the first or second kitten visit. A second vaccine should be administered 4 weeks later followed by vaccination 1 year after the last FeLV kitten vaccine.[2,7] The recommended site for administration of any FeLV vaccine is the left pelvic limb, as distally as is reasonably possible.[2] At present there is only one recombinant FeLV vaccine available (PUREVAX Recombinant Leukemia vaccine; Merial Ltd, Duluth, GA). Although FeLV is considered a noncore vaccine in adult cats because kittens are most vulnerable to infection and may be exposed if outdoors, and immunity increases with age, it is rational to vaccinate all kittens against this disease with a repeat vaccination 1 year later. If the cat is subsequently housed strictly indoors and does not live with an infected (FeLV) cat, additional vaccinations are not indicated.[2]

NONCORE FELINE PEDIATRIC VACCINES
Chlamydiosis

Chlamydophila felis, formerly known as *Chlamydia psittaci*, is a bacterium that causes upper respiratory tract disease in kittens and cats. The most common sign is conjunctivitis, but sneezing and nasal discharge may also be present. Transmission is typically through direct contact with infected cats. Kittens are most commonly affected, but usually recover fully with appropriate antibiotic therapy: either topical oxytetracycline (Terramycin ophthalmic ointment) or systemic tetracycline (Panmycin Aquadrops) or doxycycline (Vibramycin). Vaccination against this agent typically does not prevent infection but may prevent clinical signs of disease. Because the vaccine does not fully prevent infection and carries an association with adverse events that may be greater than the actual disease, routine vaccination of household pets with this product is

generally not recommended. However, it may be of use in some environments where the risk of infection is high, such as shelters or catteries with recent outbreaks.[2,44] If vaccination is deemed appropriate by the practitioner, an attenuated parenteral vaccine can be given to kittens beginning at 9 weeks, with a second dose given 3 to 4 weeks later.[45]

Bordetella

This bacterial agent causes respiratory tract disease in cats, and cats affected by stress, poor nutrition, or overcrowding seem more susceptible. Many kittens infected show mild, self-limiting disease with signs including pyrexia, sneezing, and nasal and ocular discharge, although bronchopneumonia has been documented. There is a topical, modified live bacterin vaccine designed for use in this species, but it is generally not recommended for routine use. If the practitioner feels protection against *B bronchiseptica* is warranted based on the kitten's risk of exposure, such as attendance at cat shows or visiting a boarding facility, or is in a shelter with potential contact with dogs (with a recent *B bronchiseptica* outbreak), administration of the vaccine designed for use in cats may be considered.[2] A single dose of the modified live intranasal vaccine can be given to kittens as young as 4 weeks of age.[2] The product designed for use in canines should not be used in cats.

FELINE, GENERALLY NOT RECOMMENDED

There are multiple vaccines in addition to those described and recommended here; however, many of these diseases pose a minimal risk to most of the feline population or the vaccines are minimally efficacious at preventing infection or disease, and therefore are generally not recommended. Additional reasons not to use some of these products are vaccine interference with screening tests and adverse events associated with some vaccines.

Feline Immunodeficiency Virus

A retrovirus, feline immunodeficiency virus (FIV) primarily affects cats by compromising their immune system, leaving them vulnerable to opportunistic infections. In addition to immunosuppression, with most of the effect targeted against the cell-mediated (T-cell) immune response, infection with FIV also carries an increased risk for development of certain types of neoplasia, B-cell lymphoma being the most common. Transmission occurs most commonly from breeding and fighting.[46] The virus is not spread through casual contact between housemates not engaging in the behaviors stated, nor is it spread through casual encounters between nonbreeding, nonfighting cats outside. Naturally occurring infection of kittens from queens is rare; however, kittens can become FIV-antibody positive via passive transfer from ingestion of colostrum of FIV-positive queens or queens previously vaccinated against FIV.[43,45] FIV-antibody levels acquired from maternal transfer in kittens who are actually FIV-virus negative decline over the first several months of life. The standard screening test for FIV is an ELISA test designed to detect FIV antibody. The ELISA was designed to detect antibody rather than antigen, because infected cats produce high levels of circulating antibody in contrast to low levels of circulating virus.[45] Because kittens may have circulating FIV antibody although actually may be FIV-antigen negative, it is generally not recommended to test kittens younger than 6 months. If a kitten is tested and a positive result is obtained, the test result should be repeated with a different methodology (Western blot or polymerase chain reaction [PCR]) and should be repeated once the kitten is more than 6 months old.[43] If a kitten is truly not infected,

the maternal antibody will wane by 6 months of age, leading to seroconversion. If, however, a kitten or cat remains seropositive, the recommendation is made to keep the cat indoors only from that point, both to prevent infection of other cats and to decrease exposure to potential environmental pathogens. FIV-infected cats can live for years and, unless otherwise indicated by concurrent disease, euthanasia is generally not indicated for most owned pets. There is a killed FIV vaccine available, but the efficacy of this product is still unknown. There are 5 known subtypes of FIV virus, and the vaccine has been formulated to protect against subtypes A and D; however, the predominant subtype infecting cats in North America and Europe appears to be subtype B. It is unknown whether cross-protection exists between the different subtypes.[45] Because the vaccine elicits a strong antibody response, vaccinated kittens and cats will become seropositive on both ELISA and Western blot tests, as both tests detect antibody. A PCR test is available but is currently only performed at certain laboratories, and results and reliability vary with testing centers. Because of the increased technological needs and increased costs of this test, it is not considered the standard screening test. If done under specific conditions it can detect virus, and therefore may be of benefit in differentiating between cats with viremia (truly infected cats) and kittens or cats with circulating antibody, attributable either to maternal transfer or vaccination. Because of the nature of transmission of the virus and interference with the standard screening methods for infection, the vaccination against FIV is not currently recommended. Keeping cats indoors if possible, neutering all cats going outside, and preventing exposure to stray or feral cats that may be more likely to engage in fighting behaviors remain the gold standards for preventing this disease.[45,46]

Feline Infectious Peritonitis

The disease feline infectious peritonitis (FIP) is caused by a member of the Coronaviridae. Feline enteric coronavirus (FECV) and FIP virus are 2 phenotypes of the same virus. FECV transmission occurs through the fecal-oral route where it typically infects intestinal epithelium, but the organism can be transmitted via fomites and persists for long periods of time in the environment. Most cats infected with FECV either do not show clinical signs of disease or may have transient diarrhea, and some will persistently shed the virus in their feces.[47] FECV can, however, undergo random mutations within a host, creating FIP virus, although in most cats the virus does not mutate into this form and most cats will not develop FIP. The FIP virus enters and replicates within macrophages where it can then be disseminated throughout the body. Clinical signs are numerous, but commonly include weight loss, failure to thrive, diarrhea, pyrexia, and chronic respiratory tract disease. Two main types of the disease exist, the dry (noneffusive) and the wet (effusive) forms. Both are ultimately fatal diseases.[48] Although there is a vaccine available, its efficacy and indication for use is believed to be minimal, if at all.[48] The current recommendation is not to use this vaccine, based on efficacy concerns and the minimal risk of infection in most kittens and cats. Infection with FECV and mutation with subsequent development of disease occurs most commonly in multiple-cat households ($\geq$5), catteries, and shelters. The standard screening test for FIP is a serologic, indirect immunofluorescent antibody (IFA) test designed to detect antibody. This test may be of some value, but results need to be interpreted with caution, and concomitantly with signalment, clinical signs, and other laboratory data. Prior vaccination against FIP will yield positive IFA results, further posing potential complications in routing screening of this disease. In general, kittens are most vulnerable to this disease, with greater than 50% of cats with FIP being younger than 2 years.[48] Prevention is directed toward decreasing stress in kittens and cats in multiple-cat households, preventing exposure of naïve kittens and cats

in environments known to have high endemic levels of feline enteric corona virus, and at depopulating catteries known to have high prevalence rates of FECV and FIP.[47,48] Because of the complexity of this disease and the limited space and objectives of this discussion, readers are encouraged to review *Infectious Diseases of the Dog and Cat*, 3rd edition, by Greene, and *Textbook of Veterinary Internal Medicine*, 7th edition, by Ettinger and Feldman, for a more comprehensive review of this disease.

ADVERSE EVENTS ASSOCIATED WITH VACCINES

Vaccines are potent biological agents designed to prevent disease. Any foreign product administered to an animal has the potential to be associated with an unexpected response by that animal. While vaccines must meet USDA requirements for safety, efficacy, potency, and purity, there still exists the potential for adverse events with products that have met these standards. Veterinarians should always report adverse events associated with vaccination to the vaccine manufacturer. Some adverse events are more likely to occur with certain agents, whereas others appear to have an increased rate of occurrence in certain breeds. Still others may be idiosyncratic and are not predictable. The following is offered as a brief overview of some types of adverse events associated with vaccination, with suggestions as to how a practitioner might best respond to and prevent such events from recurring.

The reactions seen most commonly are local inflammation at the site of the injection or general malaise, pyrexia, and anorexia for 1 to 2 days after vaccination.[12] Most of these reactions are self-limiting and require nothing more than monitoring by the animal owner. It is appropriate for the practitioner to note any reaction along with a description of signs documented in the medical record, and offer supportive care if indicated. In some instances administration of an MLV vaccine will cause transient mild clinical disease. Supportive care and isolation from unvaccinated animals is recommended, as the vaccinated animal showing clinical disease will shed the vaccinal organism and is potentially infectious to other animals.[9] Contact information for vaccine manufacturers, support agencies, and disease-reporting organizations is included in **Table 4**.

Feline Injection-Site Sarcomas

Feline injection-site sarcomas (FISS), formerly known as feline vaccine-associated sarcomas or fibrosarcomas, develop secondarily to local inflammation at injection sites. Originally it was thought that there was an increased risk for development of these tumors associated with specific adjuvants and vaccines; however, it is now accepted that all vaccines and repositol agents such as long-acting penicillin and corticosteroid injections, in addition to other injections, can be associated with the formation of FISS.[41] Measures to prevent these tumors are aimed at decreasing the local inflammatory response by avoiding the use of adjuvants in this species and administering only those vaccines indicated for the individual animal.[49,50] Multiple vaccines should not be administered in one site, as this may increase the amount of inflammation in that site. Following the recommended sites for injection is strongly recommended (see individual vaccine sections for specific sites)[2,6] and avoiding adjuvanted products when there is a reasonable alternative (MLV or recombinant) product available is ideal, as a recent study confirmed an increased association of tumor formation with adjuvanted vaccines compared with recombinant vaccines, although no vaccine was risk free.[51,52] There are specific guidelines as to how a practitioner should proceed if a cat develops a swelling at the site of a vaccine or injection. The practitioner is advised to monitor the patient closely, documenting 3-dimensional measurements and temporal association if a mass or swelling develops at the site of a vaccine. The 3-2-1 rule developed by the

Table 4
Support organizations, regulatory and disease reporting agencies, and vaccine manufacturers

Agency or Company	Address	Web Site and Phone Number	Support Available
American Animal Hospital Association	12575 West Bayaud Avenue, Lakewood, CO 80228, USA	www.aahanet.org 303.986.2800 Email: info@aahanet.org	Position statements on current vaccination guidelines, life-stage recommendations, standards for care and conduct
American Association of Feline Practitioners	390 Amwell Road, Suite 402, Hillsborough, NJ 08844, USA	www.catvets.com 800.874.0498	Position statements on viral screening, vaccination guidelines, life-stage recommendations, cat-friendly practice requirements
American Veterinary Medical Association	1931 North Meacham Road, Suite 100, Schaumburg, IL 60173-4360, USA	www.avma.org 800.248.2862	Links available to multiple sites, position statements on vaccination guidelines, zoonotic disease prevention and adverse event reporting (Feline Vaccine Sarcoma Task Force)
Centers for Disease Control and Prevention	1600 Clifton Road, N.E., Atlanta, GA 30333, USA	www.cdc.gov 800.CDC-INFO (800.232.4636)	United States government agency (department of Health and Human Services). Current information regarding infectious and noninfectious diseases

Center for Veterinary Biologics	USDA Animal and Plant Health Inspection Service	www.aphis.usda.gov 515.337.6100	Division of United States Department of Agriculture (USDA), contact agency for reporting adverse events associated with veterinary biologics
National Association of State Public Health Veterinarians, Inc	National Association of State Public Health Veterinarians	www.nasphv.org	Compendium of Animal Rabies Prevention and Control, rabies vaccination certificates available. List of all state veterinarians available online
Boehringer Ingelheim Vetmedica, Inc	3902 Gene Field Road, St Joseph, MO 64506, USA	www.boehringer-ingelheim.com Technical services: 800.325.9167	Manufacturer
Heska Corp	3760 Rocky Mountain Ave, Loveland, CO 80538, USA	www.heska.com 1.800.GO-HESKA (1.800.464.3752)	Manufacturer
Merck Animal Health	556 Morris Avenue, Summit, NJ 07901, USA	www.merck-animal-health-usa.com Companion Animal (dogs and cats): 800.224.5318	Manufacturer
Merial Ltd	3239 Satellite Blvd, Building 500, Duluth, GA 30096-4640, USA	www.merial.us Technical services: 1.888.MERIAL1, ext. 3 (1.888.637.4251, ext. 3)	Manufacturer
Virbac Corp	3200 Meacham Blvd, Ft Worth, TX 76137-4611, USA	www.virbacvet.com Technical services: 800.338.3659	Manufacturer
Zoetis	100 Campus Drive, Florham Park, NJ 07932, USA	www.zoetis.com 1.973.822.7000	Manufacturer

Feline Vaccine-Associated Sarcoma Task Force should be closely applied. "Three" refers to persistence of the mass for 3 months or greater; "2" refers to a size of 2 cm or greater; and "1" applies if the mass increases in size after 1 month. If any of these criteria are met, the mass should be biopsied with wedge technique or needle biopsy allowing for complete resection of the biopsy margins in the future, and subsequent referral to an oncologist or surgical oncologist if fibrosarcoma is confirmed. Fine-needle aspiration is not recommended for evaluation of potential injection-site sarcomas.[49,50] Most vaccine manufacturers have programs established to help defray the medical and surgical costs associated with these tumors, and the practitioner is advised to always notify the vaccine manufacturer any time an adverse event is seen.

Type I Hypersensitivity

Type I hypersensitivity, also known as immediate hypersensitivity and, in some cases, anaphylaxis, is mediated by immunoglobulin E antibody. The host's immune system may react to anything contained within the vaccine product, including cellular products used for culture, adjuvant, preservative, and the antigen itself, and reaction typically occurs within 2 to 3 hours after the administration of a vaccine. In the dog, signs range from urticaria, angioedema, and pruritus (Fig. 2) to respiratory distress and fulminant vascular collapse (anaphylaxis). In the cat, acute onset of vomiting and diarrhea with associated hypovolemia and respiratory and vascular shock may be seen.[12] If an animal develops any of these signs within the first several hours after vaccination, it should be presented to the veterinarian immediately for emergency medical care and support. It is not the goal of this review to offer therapies for shock, so the reader is referred to emergency veterinary literature for recommended therapies. The point here is to advise the practitioner to proceed with caution when using vaccines that may have a higher incidence of these reactions, or in breeds that may be at increased risk for immediate hypersensitivity. The increased association between killed bacterin vaccines and type I reactions is well documented, and there are reports that toy breeds may be at increased risk for type I reactions associated with these vaccines. If an animal does have a type I reaction to a vaccine, the signs shown by the patient, interval between vaccine and onset of signs, and therapeutics administered should be well documented in the medical record, as well as plans for future vaccination of the patient in question. Once an animal has this type of reaction to a vaccine, ideally the product should not be used again in that patient. All subsequent vaccines should be administered after a complete physical examination, and the vaccine should be given

Fig. 2. Type I hypersensitivity (angioedema) in a Labrador retriever puppy after vaccination. (*Courtesy of* Dr Autumn Davidson, DVM, DACVIM, Davis, CA.)

early in the day to allow monitoring of the patient in the hospital for several hours. However, if this is not possible the patient should remain in the veterinary hospital for monitoring for at least 30 minutes followed by subsequent monitoring by the owner at home for several hours. Pretreatment with diphenhydramine (Benadryl) is an option, given parenterally (subcutaneous or intramuscular routes) at the dose of 1.0 mg/kg 15 to 30 minutes before vaccination if hypersensitivity is a concern. However, administration of corticosteroids concurrently with vaccination to prevent a hypersensitivity reaction is neither appropriate nor recommended because of potential immunosuppression and vaccine interference.[9] The patient's medical record should be identified, outside and inside, to prevent future accidental readministration of the product. Advising the owner that the patient should never receive that product again is important.

Type II Hypersensitivity

Type II hypersensitivity reactions (autoimmune reactions) are suspected to occur in dogs secondarily to vaccine administration. Although this theory is yet unproved, there are reports of dogs developing immune-mediated thrombocytopenia and immune-mediated hemolytic anemia temporally associated with recent vaccination. If a dog develops either of these conditions within 1 to 2 months after vaccine administration, the practitioner is advised to strongly consider the risk/benefit ratio of subsequent use of that product in the patient.[9,53]

Type III Hypersensitivity

Type III hypersensitivity reactions are immune complex reactions. Examples include the anterior uveitis associated with use of the CAV-I vaccine and the complement-mediated rabies vaccine induced vasculitis-dermatitis seen in dogs. Other examples include glomerulonephritis and polyarthritis. Antihistamine administered at the time of vaccine will do nothing to prevent the reaction, nor is it recommended to administer corticosteroids concurrently with vaccination. Once an animal has had this type of reaction, subsequent use of the product should be avoided in that patient.[9,54]

Type IV Hypersensitivity

Type IV hypersensitivity reactions are cell-mediated responses occurring locally or systemically. Examples include sterile granulomas at the sites of vaccine administration or polyradiculoneuritis. Many sterile granulomas resolve without any intervention, but for more severe reactions the practitioner is referred to various medicine texts for recommendations.[9,53]

SPECIAL CIRCUMSTANCES

The foregoing discussion applies mainly to puppies and kittens owned by individuals. Puppies and kittens housed in shelters face unique challenges, as do orphaned animals. These animals may not have received colostrum, and it is more likely that their mothers were not adequately vaccinated. The implications are that these animals are less likely to have received maternal antibodies, leaving them more vulnerable in the earliest stages of life. In addition, they frequently are malnourished, have an increased parasite burden, and are placed in crowded environments possibly with high numbers of endemic pathogens. The American Animal Hospital Association Canine Vaccination Task Force and American Association of Feline Practitioners have developed recommendations specifically designed for puppies and kittens in these environments. In general, neonates who may not have

received colostrum or who are housed under the aforesaid conditions may be vaccinated at an earlier age, and ideally should be vaccinated before or at the time of entry into the shelter. Use of recombinant products may be of benefit in these animals, as well as additional vaccines (noncore vaccines). Husbandry is extremely important in these animals: providing proper nutrition, anthelmintics, and clean, dry housing is paramount. In general, these animals are special subsets of the general population facing challenges most young animals do not experience. Fiscal considerations and overall population health applies in these cases much more so than to individual, client-owned pets.

SUMMARY

Vaccines are perhaps one of the practitioner's greatest tools in preventing disease and maintaining individual and population health. Vaccination is to be used with forethought based on the risk of disease to the population and the individual, balanced with assessment of the risks associated with individual vaccines. It is the practitioner's role to educate pet owners regarding actual risks associated with both undervaccination and overvaccination. The goal is to reach the highest level of overall animal health with the minimum number of adverse events, based on scientific and epidemiologic merit.

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