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Current Vaccination Strategies in Puppies and Kittens

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It is far better to prevent rather than experience disease. This should be the philosophy and goal of every veterinarian as well as 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 those diseases attributable, in a large part, to the development of effective vaccines. Veterinary practice staff members have done a remarkable job in sending reminder cards, ensuring 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 pet fall behind on its 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. This information may not be accurate, however. It is our duty to educate pet owners; in fact, it should be seen as an opportunity. Who better to disseminate knowledge 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 discuss and understand how to make appropriate choices regarding pediatric vaccinations adequately, a brief review and discussion of terms relative to basic immunology are warranted. Passive immunization occurs when maternal antibody is transferred by the dam or queen to the fetus via the placenta, which

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has a minimal effect in these species. It also occurs during initial suckling through the ingestion of colostrum and lactation, which have more significant effects in these species [1]. This maternal immunity does provide initial protection against many pathogens but, of course, is dependent on the health and immune status of the mother as well as the health of the fetus and neonate. Although this may result in temporary protection for the infant, in the long term, it may be deleterious to that individual's health by essentially keeping that animal naive 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 the species; amount of maternal antibody produced, transferred, and absorbed; and individual health status of the neonate), most puppies and kittens have maternal antibody levels below protective levels. If present at high enough levels, however, maternal antibodies can interfere with the neonate's ability to respond to vaccination, because 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 for multiple sequential vaccines in kittens less than 12 weeks of age and puppies less than 16 weeks of age. 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 and/or 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, and various cytokines, such as tumor necrosis factor- α and interleukins, as well as various vasoactive molecules, such as histamine [2].

Active immunization is the process of the individual responding to an antigenic stimulus appropriately by natural infection or vaccination. Active immunization is processed through the acquired immune system. The two 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 are dependent 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 [3].

Kittens and puppies have varying degrees of ability to respond to antigens, whether attributable to 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 naive 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. This initial exposure and recognition process and the ability to produce antibody to respond to the antigen typically take 10 to 14 days. Subsequent exposures to the same antigen elicit a stronger response; a greater amount of antibody is produced, and the subsequent response is faster. This is known as the secondary, or anamnestic, immune response. 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 has previously been exposed [2].

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 the 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 of safe efficacious vaccines available is critical. In essence, we must assess each patient 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 concept of *core* and *non-core* vaccines, two terms commonly used when discussing vaccination within the veterinary field. Criteria for assigning vaccines into these categories as well as a third category, "generally not recommended," are based on the following factors [4–8]:

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. Prevalence 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 a risk to the individual or population)
3. Risk of the individual for exposure to the disease (eg, indoor-only animal versus free-roaming individual, regional variations of occurrence)
4. Efficacy of the vaccine (does the vaccine prevent infection or simply ameliorate some signs or length of the disease?)

5. Risks associated with administering the vaccine (are the risks associated with that vaccine greater than the risk of the disease?)
6. Potential for zoonotic disease
7. Route of infection or transmissibility

When these criteria are assessed, general guidelines may be generated for the individual practitioner as well as for 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. They are, simply stated, 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 [pathogen and host], owner concerns, and current vaccine technologies) [4–8].

TYPES OF VACCINES

There are multiple vaccines available for our canine and feline patients; yet, most vaccines fall within three basic categories. Assignment of vaccine products (which are considered biologic agents rather than drugs and are therefore assessed and approved by the US Department of Agriculture [USDA] rather than the US Food and Drug Administration [FDA]) into these categories is based on how the product is created. Simply stated, modified-live vaccines (ML) 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. Modified-live virus vaccines (MLV) are therefore vaccines containing live but avirulent virus. 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. There are multiple types of recombinant vaccines, and this category itself has three subcategories. These vaccines use genetic technologies to introduce genetic material directly into the host (no vector is used [eg, purified subunit vaccines, type I recombinant]), 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 recombinant rabies, type III recombinant) [9,10]. Within the near future, multiple new technologies are likely to provide us with even more choices, hopefully providing our patients with better protection against disease with minimal vaccine-associated risks. 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 ensure consistent levels of antigen and adjuvant in individual doses from a single vial [4,8]. Multivalent vaccines are not recommended in cats other than the core feline vaccine designed to protect against feline panleukopenia, feline herpesvirus I (FHV-1), and feline calicivirus (FCV). Because of increased inflammation at the site of multivalent vaccines,

all other vaccines should be given as a separate vaccine at the indicated site (see discussion on feline core and noncore vaccines) [5,8]. Allowing vaccines to acclimate to room temperature before administration, particularly in cats, is recommended, because the administration of cold vaccines was found to have an increased association with tumorigenesis in cats [11].

The practitioner is advised always to follow manufacturer's directions for dose and route of administration. Using a topical product parenterally or splitting doses should never be done. Administration of a modified-live bacterin vaccine designed for topical administration yet administered parenterally may have serious and potentially fatal consequences (Fig. 1). 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 [4,12].

The interval between various vaccines, whether using the same product serially in the initial series or using different products in an adult animal, should never be less than 2 to 3 weeks. Interference between the first product administered and a second vaccine product may lead to failure to respond to that second vaccine optimally. The exact mechanism of this interference is unknown but may be associated with interferon produced by cells processing an ML agent or by transient immunosuppression by an ML agent. Multiple vaccines administered at the same time do not seem to elicit this interference and is therefore an acceptable practice [6,9]. The reader is referred to Tables 2 and 3 for a 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 or mortality; they are of public health concern, are readily transmissible, or may be ubiquitous in the environment. In addition, safe efficacious vaccines are available and provide sterile immunity (prevent infection) or confer a high degree of protection (do not prevent infection but may confer protection, such that the animal does not develop clinical signs of disease) [4,5]. Essentially, the vaccines that fall within this category are recommended for each individual within the population regardless of that animal's lifestyle or locale.

Distemper

Canine distemper virus (CDV), an enveloped morbillivirus, has been well controlled because of widespread vaccination programs over the past several decades. The disease still persists, however, and in addition to high virulence, it is readily 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 beginning at 6 to 9 weeks of age and to give serial vaccines every 3 to 4 weeks until

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) | <p>Virus or bacteria made less virulent via cell or tissue passage</p> <p>Attenuated viruses able to enter host's cells and replicate</p> <p>Stimulates cell-mediated and humoral immunity</p> | <p>Mimics natural infection</p> <p>Rapid response by host's immune system</p> <p>Many products able to stimulate adequate immune response with a single dose</p> <p>Does not require use of adjuvant</p> <p>Vaccination of a single individual leads to viral shedding, which may be useful in a herd health situation when rapid exposure of multiple animals with an attenuated organism is desired</p> | <p>Potential to cause disease in some individuals (should not use in immune-compromised animals)</p> <p>Potential of organism to revert to more virulent form and cause disease even in healthy animals</p> <p>Special handling of vaccines required (temperature sensitive, shorter shelf life than killed products)</p> <p>Vaccinates shedding the modified-live vaccinal organisms may lead to disease outbreaks in certain environments</p> <p>Parenteral administration of topical modified-live bacterin products may lead to serious disease (eg, abscess at vaccine site, sepsis)</p> |

| | | | |
|-----------------------------|---|--|--|
| <p>Killed (inactivated)</p> | <p>Virus or bacteria chemically or heat inactivated Organism unable to enter host's cells actively, unable to replicate Stimulates cell-mediated and humoral immunity</p> | <p>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</p> | <p>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 enter host's immunocytes actively 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 two doses to stimulate protective response Greater potential for contamination and adverse reactions (require higher antigen load and adjuvants may cause adverse effects)</p> <p><i>(continued on next page)</i></p> |
|-----------------------------|---|--|--|

Table 1
(continued)

| Vaccine type | Manufacturing process, method of action | Associated benefits and recommendations | Associated precautions and contraindications |
|---|--|---|--|
| Recombinant (subunit, gene deleted, vectored) | <p>Genetic material from pathogen altered in some way; three categories of recombinant vaccine technology use various techniques</p> <p>Subunit vaccines are created by inserting specific genomic regions from the desired pathogen into nonpathogenic bacteria; bacteria then produce protein as coded by the inserted genome; desired protein is then harvested, purified, and used as a vaccine</p> <p>Vectored virus vaccines incorporate immunogenic genomic regions from pathogen into an attenuated non-pathogenic virus</p> | <p>Vector able to penetrate host's cells, delivering genetic material from pathogen into the cell; therefore, no need for adjuvant</p> <p>Rapid onset of immunity</p> <p>Stimulates cell-mediated and humoral immunity</p> <p>No potential for reversion to virulence</p> <p>May be able to overcome maternal antibody interference earlier than modified-live or killed products</p> <p>Does not cause disease in healthy or immune-compromised animals (appropriate for use in FIV+ and FeLV+ cats)</p> <p>Vaccinates do not shed virus</p> | <p>Requires handling similar to modified live products (shorter shelf life, temperature sensitive)</p> <p>Increased cost in manufacturing and therefore increased cost to consumer</p> |

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

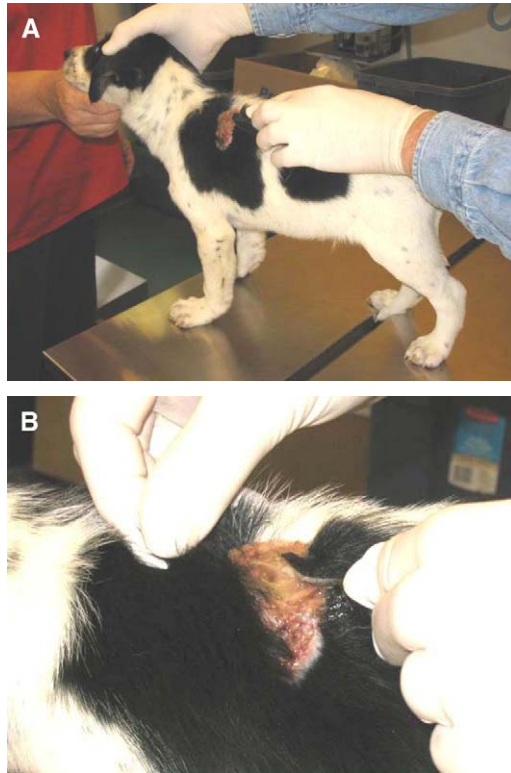


Fig. 1. (A) Puppy with an abscess secondary to parenteral administration of a modified-live *B bronchiseptica* vaccine designed for intranasal (topical) administration. (B) Close-up of the abscess in A. (Courtesy of Richard Ford, DVM, Raleigh, NC.)

the puppy has reached 14 to 16 weeks of age [4,9,14]. Currently, there is one product that contains modified-live distemper virus, canine adenovirus type II (CAV-II), and canine parvovirus (CPV) (Continuum; Intervet, Millsboro, Delaware), but there are numerous vaccines with high safety and efficacy records that also include canine parainfluenza virus. There is also a vaccine that combines a recombinant canarypox-vectored CDV with modified-live adenovirus II, parainfluenza, and parvovirus (Recombitek; Merial Ltd, Duluth, Georgia), and this vaccine seems to be less affected by maternal antibody interference than MLV vaccines [15]. Other studies support the improved ability of recombinant vaccines to overcome maternal antibody interference as compared with MLV vaccines [16,17]. Most puppies receive two or three distemper vaccinations, depending on the age when they are first presented to the veterinarian. It is, however, 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

Table 2

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

| Canine | Core | Noncore | Not recommended |
|--|--|--|---|
| CDV | MLV or recombinant beginning at 6–9 weeks, given every 3–4 weeks until ~16 weeks of age | | |
| 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 weeks) | | |
| Leptospirosis | | Killed bacterin or purified subunit product beginning at 12 weeks, 2 to 3 doses given at 4-week intervals | |
| <i>Bordetella bronchiseptica</i> | | Attenuated bacterin, a single dose of an intranasal vaccine given 1 week before potential exposure (minimum of 4 weeks of age) | |
| Parainfluenza | | MLV, either use topical product combined with <i>B bronchiseptica</i> or parenteral vaccine contained in multivalent DAPP products | |
| Lyme disease (<i>Borrelia burgdorferi</i>) | | Recombinant subunit vaccine (OspA) before exposure to ticks, 2 doses given 4 weeks apart beginning at 9 weeks of age | |
| Measles | | | No longer recommended, use recombinant distemper vaccine for high-risk puppies instead of measles (continued on next page) |

Table 2
(continued)

| Canine | Core | Noncore | Not recommended |
|------------------------|------|---------|---|
| Coronavirus | | | Not recommended |
| <i>Giardia lamblia</i> | | | Not recommended |
| Rattlesnake vaccine | | | Insufficient data to evaluate efficacy; prevention of exposure, aversion training, and immediate veterinary attention after exposure highly recommended |
| CAV I | | | Not recommended; CAV II to prevent CAV I infection is highly recommended |

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

risk of vaccine failure that may occur when only one 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 [2]. Potential causes for vaccine failure include an MLV vaccine that was improperly stored and therefore 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), and maternal interference [9]. In theory, if a puppy were kept "sequestered" from exposure to this virus, one MLV distemper vaccine administered after 16 weeks of age would confer protection for at least 1 year [1,4]. In reality, however, 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 to decrease behavior problems in young adult and mature dogs [18]. 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 old) for administration of another dose of distemper vaccine. After the first "annual" vaccination, triennial immunization is recommended for MLV vaccines [4,19]. Annual revaccination is currently recommended if the recombinant product is used [4,9].

Canine Adenovirus

There are two types of adenovirus that cause disease in our 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

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

| Feline | Core | Noncore | Not recommended |
|---|--|---|-----------------|
| Feline herpesvirus FVR | MLV, give 2 to 3 doses of parenteral product beginning at 6 to 9 weeks of age every 3 to 4 weeks until ~12 weeks of age | | |
| Calicivirus | MLV, frequency as for FVR | | |
| Panleukopenia | MLV, frequency as for FVR | | |
| Rabies | Recombinant canarypox-vectored product, single dose at minimum age of 8 weeks of age but varies dependent on state and local regulations | | |
| FelV ^a | | After viral screening confirming negative viral FelV status, recombinant canarypox-vectored or killed product, 2 doses given 4 weeks apart as early as 8 weeks of age | |
| Chlamydiosis (<i>Chlamydomphila felis</i>) | | In high-risk environments, use parenteral attenuated bacterin product, 2 doses given 4 weeks apart beginning at 9 weeks of age | |

| | | |
|----------------------------------|---|---|
| <i>Bordetella bronchiseptica</i> | In high-risk environments, topical attenuated bacterin product designed for use in this species, single dose as early as 4 weeks of age | |
| Feline immunodeficiency virus | | Not generally recommended in kittens; viral testing in kittens less than 6 months of age may yield false-positive results because of PMA; vaccination causes positive Ab test |
| Feline infectious peritonitis | | Not recommended; vaccination causes positive Ab test |
| <i>Giardia lamblia</i> | | Not recommended |

Abbreviations: Ab, antibody; FeLV, feline leukemia virus; FVR, feline viral rhinotracheitis; MLV, modified-live virus; PMA, persistent maternal antibodies.

^aBecause of increased susceptibility for infection in kittens, vaccination against FeLV is strongly recommended for all kittens. In single-cat households, households with known negative viral status of all cats, and households with indoor only cats, the practitioner may elect to consider this a noncore vaccine.

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 MLV product 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 MLV because it stimulates the immune system to protect against CAV-I and CAV-II without the associated adverse reaction caused by the type I vaccine [4,14,20]. A modified-live adeno-type II virus is typically included in a multivalent injection (as mentioned previously) 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 of age. 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 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 seem to be at highest risk for developing severe life-threatening disease. The current recommendation for vaccination is to use a multivalent MLV beginning at 6 to 9 weeks of age and to repeat the vaccine at intervals as stated previously (every 3 to 4 weeks until the puppy is 14 to 16 weeks of age). There has been some concern that certain breeds may be at increased risk for contracting and developing severe parvoviral disease (eg, Doberman Pinschers, Rottweilers), but it is generally agreed that these breeds mount an appropriate response to a quality product if the last vaccine is given between 14 and 16 weeks of age [13,21]. Recent studies using MLV CPV2b strains showed a higher antibody response to CPV2 and CPV2b and that the CPV2b strain vaccines were better able to overcome maternal antibody interference than the CPV2 strain vaccines used [22,23]. An alternative would be to use serial vaccinations of killed virus if the practitioner were concerned about the potential for vaccine-induced clinical disease in one of the breeds believed to be more susceptible to this virus; however, these vaccines are less immunogenic [13]. Immunization 1 year after completing the initial puppy series is recommended, with subsequent triennial vaccinations [4,19,24].

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 behavior 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 [4,5]. It is the practitioner's professional responsibility to acquire knowledge of and maintain adherence to regional laws regarding rabies vaccination frequency [25].

NONCORE CANINE PEDIATRIC VACCINES

Vaccines in the noncore category have limited efficacy, or the organism causing disease is not readily transmissible or may have limited geographic distribution or prevalence. Additionally, the diseases these vaccines are designed to prevent may be so mild or self-limiting that the risk associated with administering the vaccines may be greater than that of the actual disease. Finally, 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 [4–7].

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 two 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 [26]. Although these organisms have the potential to cause serious disease, dogs are not likely to be at risk in a mostly urban and controlled environment (eg, housed in a fenced yard with no exposure to wildlife or livestock). A dog that frequents rural environments or has exposure to waterways or livestock is definitely at risk of infection, however, and should therefore be protected against the disease. Again, the initial puppy appointments should involve a thorough history and include the owner's plans for that dog's future use. If an owner brings a Labrador Retriever puppy to the veterinarian for "whatever vaccines it needs," it is up to the practitioner to ask: "Will it be a hunting dog, will it be used in field trials, or will it be exposed to wildlife and waterways?" The Border Collie that lives on a working sheep ranch surely should be vaccinated as well. Conversely, a long-haired Miniature

Dachshund that spends its days on its owner's lap is at minimal risk of exposure; therefore, vaccination is most likely not warranted. In essence, the regional distribution, seasonality (increased prevalence during and immediately after the rainy season), and lifestyle of the puppy should factor 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 of age; at that 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 those serovars known to cause disease in a given region is recommended. Currently, there is one killed purified subunit vaccine (LeptoVax; Fort Dodge Animal Health, Overland Park, Kansas) that contains four serovars (*icterohaemorrhagiae*, *canicola*, *pomona*, and *grippotyphosa*); however, the duration of immunity against *grippotyphosa* and *pomona* is unknown, and there are no vaccines available for *autumnalis* or *bratislava*. An initial series of two to three vaccinations should be administered monthly and repeated at least annually thereafter as long as exposure to the agent exists [27]. 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 this vaccine and to increase the likelihood of a complete immune response minimizing ineffective vaccinations [4,28].

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 (eg, canine parainfluenza virus, 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 an avirulent live bacterin for *B bronchiseptica* and a modified-live canine parainfluenza virus. Although the vaccine can be administered to puppies as young as 3 to 4 weeks of age, it is generally not indicated unless the puppy is in a kennel environment [28]. Many organized 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 because they stimulate rapid local immunity [5,9]. If the puppy is intermittently exposed throughout the year (eg, traveling to shows or boarding or grooming facilities), the vaccine should be administered every 6 months.

Parainfluenza

As stated previously, parainfluenza may occur in concert with other respiratory tract agents. The vaccine recommendations are as stated for *B bronchiseptica* if indicated. There are multiple products available, but the product currently recommended is the combination intranasal vaccine containing a modified-live

parainfluenza virus with an attenuated *B bronchiseptica* bacterin. For optimal protection, the vaccine should be administered every 6 months to annually if indicated. Alternatively, many multivalent products containing modified-live CDV, CAV II, CPV, and parainfluenza are available and appropriate for use [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; therefore, the risk to human beings and other pets is thought to be minimal. If a puppy has a significant burden with infected ticks, this, of course, increases the exposure to others in the household; however, because ticks typically do not reattach once they have taken a complete meal, the risk is thought to be quite small unless appropriate tick control is not instituted [29]. Vaccination to protect against Lyme disease is controversial, because the duration of immunity and degree of protection provided by vaccination are unknown and vaccination with some vaccines interferes with standard screening diagnostics [30]. Therefore, vaccination against Lyme disease is warranted only if a puppy is at high risk for tick exposure and only if it lives in a *Borrelia* endemic area. There are killed and recombinant (outer surface protein A [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 of age and should be repeated 3 to 4 weeks later [28]. The best prophylaxis is likely achieved by using appropriate tick prevention, such as fipronil with methoprene spray or spot-on products (Frontline Top Spot; Merial Ltd, Iselin, New Jersey), amitraz collars (Preventic collar; Virbac, Fort Worth, Texas), or an imidacloprid/permethrin topical product (Canine Advantix; Bayer Animal Health, Shawnee Mission, Kansas) [30,31]. These products should be chosen and recommended carefully by the veterinarian based on household situations, owner concerns, and age of the puppy.

CANINE PEDIATRIC VACCINES NOT GENERALLY RECOMMENDED

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 not adequate to protect against infection. If indicated (see discussion of special circumstances), a single vaccination with an MLV vaccine should be given intramuscularly as early as 6 weeks of age. Subsequent immunizations with MLV CDV vaccines should be given serially as recommended previously (see section on CDV) [1,4,32]. Canine measles

vaccines should never be administered to female puppies older than 12 weeks of age because they may develop an acquired immune response to the virus. This could be problematic if a female puppy vaccinated against measles at 14 weeks of age, for example, later became pregnant. If the dog developed antibodies to the measles virus and maintained immunologic memory, it would confer measles antibody to 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 interference [15] (Autumn Davidson, DVM, Davis, CA, personal communication, 2005; regarding the American Animal Hospital Association Canine Vaccine Task Force 2005 guidelines, work in progress).

Canine Coronavirus

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 of the disease is unknown. Those most likely to be infected and develop clinical disease are neonates less than 6 weeks of age. Clinical signs may include diarrhea, possibly hemorrhagic but typically self-limiting. The general recommendation is to vaccinate puppies against CPV (as recommended previously), because this practice seems to confer protection against coronavirus in addition to preventing infection with CPV-2 [4,14].

Giardia lamblia

This protozoal parasite causes diarrhea in canine and feline patients as well as in many other mammalian species, including human beings. Transmission is via the fecal-oral route, with animals contracting the agent from contaminated feces or water. There is a killed vaccine available; however, vaccination against this agent is typically not recommended, because most animals are not at risk to contract the parasite, the vaccine does not prevent infection (it may ameliorate clinical signs and decrease cyst shedding), and the disease is readily amenable to therapy (fenbendazole, albendazole, and metronidazole are off-label uses but commonly accepted as standard of care). Because puppies should be prophylactically dewormed at regular intervals, it is unwarranted to use this vaccine even if the disease is suspected, because a standard anthelmintic dose of fenbendazole given for several days should resolve the infection [4,14,33,34].

Rattlesnake Vaccine

A vaccine designed to protect against envenomation by *Crotalus atrox*, the Western Diamondback rattlesnake, was released onto the market recently. The original provisional licensure was granted to provide possible protection against that single species of snake and was granted for use only in California. Recently, the company was granted extended provisional licensure for multiple states and has extended their claim for potential protection against multiple

species of members of the Crotalidae (pit vipers). At this time, 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 anecdotal reports of protection of naturally occurring envenomation [35]. The manufacturer does not claim that vaccination with this product completely protects against the effects of envenomation; rather, the manufacturer claims that it may slow the onset of clinical signs and decrease the severity of signs. Immediate veterinary care is still the “gold standard” for any snakebite. Because of the great potential for variability in envenomation (site of bite on an animal, size of the snake, amount of venom injected into an animal, and species of snake), field observations and anecdotal reports of protection are difficult to substantiate. Challenge studies done under controlled conditions are likely necessary to validate the efficacy of this product. At present, because of the preceding statements, this vaccine is not recommended for general use. Aversion training and keeping dogs out of areas known to favor rattlesnake habitation as well as immediate veterinary evaluation and care are still the standard recommendations for preventing and treating disease associated with rattlesnake envenomation.

Canine Adenovirus Type I

As stated in the canine core vaccine section, CAV-I causes serious disease in dogs; however, the use of the CAV-I vaccine is associated with a high incidence of adverse events. Vaccination with the CAV-II vaccine induces an immune response that is protective against CAV-I and CAV-II without the adverse effects. The recommendation is to use the CAV-II vaccine as part of the canine core vaccination program; the CAV-I vaccine should not be used [4].

CORE FELINE PEDIATRIC VACCINES

Feline Panleukopenia Virus

Feline panleukopenia, a nonenveloped parvovirus closely related to CPV, causes serious and often fatal disease in kittens. Transmission typically occurs from direct contact with infected animals, although in utero infection and fomite transmission also occur. Clinical signs typically include pyrexia, anorexia, lethargy, and 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 using MLV 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 a higher incidence of postvaccinal viral shedding and potential for clinical disease induced by the more virulent viruses in these vaccines) [4,5,8,9]. As is the case for canine CDV, CAV, and CPV, the core feline diseases, with the exception of rabies, are typically administered in a multivalent product in a series. There are numerous vaccine products containing feline panleukopenia virus, herpesvirus I, and calicivirus (see additional discussion). The current

recommendation is to choose an MLV nonadjuvanted product from a reputable manufacturer. Vaccines are administered subcutaneously in the right thoracic limb and given every 3 to 4 weeks until the kitten is 12 to 14 weeks of age. Repeat administration is recommended 1 year later before instituting a triennial schedule [4,8,36].

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 and/or lingual ulcerations and associated hypersalivation. In some cases, ulcerative crusting dermatitis that may mimic other dermatologic disease occurs [37]. 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 “recover” and do not show clinical signs. Cats infected with FHV-I may have recurrent “outbreaks,” especially in 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 in controlling this disease [37,38]. Vaccination with an MLV or recombinant vaccine beginning as early as 6 to 9 weeks of age is recommended. This is commonly administered as part of a multivalent product and is 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 at least 12 weeks old. The vaccine should be given 1 year later before beginning the triennial schedule [4,8].

Feline Calicivirus

FCV 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 FHV-I and FCV is through direct contact, exposure to contaminated secretions, aerosolization, and fomites [37,38]. A newer highly virulent strain of FCV was recently identified and carries a high incidence of mortality. Transmission is through direct contact or via fomites. Prior vaccination against FCV does not seem to be protective against this strain, and adult cats seem to be more severely affected than kittens [39,40]. The current recommendation is as previously discussed for panleukopenia and FHV-I: administering an MLV or recombinant virus parenteral vaccine beginning at 6 or 9 weeks of age, with a subsequent dose of vaccine 4 weeks later (last vaccination should be when the kitten is at least 12 weeks old). A booster vaccination should be administered 1 year later and then every 3 years [4,8].

Rabies

As stated previously, rabies virus affects all mammals; in this country, most documented rabies cases in pet animals occur in cats [41]. Because of the significant risk to pets, wildlife, and human beings, vaccination against rabies virus is highly recommended for all kittens and cats, even those kept inside [5,8]. Local requirements vary, but the general recommendation is that all kittens should be vaccinated beginning at 12 weeks of age with the recombinant rabies vaccine designed for use in cats [6]. This 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 is attenuated and 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 cell-mediated and humoral immune responses. In addition to the benefit of stimulating both types of immunity, the fact that no adjuvant is needed is beneficial [10]. 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 not appropriate. Currently, there is only a recombinant rabies vaccine approved for use in cats (PUREVAX Feline Rabies vaccine; Merial Ltd, Duluth, Georgia). The current USDA approval and label state 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 and a subsequent vaccination 1 year later. These products are highly efficacious but may carry an increased association with the development of fibrosarcoma formation because they contain adjuvants [5,6,8,11,42]. Because regulations vary depending on the state or region, the veterinary practitioner must be familiar with local laws regarding rabies vaccination in this species [25].

NONCORE FELINE PEDIATRIC VACCINES

Feline Leukemia Virus

Feline leukemia virus (FeLV) is a retrovirus affecting cats of any age, but kittens and juvenile cats seem to be most susceptible to infection [43]. Clinical signs are numerous and nonspecific, and they include pyrexia, failure to thrive, and 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 the queen to the kitten during lactation and grooming. Transmission also occurs through direct and usually prolonged contact with other infected cats from behaviors like grooming and sharing food and water bowls as well as litter boxes. Viral screening using an 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 [44]. If a kitten is antigen-negative, the current recommendation is to administer a recombinant vaccine on the second visit. A second dose of vaccine should be administered 4 weeks later, followed by vaccination 1 year after administration of the last FeLV vaccine in the kitten [6,8]. The recommended site for administration of any FeLV vaccine is the left pelvic limb as distally as is reasonably possible [8]. Currently, there is only one recombinant FeLV vaccine available (PUREVAX Recombinant Leukemia vaccine; Merial Ltd, Duluth, Georgia). This vaccine is administered with a needle-free high-pressure device that deposits the vaccine in skin, subcutaneous, and muscle tissues (VETJET delivery system, Merial Ltd, Duluth, Georgia, which is manufactured by BIOJECT, Tualatin, Oregon) [45]. There are killed virus vaccines that are efficacious; however, because they contain killed virus, they require an adjuvant to maximize the host's immune response. Because of documented associations between adjuvants and the formation of fibrosarcomas, the use of adjuvants in cats should be avoided when adjuvant-free products with comparable efficacy are available. The most recent findings linking injections of any type with fibrosarcoma formation in this species further support the use of a needle-free system as a viable means of vaccine delivery [6,11,42]. Under the current vaccine guidelines released in 2002 in the American Veterinary Medical Association Council on Biologic and Therapeutic Agents' report on cat and dog vaccines, vaccination against FeLV is only indicated if a kitten or cat is allowed to go outside or if the kitten or cat lives with an FeLV-positive cat. Because kittens are most vulnerable to infection and may have exposure if outdoors and because immunity increases with age, it is rational to vaccinate all kittens against this disease with a repeat vaccination 1 year later. Subsequent to that, if the cat is housed strictly indoors and does not live with an infected (FeLV-positive) cat, additional vaccinations are not indicated [8].

Chlamydiosis

Chlamydomphila 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—topical oxytetracycline (ophthalmic ointment) or systemic tetracycline or doxycycline. 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. It may be of use in some environments in which the risk of infection is high, however, such as shelters or

catteries [8,46]. If vaccination is deemed appropriate by the practitioner, an attenuated parenteral vaccine can be given to kittens beginning at 9 weeks of age, with a second dose given 3 to 4 weeks later [47].

Bordetella

This bacterial agent causes respiratory tract disease in cats, and cats affected by stress, poor nutrition, or overcrowding seem to be more susceptible. Although many infected kittens show mild self-limiting disease with signs that include pyrexia, sneezing, and nasal and ocular discharge, 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 thinks protection against *B bronchiseptica* is warranted based on the kitten's risk of exposure (eg, attends cat shows, goes to a boarding facility), administration of the vaccine designed for use in cats may be considered [8]. A single dose of the ML intranasal vaccine can be given to kittens as young as 4 weeks of age [47]. The product designed for use in dogs should not be used in cats.

FELINE PEDIATRIC VACCINES NOT GENERALLY RECOMMENDED

There are multiple vaccines in addition to those described and recommended previously; 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 carries an increased risk for development of certain types of neoplasia, with B-cell lymphoma being the most common. Transmission occurs most commonly from breeding and fighting. The virus is not spread through casual contact between housemates not engaging in the behaviors stated previously, nor is it spread through casual encounters between nonbreeding and 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 [48]. FIV antibody levels acquired from maternal transfer in kittens that are actually negative for FIV virus 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 [49]. Because kittens may have circulating FIV antibody, although actually being negative for FIV antigen, it is generally not recommended to test kittens less than 6 months of age. 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 older than 6 months of age [44]. If a kitten is truly not infected, the maternal antibody wanes 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 on so as to prevent infection of other cats and to decrease exposure to potential environmental pathogens. FIV-infected cats can live for years; 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 five 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 seems to be subtype B. It is unknown if cross-protection exists between the different subtypes [49]. Because the vaccine elicits a strong antibody response, vaccinated kittens and cats become seropositive on ELISA and Western blot tests, because both tests detect antibody. A PCR test is available but is currently only performed at certain laboratories. Because of the increased technologic 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 to maternal transfer or vaccination. Because of the nature of transmission of the virus and interference with the standard screening methods for infection, 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 [48,49].

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 two phenotypes of the same virus. FECV transmission occurs through the fecal-oral route, where it typically infects the intestinal epithelium, but the organism can be transmitted via fomites and persists for long periods in the environment. Most cats infected with FECV do not show clinical signs of disease or may have transient diarrhea; some persistently shed the virus in their feces [50]. FECV can, however, undergo random mutations within a host, creating FIP virus, although the virus does not mutate to this form in most cats and most cats do 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 [51]. Although there is a vaccine available, efficacy and indication for use are believed to be minimal, if at all [51]. 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 occur most commonly in multiple-cat households (five or more), 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 yields positive IFA results, further posing potential complications in routine screening of this disease. In general, kittens are most vulnerable to this disease, with greater than 50% of cats with FIP being less than 2 years of age [50]. Prevention is directed toward decreasing stress in kittens and cats in multiple-cat households and preventing exposure of naive kittens and cats in environments known to have high endemic levels of FECV and at depopulating catteries known to have high prevalence rates of FECV and FIP [50,51]. Because of the complexity of this disease and the limited space and objectives of this discussion, readers are encouraged to review the texts by Greene [52] and Ettinger and Feldman [53] for a more comprehensive review of this disease.

Giardia lamblia

As discussed in the canine section, vaccination with this product does not prevent infection but may decrease fecal shedding of infective cysts. Because vaccination does not prevent infection and the organism is readily treated with fenbendazole or metronidazole, routine use of this product in cats is generally not recommended [8].

ADVERSE EVENTS ASSOCIATED WITH VACCINES

Vaccines are potent biologic 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. Although vaccines must meet USDA requirements for safety, efficacy, potency, and purity, there still exists the potential for adverse events with products that have met those standards. Veterinarians should always report adverse events related to vaccination to the vaccine manufacturer. Some adverse events are more likely to occur with certain agents, whereas others seem 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 and to offer suggestions as to how a practitioner might best respond to and prevent those 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 exhibited, in the medical record and to offer supportive care if indicated. In some instances, administration of an ML causes transient mild clinical disease. Supportive care and isolation from unvaccinated animals are recommended, because the vaccinated animal showing clinical disease sheds 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, also known as feline vaccine-associated sarcomas or fibrosarcomas, develop secondary to local inflammation of injection sites. There is an increased risk for development of these tumors associated with adjuvants and certain repositol agents, such as long-acting penicillin and corticosteroid injections [42]. 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. Multiple vaccines should not be administered in one site because 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) [5,8]. There are specific guidelines as to how a practitioner should proceed if a cat develops a swelling at the site of a vaccination or injection. The practitioner is advised to monitor the patient closely, documenting three-dimensional measurements and temporal association if a mass or swelling develops at the site of a vaccination. The “three-two-one rule” developed by the Feline Vaccine-Associated Sarcoma Task Force should be closely applied. “Three” refers to persistence of the mass for 3 months or longer, “two” refers to a size of 2 cm or greater, and “one” applies if the mass increases in size after 1 month. If any of these criteria are met, the mass should be biopsied using 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 [54,55]. Most vaccine manufacturers have programs established to help defray the medical and surgical costs associated with these tumors, and the practitioner is advised always to notify the vaccine manufacturer whenever an adverse event is seen.

Type I Hypersensitivity

Type I hypersensitivity, also known as immediate hypersensitivity and, in some cases, anaphylaxis, is mediated by IgE 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 such a reaction typically occurs within 2 to 3 hours after the administration of a vaccine. In the dog, the most common signs are angioedema (Fig. 2),

urticaria, and pruritus, but symptoms may progress to respiratory distress and fulminant vascular collapse (anaphylaxis). In the cat, the 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; thus, 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 leptospirosis vaccines and type I reactions is well documented, and there are reports that toy breeds, particularly Miniature Dachshunds, may be at increased risk for type I reactions associated with leptospirosis vaccination [9]. If an animal does have a type I reaction to a vaccine, the signs exhibited by the patient, interval between vaccine administration and onset of signs, and therapeutics administered should be well documented in the medical record as well as plans for future vaccination of that patient. Ideally, once an animal has this type of reaction to a vaccine, that 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 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 is an option; it is given parenterally (subcutaneous or intramuscular route) at a dose of 1.0–2.0 mg/kg 15 to 30 minutes before vaccination if hypersensitivity is a concern. Administration of corticosteroids concurrently with vaccination to prevent a hypersensitivity reaction is neither appropriate nor recommended because of potential immunosuppression and vaccine interference, however [9,56]. The patient's medical record should be identified, outside and inside, to prevent future accidental readministration of that 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 secondary to vaccine administration. Although this theory is yet unproven, 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 would be advised to consider the risk/benefit ratio of subsequent use of that product in that patient [9,57].

Type III Hypersensitivity

Type III hypersensitivity reactions are immune complex reactions. Examples include the anterior uveitis associated with the use of the CAV-I vaccine and

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

| Agency or company | Address | Website and telephone number | Support available |
|--|--|--|--|
| American Animal Hospital Association | American Animal Hospital Association 12575 West Bayaud Avenue Lakewood, CO 80228 | www.aahanet.org 303.986.2800 | Position statements on current vaccination guidelines, standards for care and conduct |
| American Association of Feline Practitioners | American Association of Feline Practitioners 203 Towne Center Drive Hillsborough, NJ 08844-4693 | www.aafponline.org 800.204.3514 | Position statements on viral screening, vaccination guidelines |
| American Veterinary Medical Association | American Veterinary Medical Association 1931 North Meacham Road, Suite 100 Schaumburg, IL 60173-4360 | www.avma.org 847.925.8070 | Links to available multiple sites; position statements on vaccination guidelines, zoonotic disease prevention, and adverse event reporting (Feline Vaccine Sarcoma Task Force) |
| Centers for Disease Control | Centers for Disease Control and Prevention 1600 Clifton Road NE, Atlanta, GA 30333 | www.cdc.gov 800.311.3435 | United States government agency (Department of Health and Human Services), current information regarding infectious and non-infectious diseases |
| Center for Veterinary Biologics | Center for Veterinary Biologics 510 South 17th Street Suite 104 Ames, IA 50010 | www.aphis.usda.gov 800.752.6255 | Division of United States Department of Agriculture, contact agency for reporting adverse events associated with veterinary biologics |

| | | | |
|---|--|---|--|
| National Association of State Public Health Veterinarians | 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 on-line |
| Bio-Ceutic | Boehringer Ingelheim Animal Health 2621 North Belt Highway St. Joseph, MO 64506 | www.boehringer-ingelheim.com Technical services: 800.325.9167 | Manufacturer |
| Delmont Laboratories | Delmont Laboratories 715 Harvard Avenue PO Box 269 Swarthmore, PA 19081 | www.delmont.com Technical services: 800.562.5541 | Manufacturer |
| Fort Dodge Animal Health | Fort Dodge Animal Health 9225 Indian Creek Parkway, PO Box 25945 Overland Park, KS 66225 | www.wyeth.com Technical services: 800.533.8536 | Manufacturer |
| Heska Corporation | Heska Corporation 3760 Rocky Mountain Avenue, Loveland, CO 80538 | www.heska.com Technical services: 888.437.5287 | Manufacturer |
| Intervet | Intervet 29160 Intervet Lane, PO Box 328 Millsboro, DE 19966 | www.intervetusa.com Technical services: 800.992.8051 | Manufacturer |
| Merial Ltd | Merial Ltd 3239 Satellite Boulevard Duluth, GA 30096-4640 | us.merial.com Technical services: 888.637.4251, ext.3 | Manufacturer |
| Pfizer Animal Health | Pfizer Animal Health Whiteland Business Park 812 Springdale Drive Exton, PA 19341 | www.pfizer.com Technical services: 800.366.5288 | Manufacturer |
| Schering-Plough Animal Health Corporation | Schering-Plough Animal Health Corporation 1095 Morris Avenue Union, NJ 07083 | www.spah.com Technical services: 800.224.5318 | Manufacturer |
| Virbac Corporation | Virbac Corporation 3200 Meacham Boulevard Ft. Worth, TX 76137 | www.virbaccorp.com Technical services: 800.338.3659 | Manufacturer |



Fig. 2. Type I hypersensitivity. Angioedema in a 12-week-old puppy secondary to administration of a distemper, adenovirus type II, parainfluenza, parvovirus, and leptospirosis vaccine. (Courtesy of Autumn Davidson, DVM, Davis, CA.)

the complement-mediated rabies vaccine-induced vasculitis-dermatitis seen in dogs. Other examples include glomerulonephritis and polyarthritis. Antihistamine administered at the time of vaccine does 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 that product should be avoided in that patient [9,58].

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; however, for more severe reactions, the practitioner is referred to various medical texts for recommendations [9,57].

SPECIAL CIRCUMSTANCES

The previous 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 Task Force is currently developing recommendations specifically designed for puppies in these environments. In general, neonates that may not have received colostrum or are housed under these conditions may be vaccinated at an earlier age and ideally should be vaccinated before or at the time of entry into the shelter. The recombinant distemper vaccine could be given in this circumstance and should be administered

every 2 to 3 weeks (Autumn Davidson, DVM, Davis, CA, personal communication, 2005; regarding the American Animal Hospital Association Canine Vaccine Task Force 2005 guidelines, work in progress). Vaccination against additional diseases (canine and feline upper respiratory diseases) is indicated as well (see previous vaccine sections). Husbandry is extremely important in these animals: providing proper nutrition, anthelmintics, and clean and dry housing is paramount. In general, these animals are special subsets of the general population facing challenges that 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. They 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 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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