Canine Vaccines

Vaccination is widely employed to protect dogs against infectious diseases. As might be anticipated, some of these diseases are more important than others. This has led to the designations "core" and "noncore" to denote those vaccines that are essential and those that are less important. Core vaccines are those that all dogs, regardless of circumstances or location, should receive. They protect the animals from severe, life-threatening disease. The three core vaccines for dogs in North America are those against canine distemper virus (CDV), canine adenovirus 2 (CAV-2), and canine parvovirus type 2 (CPV-2). Additional vaccines may also be considered to be essential by the attending veterinarian based on their professional judgment. One obvious such example is rabies vaccine, especially in countries where rabies is endemic. Rabies vaccination is also legally required in many jurisdictions and is mandatory for international travel. Noncore vaccines are those whose use is also based upon careful risk assessment by a veterinarian in consultation with the dog owner. These risks will vary with the type of vaccine used, geographic location, local environment, degree of exposure to other dogs, and the dog's lifestyle (Box 13.1).

SPECIES CONSIDERATIONS

One unique feature of dogs is their extreme size variation. This presents problems regarding vaccine safety and efficacy. It has been conventional procedure to administer an identical dose of vaccine to all dogs irrespective of their size. Although it has long been thought that the canine immune system was somewhat indifferent to antigen dose, this is not the case. Postvaccinal antibody titers vary inversely according to a dog's body weight. For example, antibodies against CPV-2, CDV, and CAV-2 have been measured in adult dogs over a large size range, 12 months after receiving a conventional vaccine. All the dogs developed a protective level of antibodies. CPV-2 antibody titers were significantly higher in very small dogs (<5 kg) than in medium sized dogs (10–20 kg) or in large dogs (>20 kg). CDV antibody titers were significantly higher in the very light, light, and medium groups, than in the heavy group. Interestingly there were no significant differences between the size groups with respect to CAV-2 antibody titers. In another study investigating rabies vaccine failures, the proportion of dogs failing to make sufficient antibodies—their median antibody titers—decreased whereas the vaccine failure rate increased with increased dog sizes. There is also a difference in the frequency of adverse reactions to vaccination in dogs depending upon their size (Fig. 10.1). Small dogs suffer more adverse events than large dogs.

Other issues associated with dogs are the major differences in vaccine responses associated with different breeds. These breed differences, resulting largely from a loss of genetic variability, are reflected in differences in their responses to vaccines and also differences in their susceptibility to vaccine-induced adverse events.

Antibacterial Vaccines

BORDETELLA BRONCHISEPTICA

Bordetella bronchiseptica is a gram-negative bacterium, one of the complex mixture of agents that are associated with canine respiratory disease. Its importance was recognized in 1910 when it was wrongly believed to be the cause of canine distemper (Chapter 1). *B. bronchiseptica* is a primary pathogen because it can impair ciliary function and thus predispose to secondary opportunistic infections. It can also be a secondary invader following infection with other respiratory pathogens. Bordetella infection is associated with mild to moderate tracheobronchitis resulting in coughing, retching, sneezing, and nasal discharge. Monovalent and combined vaccines are available for administration parenterally or intranasally. Most of these are combined vaccines that contain multiple antigens against diverse respiratory pathogens.

A nonadjuvanted acellular *B. bronchiseptica* vaccine containing selected bacterial antigens may be administered by the subcutaneous route. Several different modified live intranasal *B. bronchiseptica* vaccines are also available as well as single component oral vaccines. The oral vaccines may be administered into the buccal pouch as early as 7-8 weeks of age.

Onset of immunity develops by 48 hours following oral and intranasal vaccination and the duration of immunity is 12 to 14 months so annual revaccination is recommended. These vaccines may be administered in combination with canine parainfluenza and CAV-2 vaccines. Intranasal or oral vaccines must never be delivered by parenteral injection since these live vaccines retain some virulence and may therefore cause severe adverse reactions and possibly death.

LEPTOSPIROSIS

Leptospira are aerobic gram-negative spirochetes. The taxonomy of Leptospires is complex and confusing. Three species are common animal pathogens, *Leptospira interrogans, Leptospira borgpetersenii,* and *Leptospira kirchneri*. These are each divided into multiple serogroups and serovars (Table 13.1). More than 250 serovars of Leptospira have been identified and immunity is highly serovar specific. Before the introduction of vaccination, the important serovars were considered to be canicola and icterhaemorrhagiae. Following the widespread use of vaccines against these two, the prevalence of serovars has changed. In North America, the important serovars are now considered to be Pomona, Autumnalis, Bratislava, and Grippotyphosa, whereas in Europe the important serovars are Bratislava, Grippotyphosa, and Sejroe.

TABLE 13.1 ■ **A Simple Classification of the Most Common Leptospires Discussed in the Text**

Species	Serogroup	Serovar
L. interrogans	Icterohemorrhagiae	Icterohemorrhagiae
		Copenhageni
	Grippotyphosa	Grippotyphosa
	Canicola	Canicola
	Australis	Australis
		Bratislava
	Pomona	Pomona
		Kennewicki
	Sejroe	Sejroe
		Hardjo
Leptospira borgpeterseni	Sejroe	Hardjo
		Hardjo-bovis
	Australis	Australis
Leptospira kirschneri	Icterohemorrhagiae	Icterhemorrhagiae
	Grippotyphosa	Grippotyphosa
	Canicola	Canicola
	Australis	Australis

Note that certain serovars such as Hardjo are found in more than one species.

Antileptospiral immunity is primarily antibody-mediated and is directed against the bacterial lipopolysaccharide (LPS). (Experimentally, polyclonal and monoclonal antibodies against this LPS can transfer immunity to susceptible animals.) However, it also appears that cell-mediated responses are required to protect against some serovars such as Hardjo in cattle. Whole, inactivated Leptospira bacterins have been used for many years but are associated with adverse reactions, in addition to serovar-specific immunity.

In the United States, dogs receive bacterins containing four serovars: Canicola, Icterhaemorrhagiae, Pomona, and Grippotyphosa. There is limited cross protection between these serovars. Some may protect against clinical disease and reduce but not prevent renal colonization and shedding. Antibodies last for about 1 year (at least 15 months in the case of Grippotyphosa). In other countries these bacterins may contain up to 8 different serovars. (Box 13.2).

BORRELIA BURGDORFERI

Borrelia burgdorferi is the cause of Lyme disease predominantly spread by the deer tick, *Ixodes scapularis*. Four different vaccines are available in North America. All induce antibodies to OspA, the antigenic outer membrane lipoprotein of the spirochete. OspA is expressed by the organisms within the tick mid-gut but is downregulated within the vertebrate host. When blood is ingested by a feeding tick, the antibodies to OspA attack the spirochetes and thus halt transmission. AntiOspA antibody titers are however not boosted by natural exposure and wane in vaccinates allowing host infection. Recently vaccines containing OspC have also been investigated. OspC is the dominant surface antigen expressed within the vertebrate host. AntiOspC antibodies and T cells induced by these vaccines may therefore eliminate organisms within the host. Available vaccines include a killed whole cell bacterin (OspA), a bacterin containing OspA and OspC, a recombinant OspA vaccine and a chimeric recombinant containing OspA plus OspC. All are administered subcutaneously. The reported efficacies of these vaccines are highly variable ranging from 50% to 100%. Vaccination of infected dogs is of no benefit so puppies should be tested to ensure that they are not infected before vaccination. Vaccination is also advisable if a dog travels

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BOX 13.2 ■ Leptospirosis

Given the diversity and potential for change of *Leptospira* serovars it is important to review their use from time to time to ensure that we are vaccinating dogs against the correct ones. For example, vaccines traditionally contained serovars Canicola and Icterohemorrhagiae. In North America, epidemiological changes resulted in adding Grippotyphosa and Pomona to the bacterin mixture. In Europe the most common serovars affecting dogs are Icterohemorrhagiae, Bratislava, Grippotyphosa, Sejroe, and Canicola. Their geographical distribution may however be different. For example, Grippotyphosa is not found in the United Kingdom but is common across mainland Europe. Bratislava is widespread across Europe. In contrast, Pomona is very uncommon across Europe even although it is of major importance in North America. Infections with Canicola appear to be declining and it is now uncommon. Canicola is maintained by dogs and has no other natural hosts. It is possible that years of vaccination against this organism have had an effect. Thus Bratislava and Grippotyphosa have recently been added to the list of recommended Leptospirosis bacterins used in dogs in Europe.

(From Ellis, W.A. [2010]. Control of canine leptospirosis in Europe: time for a change? *Vet Rec,* 167, 602–605.)

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from a nonendemic area to an endemic one. Vaccination must be part of a comprehensive program to reduce disease risks including adequate tick control, preferably with products that prevent tick attachment or kill ticks during early feeding.

CANINE RESPIRATORY DISEASE COMPLEX

As with other species, dogs may suffer from chronic infectious respiratory disease caused by diverse pathogens. An initial viral infection may cause tissue damage and immunosuppression leading to secondary bacterial invasion. The primary viral pathogens include canine parainfluenza, adenovirus 2, or distemper. Other viruses that may play a role include reoviruses, respiratory coronavirus, herpesvirus, influenza virus, pneumovirus, and adenovirus 1. *Bordetella bronchiseptica* may act as a primary or secondary pathogen. Other potential bacterial pathogens include Mycoplasmas, *Streptococcus equi* subspecies *zooepidemicus*, and *Chlamydophila psittaci*. Vaccines are not available against every one of these agents and the viral components are discussed in the viral section later.

Many of the available vaccines are designed to be administered intranasally. It should be pointed out that there are major differences in the nature of the immune response triggered by intranasal and injected vaccines. Thus intranasal administration with a modified live vaccine will trigger local innate responses in addition to a local immunoglobulin A (IgA) response. Parenteral immunization with an acellular vaccine will trigger a systemic immunoglobulin G (IgG) response. Both of these are protective responses. In theory, the best result may be obtained by administering the injected vaccine first and boost with the intranasal product (or vice versa). This prime boost technique has worked very well in humans vaccinated against polio. However, there is as yet, no data to support this method in dogs.

Antiviral Vaccines

CANINE DISTEMPER

Canine distemper caused by canine morbillivirus infection remains one of the most significant and lethal viral diseases of dogs. It affects the gastrointestinal and respiratory tract in addition to the nervous system.

There are currently 50 licensed distemper vaccines available in the United States; however, only one of these is directed against canine distemper virus alone. Distemper vaccine is usually combined with those against canine adenovirus 2, canine parvovirus, and canine parainfluenza. These combinations may also contain coronavirus, leptospirosis, and Borrelia vaccines. Three different types of vaccine are available to prevent canine distemper.

Inactivated CDV vaccines generally give inferior protection and are best used in susceptible wildlife species.

Modified live virus vaccines contain attenuated virus strains such as the Snyder Hill and Rockborn strains attenuated by prolonged canine cell culture, or the egg adapted Onderstepoort strain, now adapted to tissue culture. Antigenic differences between these strains are not significant and all are protective when used appropriately. Note that the modified live virus (MLV) distemper vaccines, although safe in domestic dogs, can cause disease in related wildlife such as gray foxes and the black-footed ferret. Indeed, the black-footed ferret, a highly endangered species was nearly wiped out as a result of the inappropriate use of MLV distemper vaccines (Chapter 20).

A canarypox vectored recombinant vaccine is available in some countries. The genes encoding two immunogenic CDV antigens, the hemagglutinin (HA) and fusion proteins have been inserted into an ALVAC canarypox vector (Chapter 5). This vaccine is able to overcome some maternal immunity and appears to immunize puppies about four weeks earlier than conventional MLV vaccines. The vectored vaccine has the additional advantage that it is unable to cause postvaccinal distemper encephalitis.

The recombinant and MLV vaccines perform similarly with respect to onset and duration of immunity. Measuring serum antibodies provides a reasonable assessment of protective immunity. Duration of immunity after vaccination is at least five years.

HETEROTYPIC IMMUNIZATION

Measles and canine distemper viruses are very closely related morbilliviruses; their fusion proteins are almost identical. As a result, an attenuated measles vaccine has been used for many years to provide early protection of puppies against distemper. The differences between the HA antigens of these viruses are such that maternal antibodies against distemper virus cannot completely neutralize the measles vaccine. As a result, measles vaccine may be administered somewhat earlier than distemper vaccine to effectively immunize puppies. It is given intramuscularly between 6 and 12 weeks of age. (Use the dog vaccine, not the human one. There is not enough antigen in the human one.) It is vitally important, however, that puppies also be vaccinated using a distemper vaccine at the appropriate time. Heterotypic immunity should not be relied on after 16 weeks of age.

CANINE ADENOVIRUS 2

CAV-2 is a respiratory pathogen transmitted by the oronasal route. The virus damages bronchial epithelial cells resulting in fever, cough, nasal discharge, and pharyngitis.

Inactivated CAV vaccines are usually administered in combination with CDV and CPV.

The preferred vaccines against canine adenoviruses are modified live products. These MLV also provide immunity against infectious canine hepatitis caused by CAV-1 and against tracheobronchitis caused by CAV-2. Immunity develops about five days postvaccination with the MLV. However, CAV-2 infection or vaccination will not induce the hypersensitivity reaction known as blue-eye caused by CAV-1 (Fig. 10.5). Both injectable and intranasal forms of CAV-MLV vaccines are available. Because CAV-2 is a contributor to the canine respiratory disease complex, it is commonly used in combination with other respiratory pathogen vaccines such as those against *Bordetella bronchiseptica* and canine parainfluenza virus. The duration of immunity after

vaccination is at least nine years. The presence of serum antibodies indicates protection, making serology a useful guide to revaccination.

CANINE PARVOVIRUS

CPV is one of the major causes of canine acute gastroenteritis. Young puppies two to six months of age are most susceptible, but cases are increasingly recognized in adult dogs. Clinical signs include anorexia, depression, vomiting, and diarrhea that is often hemorrhagic.

The original canine parvovirus (CPV-2) first appeared in the 1970s and was likely a host variant of feline panleukopenia or a related virus. Since then new circulating variants have appeared. For example, CPV-2a and -2b appeared in the 1980s and CPV-2c in 1996. All these variants are antigenically related so that currently available MLV-CPV vaccines are believed to protect against the variants circulating in North America.

The inactivated vaccines are not as effective and are relatively slow to induce protective immunity when compared with the MLV vaccines. As a result, they are not recommended for routine use except possibly in situations such as in an immunosuppressed dog where the use of a live vaccine may be hazardous.

In the absence of maternal antibodies, MLV parvovirus vaccines may be protective within three days. This is probably because of early interferon production rather than antibodies (Fig. 4.1). These MLV vaccines can replicate in the dog intestine and thus are intermittently shed in the feces of vaccinated dogs. This shedding occurs irrespective of the presence of antibodies. MLV-CPV vaccines should not be used in wildlife as they may be insufficiently attenuated. Inactivated vaccines are safer in other species. Duration of immunity is thought to be life-long, especially following the use of MLV vaccines.

RABIES

The use of rabies vaccines in the United States is regulated by individual states or other jurisdictions. As a result, requirements may be conflicting and inconsistent. In most, but not all states, vaccination is mandatory. It is essential that practicing veterinarians are fully aware of the appropriate legislation and regulations that govern rabies vaccination.

Although modified live vaccines have been proven safe in dogs, the World Health Organization stopped recommending these vaccines in 2004. As described elsewhere (Chapter 10), self-inoculation incidents result in an unacceptable risk to humans. No modified live rabies vaccines are currently marketed in the United States.

Inactivated rabies vaccines are commonly used in mass vaccination programs where maintaining the cold chain is less critical and safety is not an issue. These viruses are generally grown to high titer in tissue culture and then inactivated with beta-propiolactone, acetylethylamine, or binary ethyleneimine (Fig. 3.2). Once inactivated, adjuvants such as aluminum hydroxide, aluminum phosphate, or saponin are added.

Vectored recombinant rabies vaccines express the highly immunogenic rabies glycoprotein G gene. Vectors used include vaccinia, canarypox, and adenoviruses. The vaccinia and adenovirus vectored vaccines may be used in North America and Europe for wildlife vaccination. It is interesting to note that injectable rabies vaccines may be of little use in less developed countries where most cases of canine-induced rabies occur. In these countries there are large numbers of stray dogs and it is not possible to catch and vaccinate them all. In such cases, encouraging results have been obtained by distributing oral recombinant vaccines similar to those used in wildlife (Chapter 20). Blister packs containing the vaccines may simply be offered to these dogs by hand, enclosed in chicken heads, meatballs or a short segment of boiled beef or pig intestine. The vaccinator can also

note that the dog has punctured the vaccine blister and recover used packs. This technique is a viable strategy to supplement parenteral vaccination in otherwise unreachable dog populations.

In many jurisdictions it is a requirement that domestic dogs, cats, and ferrets are to be vaccinated. In general, they are not considered to be vaccinated until 28 days after the initial vaccine dose. The interval between doses is determined by the manufacturer and indicated on the product label, but legally they are considered unvaccinated one day after the vaccine's official duration of immunity (one year or three years). In most (but not all) states, only a licensed veterinarian is authorized to administer rabies vaccine.

The definition of exposure to rabies also varies between states. This is determined by the state Department of Health, not by the veterinarian. Most properly vaccinated dogs are immune to rabies. Should such a dog be bitten by a rabid animal, they should be quarantined for 45 days. Unvaccinated animals should be quarantined for four months. They should be vaccinated within 96 hours of exposure on entry into quarantine.

If multiple doses of vaccines are administered to small-breed dogs (<10 kg), this may increase the risk of adverse reactions. Given the importance of the size of the dog, it has been suggested that veterinarians consider delaying administration of noncore vaccines to small dogs until two to four weeks after completion of the core vaccination process.

There is currently no data available to support the practice of reducing vaccine dose or frequency of administration in small dogs. Dose reduction increases the chances that the dog will receive an insufficient dose to confer protective immunity. Likewise, there is no data to suggest that dose reduction will reduce the incidence of adverse events. After all, if the animal is already allergic to a vaccine component, even a reduced dose may trigger a reaction.

Note that vaccination of dogs against rabies has saved millions of humans from a horrible death. This is yet another triumph for the science of immunology.

CANINE PARAINFLUENZA

Canine parainfluenza (CPiV) is a Rubulavirus in the family Paramyxoviridae. It is one of the main contributors to "kennel cough." The virus causes transient mild respiratory disease and damages local defense mechanisms in the respiratory tract by destroying ciliated epithelium. As a result, secondary opportunistic infections by viruses and bacteria are common. It is usually a component of combination vaccines. The duration of immunity to this virus is unclear and it may be less than three years.

CANINE INFLUENZA

Canine influenza was first described in 2004 when it appears to have been transmitted from horses to racing greyhounds. The original outbreak began as a severe hemorrhagic pneumonia with high mortality. Viral virulence has declined since then and the canine disease is now primarily a tracheobronchitis.

An inactivated canine influenza vaccine (H3N8) may be given subcutaneously. Immunity develops approximately seven days after the second dose although vaccinated dogs may still develop mild clinical signs. This is a noncore vaccine because this strain of influenza is largely restricted to North America.

An inactivated influenza vaccine against a second influenza strain (H3N2) is also available as is a bivalent vaccine directed against both strains. This strain of influenza is also currently geographically restricted to North America. H3N2 is shed in much greater amounts than H3N8, making it that much more contagious. Ideally dogs should receive vaccines against both strains if the veterinarian perceives them to be at risk.

Influenza viruses continue to evolve rapidly. The highly pathogenic strain of influenza, H5N1, was transmitted to dogs in Central Asia after they had been exposed to infected duck carcasses. It is essential that veterinarians be aware of the inevitability of the emergence of new strains of influenza virus capable of infecting both companion animals and their owners.

COMBINATION VACCINES

Most of the vaccines used in dogs contain combinations of antigens. These are generally administered as subcutaneous modified live or recombinant canine distemper vaccine (D) plus adenovirus 2 (A), parvovirus (P), and parainfluenza (P) vaccines (DAPP). Other vaccine combinations may include leptospira.

Other Noncore Vaccines

CANINE CORONAVIRUSES

There are two groups of canine coronaviruses. Group 1 causes enteric disease. Group 2 causes a mild self-limiting respiratory disease. Although both inactivated and modified live vaccines against the group 1 virus are available, their use is not usually recommended because this virus usually only causes a mild, self-limiting or inapparent gastroenteritis with anorexia, fever, and diarrhea. It usually affects puppies younger than six weeks old and lasts for a few days. The vaccine appears to protect dogs from disease but not from infection.

CANINE HERPESVIRUS

Canid herpesvirus 1 may produce mild upper respiratory disease and inapparent infections in adult dogs. However, it causes fatal infections in newborn puppies. This susceptibility is highly age related and puppies over two weeks of age rapidly develop resistance. The clinical disease is nonspecific. Puppies vomit, show rapid shallow breathing, and die within two days. The virus may also cause abortion, stillbirth, and infertility.

Although a vaccine is not available in North America, an adjuvanted subunit vaccine is marketed in Europe (Eurican Herpes 205, Boehringer Ingelheim). It consists of purified glycoprotein subunits (especially gB glycoprotein) of the F205 strain with an oil adjuvant. It is administered subcutaneously when the female is in heat or 7 to 10 days after mating. A second dose is given one to two weeks before whelping. Revaccination during each subsequent pregnancy is recommended. As with other such vaccines its effectiveness depends upon the puppies ingesting adequate colostral antibodies.

CROTALID VACCINE

A toxoid directed against the Western Rattlesnake (*Crotalus atrox*) venom is available. It is administered to dogs that may be exposed to Western Diamondback Rattlesnakes. There is limited cross protection against other rattlesnake species. Two subcutaneous doses are given after four months of age, and annually thereafter. Although this vaccine may mitigate the severity of the venom, snake-bitten dogs must still receive immediate veterinary attention.

Vaccination and Maternal Antibodies

Current high-quality core vaccines induce high levels of antibodies in dogs. As a result, canine colostrum also contains high antibody titers. These maternal antibodies are highly effective in blocking antibody responses in young puppies (Fig. 13.1). As a result, maternal antibodies persist
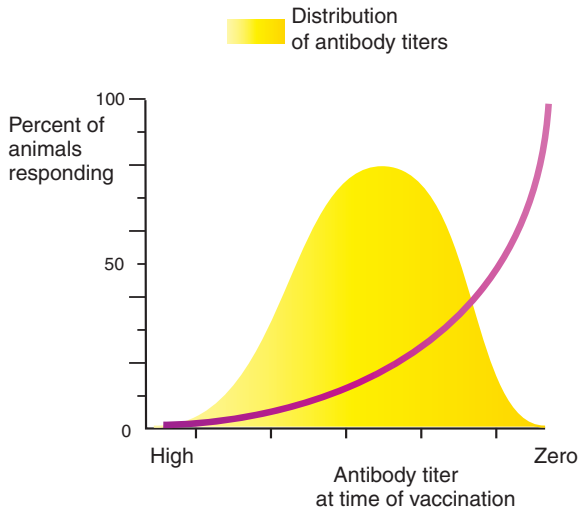
Fig. 13.1 The effect of maternal antibody titer on the response of newborn animals to vaccination. The presence of specific maternal antibodies profoundly suppresses the animal's immune response to a vaccine and the higher the maternal antibody titer, the greater the suppression. However, antibody titers are normally distributed so that as maternal antibody titers decline, more and more individuals will respond to the vaccine until only a few very high responders remain.

longer and many puppies cannot be primed, even by 12 weeks of age. Most puppies that have suckled successfully and received sufficient colostrum will be protected up to approximately 8 to 14 weeks of age. However, not all mothers are immune and not all puppies receive sufficient colostrum. As a result, at least three doses of the core vaccines must be administered every 3 to 4 weeks beginning between 6 and 8 weeks of age with the final dose administered on or after 16 weeks of age to ensure that a susceptibility gap does not develop between the loss of maternal immunity and vaccination. An optional fourth dose may be administered at 18 to 20 weeks of age. This is recommended if confirmed distemper or parvovirus infections have occurred in young dogs that had received the initial three-dose series.

It has been normal practice to boost puppies by vaccination at one year of age. The rationale for this is to ensure that any dog that fails to respond to the initial series of vaccines will thus be protected and the primed dogs will be boosted. It makes sense to give this vaccine at six months rather than a year. In this way the window of susceptibility of any unvaccinated dogs is reduced significantly and still providing an effective boost to their immune responses.

It is also important to point out that multiple sources of evidence support the contention that core vaccines confer a minimum duration of immunity of three years (except for one-year rabies vaccines). Vaccines are not innocuous and should consequently be given no more than necessary. Note that immunity to bacterins such as those from Bordetella, Borrelia, and Leptospira is relatively short lived, and these should be boosted annually if deemed necessary.

Management Issues

RISK FACTORS

The lifestyle of a dog should be considered when making specific vaccine recommendations. For example, how much interaction does the dog have with other dogs? Staying in a boarding kennel,

attending dog shows, visits to dog parks, or living in a shelter may significantly increase a dog's risk of acquiring infections from others. Likewise, exposure to wildlife or domestic livestock and possible exposure to contaminated water sources increases risks from leptospirosis. Hunting dogs at high risk of getting bitten by ticks will be at increased risk of Lyme disease.

CORRELATES OF PROTECTION

We cannot always assume that a vaccinated animal is protected or that revaccination is necessary. We require a method of objectively assessing immunity. It is now possible to make informed decisions regarding the need for revaccination by testing animals for the presence of antibodies. A veterinarian should always assess the relative risks and benefits to an animal in determining the need for any vaccination. In the past this assessment was largely a matter of conservative tradition. Rapid, simple point-of-care test kits are now available to detect canine antibody responses. It is therefore good practice to use serum antibody assays such as rapid test ELISA kits or lateral flow assays, if available, to provide guidance on revaccination needs. Persistent antibody titers determine whether an animal requires additional protection. These tests not only identify those animals that have responded to vaccination, they can determine if an animal is a nonresponder, a problem associated with immunity to parvovirus infections. They can determine if an animal that previously suffered from an adverse event really requires revaccination. They can determine whether an animal with an undocumented vaccine history needs to be vaccinated and with which vaccines. They can determine which animals in a shelter undergoing a disease outbreak are susceptible and require vaccination. They can also determine whether revaccination is really necessary at three years. Note, however. that animals with low or undetectable serum antibody levels may still be protected as a result of persistence of memory B and T cells capable of responding rapidly to reinfection. "Blind" revaccination should be avoided if appropriate antibody assays are available. Point of care tests are usually reported as positive versus negative. In general, a negative test may indicate susceptibility. Nevertheless, false negative results do occur as a result of errors, and poor timing, and so on. Generally, however these point of care tests have been carefully standardized against gold-standard tests such as virus neutralization or hemagglutination tests.

It is known that after vaccination most dogs retain protective antibodies against CDV, CPV-2, CAV-1, and CAV-2 for many years. Thus any dog that is seronegative should be revaccinated unless contraindicated by some other problem. There is a poor correlation between antibody levels and protection after vaccination against Leptospirosis.

Studies have demonstrated that dogs receiving a modified live CDV vaccine were protected for over four years and detection of virus neutralizing antibodies implied resistance. A positive response was considered to be a two-fold increase above the assay cut-off. A negative response was considered to be an antibody titer of less than 16. However, many vaccinated dogs had a titer of less than 16 at 4 years but were still protected when challenged. In other words, a negative titer has little predictive value. Conversely all the dogs with a positive titer were also protected so its predictive value was 100% (i.e., there were no false positive results).

SHELTER-HOUSED DOGS

In general, dogs in shelters represent a random collection of dogs with no known vaccination history and a high risk of infectious diseases. The high likelihood of disease transmission demands that a comprehensive vaccination strategy be established and adhered to. All dogs entering a shelter should be vaccinated before entry with the core vaccines. It would be desirable to test dogs on admission for the presence of antiviral antibodies. In the absence of evidence of immunity or vaccination, as many dogs as possible should be vaccinated before or on admission to the

facility to establish herd immunity. However, remember that onset of immunity is not immediate, but intranasal vaccines may induce immunity faster than injected ones.

As elsewhere, vaccination is only one component of an infection control strategy for an animal shelter. Managers must pay attention to factors such as cleaning and disinfection protocols, personal protective equipment, segregation of susceptible animals crowding, climate management, and stressors that may influence disease resistance.

Similar considerations apply to boarding kennels (and catteries), dog or cat shows, pet day-care facilities, and any situation where these animals might gather in significant numbers.

OBESITY

It is abundantly clear from the human and mouse literature that obesity reduces the immune response to vaccination. A high body mass index in humans is associated with a reduced response to vaccines. This has been well demonstrated with respect to influenza vaccination. Obese mice mount significantly lower virus-specific antibody responses when compared with lean mice. When infected, their viral loads are much higher even after vaccination. Similar effects have been reported for hepatitis B, tetanus, and rabies vaccines. (Box 13.3) Only limited studies have been performed on obese dogs and the results did not show significant differences in responses to canine core vaccines. Nevertheless, obesity should be considered a risk factor for an inadequate vaccine response. Great care should be taken to avoid injecting antigens directly into adipose tissue.

Adverse Events

Vaccines should be administered with a minimal interval of three to four weeks between doses regardless of the vaccine or the age of the patient.

LOCAL REACTIONS

Transient injection-site reactions result from local innate immune responses. These may produce visible or palpable lumps, with pain or pruritus. Permanent hair loss as a result of ischemic vasculitis and focal skin necrosis has resulted from a vasculitis following rabies vaccination.

GENERALIZED REACTIONS

Transient nonspecific effects of the innate immune response such as lethargy, anorexia, fever, and lymphadenopathy are common in vaccinated dogs (see Fig. 13.2). They generally last for less than 24 to 48 hours.
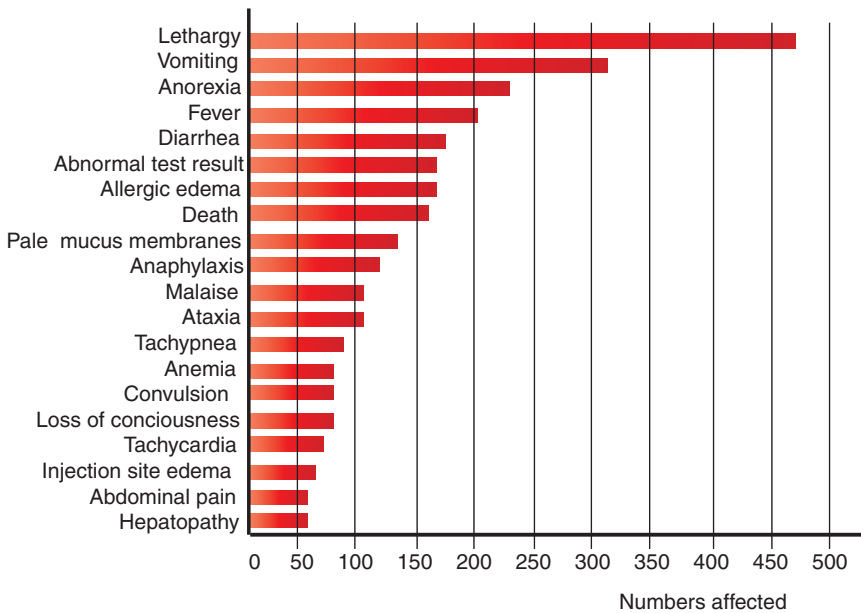
Fig. 13.2 The clinical signs of adverse events associated with administration of canine core vaccines in the UK. Note that these are the number of reports received by the Veterinary Medicines Directorate. Veterinary Pharmacovigilance in the United Kingdom, Annual Review, 2014. With permission.

Hypersensitivity reactions are the consequence of vaccination in some animals. The most important of these is a type 1 anaphylactic response. Dogs differ from the other domestic mammals in that their major shock organ is not the lung but the liver, specifically the hepatic veins. Dogs undergoing anaphylaxis show initial excitement followed by vomiting, defecation, and urination. As the reaction progresses, dogs may collapse with weakness and depressed respiration, become comatose, convulse, and die. All these signs result from occlusion of the hepatic vein because of a combination of smooth muscle contraction and hepatic swelling. This results in portal hypertension and visceral pooling, in addition to a decrease in venous return, cardiac output, and arterial pressure. This is secondary to generalized vasodilation. Identified mediators include histamine, prostaglandins, and leukotrienes. Treatment involves the prompt administration of epinephrine (Box 10.2).

TRANSIENT IMMUNOSUPPRESSION

When certain combination vaccines that contain MLV-CDV plus adenoviruses-1 or -2 are administered to puppies, there is a transient suppression of T cell responses to mitogen for several days. Some canine parvovirus-2 vaccines can cause a mild immunosuppression. This is unlikely to be clinically significant.

RESIDUAL VIRULENCE

Modified live vaccines are usually good immunogens, but their use may involve certain risks. The most important theoretical problem encountered is residual virulence. This has been a problem

in the past. One serious example of this was the development of clinical rabies in some dogs and cats following administration of older strains of MLV rabies vaccine. Another example is that of the Rockborn strain of CDV that can revert to virulence in zoo and wildlife species. Postvaccinal cough or sneezing may be associated with administration of attenuated intranasal vaccines against *B. bronchiseptica* and parainfluenza. As described in Chapter 10, other adverse events associated with vaccination in dogs include postvaccinal canine distemper virus encephalitis, and vaccine-induced osteodystrophy. It should be pointed out, however, that when using modern vaccines, the risk of disease developing as a result of residual virulence is minimal.

Sources of Additional Information

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Abstract: Canine vaccines can be divided into essential, core vaccines, and less essential noncore vaccines. The core vaccines are canine distemper, adenovirus-2, and parvovirus. Rabies vaccination is mandatory in many different jurisdictions. Canine respiratory disease vaccines include Parainfluenza 3, and *Bordetella bronchiseptica*. Other important bacterial vaccines include those against Lyme disease and Leptospirosis. Vaccination schedules must be initiated in puppies no earlier than 6 weeks, and the core vaccines must be readministered at frequent intervals until 16 weeks as a result of the prolonged inhibitory effects of maternal immunity. Emerging diseases such as canine influenza may also be vaccinated against.