XII. VACCINATION OF NON-DOMESTIC CARNIVORES: A REVIEW

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Since the introduction of *vaccinia* by Jenner 200 years ago, vaccines have been the first line of defense in controlling infectious diseases in man and domestic animals. Large scale domestic dog vaccination programmes against canine distemper virus (CDV) and canine adenovirus (CAV) became possible in the late 1940’s, when egg-adapted vaccines became available on a commercial basis, followed by tissue culture adapted vaccines in the late 1950’s (Piercy 1961). Before this time these devastating diseases had to be controlled through quarantine and vigilance in capturing feral domestic animals (Dolensek et al. 1977).

Historically there have always been two major types of vaccines based on the living state of the antigens. Modified live (MLV) vaccines use attenuated pathogens which reproduce in the vaccinate, thereby eliciting an immunologic response without causing disease (a “controlled” infection). The other major type of vaccine uses antigens that are non-living or inert – killed vaccine (KV). These vaccinations are preferred when safety information is not available, as they do not replicate and are therefore incapable of causing an infection. The process of inactivation however may be damaging enough to modify immunogenicity, usually resulting in an immune response that is shorter in duration, narrower in antigenic spectrum, weaker in cell-mediated and mucosal immune responses, and possibly less effective in totally preventing viral entry (Murphy et al. 1999).

Recent advances in immunology, molecular biology and biochemistry have allowed the construction of subunit vaccines based on viral or bactererial recombinants, peptides, or plasmid vectors, which may lead to safer, more efficacious vaccines that can also be used in exotic species.

Vaccines cannot be absolutely guaranteed to provide protection against disease. The principal objective of vaccination is to mimic the protective immune response induced by natural infection, ie to elicit a high titre of neutralising antibodies of the appropriate class, IgG and/or IgA, directed against the relevant epitopes on the virion (Murphy et al. 1999). Immunity induced by vaccination or infection in domestic animals has been evaluated mainly by measuring the levels of serum antibodies. The immunologic response that provides protection against infectious agents involves a cellular and a humoral response. For certain infections (e.g. CDV, CAV, canine parvovirus (CPV), feline panleukopenia virus (FPV) or *Borrelia burgdorferi*) the humoral responses, although not the only mechanism involved, tend to correlate with level of protection from clinical disease, and therefore may be a useful indicator of the immune status. Other agents (eg, *Bordetella bronchiseptica*, canine coronavirus (CCoV), feline enteric coronavirus (FCoV), canine parainfluenzavirus (CPIV) and *Chlamydia psittaci*) all replicate and cause damage on mucosal surfaces, and might require a mucosal immune response for protection. As a consequence, serum antibody titres do not necessarily correlate with protection (Pfizer 1998). A high concentration of antibodies in an
animal implies that the animal is probably protected but also could indicate that it may not be possible to stimulate an additional immune response in that animal. Cattle vaccinated with baculovirus-expressed haemaglutinin (H) and fusion (F) proteins of Rinderpest virus (RPV) were not protected against disease caused by challenge exposure despite having detectable antibody titres (Bassiri et al. 1993). For some diseases, caused by persistent intracellular pathogens (viral diseases or intracellular bacteria) the neutralising antibodies and complement may play a less important role than the cellular immunity. Jones et al. (1993, 1997) demonstrated a lack of detectable antibody titre to CDV in ferrets and to peste des petites ruminants (PPRV) in goats after vaccination with a RPV recombinant vaccine based on fowlpox expressing the F and H genes. When these animals were challenged they survived, suggesting that protection against clinical disease may be cell mediated rather than humoral. A comparable study by Fisher et al (2003) using a DNA vaccine showed clear protection after challenge with CDV, with only limited virus neutralising antibody titres. High antibody concentrations do serve to inhibit the spread of virus between cells and thus promote host resistance (Tizard & Ni 1998). Infection with feline rhinotracheitis virus, as all herpesviruses, requires local and cell-mediated immunity, and one study suggests that there is no correlation with protective immunity and antibody titre (Johnson & Povey 1985). Later studies (eg Scott & Geissinger 1999, Dawson et al. 2001) use antibody titres as indicators of protective effect. In general it can be stated that theoretically, cell-mediated immunity is the most effective arm of the immune system in controlling, if not eliminating latent/persistent infections such as those caused by herpesviruses and retroviruses (Murphy et al. 1999).

The usefulness of antibody titres to measure immunity is thus limited to only a few disease agents, and in order to obtain a more complete view of the immunologic status of an animal one therefore needs to look at the humoral and cellular responses. One should also keep in mind that an animal that has mounted an immune response after vaccination will possess memory T and B cells, which will remain for years after the antibody titre has declined. These memory cells rapidly differentiate during a subsequent infection into effector cells that can eliminate an infection before clinical signs appear, although the exact mechanism responsible for this longevity is unknown (Ahmed & Gray 1996). One can only know if the measured level of immunity is protective by challenging the vaccinated animal with the pathogen.

One of the principal causes of vaccination failures in domestic dogs is maternal antibody interference. MLV vaccines differ in their ability to evade antibodies, and may sometimes be prevented from inducing an immunologic response in the vaccinate when the antibody level is high. The duration of passive immunity is directly correlated with the metabolic size of the animal. Therefore immunoglobulins will persist longer in a larger animal (Armstrong et al. 1942). The "window of vulnerability" during which the pup is vulnerable to infection with virulent virus, but unresponsive to attenuated vaccine virus (Pollock and Carmichael 1990), has been shown to range from 2-5 weeks for parvovirus infection in domestic dogs, but varies between pathogens and vaccinate species. Females close to parturition may be hyperimmunised with an inactivated parvovirus vaccine, so that high levels of maternal antibody delay the window of vulnerability until the offspring are older and better able to withstand the effects of parvovirus infection.

The recent debate in veterinary medicine concerning issues related to vaccine efficacy and safety as well as duration of immunity induced by the currently available vaccines (Smith et al. 1995, Schultz et al. 1998, Kruth & Ellis 1998, Tizard & Ni 1998, McCaw et al. 1998, Gumley et al. 1999, Huestad et al. 1999, Twark et al. 2000) has resulted in the need for more objective and scientific data and an increase in research in domestic animals.

In non-domestic animals however, there have been only few controlled studies of vaccination (Heerden et al. 1980, Halbrooks et al. 1981, Behlert et al. 1981, Barker et al. 1983, Montali et al. 1983, Green et al. 1984, Bush et al. 1985, Hoover et al. 1985, Paul-Murphy et al. 1985,
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Challenge studies in dogs have shown a range of reported protective titres – these may differ due to the variety of techniques and standards used. In humans there is a general standardisation of assay methods to measure antibody titres. Non-standardisation of serologic tests makes comparisons between laboratories of questionable use (Luff et al. 1987):

Table 1: Reported protective titres in domestic dogs:

<table>
<thead>
<tr>
<th>Virus</th>
<th>Protective titre</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAV</td>
<td>≥30</td>
<td>Cole et al. 1998</td>
</tr>
<tr>
<td>CDV</td>
<td>&gt;2</td>
<td>Gillespie et al. 1965; Ackerman &amp; Siebel 1974.</td>
</tr>
<tr>
<td></td>
<td>≥30</td>
<td>Gillespie 1966.</td>
</tr>
<tr>
<td></td>
<td>&gt;50</td>
<td>Olson et al. 1988.</td>
</tr>
<tr>
<td></td>
<td>≥96</td>
<td>Mc Caw et al. 1998.</td>
</tr>
<tr>
<td>RV</td>
<td>≥20</td>
<td>Bunn et al. 1984</td>
</tr>
</tbody>
</table>

Twark et al. (2000) report that CDV titres above 5 are indicative of an adequate antibody response in domestic dogs, although level of protection is unknown, and recommend CDV revaccination when titres are below 32. Carmichael et al. (1983) demonstrated that dogs with a CPV titre below 100 were not protected. Titres of 200-800 were protective in some dogs, titres above 1600 appeared to be protective in all dogs.

There is still no general consensus on how often domestic animals need to be revaccinated - for most vaccines there is little information on the duration of immunity. It is, however, recognised that protective immunity to CDV following MLV vaccination is of long duration, perhaps even lifelong. For other viruses or components of combination vaccines this duration may not be of such long duration.

Vaccines used in domestic animals are approved for use in specific animals under specific conditions, and any other use is therefore extra-label. Most of the vaccines are not approved for non-domestic species, therefore there is always a potential liability to such use (Bittle 1993). MLV vaccines have been designed to be minimally virulent, while retaining maximal immunogenicity in their domestic counterparts. When used in other species or delivered by another route the residual virulence may cause disease (Tizard et al. 1990). It is not unusual to observe side-effects such as elevated temperature, swelling, and irritation at the site of injection, or systemic anaphylactic reactions like hyperaemia, hypersalivation, or vomiting (Greenacre 2003) that may in some cases be severe (Karesh et al. 1983).
Several viruses induce a suppression of the immune system, and it is known that some attenuated virus strains may still be able to cause immunosuppression, e.g. MLV CPV (Krakowka et al. 1982). Sometimes the individual vaccine strains are not detectably immunosuppressive, but when combined in a combination vaccine they may induce a suppression of blood lymphocyte counts (Phillips et al. 1989a). Enhanced virulence of canine distemper virus produced in canine cell-cultures has been reported when used in combination with CAV-1 and live CCV vaccines (Carmichael et al. 1983, Martin et al. 1985, Wilson et al. 1986), and may lead to encephalitis.

Table 2: There are many examples of vaccine-induced disease:

<table>
<thead>
<tr>
<th>Virus</th>
<th>Species</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAV</td>
<td>Domestic dog (Canis familiaris)</td>
<td>Appel et al. 1978.</td>
</tr>
<tr>
<td>CDV</td>
<td>Domestic ferret (Mustela putorius furo)</td>
<td>AVMA 1966; Wimsatt et al. 2001.</td>
</tr>
<tr>
<td></td>
<td>European mink (Mustela lutreola)</td>
<td>Sutherland-Smith et al. 1997.</td>
</tr>
<tr>
<td></td>
<td>Gray fox (Urocyon cinereaargentus)</td>
<td>Ek-Kommonen et al. 2003</td>
</tr>
<tr>
<td></td>
<td>Fennec fox (Fennecus zerda)</td>
<td>Halbrooks et al. 1981.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mehren et al. 1984.</td>
</tr>
<tr>
<td></td>
<td>Skunk (Mephitis mephitis)</td>
<td>Debbie et al. 1979.</td>
</tr>
<tr>
<td></td>
<td>Raccoon (Procyon lotor)</td>
<td>1978.</td>
</tr>
<tr>
<td>FeLV</td>
<td>Cheetah</td>
<td>Briggs et al. 1986.</td>
</tr>
<tr>
<td>FHV</td>
<td>Domestic cats</td>
<td>North et al. 1978</td>
</tr>
<tr>
<td></td>
<td>Pallas cat</td>
<td>Wallach &amp; Boever 1983</td>
</tr>
<tr>
<td>FPV</td>
<td>Felidae:</td>
<td>Behlert et al. 1981</td>
</tr>
<tr>
<td></td>
<td>Cheetah (Acinonyx jubatus)</td>
<td>Crawshaw et al. 1996</td>
</tr>
</tbody>
</table>

Preventive medicine is especially important in the management of non-domestic animals for several reasons: the ability to mask or hide illness or distress as a means of survival means that by the time signs of disease are exhibited, the underlying disease condition may have advanced to a critical stage. Another reason is that the use of anaesthesia is required to perform a proper physical examination. Active immunisation is only one of the factors (eg nutrition, parasite control, hygiene) associated with preventive medicine. Recommendations for use in exotic mammals are generally based on tradition, anecdotal/personal experiences or taken from limited precise, published data. This has led to a plethora of differing opinions and therefore the use of many different protocols in zoological collections. In general, inactivated viral or bacterial vaccines are preferred for use in exotic animals. The type, serial number, and source of product should be recorded in the medical records (Joslin et al. 1990). Use of polyvalent vaccines containing unnecessary antigen (one the species is not susceptible to) should be avoided where possible. Animals with active clinical illness should not be vaccinated. In the event of a viral disease outbreak in an animal collection, all susceptible species should be vaccinated immediately and boosteder 10-14 days later, regardless of age and last time of immunization (Phillips 1989). Some drugs, such as tetracycline, chloramphenicol, dapsone, clindamycin, griseofulvin, nalidixic acid and sulphamethoxypyridazine have been associated with an inadequate response to vaccination (Kruth – Ellis 1998). Vaccination should also be avoided in animals undergoing glucocorticoid therapy, although challenge studies have been performed which show that “immunosuppressive” doses given at the time of vaccination do not significantly affect the level of
post-vaccinial immunity to canine distemper or rabies (Dhein et al. 1986). When using remote delivery systems one must be sure that a full dose has been delivered. Syringe darts may rebound quickly on impact and fail to deliver the dose required to elicit a satisfactory immune response (Aiello 1998). Any vaccination programme should also take the current local prevalence of the pathogen into account, upon which the decision can be made if vaccination is warranted.

### Table 3: Disease susceptibility

<table>
<thead>
<tr>
<th>Family</th>
<th>CAV</th>
<th>CDV</th>
<th>FPV</th>
<th>FeLV</th>
<th>FHV</th>
<th>FCaV</th>
<th>Rabies</th>
<th>Lepto</th>
<th>Toxo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canidae</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Felidae</td>
<td>-</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Ursidae</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Procyonidae</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Mustelidae</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Viverridae</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>?</td>
</tr>
<tr>
<td>Hyaenidae</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Pinnipedia</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

**Canine distemper virus (CDV)**

All families of the order *Carnivora* are susceptible to CDV, and it is among the most significant infections of many species. Christensen (1963) recommended vaccination against CDV in susceptible zoo animals, with the addition that vaccination of young animals at an earlier stage than in dogs is preferred. CDV vaccination is recommended in all members of the *Canidae, Procyonidae* and *Mustelidae* by all authors. There is no mention of vaccination of felids against CDV in literature until several outbreaks occurred among large cats in zoos and the wild (Fix et al. 1989, Appel et al. 1994, Munson et al. 1995, Wood et al. 1995, Roelke-Parker et al. 1996, Meehan et al. 1998, Cameron et al. 1998, Miller & Anderson 2000). Following this, the vaccination of large cats is mentioned as being possible, but not recommended – unless in high risk situations - as risk of exposure is generally low, and vaccination carries some risk (Junge et al. 1995, Kennedy-Stosskopf 1996, Aiello 1998, Miller & Anderson 2000, Woodford 2001, www.5tigers.org). The susceptibility of members of the *Ursidae* and *Hyaenidae* to canine distemper virus is deemed questionable by some authors, and therefore not recommended by these authors (Fraser 1991, Aiello 1998). Although clinical disease as a result of CDV infection is rare in ursids (Poston & England 1992), serologic surveys have shown the presence of CDV specific antibodies (Munson et al. 1995, Marsilio 1997, Dunbar et al. 1998, Maack et al. 2000). Clinical disease and presence of CDV specific antibodies has been documented in spotted hyaenas (*Crocuta crocuta*) (Montali et al. 1987, Alexander et al. 1995, Haas et al. 1996, Harrison et al. 2002) and a palm civet (*Paguma larvata*) (Machida et al. 1992), therefore vaccination is recommended in these species by other authors (Fowler 1986, Phillips 1989, Miller 1989, Burroughs 1992, Junge 1995, Woodford 2001). Miller & Anderson (2000) recommend vaccination of *Viverridae*, do not recommend vaccination of *Ursidae*, and omit *Hyaenidae* from their article. In general, when vaccination is recommended, the same regime is used in the different families. Due to the possibility of immunosuppressive effects of multivalent vaccines, it is recommended that the distemper vaccine be given separately at a reasonable interval from the other components (Montali et al. 1994)

A problem faced in the prophylaxis of distemper in exotic carnivores is the variation between and within species in their reaction to MLV vaccines, with possible lethal consequences. There are two distinct types of MLV CDV vaccine, one produced in avian cells and the other in canine kidney cells, and neither is safe for use in all potential target species. Chicken embryo-adapted live virus distemper vaccines attenuated for ferrets have protected them from challenge with an infective dose of virulent virus within 48 hours after vaccination (Baker...
et al. 1952). Fromm D (Solvay Animal Health Inc.) appeared to be safe and efficacious for use in maned wolves, bush dogs and fennec foxes (Montali et al. 1983). But avian cell vaccines have caused disease in mink, ferrets and foxes (Sutherland-Smith et al. 1997, Carpenter et al. 1976, Henke et al. 1997). Fervac-D, also of avian origin caused fatal disease in 1 of 8 red pandas (Montali et al. 1994). Vaccine of canine origin has been responsible for vaccine induced distemper in a large number of species (see table ). Non-domestic canine pups can be vaccinated with a MLV measles vaccine (Klös & Lang 1982, Frankenhaus & Visee 1985) - measles and canine distemper virus are antigenically closely related, and the measles virus is not neutralised by the maternal antibodies in 6 week old puppies of domestic dogs (Appel et al. 1984). The second and all subsequent vaccinations should be with a MLV CDV vaccine. Until 1983 the use of MLV is mentioned without warning (Klös & Lang 1982, Wallach & Boever 1983, Miller 1989). After this KV are recommended for use in exotic species (Fowler 1986, Gabrisch & Zwart 1987, Franke et al. 1989, Fraser 1991, Aiello 1998) even though the efficacy of KV has been questioned (Appel et al. 1984, Sikarski et al. 1991). Currently there are no killed CDV vaccines commercially available, because there is no demand for its use in domestic dogs, and the market for zoo animals is too small (Appel & Montali 1994). Between the different commercially available MLV vaccines there is a clear difference in vaccine efficacy, as has been demonstrated in domestic dogs (Appel et al. 1987, Rikula et al. 1996, Kommonen et al. 1997). Considering the high incidence of vaccine induced disease, Miller & Anderson (2000) mention that in some cases strict isolation may be preferable to vaccination.

The large range of (highly susceptible) host species in zoos for which vaccination is recommended underpins the need for the production of a safe and efficacious vaccine. An experimental subunit vaccine incorporating the CDV F and H proteins into immuno stimulating complexes (ISCOM) has been developed for use in dogs and seals (de Vries et al. 1988, Visser et al. 1992), and proved to be capable of producing humoral and cellular immunity. Although the immunity achieved was not sterile (infection of the upper respiratory tract occurred), the vaccinated seals were protected from a potentially lethal challenge with phocid distemper virus (Visser et al. 1992). The ISCOM vaccine has since been used experimentally in several European zoos (Schaftenaar pers. comm), and its potential use in non-domestic felids has been proposed in special cases (Kennedy-Stoskopf 1996). An experimental adjuvanted killed CD vaccine produced by M.J.G. Appel has been used in red pandas and giant pandas in several zoos. The vaccine appeared to be safe and efficacious, but produced low titres with inadequate durability, requiring booster vaccinations two to three times annually (Montali et al. 1994). This vaccine is no longer produced. In Germany a small amount of inactivated vaccine is produced for use in zoos (Geyer and Matern pers. comm. 2001).

In 1997 a recombinant virus vectored CDV vaccine was introduced (Stephenson et al. 1997) and tested for its safety and efficacy along with MLV components (Pardo et al. 1997). Following vaccination experiments in mice using a vaccine expressing the H and F protein in mice, a vaccine containing the H, F and nucleocapsid (N) constructs produced highly encouraging results in domestic dogs after challenge with virulent virus, although the mechanism of protection was not clear (Cherpillod et al. 2000). Recently a monovalent canarypox-vectored vaccine expressing the H and F surface antigens of CDV has become commercially available in the US, and its efficacy and safety in domestic ferrets has been demonstrated (Wimsatt et al. 2001). In black-footed ferrets (Mustela nigriceps) x Siberian polecat (Mustela eversmanni) hybrids the use of this vaccine has produced a good immune response (Williams & Montali 1998), and has since been used and evaluated in a large number of exotic species (Montali pers. comm.). This vaccine, Purevax (Merial) is registered for use in domestic ferrets, but its off-label use in all susceptible species in zoos is recommended by the American Association for Zoo Veterinarians (AAZV) and Woodford (2001). In the European Union its use is not permitted. The main advantage of avipox-vectored vaccines is their safety, the foreign genes in the vector are expressed, inducing
protective cellular and humoral immunity in the absence of the complete virus, and therefore eliminating the possibility of infection. Members of the *Avipox* genus are distinguished by their host restriction to avian species, eliminating the potential for dissemination of the vector within the vaccinate and therefore the spread of the vector to nonvaccinated contacts or the environment (Paoletti 1996). Virus replication is blocked at a late stage of morphogenesis in mammalian cells, importantly leaving the synthesis of viral proteins unimpaired (Sutter & Moss 1992). For unknown reasons, canarypox virus appears to be superior to fowlpox virus in the induction of immune responses in mammals (Moss 1996). Recent research has shown that replication-competent CAV-2 recombinant vaccines expressing the H and F antigens of CDV triggered both a significant seroconversion and protective immunity in puppies born to CDV and CAV-2 immune dams, thereby overcoming the passive immunity (Fischer 2002).

*CDV Vaccination regime recommended in domestic dogs:*

- Initial at 6 weeks, repeat every 2 weeks until 12 weeks. Booster annually with MLV vaccine

**Table 4:**

<table>
<thead>
<tr>
<th>Species</th>
<th>Vaccine</th>
<th>Regime</th>
<th>Booster</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>All susceptible</td>
<td>MLV</td>
<td>Initial at 3-6 weeks, at 9 weeks combination vaccine. Single vaccination after 12 weeks</td>
<td>biannually</td>
<td>Klös &amp; Lang 1982</td>
</tr>
<tr>
<td>Mustelidae</td>
<td>MLV</td>
<td>10 weeks</td>
<td></td>
<td>Klös &amp; Lang 1982</td>
</tr>
<tr>
<td>All susceptible</td>
<td>KV or MLV</td>
<td>Initial at 5-6 weeks repeat every 2 weeks until 15 weeks</td>
<td>annually</td>
<td>Wallach &amp; Boever 1985</td>
</tr>
<tr>
<td>Mustelidae</td>
<td>KV for blackfoot &amp; initial</td>
<td>Initial at 8 weeks, repeat after 2-3 weeks</td>
<td>*</td>
<td>Wallach &amp; Boever 1985</td>
</tr>
<tr>
<td>Procyonidae</td>
<td>KV</td>
<td>Initial at 6-8 weeks, repeat every 2-3 weeks until 14 weeks</td>
<td>annually</td>
<td>Wallach &amp; Boever 1985</td>
</tr>
<tr>
<td>All susceptible</td>
<td>KV</td>
<td>Initial at 8 weeks, repeat after 2-3 weeks</td>
<td>annually in affected areas, otherwise every 2-3 years</td>
<td>Frankenhuis &amp; Visee 1985</td>
</tr>
<tr>
<td>All susceptible</td>
<td>KV (unavailable)</td>
<td>Initial distemper/measles at 6-8 weeks, at 12-14 weeks combination vaccine.</td>
<td>annually</td>
<td>Burroughs 1992</td>
</tr>
<tr>
<td>Procyonidae</td>
<td>Initial at 8 weeks, repeat at 12 and 16 or 18 weeks of age</td>
<td>*</td>
<td>Paré et al. 1999</td>
<td></td>
</tr>
<tr>
<td>All susceptible</td>
<td>Single dose after weaning im, monthly booster up to 4 months</td>
<td>annually</td>
<td>Fraser 1991, Aiello 1998</td>
<td></td>
</tr>
<tr>
<td>All susceptible</td>
<td>Initial at 6-8 weeks, repeat every 2-3 weeks with a total of 3 vaccinations, in special cases (ie early weaning, ill juveniles, high probability of exposure to disease) extended to 4 or 5.</td>
<td>annually</td>
<td>Phillips 1989, Cubas et al. 1996</td>
<td></td>
</tr>
<tr>
<td>All susceptible</td>
<td>ISCOM or KV (unavailable)</td>
<td>8, 11, 14 weeks of age</td>
<td>annually</td>
<td>Blijdorp</td>
</tr>
</tbody>
</table>

**Parvovirus infections**

Infections with Feline Parvovipovirus (FPV) have been reported in captive felids since the 1930's (Hindle & Findlay 1932, Goss et al. 1942), and have since been reported in a large number of feline species. All members of the *Canidae, Felidae, Viverridae, Mustelidae* (except for the domestic ferret, Parrish et al. 1987), *Procyonidae* and *Ursidae* are susceptible and vaccination is recommended. Although there is some difference of opinion on the susceptibility of *Hyaenidae*, vaccination is recommended (Junge 1995). Vaccination regimes
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reported by these authors are as those for the exotic cats. In 1947 a new viral gastroenteritis was observed in farmed mink (*Mustela vison*) in Canada (Schofield 1949). That virus, closely related biochemically and serologically to FPV, was later named mink viral enteritis, and currently probably occurs wherever mink are farmed (Pollock and Larsen 1990). In 1978 a virus infecting canine species emerged with clinical similarities to FPV infection in cats (Appel 1979). This virus, referred to as canine parvovirus type 2 (CPV-2) is closely antigenically and pathogenically related to FPV. Members of the *Canidae, Mustelidae, Viverridae* and *Procyonidae* are considered to be susceptible, but the virus has not got the ability to replicate in *Felidae*. In 1979 and around 1984 new antigenic types of CPV (CPV-2a and CPV-2b) emerged with an increased host range including both domestic and large cats (Steinel et al. 2000), although the large cats appear to have a higher susceptibility for these virus types (Steinel et al. 2001). For all susceptible species vaccination is recommended (Fraser 1991, Aiello 1998, Steinel et al. 2001). Other authors recommend vaccination of canidae only (Wallach & Boever 1985, Cubas et al. 1996). Canidae may be vaccinated with a FPV vaccine, and *Felidae* may be vaccinated with CPV vaccine due to the close antigenic relationship (Pollock & Carmichael 1983). In general, when vaccinating non-domestic species, the vaccine selected should be based on the similarity of the hosts (e.g. CPV in coyotes) or the known or probable virus susceptibility of the host to be vaccinated (e.g. FPV vaccine in raccoons) (Barker and Parrish 2001). It is recommended to vaccinate members of the *Canidae* with CPV-2 vaccines, and considering the high incidence of infections with CPV-2a and CPV-2b in large cats an inactivated vaccine containing these types rather than CPV-2 would be desirable, but is not yet commercially available.

There is debate over vaccine dose in relation to size of species, and the use of KV and MLV vaccines. Povey and Davis (1977) suggest that it is probably unnecessary to increase the dose or antigen mass when using KV in large species, due to the antigenic efficiency of parvoviruses and the use of adjuvants. Increased or double doses have been recommended for the vaccination of large cats >50 kg, which will subsequently develop higher antibody titres (Fowler 1977, Wallach - Boever 1983, Fraser 1991, Aiello 1998). In other studies antibody titre does not appear to be dose dependent (Wack 1991), large felids do not require larger doses than the 1ml dose used in domestic cats to develop protective titres (Bush et al. 1981). MLV vaccines probably overcome the consideration of animal size in relation to dose of vaccine (Povey and Davis 1977), although the increased potency may result in decreased safety. Some MLV vaccines reported to be safe for one species may be insufficiently attenuated for use in another species, and have caused vaccine-induced disease (Klöss & Lang 1982, Wallach & Boever 1983, Frankenhaus & Visee 1985, Appel et al., Fraser 1991, Aiello 1998, Woodford 2001). Christensen (1963) reported abortive cases of depression and diarrhoea with recovery after 1 or 2 days' symptoms following the introduction of systematic FPV vaccination. Visee (pers. comm. 1974 & 1975) reported clinical panleukopenia in 3 vaccinated Siberian tigers and 1 leopard (*panthera pardus*), of which 2 fatal. Therefore the use of KV is generally recommended in exotic species, although the production of antibodies is not as effective and the duration of immunity is shorter. KV FPV vaccine used in bush dogs (*Speothos venaticus*) did not protect them from infection – protective titres were not reached before 23 weeks of age during which period they were susceptible to infection (Janssen et al. 1982). Fowler (1977) reports that MLV vaccines have been used in different wild felid species, and are apparently safe. Many authors after this recommend the use of the highly antigenic KV vaccine (Klöss & Lang 1982, Wallach & Boever 1983, Appel et al., Fraser 1991, Aiello 1999), or at least for the initial vaccinations which can then be boostered with MLV (Frankenhaus & Visee 1985, Fowler 1986, Gabrisch & Zwart 1987). Phillips (1989) recommends the use of KV without components for the feline respiratory viruses in mustelidea, procyonidae and viverridae. MLV vaccine should never be used in pregnant felidae, foetal infection results in cerebellar hypoplasia with clinical ataxia in the kitten (Fowler 1986).
Many different regimes have been tried, in which the timing of the initial vaccination is one of the main variables. Interference with primary immunisation by maternal antibodies is the commonest cause of “vaccine failure” in both domestic (Greene 1990) and non-domestic carnivores (Janssen et al. 1982; Wack et al. 1993). Vissee (pers. com. 1975) reported that after a change in the vaccination regime (6, 12, 26 weeks to 12, 16, 20 weeks) no clinical signs were reported following MLV vaccination, suggesting that maternal antibodies interfere with vaccination during the first 3 months. No controlled studies on the half-life of maternal antibodies to FPV in non-domestic species have been performed, and it should not be directly extrapolated from the 9.5 days determined in domestic cats (Scott 1970). Therefore the vaccination recommendations for non-domestic species are the same as those used in domestic species during maternal immunity.

Combination vaccines containing MLV CDV, CAV-2, CPI-3, and FPV/CPV have been used in wild canidae without adverse effects, but with variable results, especially among non-canine species. Burroughs (1992) recommends its use in canidae, viveridae and hyaenidae. A multivalent KV vaccine (Fel-O-Vax PCT, Fort Dodge Lab Inc.) provides good antibody titres to the three major infectious viral diseases of domestic cats (panleukopenia, rhinotracheitis and calicivirus). The European Endangered Species Program (EEP) recommends 1 ml of Fel-O-Vax be used for boosters in adults; juveniles should be vaccinated at 8, 12, and 16 weeks, repeated at 6 months, and then given annual boosters. This is the same schedule used in domestic cats. Another regime recommended is repeated vaccinations with 2 week intervals for 3 injections or until 16 weeks of age (Woodford 2001). When cheetah cubs are vaccinated every 4 weeks from 8-16 weeks they may not develop and maintain protective antibody titres during their first year of life. When these cubs are vaccinated every 2 weeks from 8-16 weeks will develop protective titres. A booster may need to be given at the age of 40 weeks to insure that titres are maintained during the first year of life. There is much individual variation – boosters every 3 months may be warranted in high risk situations (Wack et al. 1993) - but a single annual vaccination may be adequate to maintain protective antibody titres (Wack 1991).

**FPV vaccination recommendation in domestic cats:**
- 8, 12, 16 weeks, booster at 6 months, then annually (Fel-O-Vax, Fort Dodge)

**Table 5:**

<table>
<thead>
<tr>
<th>Species</th>
<th>Vaccine Regime Recommended for use in non-domestic species</th>
</tr>
</thead>
<tbody>
<tr>
<td>All susceptible</td>
<td>MLV 6, 12, 26 weeks</td>
</tr>
<tr>
<td>All susceptible</td>
<td>MLV or KV 12, 16, 20 weeks</td>
</tr>
<tr>
<td>All susceptible</td>
<td>KV or MLV 4, 8, 12, 16 weeks annually when using KV</td>
</tr>
<tr>
<td>All susceptible</td>
<td>4, 8, 16 weeks (bi-)annually</td>
</tr>
<tr>
<td>All susceptible</td>
<td>6-8 weeks, repeat every 2-3 weeks until 14 weeks of age</td>
</tr>
<tr>
<td>All susceptible</td>
<td>1-2 doses KV, then after 3 weeks MLV, MLV at 8, 11 weeks.</td>
</tr>
<tr>
<td>All susceptible</td>
<td>2, 4, 8, 12, 16 weeks (colostrum deprived), 8, 12, 16 weeks (natually weaned)</td>
</tr>
<tr>
<td>All susceptible</td>
<td>3 x KV with 2 weeks interval, then 2 x MLV with 4 weeks interval (colostrum deprived), 3 x MLV with 3-4 weeks interval starting at 7-8 weeks.</td>
</tr>
<tr>
<td>Skunks</td>
<td>Initial at 8-10 weeks, repeat after 3 weeks</td>
</tr>
</tbody>
</table>

**Reference**
- Visee pers comm 1974
- Visee pers comm 1975
- Fowler 1977
- Klöss & Lang 1982
- Wallach & Boever 1983
- Frankenhuys & Visee 1985
- Fowler 1986
- Gabriisch & Zwart 1987
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All susceptible pregnant females should be boosted during gestation annually Sacramento zoo 1990

Felidae KV, (unavailable) Initial KV at 3 months, MLV combination vaccine at 4 months annually

Initial at weaning and repeated at least twice with 2 week intervals annually Junge 1995

All susceptible 8 and 12 weeks annually Meitzer et al. 1996

2 x with 2 weeks interval 6-12 months Fraser 1991, Aiello 1998

All susceptible KV 8, 10, 12, 14, 16 weeks, repeat at 6 months annually Miller & Anderson 2000

All susceptible KV 8, 11, 14 weeks annually Blijdorp

Table 6:
CPV vaccination Regimes recommended for use in non-domestic species

<table>
<thead>
<tr>
<th>Species</th>
<th>Vaccine</th>
<th>Regime</th>
<th>Booster</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>All susceptible</td>
<td>Initial at 8-12 weeks, 2nd vaccination 3 weeks later</td>
<td>annually, every 6 months in endemic areas</td>
<td>Wallach &amp; Boever 1985</td>
<td></td>
</tr>
<tr>
<td>All susceptible</td>
<td>As in domestic dogs</td>
<td></td>
<td>Frankenhuis &amp; Visee 1985</td>
<td></td>
</tr>
<tr>
<td>All susceptible</td>
<td>Initial at 3 months</td>
<td>annually</td>
<td>Burroughs 1992</td>
<td></td>
</tr>
<tr>
<td>All susceptible</td>
<td>Initial at 8 weeks, repeat 3-4 times with 2-3 week intervals</td>
<td></td>
<td>Cubas et al. 1996</td>
<td></td>
</tr>
<tr>
<td>All susceptible</td>
<td>8, 11, 14 weeks</td>
<td>annually</td>
<td>Blijdorp</td>
<td></td>
</tr>
</tbody>
</table>

Infectious canine hepatitis / Canine Adenovirus-1 (CAV-1)

Canidae, Ursidae and Mustelidae are susceptible to canine adenoviruses (Mann et al. 1980, Whetstone et al. 1988). Annual vaccination of Ursidae is recommended by some authors (Sacramento zoo 1990, Fraser 1991, Aiello 1998), depending on risk of exposure (Fowler 1986, Appel 1987) or not at all (Wallach & Boever 1983, Frankenhuis & Visee 1985, Junge et al. 1995, Miller & Anderson 2000). Burroughs (1992) recommends vaccination of Canidae and Hyaenidae. KV has been recommended for use in genera other than Canidae, as MLV may prove virulent (Klös & Lang 1982, Appel 1987). Currently there is no KV commercially available. The diluent portion of Adenomune-7 however, contains a killed CAV-2 antigen that may be used in highly susceptible species like maned wolves (Woodford 2001). Commercial combination vaccines that include CDV and MLV CAV-1 or CAV-2 are generally used. CAV-1 is the causative agent of of infectious canine hepatitis, CAV-2 is the causative agent of respiratory disease. The two viruses are closely antigenically related, and vaccination with CAV-2 provides cross-protection against CAV-1 without causing adverse postvaccinial reactions like corneal opacity, common in domestic dogs after vaccination with MLV CAV-1, and reported in maned wolves by Thomas-Baker et al. (1985). Although clinically dramatic, the oedema usually resolves after a few days without consequence. Another reason was the diminution of postvaccinial encephalitis which was noted after substitution of CAV-2 for CAV-1 in combination vaccines (Carmichael 1999).

Table 7:
CAV vaccination Regimes recommended for use in non-domestic species

<table>
<thead>
<tr>
<th>Species</th>
<th>Vaccine</th>
<th>Regime</th>
<th>Booster</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>All susceptible</td>
<td>Initial at 3-6 weeks</td>
<td>bi-annually</td>
<td>Klös &amp; Lang 1982</td>
<td></td>
</tr>
<tr>
<td>All susceptible</td>
<td>MLV or KV</td>
<td>Initial at 11-12 weeks, repeat after 2-3 weeks</td>
<td>annually</td>
<td>Wallach &amp; Boever 1983</td>
</tr>
<tr>
<td>All susceptible</td>
<td>As in domestic dogs</td>
<td></td>
<td>Frankenhuis &amp; Visee 1985</td>
<td></td>
</tr>
</tbody>
</table>
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Herpesvirus infections

All smaller exotic Felidae are susceptible to feline herpesvirus (FHV), larger Felidae have no or mild symptoms. Vaccinations currently available are KV or MLV, but KV is recommended. Vaccines commercially available (eg Fel-O-Vax) are usually in combination with other agents (eg FPV, FCaV, Chlamydia). Humoral titres are usually short-lived and boosters every 3 months may be required in high-risk situations (Wack et al. 1993). Klös and Lang (1982) recommended vaccination of Mustelidae and Viverridae, all other authors regard Felidae as the only susceptible animals.

Fatal phocine herpesvirus type 1 (PhHV-1) infections have been reported in young and immunocompromised harbour seals in rehabilitation centres (Osterhaus et al. 1985, Borst et al. 1986, Gulland et al. 1997, Harder et al. 1997). An experimental sub-unit vaccine using the gB protein of PhHV-1 has been produced that proved to be safe and provided protective immunogenicity after challenge infection in domestic cats. Humoral and cellular immunogenicity was produced in harbour seals (Martina et al. 2001; 2003).

Table 8:

<table>
<thead>
<tr>
<th>FHV vaccination Regimes recommended for use in non-domestic species</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Species</strong></td>
</tr>
<tr>
<td>All susceptible</td>
</tr>
<tr>
<td>All susceptible</td>
</tr>
<tr>
<td>All susceptible</td>
</tr>
</tbody>
</table>

**Table 8:**

<table>
<thead>
<tr>
<th>FHV vaccination Regimes recommended for use in non-domestic species</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Species</strong></td>
</tr>
<tr>
<td>All susceptible</td>
</tr>
<tr>
<td>Felidae</td>
</tr>
<tr>
<td>Felidae</td>
</tr>
<tr>
<td>Felidae</td>
</tr>
<tr>
<td>Felidae</td>
</tr>
<tr>
<td>Felidae</td>
</tr>
<tr>
<td>All susceptible</td>
</tr>
<tr>
<td>All susceptible</td>
</tr>
</tbody>
</table>

**Feline Leukemia virus (FeLV)**

Has been reported in exotic felids, and efficacy of a subunit vaccine has been demonstrated (Briggs et al. 1986, Citino et al. 1988, Pettan et al. 1992). It is recommended to serologically test all Felidae for exposure. In 1986 vaccination with the then recently developed Leucocell vaccine was recommended by Gabrisch & Zwart. Due to the low prevalence in exotic cats, and the interference with serologic antibody screening, vaccination is not generally done (Citino et al. 1988, Phillips 1989, Junge et al. 1995, Kennedy-Stosskopf 1996), but may be done when there is close contact with feral cats (Miller & Anderson 2000).
Leptospirosis

Canidae, Procyonidae, Ursidae, Mustelidae, and Pinnipedia are susceptible (Shotts 1981). A recent study in Rio de Janeiro Zoo, Brazil revealed an antibody prevalence of 37.7% of all animals tested – carnivores and non-carnivores - belonging to 10 families, out of which seroprevalence was most common in Canidae and Procyonidae (Lilenbaum et al. 2002). Raccoons, opossums, and rodents can act as reservoirs and concurrently transmit infection to zoo animals. Vaccination is highly serovar specific: the carnivores should be vaccinated with bacterins that contain immunogens against Leptospira interrogans serovar canicola and icterohaemorrhagiae. Vaccinations may influence the immune response in young animals - vaccination of pups younger than 9-10 weeks of age is not recommended (Appel et al. 1999). Vaccination does not necessarily prevent shedding of the organism (Aiello 1998).

Table 9:

<table>
<thead>
<tr>
<th>Leptospirosis vaccination Regimes recommended for use in non-domestic species</th>
<th>Species</th>
<th>Vaccine</th>
<th>Regime</th>
<th>Booster</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canidae</td>
<td>Initial at 12 weeks, repeat after 2-3 weeks</td>
<td>annually</td>
<td>Wallach &amp; Boever 1983</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Procyonidae / Mustelidae</td>
<td>Initial at 12-14 weeks</td>
<td>annually</td>
<td>Wallach &amp; Boever 1985</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All susceptible</td>
<td>As in domestic dogs</td>
<td></td>
<td>Frankenhuys &amp; Visee 1985</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ursidae</td>
<td>Initial at 8 weeks, repeat at 12 and 16 weeks of age</td>
<td>annually</td>
<td>Sacramento zoo 1990</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All susceptible</td>
<td></td>
<td>annually</td>
<td>Junge et al. 1995</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All susceptible</td>
<td>1-2 ml dose im or sc at 6-8 weeks, repeat after 2 weeks</td>
<td>bi-annual</td>
<td>Fraser 1991, Aiello 1998</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Canidae/ Procyonidae</td>
<td></td>
<td>bi-annual</td>
<td>Woodford 2001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Rabies

All mammal species are susceptible. Previously rabies vaccination was recommended in all circumstances (Klös & Lang 1982, Wallach & Boever 1983, Fowler 1986, Appel 1987). More recently recommendations are to vaccinate depending on location, risk of exposure, or possible outbreak (Fraser 1991, Junge et al. 1995, Aiello 1998). In areas where the incidence of rabies in local wildlife (skunks, raccoons, foxes) is high, vaccination is recommended. Local veterinary authorities should be contacted regarding the legal aspects of extra-label vaccination, as some areas may have restrictions. Klös & Lang (1982) recommended use of MLV, except for younger animals. All other authors agree that non-domestic animals should be vaccinated with KV only. MLV vaccines have not been available commercially after rare occasions where the vaccine caused rabies-like disease in dogs. The efficacy of KV vaccines were questioned by Fowler (1986), but a KV vaccine (Imrab, Pitman Moore) has proven to be efficacious and safe, and been approved for use in domestic ferrets (Rupprecht et al. 1990). A great reduction in wildlife rabies has been accomplished by oral immunization (see below).

Table 10:

<table>
<thead>
<tr>
<th>RV vaccination Regimes recommended for use in non-domestic species</th>
<th>Species</th>
<th>Vaccine</th>
<th>Regime</th>
<th>Booster</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>All susceptible</td>
<td>KV</td>
<td>Initial at 4-6 months</td>
<td>annually</td>
<td>Wallach &amp; Boever 1983; Junge et al. 1995</td>
<td></td>
</tr>
<tr>
<td>Felidae</td>
<td>KV</td>
<td>Initial at 6 months</td>
<td>annually</td>
<td>Wallach &amp; Boever 1983</td>
<td></td>
</tr>
<tr>
<td>All susceptible</td>
<td>KV</td>
<td>Initial at 6 months</td>
<td>annually</td>
<td>Sacramento zoo 1990</td>
<td></td>
</tr>
<tr>
<td>All susceptible</td>
<td>KV</td>
<td>Initial at 3-4 months</td>
<td>annually</td>
<td>Fraser 1991, Aiello 1998</td>
<td></td>
</tr>
</tbody>
</table>
Toxoplasmosis

Many species of zoo mammals (but also birds) are highly susceptible to *Toxoplasma Gondii* infections, especially New World monkeys and marsupials, although members of the *Felidae* family are the definitive host, and the only animals that pass the oocyst in the faeces. This protozoan parasite has been reported in several species of non-domestic felidae, of which the Pallas cat appears to be highly susceptible (Dubey et al. 1988, Dorny et al. 1989, Ocholi et al. 1989, Swanson et al. 1999, Silva et al. 2001). There are a number of different vaccines, of which New Zealand S48 vaccine containing live tachyzoites, proved to be capable of inducing acute, fatal toxoplasmosis and is therefore considered to be unsuitable for use in macropods (Lynch et al. 1993). An alternate study suggested that oral vaccination with *Hammondia Hammondi* oocysts – a closely related non-pathogenic protozoan - may offer partial protection to the clinical effects, but does not prevent infection by *T. gondii* (Reddacliff et al. 1993). Recently an experimental recombinant FHV vaccine expressing the ROP2 antigen of *T. gondii* has been developed and proven efficacious in domestic cats (Mishima et al. 2002), but this is not yet commercially available.

Vaccination of free-ranging wildlife

Should free-ranging wildlife be vaccinated? It is an interference of the natural selection, and therefore a topic under discussion. Re-introduced or translocated animals will not have been challenged under natural conditions with the local pathogens when young (and maternal immunity is still present), and therefore need to be vaccinated to obtain a level of immunity against these pathogens. Recently IUCN guidelines for the reintroduction of captive animals into the wild have been published (Woodford 2001). Pre-release vaccination of animals to be rehabilitated or translocated should be considered by the veterinarian after evaluating the immunological status, and the risk of infection upon release into the destined area.

When vaccinating wildlife it is of utmost importance to consider the fact that MLV vaccines may not be sufficiently attenuated for exotic species, and that vaccine induced disease or shedding of virulent virus may occur, thereby infecting free-living populations. Another problem faced is the difficulty to booster under field conditions, so that the level of immunity may not be sufficient. It is therefore recommended to complete the vaccination regime before release when possible. When this vaccination is carried out during the “preparation stage”, sufficient time is allowed to develop the required immunity and detect possible adverse effects.

Following the phocine distemper (PDV) epidemic of 1988 (Osterhaus et al. 1988, Osterhaus & Vedder 1988, Kennedy et al. 1988) and the development of an experimental ISCOM (Osterhaus et al. 1989, Visser et al. 1992), all rehabilitated seals from the rehabilitation and research centre Pieterburen have been vaccinated before release. The duration of protective immunogenicity following this vaccination is unknown, and is intended to last for the duration of stay in the rehabilitation centre. The discussion of whether to start vaccinating the wild population flared up during the recent PDV epidemic of 2002, but was not considered a viable option (Trilateral seal expert meeting 2002, DEFRA 2002). Vaccination of seals with a MLV vaccine is contraindicated (Kennedy et al. 2001).

Vaccination of endangered species to infectious diseases may aid in the survival of these species. African wild dog (Visee et al. 2001) and black-footed ferret (Williams & Thorne 1999) conservation projects have been severely affected by CDV outbreaks, and much work
is done on the production of a safe and efficacious vaccine (Montali et al. 1998, Visee 2001, van de Bildt et al. 2002).

Vaccination of a wild population of Mediterranean monk seals (*Monachus monachus*) was considered during a morbillivirus epizootic in the Mediterranean in 1992 (Osterhaus et al. 1992). During the PDV outbreak among Northern European Harbour seals in the summer of 2002, vaccination was also considered in the UK, but not deemed feasible (DEFRA 2002).

The zoonotic and economic aspects of rabies infection have resulted in prophylactic immunization of domestic dogs and the eradication of canine rabies in several countries (Bögel 1982). Following this achievement attention was focused on free-ranging vector species, which were much more difficult to vaccinate. The development of a MLV vaccine which vaccinated foxes by the oral route (Baer 1971) was a major step in the right direction, which proved its value when an advancing epidemic was stopped by the vaccination zone (Steck et al. 1982). This vaccine has since been replaced by a vaccinia recombinant vaccine (Pastoret 1997), which has proven to be efficacious, and safe for the target species, the fox, as well as for numerous non-target species (Black et al 1993). To be effective the vaccine must be brought into contact with oral and/or pharyngeal mucosa in a sufficient number of target animals via bait. Factors affecting uptake: size, texture, shape of bait and vaccine container, as well as physical and chemical characteristics. One should take into account bait density, distribution method (manual, aerial or both), sequence and frequency of bait distribution, season, selection of specific baiting areas, strategies for expansion of baiting areas and the overall duration of vaccination campaigns (Rupprecht et al. 2001). Research is being conducted on the development of ideal baits and baiting systems for different species (Steelman et al 1998, Knobel et al 2002, Linhart et al 2002).

Oral vaccination may be used in the eradication of other diseases of wildlife in the future. Wimsatt (1999) reported potential oral efficacy of an experimental canarypox vectored recombinant CDV vaccine in a preliminary study, and this oral efficacy was demonstrated in Siberian polecats (Wimsatt 2003) but more research is needed to evaluate its efficacy and safety in other species.
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