

Practical Exotic Mammal Vaccine Strategies

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Session #126

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Abstract: Few guidelines exist for vaccination of exotic pet mammals. Practitioners must have a clear understanding of individual disease susceptibility, product availability, and consider vaccine risk vs. benefit.

Introduction

Vaccination against infectious disease is a proven preventative therapy in domestic species. Vaccination is also practiced in non-traditional and exotic pet species, at the practitioner's discretion and without benefit of trials demonstrating safety and efficacy.

The goal of vaccination of exotic species is to derive the benefit of protection from disease. Disadvantages of vaccination include unproven efficacy, lack of trials demonstrating safety, and the possibility of vaccine-induced disease. A number of commercial vaccine products are available for use in veterinary medicine, including single or multiple agent vaccines, killed or deactivated vaccines, and recombinant subunit vaccines containing DNA segments.

Legalities of Vaccine Use in Exotic Pet Medicine

Vaccines are approved for use in only one common exotic pet species, the ferret.

Vaccines are regulated by the Animal Plant and Health Inspection Service-United States Department of Agriculture (APHIS-USDA), which "regulates veterinary biologics (vaccines, bacterins, antisera, diagnostic kits, and other products of biologic origin) to ensure that the veterinary biologics available for the diagnosis, prevention and treatment of animal diseases are pure, safe, potent and effective."¹

APHIS-USDA does not regulate veterinary use of these products; therefore, veterinarians can legally use vaccines in a discretionary manner. This does not even fall under the heading "off-label" usage, as this term specifically applies to animal drugs, which are regulated by the Food and Drug Administration's Center for Veterinary Medicine (FDA-CVM).²

The Centers for Disease Control Morbidity and Mortality Weekly Report (CDC-MMMR) publishes the Compendium of Animal Rabies Prevention and Control, 2005, prepared by the National Association of State Public Health Veterinarians. The bulletin gives up-to-date recommendations for prevention and control of rabies virus. The only statement referring to use of rabies vaccine in exotic animals reads, "No parenteral rabies vaccines are licensed for use in wild animals or hybrids. Wild animals or hybrids should not be kept as pets."³

The American Veterinary Medical Association (AVMA) does not specifically recommend against vaccination of exotic pet mammals, but neither does it endorse it. The official AVMA position can be summed up in

recommendations for the use of rabies vaccine in wildlife and hybrid animals: “The safety and efficacy of parenteral rabies vaccination of wildlife and hybrids have not been established, and no rabies vaccines are licensed for these animals.” AVMA goes on to encourage zoos and research institutions to establish rabies vaccination programs in order to protect valuable animals, with the caution that vaccination must not “replace appropriate public health activities that protect humans.”⁴

Liability may be a concern when using a vaccine on a non-approved species. In a position paper on the vaccination of wolf hybrids, AVMA Professional Liability Insurance Trust (PLIT) recommends first checking on the legal status of the animal in question. If the animal were legal as a pet, the trust would consider vaccination of the animal as a “discretionary use of a biologic by the veterinarian, an act which the policy does not specifically exclude.” However, if a veterinarian vaccinates an animal kept illegally, vaccination is considered an illegal act, and likely not covered under the AVMA professional liability act.⁵

AVMA-PLIT specifically recommends the following when considering vaccination of a non-approved species: (Linda Ellis, DVM, Trust Representative, AVMA-PLIT, March 2006)

1. Confirm that possession of the animal is legal per state, community, and other applicable laws.
2. Obtain informed consent from the owner, and note this consent in the medical record. Informed consent assures that the owner understands there are no safety and efficacy trials associated with the use of the vaccine in their pet.
3. Use products and vaccination procedures with some “track record” of success, for example vaccines and protocols used by zoos, even if use is non-published or anecdotal.

Using products with some history of success allows support of vaccination as following the current “standard of care.” The trust representative cautioned against being the first to try a new product in an unapproved species as successful legal defense in the case of death or adverse effect will be much more difficult.

Determining Vaccination Protocols

The principles of determining what vaccines are beneficial in any single exotic species include:

1. Determination of individual susceptibility of the species in question for the diseases for which vaccines are available
2. Determination of the likelihood of that particular animal encountering a particular disease
3. Determination of potential products that might be useful
4. Acquisition of information regarding reported or anecdotal benefits and dangers of the use of each particular vaccine in a particular species
5. Determination of zoonotic potential of the particular disease

Determining Vaccine Protocols: Individual Susceptibility and Likelihood of Encountering Disease

Most information on the susceptibility of non-traditional pet species to infectious diseases comes from studies in wildlife, and is generally reported in wildlife journal and textbooks. Information on susceptibility and natural transmission can be useful to determine the probability a specific animal will encounter and become sick from a specific disease. Outbreaks of disease in exotic mammals kept as pets are occasionally reported in the literature as well. Table 1 is a summary of domestic and wildlife species and their reported susceptibility to viral diseases for which commercial vaccines are available (Table 1). The author was unable to find information on feline herpesvirus in exotic mammals.

Canine Distemper Virus (CDV)

All members of the taxon Carnivora are thought to be susceptible to CDV. This includes raccoons, foxes, skunks, ferrets, coatimundi, kinkajou, and certain exotic felids as well.⁶ CDV outbreaks have been documented to occur in free-living raccoons, and varying levels of morbidity and mortality are linked to variable virulence of the CDV strain.⁷ The striped skunk is thought to be moderately resistant to CDV,⁶ but the author is aware of several confirmed cases.

Rabies

All mammals are considered susceptible to rabies virus infection.⁵ Raccoon-variant rabies virus was confirmed in 1 guinea pig and 7 pet rabbits in New York State, necessitating post exposure treatment in several adults and children. 4 animals were exposed to raccoons, one exposed to a skunk, and exposure of the 3 remaining animals was unknown.⁷ In the United States, significant reservoirs appear to be bats, skunks, raccoons, coyotes, and foxes.⁵

Parvovirus

The susceptibility of exotic animals to canine parvovirus (CPV) and/or feline parvovirus (FPV) varies.⁵ CPV is mostly a disease of canids, while FPV is reported in felids, raccoons, and mink. Skunks appear resistant to both feline and canine parvovirus. Raccoons, however, are susceptible to disease produced by FPV but not CPV. (Note: the most important infectious diseases of raccoons appear to be rabies virus, CDV, and FPV.⁵ Numerous studies of free-living wildlife indicate antibodies for CPV are present in species such as foxes and martens.^{8,9} While mink are susceptible to FPV, ferrets are not, except when inoculated in utero or within several days of birth.⁵

Infectious canine hepatitis

This disease was first described in the silver fox, and many members of Canidae, Mustelidae and Ursidae family are susceptible, including skunks, raccoons, mink, ferrets, wolves, and bears.⁵

Canine coronavirus

Infection of exotic mammals is considered rare, but possible. There are many species-specific strains of coronavirus, and each appears limited only to closely related species only, for example canine coronavirus between dogs and cats, and porcine coronavirus from pigs, to dogs to foxes.⁵

Table 1. Susceptibility of domestic and exotic mammals to selected viral diseases for which commercial vaccines are readily available in the United States. From: Williams S, Barker IK. *Infectious Diseases of Wild Mammals*. Ames, IA: Blackwell; 2001, unless otherwise indicated.

Disease	Viral Class	Natural Infection	Reservoir Range in US	Transmission, Incubation	Zoonosis
Rabies	Rhabdovirus Lyssavirus	Carnivores Fennec fox Skunk Wild gerbils Wild rats Raccoon Coati Guinea pig ⁶ Rabbit	Skunk, raccoon, coyote, fox, bat	Bite, saliva 1–3 months, but could be days to several years	Yes
Canine Distemper CDV	Paramyxovirus Morbivirus	All Carnivora: Canidae Mustelidae, Procyonidae Hyaenidae Ursidae, Viverridae Felidae Marine mammals Peccary ²⁴	Raccoon Black Bear Coyote Wolves Fox	Close association with many secretions, aerosol; 1–2 weeks	No; Controversial connection with Paget's disease
Western Equine Encephalitis WEE	Arbovirus	Squirrel Opossum Mice Vole Wild rabbits	Birds Jackrabbit	Mosquito vector	Rare
Eastern Equine Encephalitis EEE	Arbovirus	Opossum Mice Rats Other rodents Monkey Bats	Birds	Mosquito vector	Rare
Feline Panleukopenia FPV	Parvovirus	Felidae Canidae, Procyonidae Mustelidae Suspected: Ursidae Viverridae	Felidae	Contact with feces and fecal contaminated environment	No
Canine Parvovirus CPV	Parvovirus	Canidae	Coyote, wolves	Same	No

Table 1 cont'd.

Disease	Viral Class	Natural Infection	Reservoir Range in US	Transmission, Incubation	Zoonosis
Infectious Canine Hepatitis CAV-1	Adenovirus	Canidae, Mustelidae, Ursidae, raccoon	Fox, wolves, coyote, skunk, raccoon, mink, ferret, bears	Direct contact, infected fomites	No
Feline Leukemia Virus (FELV)	Retrovirus	Domestic Felids, rare non-domestic felids: cougar leopard cheetah bobcat ¹⁰	Domestic felids	Excretions, secretions	No
Feline Immunodeficiency Virus (FIV)	Retrovirus	Domestic felids, rare in non-domestic felids: Puma, lion, cheetah, leopard	Domestic felids	Saliva-bite	No
Canine Coronavirus	Coronavirus	Rare in wildlife, but considered possible	Domestic canids	Upper respiratory or GI mucosal secretions	No
Feline Calicivirus	Calicivirus	Domestic felids, wild felids probably susceptible: cheetah, lion, tiger, panther, bobcat ⁹	Domestic felids	Direct contact, aerosol	No
Feline Infectious Peritonitis	Coronavirus	Domestic felines, many exotic felids			No

Feline Leukemia Virus (FeLV) and Feline Immunodeficiency Virus (FIV)

FeLV and FIV are predominantly a disease of domestic cats.⁵ However, rare cases have been reported in exotic felids, including a case of fatal FeLV in a captive bobcat.¹⁰ The source was presumed to be a domestic cat that served as a surrogate nurse.

Feline Calicivirus (FCV)

Feline Calicivirus is primarily a disease of domestic cats.⁵ Antibodies against FCV have been detected in wild bobcats in California.⁹

Feline Infectious Peritonitis (FIP)

FIP is emerging as a potential pathogen in exotic felids, and may be concern for endangered populations. Multiple surveys of wild and captive exotic felids demonstrated positive animals by one or more detection methods. Some wild felids had evidence of infection as well.^{11,12}

Eastern Equine Encephalitis (EEE) and Western Equine Encephalitis (WEE)

These viruses are not considered significant pathogens of exotic animals. Both viruses have been occasionally isolated from a number of wild mammals including squirrels and Virginia opossums. Experimental infection of several rodent species did not produce mortality.⁵

Bacterial Diseases

Leptospirosis

Leptospirosis appears to be a re-emerging infection in domestic dogs, and surveys in wildlife indicate the presence of one or more serovars in wild raccoons, skunk, and squirrels, but not in tested opossums. Results of this study suggested wildlife might be a source of infection in domestic dogs.¹³

All mammal species can be reservoirs of leptospirosis, which is transmitted directly via urine, or through contaminated surfaces. In most cases, the organism exists in a stable host-parasite relationship without evidence of clinical disease. However, disease can be severe to fatal. Multiple serovars exist, and have different levels of pathogenicity and likelihood of apparent infection in different hosts. For example, *L. gryppotyphosa* is maintained in raccoons, skunks, and rodents, *L. icterohaemorrhagiae* in rodents, and *L. pomona* in ungulates.⁵ Leptospirosis has potential zoonotic potential, including documentation of transmission from raccoon and rat to human. Most cases of Leptospirosis in humans are linked to exposure to contaminated water.¹⁴

Bordetella bronchiseptica

Bordetellosis is a disease problem in dogs, cats, rabbits, rats, monkeys, humans, pigs, and guinea pigs. In rabbits, *B. bronchiseptica* is primarily an opportunistic organism, often acting as a co-pathogen with another organism, for example, *Pasteurella multocida*. As the organism is commonly present but seldom causes disease in rabbits, attempts to eradicate the bacterium is seldom attempted.¹⁶

B bronchiseptica can be a significant cause of morbidity and mortality in guinea pigs, with younger pigs most severely affected. Older pigs are often inapparent carriers, and outbreaks are often related to stress. Most pigs will eventually develop immunity and clear the organisms.¹⁶ Most references make the assumption that interspecies transmission can occur.

Comments on Ferrets and CDV

Ferrets are often used as a model for distemper studies, as mortality in this species approaches 100%. They are apparently susceptible to several related strains, including 2 separate strains of lion morbillivirus.¹⁶ As ferrets with distemper often do not survive long enough to spread the disease to other ferrets, most ferret disease is likely due to exposure to sick dogs. Distemper in dogs appears to be mainly clustered in areas with high numbers of immigrant populations and unvaccinated pets, for example Tucson and Phoenix, Arizona, as well as shelters in large cities (Chicago, Illinois, and Dallas, Texas) (Rich Ford, oral communication, February 2006). However, there is a paucity of data on the current incidence of CDV in dogs, as this is not a reportable disease.

An informal survey of veterinary colleagues treating exotic pet revealed that confirmed CDV is uncommon in ferrets. Most reported only sporadic cases, averaging one case per 5–6 years. The respondent with the highest reported incidence (1–2 per year) practices in a CDV endemic area, with several confirmed cases of the disease in dogs per month.

Most reported cases of confirmed CDV seems to occur in stray animals brought into animal shelters, presumably in contact with dogs.

An exotic animal pathology services reported about 5 suspected or confirmed cases per year (Michael Garner, Northwest ZooPath, oral communication, February 2006).

Another exotic animal pathologist reported a cluster of suggestive cases in 1998, all coming from a single retail source that also sold large numbers of puppies (D. Reavill, Zoo/Exotic Pathology Service, oral communication, February 2006).

Determining Vaccine Protocols: Finding Products that Might be Useful, and Information Regarding Use of these Products in Pet Exotic Mammals

A number of manufacturers produce vaccines for domestic animals. Only 3 are licensed for use in an exotic pet mammal, the ferret (Table 2). Adverse reactions to vaccination of exotic species occur, and are mostly anecdotally reported. An example of an exception is a report on morbidity and mortality associated with the use of live attenuated CDV vaccine in mink.¹⁸ Others include reports of mortality from the use of modified live CDV vaccines in ferrets, fennec foxes, and kinkajous.⁶ There are even fewer reports of limited vaccine challenge trials, with the exception of the ferret. Since most anecdotal reports of vaccine-induced illness are related to the use of live attenuated vaccine products, most vaccine protocols suggest use of killed or DNA subunit products in exotic species.

Table 2. Vaccine products of potential use in exotic mammal species.

Product and Manufacturer	Vaccine Type	Approved Species
Purevax Merial	Modified live canary pox vector with DNA segment of CDV	Ferret
Imrab 3 Rhône-Mérieux	Killed rabies virus	Dog, cat, ferret, horse, cattle, sheep
Fervac United Vaccine	Modified live CDV	Ferret
Felovax Fort Dodge	Killed feline panleukopenia feline herpes virus and calicivirus	Cat
Leptovax Fort Dodge	Modified live <i>L. grippotyphosa</i> , <i>L. pomona</i> , <i>L. icterohaemorrhagiae</i> , <i>L. canicola</i>	Dog
Fel-O-Vax Lv-K Fort Dodge	Killed Feline Leukemia Virus	Cat

The American Zoo and Aquarium Association is creating standardized husbandry guidelines for multiple species, and information from these guidelines can be useful to practitioners dealing with these species kept as pets. At this time, husbandry guideline drafts have been proposed for a number of mammalian and avian species, with the goal to have all zoo species covered in the coming years. Access to husbandry guidelines requires membership, which is inexpensive and worthwhile for veterinarians treating a significant number of exotic pets.¹⁹

An example includes recommendation for vaccination taken from the Felid Taxon Advisory Group (TAG) Husbandry Manual for Small Felids, which recommends vaccination of valuable exotic felids with 1 ml of Fel-o-vax (Fort Dodge Laboratories Inc, Fort Dodge, IA, USA). Cubs are vaccinated once every 2 weeks from 8–16 weeks of age, or a single vaccine for adult animals.¹⁹ Also recommended in rabies endemic areas is vaccination against rabies with Imrab (Rhône-Mérieux, Inc, Athens GA, USA). The TAG does not recommend vaccination against FeLV or any other feline disease, but suggests vaccine against Leptospirosis in endemic areas.¹⁹ Similar recommendations are being developed for other species.

Some practitioners advocate vaccination of guinea pigs against *B. bronchiseptica*. Many commercial vaccines, including *B. pertussis* vaccine for humans, and commercial porcine and canine vaccines have been shown to afford protection due to the close relationship among strains of *B. bronchiseptica* and substantial antigenic cross-reactivity. In most cases vaccination prevented disease but did not completely eliminate the organism from the respiratory tract.^{20,21} In the author's experience, most cultures of guinea pigs with respiratory disease reveal a wide range of organisms, and only occasionally *B. bronchiseptica*. Practitioners noting high morbidity and mortality due to *B. bronchiseptica* might consider vaccination of at-risk guinea pigs.

Commercial ferret distemper vaccines have been tested for safety and efficacy. Commercial vaccines appear protective against a number of related strains, including 2 strains of lion CDV.¹⁶ Reaction in ferrets after administration of vaccines is high. In one study comparing vaccine reaction rates in 143 ferrets after administration of a modified live avian cell culture canine distemper virus vaccine alone, an inactivated rabies vaccine alone or

both together were 5.9%, 5.6%, and 5.6%.²² Another study of 3578 animals indicated a much lower vaccine reaction rate. Rates were 0.51% for rabies vaccine administered alone, 1.0% for one of either approved distemper vaccine for ferrets alone, and 0.85% for both products administered simultaneously.²³ It is unclear why reaction rates were so different in these 2 studies.

Zoonosis

Occasionally vaccination decisions are made with consideration of the zoonotic potential of the disease in question, in particular vaccination against rabies virus. While all mammals are susceptible, probability of exposure to rabies is minimal in many exotic mammals caged and maintained indoors.

Of the diseases mentioned in this paper, rabies virus, EEE, and WEE are considered by CDC to be reportable.³

Future of Vaccinations in Exotic Mammals

Among the most valuable advances for exotic mammal vaccines would be successful safety and efficacy trials in these species, which is unfortunately unlikely to happen due to the lower economic value of sales of vaccines for unusual species. Vaccination trials in endangered species may involve measurement of antibody titers, but are unlikely to involve challenge studies.

Measurement of post vaccination antibody titers may be useful in exotic mammals, and several reference laboratories offer measurement of titers for CDV, CPV, FPV, and other viral diseases. However, interpretation of test results is problematic in exotic mammal species.

Development of additional DNA subunit or killed vaccines may prove useful in the prevention of vaccine-induced disease. In January 2006, Dow AgroSciences announced registration for the first plant-made vaccines, where antigen DNA is inserted into plant cells, with no possibility of vaccine-induced disease or post-vaccine viral shedding.²⁵ It remains to be seen whether this technology may one day prove beneficial for exotic mammals.

Acknowledgments: The author thanks the following colleagues for their contributions to this paper: Sue Biolsi, DVM; Brad Brusnskill, DVM; Peter Fisher, DVM; David Hannon, DVM; Astrid Kruse, DVM; George Messenger, DVM; Andres Montesinos, DVM; and Greg Rupp, DVM.

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