Canine Distemper Vaccination is a Safe and Useful Preventive Procedure for Southern Sea Otters (*Enhydra lutra nereis*)


Published By: American Association of Zoo Veterinarians

DOI: [http://dx.doi.org/10.1638/2008-0080.1](http://dx.doi.org/10.1638/2008-0080.1)

CANINE DISTEMPER VACCINATION IS A SAFE AND USEFUL PREVENTIVE PROCEDURE FOR SOUTHERN SEA OTTERS (ENHYDRA LUTRA NEREIS)


Abstract: From 2002 to 2006, eight captive southern sea otters (Enhydra lutris nereis) at research and display institutions in California at risk of exposure to potentially lethal morbilliviruses were vaccinated with a commercial recombinant poxvirus vectored canine distemper (CD) vaccine. Serum-neutralizing (SN) antibody responses were followed for several years. The goal of this study was to determine whether 1) CD vaccination was a safe preventive medicine procedure for this species; 2) sea otters produce detectable SN antibodies in response to vaccination with this product; and 3) if this type of vaccination might be useful in response to a morbillivirus disease outbreak in free-ranging sea otters. Results indicate that a commercial recombinant vaccine is safe, provokes a measurable SN antibody response, and that vaccination may provide some protection from infection for free-ranging sea otters. It also resulted in the reevaluation of CD serology data that were previously published for free-ranging sea otters.

Key words: Canine distemper, Enhydra lutris nereis, morbillivirus, sea otter, serology, vaccination.

INTRODUCTION

A small number of federally listed “threatened” southern sea otters (Enhydra lutris nereis) are held in captivity at the Marine Wildlife Veterinary Care and Research Center (MWVCRC; Santa Cruz, California, USA) and the Monterey Bay Aquarium (MBA; Monterey, California, USA) for rehabilitation, display, and research. Both institutions identified significant risks of exposure to canine distemper (CD) virus in daily operations for captive sea otters in their care. MBA receives injured and sick wild southern sea otters for treatment and rehabilitation while also housing display and research animals. MWVCRC houses only research animals but is adjacent to heavily vegetated lands with abundant raccoon (Procyon lotor) and other small carnivore populations, and despite the use of physical barriers, raccoon have occasionally been able to intrude into otter holding areas. The initial objective of this study was to determine if a commercially available CD vaccine that had proven effective for protection of black-footed ferrets (Mustela nigripes) could be used safely and effectively on captive sea otters and if it might provide protective antibodies.

As part of efforts to promote the recovery of the southern sea otter, both institutions assist the U.S. Fish and Wildlife Service (USFWS) in the development of preventive medicine procedures and potential response strategies. CD is considered to be highly infectious in, and highly lethal to, most mustelid species. Although sea otters are seldom kept in captivity in large numbers, during oil spills dozens to hundreds may be taken into captivity for washing and recovery, and these animals may have preexisting health problems and stress associated with capture may render them even more susceptible to infectious diseases. Thus, it is necessary to determine whether vaccination of captive or free-ranging sea otters might be an effective and potentially useful tool should wild sea otters need to be taken into captivity or should a CD outbreak occur in a sea otter population in North America.

Serologic surveys of wildlife populations are frequently conducted to determine whether particular diseases are present or absent and widespread or clustered in populations. Where antibodies to highly infectious diseases are absent, it is often assumed that the population is unexposed and may be vulnerable to a potential epizootic. However, simple serosurveys have a number of shortcomings, including potentially insufficient sensitivity and specificity of various methods for...
detecting CD antibodies or variations between laboratories using the same methods, which can lead to differing conclusions.

MATERIALS AND METHODS

Four adult male southern sea otters held at MWVCRC came to MBA as orphaned pups, and despite efforts to rehabilitate and release them, they failed to adapt to a free-living situation or were involved in inappropriate or dangerous activities that resulted in them being deemed unsuitable for release by the USFWS. These four animals (Taylor, Morgan, Wick, and Jacob) had lived among wild sea otters from 0.5–4 yr prior to being permanently placed in captivity. They had been in captivity and under regular veterinary observation for 1–8 yr prior to the beginning of this work.

Four female sea otters maintained at the Monterey Bay Aquarium were similarly acquired through a stranding program. Three (Mae, Joy, and Rosa) of the four were originally brought in as dependent pups, ranging in age from 4 day of age to approximately 6 mo of age. The fourth otter (Toola) was a mature, breeding-age female that was approximately 7 yr of age. This animal was part of the free-ranging sea otter population until it stranded. Two of the otters (Joy and Rosa) had been released for 14 and 24 mo, respectively, before being returned to captivity permanently as a result of inappropriate behavior within the wild population. The remaining otter (Mae) was never returned to the wild; however, she was approximately 6 mo of age before stranding.

All sea otters were kept in relatively large pools (1–5,000 gallons) of ambient-temperature seawater (44–54°F). At both institutions, water quality was monitored regularly. The otters were fed a diet of very high-quality shellfish and fish four to five times per day. These animals are trained to facilitate husbandry and medical behaviors. Holding of nonreleasable sea otters at both MBA and MWVCRC was permitted by USFWS (permits MA032027-0 and MA 095276-1, respectively). The care and management protocols for sea otters at both institutions are subject to their respective institutional animal care and use committees and to review and inspection by the U.S. Department of Agriculture under the Animal Welfare Act (license numbers 93-R-0476 and 93-C-0288, respectively).

All eight otters were deemed healthy by the attending veterinarians and remained “normal” in terms of behavior, diet, and general health prior to vaccination and throughout the vaccination trials. Their ages and sexes are shown in Table 1. On day 0 (day of vaccination), each otter was anesthetized for a health examination with intramuscularly administered fentanyl citrate (Fentanyl Citrate for injection, Central Avenue Pharmacy, Pacific Grove, California 93950, USA; 0.22 mg/kg) and midazolam HCL (Ben Venue Laboratories, Inc., Bedford, Ohio 44146, USA; 0.07 mg/kg) anesthesia, which was reversed with intramuscular naltrexone HCL (ZooPharm, Ft. Collins, Colorado 80526, USA; 0.66 mg/kg). All other handling and sampling procedures were similar to those previously described for sea otters. Blood was taken via jugular venipuncture for complete blood count (CBC) and blood chemistry. Blood was allowed to clot, and serum was separated and stored at −70°F to determine whether the animal had any serum-neutralizing (SN) antibodies before vaccination and at various intervals thereafter, on a schedule largely determined by the dates of quarterly health checks. SN antibodies were measured at the Animal Health Diagnostic Center (AHDC) at Cornell University (Ithaca, New York 14853, USA). Samples were considered positive at or above a dilution of 1:8.

A commercial recombinant CD vaccine (Pure-vax, Merial, Athens, Georgia 30602, USA) expressing poxvirus F and H glycoprotein was selected

<table>
<thead>
<tr>
<th>Institution</th>
<th>Otter name</th>
<th>Sex</th>
<th>Age at vaccination (yr)</th>
<th>Subsequent vaccination protocol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marine Wildlife Veterinary Care and Research Center</td>
<td>Taylor</td>
<td>M</td>
<td>10</td>
<td>booster vaccination days 30 and 60</td>
</tr>
<tr>
<td></td>
<td>Jacob</td>
<td>M</td>
<td>1</td>
<td>booster vaccination days 30 and 60</td>
</tr>
<tr>
<td></td>
<td>Morgan</td>
<td>M</td>
<td>6</td>
<td>booster vaccination days 30 and 60</td>
</tr>
<tr>
<td></td>
<td>Wick</td>
<td>M</td>
<td>4</td>
<td>booster vaccination days 30 and 60</td>
</tr>
<tr>
<td>Monterey Bay Aquarium</td>
<td>Rosa</td>
<td>F</td>
<td>5</td>
<td>booster vaccination days 30 and 60</td>
</tr>
<tr>
<td></td>
<td>Mae</td>
<td>F</td>
<td>4</td>
<td>booster vaccination days 30 and 60</td>
</tr>
<tr>
<td></td>
<td>Toola</td>
<td>F</td>
<td>10</td>
<td>booster vaccination days 30 and 60</td>
</tr>
<tr>
<td></td>
<td>Joy</td>
<td>F</td>
<td>6</td>
<td>booster vaccination days 30 and 60</td>
</tr>
</tbody>
</table>

* M, male; F, female.
for these trials, as it had been proven safe and effective\textsuperscript{11} even when used on hybrid ferrets.\textsuperscript{15,18} Vaccination was carried out by intramuscular injection, as per instructions for commercial use. Two to three booster vaccinations were given to each animal at approximately 30-day intervals (Table 1).

RESULTS

No behavioral changes, clinical signs of pain, anaphylaxis, or side effects that could be associated with vaccination were noted in any of the vaccinated sea otters over the several years during which these trials were conducted. All postvaccination CBC and serum chemistry parameters were within reference ranges and were not indicative of inflammation, infection, or systemic illness during these vaccination trails.

SN antibody titers from MWVCRC and MBA animals conducted at Cornell University’s AHDC are shown in Figure 1a and b. In most vaccinated otters, serum samples submitted to AHDC demonstrated a 50–100-fold rise in antibody titer within 30 day of vaccination and a 100–500-fold rise in titer within 60 day of vaccination. Postvaccination antibody titers were generally in the range thought to be protective against CD virus challenge in other species for at least a year. As shown in Figure 1a and b, detectable antibody titers lasted for several years in most otters.

In a previous publication,\textsuperscript{4} it was reported that serum samples collected between 1995 and 2000 from captive and free-ranging sea otters in California and Alaska were tested at the Marine Mammal Immunology Laboratory at the University of California, Davis (U.C. Davis; California 95616, USA) for morbillivirus antibodies using an enzyme-linked immunosorbent assay (ELISA). All samples were negative at the cutoff established for this ELISA test. These same sera from the same California otters tested by ELISA at U.C. Davis were sent to AHDC for testing by SN. Summary results for California otters by coastal area are shown in Table 2.
Table 2. Comparison of canine distemper (CD) serum-neutralizing with CD enzyme-linked immunosorbent assay (ELISA) results by area for southern sea otters.

<table>
<thead>
<tr>
<th>Location</th>
<th>Reciprocal Serum Neutralizing Titer</th>
<th>Animal Health Diagnostic Center</th>
<th>Hanni et al. ELISA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monterey</td>
<td>1:12–1:64</td>
<td>99% (94/95) +</td>
<td>all negative</td>
</tr>
<tr>
<td>Big Sur</td>
<td>1:8–1:32</td>
<td>100% (10/10) +</td>
<td>all negative</td>
</tr>
<tr>
<td>Piedras Blancas</td>
<td>1:8–1:64</td>
<td>100% (51/51) +</td>
<td>all negative</td>
</tr>
<tr>
<td>Gaviota</td>
<td>1:12–1:48</td>
<td>100% (15/15) +</td>
<td>all negative</td>
</tr>
<tr>
<td>San Nicholas</td>
<td>1:8–1:48</td>
<td>100% (16/16) +</td>
<td>all negative</td>
</tr>
</tbody>
</table>

**DISCUSSION**

CD, caused by a paramyxovirus of the genus *Morbillivirus*, is one of the most important diseases of free-ranging carnivores, and it may have a significant negative impact on wild populations of highly susceptible species. Recent emergence of CD infections in species not previously known to be naturally infected, their significant impact on endangered species, and emergence of morbilliviruses in marine mammals make these viruses a major concern for managers of free-ranging wildlife. CD is also among the most important infectious diseases of carnivores in captivity and must be considered in the design of husbandry protocols, including vaccination and housing arrangements.

CD has been reported in mustelids in many parts of the world, including epidemics in European badger (*Meles meles*), polecat (*Mustela putorius*), and stone marten (*Martes fiona*). In North America, black-footed ferrets are extremely susceptible, but species like striped skunk (*Mephitis mephitis*) appear to be more resistant. Mortality is variable in adult mink (20–90%). Mortality is approximately 90% in mink kits, and CD is considered 100% fatal in domestic ferrets (*Mustela putorius furo*). Neither CD nor marine mammal morbillivirus infections have been reported in sea otters, but as mustelids, they must be considered potentially very susceptible.

The southern sea otter is found only off California’s central coast, and yearly counts show that the current population numbers approximately 3,000 animals. This is only a small increase since 1994, when the population began a period of decline and stasis. The primary cause of this decline is high rates of mortality in prime-age adult animals that should live and reproduce for longer periods of time. The southern sea otter was listed as “threatened” under the Federal Endangered Species Act in 1977 and is managed under a Recovery Plan. A high percentage (40–50%) of adult sea otter mortality is attributed to infectious diseases and intoxications. Although the Recovery Plan considers a large oil spill the most likely stochastic event to cause catastrophic reduction to this population, disease epidemics are also a serious concern. Should a major oil spill occur in the limited geographic range of the southern sea otter, many oiled animals would be captured, washed, and housed at MWVRC, MBA, and other locations where there is potential exposure to CD and rapid spread among and between groups of otters. Previous serosurvey efforts had not revealed the presence of antibodies to CD or three other marine mammal morbilliviruses, so it was assumed that southern sea otters were not yet exposed to morbilliviruses and were likely a completely naïve population.

Vaccine-induced infections due to modified live CD vaccination have been reported in a number of sensitive species, and so vaccination is generally not recommended. These trials were conducted primarily to provide valuable, intensively trained, relatively easy-to-handle and at-risk research and display sea otters with protection against potential infection by virulent CD virus. Based on the lack of negative side effects seen in the eight captive sea otters and the production of 100-fold or greater rises in CD SN antibodies with the somewhat varied dosage regimes, it appears that a commercial recombinant poxvirus CD vaccine (Purevax) is potentially both safe and effective for CD prophylaxis.

A number of endangered species, including giant panda (*Ailuropoda melanoleuca*) and black-footed ferrets, have been vaccinated with this canary-pox vectored CD vaccine. SN antibody titers in giant panda lasted over 2 yr in one animal given two doses subcutaneously (6 day apart) and in another animal given two doses intramuscularly (4 mo apart). Significantly, elevated SN antibody titers in sea otter sera submitted to AHDC were found for up to 3 yr in some otters following the vaccination protocol. Although not surprising, the findings of this study were promising, as some related species, including river otters (*Lutra canadensis*), failed to develop antibodies when vaccinated with modified live CD vaccine. SN antibody levels of >1:100 are considered protective against virus challenge in domestic dogs.
vaccinated with modified live vaccines. Studies testing recombinant virus vaccines have shown that lower SN titers can be protective for dogs and Siberian polecat (*Mustela eversmanni*).  

The results indicate that in response to a three-shot series of injections with Purvax, most southern sea otters produce significant SN antibodies, probably immunoglobulin G, for at least a year or more. However, protection may last considerably longer as a result of the mixed nature of humoral and cell-mediated response to vaccination and viral infection.

These trails utilized captive sea otters and a multiple-vaccination protocol. Should vaccination of wild sea otters be desired, the vaccination protocol would have to be modified. Multiple captures of free-ranging otters for booster vaccination at optimal intervals is unlikely, and retaining otters in captivity for multiple injections is stressful, expensive, and may not be necessary or warranted. It appears that an initial injection of Purvax does elicit a SN response to CD. SN antibodies were detected after a single vaccination in several of our otters within 30 day of their first vaccination. Despite the limitations posed by a disease emergency in free-ranging sea otters, the use this type of vaccine as a potential lifesaving and genetic salvage tool may be considered.

Serologic surveys are a commonly used method of determining baseline exposure rates of groups of animals to pathogenic organisms, but they are subject to limitations. Wildlife serosurveys usually rely on a single sampling in time. They rely on the assumptions that testing methods are relatively sensitive, specific, and adequate for detecting antibodies, even in species for which they have not been validated, and they rely as well on assumptions that disease-specific antibodies will be relatively long lasting and detectable through time. These assumptions are sometimes inappropriate, so testing by multiple methods or interlab comparison may be valuable. Earlier efforts using an ELISA indicated that CD and cross-reacting virus were essentially nonexistent in southern sea otters. To further test this hypothesis, and because some of the captive sea otters demonstrated evidence of low levels of preexisting antibody titers to CD, serum samples from the same sea otters previously tested by ELISA were submitted to AHDC for testing by SN. Although low titers (less than 1:16) may be interpreted as inconclusive (Dubovi, pers. comm.), results from AHDC using SN, a method that is more specific for protective CD antibodies, indicate that CD or a virus stimulating cross-reacting antibodies may be widely prevalent in the southern sea otter population (Table 2). Hence, it is presumed that the earlier published conclusions regarding CD in southern sea otters were in error.

**CONCLUSIONS**

Sea otters may be safely and successfully vaccinated with nonferret lethal recombinant CD vaccines, and such vaccines, when given in a three-shot series with injections scheduled a month apart, should impart significant resistance to infection for several years for captive sea otters. Although it was not tested under field conditions, it is believed that vaccination of otherwise-healthy wild sea otters prior to an outbreak of CD, and perhaps of similar morbiliviruses for which there are no vaccines, could confer some level of resistance to infection and help prevent disease and death in this sensitive species. This statement is based on both the SN responses in the experimentally vaccinated otters and the fairly common cross-species use of morbilivirus vaccines.

**Acknowledgments:** The authors thank Dr. Ed Dubovi, Christine Arnold, Erin Dodd, and Sharon Toy-Choutka of the Marine Wildlife Veterinary Care and Research Center staff; Jennifer Coffey, Brett Long, and Tracy Fink of the Long Marine Laboratory Marine Mammal Training Program; and various members of the Monterey Bay Aquarium staff.

**LITERATURE CITED**


Received for publication 20 May 2008