**RECOMBITEK CANINE DISTEMPER VACCINE AS AN ALTERNATIVE FOR PUREVAX DISTEMPER VACCINE IN ENDANGERED BLACK-FOOTED FERRETS (MUSTELA NIGRIPES).**

Wright ML, Livieri TM, Santymire RM.

Journal of Zoo and Wildlife Medicine. 2022;53(1):194-199

Black-footed ferrets (Mustela nigripes) are an endangered species in North America that are highly sensitive to canine distemper virus (CDV) infections and any exposure could be devastating to species recovery. The U.S. Fish and Wildlife Service recovery program has safely used a recombinant DNA (rDNA) canarypox-vectored CDV vaccine, Purevax® Ferret Distemper (PFD), to vaccinate black-footed ferrets. Because of a PFD shortage in 2015, an rDNA vaccine labeled for use in dogs, Recombitek® CDV (rCDV), was chosen to vaccinate black-footed ferrets. Our goal was to compare the serum neutralizing (SN) titers after vaccination of 17 captive and 18 wild black-footed ferrets with rCDV or PFD, respectively, considering ≥1:128 as a protective titer. Both vaccines produced comparable 1 yr postvaccination protective titers in captive and wild black-footed ferrets. In wild black-footed ferrets, one PFD vaccination produced SN titers similar to two PFD vaccinations at 1 yr postvaccination. One year after vaccination with rCDV, SN titers in captive black-footed ferrets were higher than in wild ferrets. These results indicate rCDV may be an effective alternative CDV vaccine in captive black-footed ferrets and PFD should be prioritized for wild ferrets because one dose was effective for animals that can be difficult to recapture.

**Background**

* Black-footed ferret (*Mustela nigripes*): NA mustelid, endangered, sensitive to CDV
	+ Historical deaths from MLV and natural infections, inactivated appears safe
* Purevax – recombinant (rDNA) canarypox-vectored vaccine, safe for BFF, authorized for use in BFF by US FWS, shortage in 2015
* Recombitek – rDNA, antigenically similar to Purevax but few plaque-forming units
	+ May produce a lower antibody response, mixed results in multiple spp (red pand, two-toed sloths, maned wolves, red fox, tigers, snow leopards)

**Key Points**

* Vaccinated captive BFFs with Purevax or Recombitek at 8wk and 2-4 wk booster
	+ Also vacc wild BFF with Purevax or Recombitak at 14 wk +/- booster of same vacc
	+ Tested for serum neutralizing titers (>1:128 considered protective)
* Captive: all had protective titers at 30d and most (92%) at 1 year with both vaccines
	+ Titers for Recombitek were higher than Purevax
* Wild: no significant titers prior to vacc
	+ 2 doses of Purevax had similar titers to Recombitek at 1 year but 50% Recombitek did not have protective titers at 1 year
	+ 1 dose of Purevax had similar titers as 2 doses at 1 year and 92% maintained protective titers
	+ Titers at 30 days were similar to 1 year for both vaccines
* Captive vaccinated had higher 1 year titers than wild for both vaccines – possibly age at vacc or maternal antibodies from vaccinated captive mothers

**Conclusion**

* Both Recombitek and Purevax produced protective titers in captive BFF to at least 1 year
* Recombitek may be a suitable alternative to Purevax in captive BFF
* 1 dose of Purevax in wild BFF was just as effective as 2 doses
	+ Possibly prioritize use of limited Purevax supplies for wild and use either in captive

**CANINE DISTEMPER AND PARVOVIRUS VACCINATION WITH RECOMBITEK C3 IN AFRICAN WILD DOGS (LYCAON PICTUS).**

Mulreany LM, Cushing AC, Ramsay EC.

Journal of Zoo and Wildlife Medicine. 2021;52(4):1229-1233.

Infectious disease threats are increasingly recognized as a major contributor to mortality in wild populations of African wild dog (Lycaon pictus, AWD). Canine distemper virus (CDV) infection has been implicated as a cause of pack mortality in both captive and wild AWD populations. **Ten animals were vaccinated with RecombitekTM C3, a vaccine containing a recombinant CDV, and modified live canine parvovirus (CPV) and adenovirus-2 components, at 8, 12, and 16 wk of age. Half of the pups received the vaccine IM and the other half SC.** All ten pups had a positive serological response to CDV after the second vaccination, which decreased or stagnated after the third vaccination. Half of the pups had CDV titers ≥32 at 20 wk of age. Titers to CPV were high in all pups prior to vaccination and dropped precipitously over the course of the vaccine series. At the last sampling period, only 50% of the pups had measurable CPV titers. An initially higher titer was seen for CDV in the IM administration group; however, this was not significant at later time points. Vaccination with Recombitek C3 appears to be safe and effected a sustained serological response to CDV in AWD.

**Background**

* African wild dog declines - habitat fragmentation, human conflict, and decreased prey density, infectious disease \*distemper significant threat in the wild
* Cases of MLV vaccine-induced distemper reported in African wild dogs
* Purevax in AWD had seroconversion after 3 vacc series but only half had protective titers at 6.5 mo and none at 21.5 mo

**Key Points**

* No adverse effects
* Distemper
	+ 16 wks - all had increasing titers, 9/10 had protective titers, sig higher IM than SQ
	+ 20 wks - all had detectable but only half had protective
	+ Less robust response than previous study in canarypox-vectored distemper vaccine
* Parvo
	+ All had high titers before vaccination, decreasing with age despite vaccination
	+ 20 wks - half had detectable titers
	+ No diff between IM and SQ

**Conclusions**

* Recombitek C3 in African wild dog pups had initial serologic response to distemper after 2 vaccinations but titers declined or stagnated at 20 wks old with only half having protective titers.
* All African wild dog pups had high parvo titers before vaccination that declined over the course of the vacc series, all below protective

**References**

Woodroffe R. Modified live distemper vaccines carry low mortality risk for captive african wild dogs, lycaon pictus. Journal of Zoo and Wildlife Medicine. 2021;52(1):176-184.

Connolly M, Thomas P, Woodroffe R, Raphael BL. Comparison of oral and intramuscular recombinant canine distemper vaccination in African wild dogs (Lycaon pictus). Journal of Zoo and Wildlife Medicine. 2013;44(4):882-888.

*JWD* 2021 57(1):104-115

[**Comparison of two surveillance components for investigating the epidemiology of canine distemper virus in raccoons (*Procyon lotor*)**](https://doi.org/10.7589/jwd-d-19-00001)

Giacinti JA, Pearl DL, Ojkic D, Jardine CM

**ABSTRACT:** Canine distemper virus (CDV) has a broad mammalian host range. In Ontario, Canada, CDV is frequently encountered in wild carnivores and is the most common infectious cause of death for raccoons (*Procyon lotor*). The isolation of wild-type CDV strains genetically distinct from vaccine strains in North America has renewed interest in the epidemiological patterns of this virus. However, wildlife surveillance is challenging and often utilizes a combination of surveillance methods with aggregation of data from multiple sources. Our objective was to compare raccoon CDV data generated through two separate surveillance components operated by the Ontario-Nunavut node of the Canadian Wildlife Health Cooperative. The raw data generated by each component in addition to the results of multilevel logistic regression and spatial scan statistics, were compared between the datasets. A total of 498 raccoons obtained via passive surveillance between 2007 and 2017 and 887 raccoons obtained via enhanced-passive surveillance between 2014 and 2017, were tested for CDV. The number and geographic distribution of reports, proportion of yearly reports classified as CDV-positive, and characteristics of CDV-positive raccoons differed between passive and enhanced-passive surveillance components. Geographical data demonstrated that CDV infection was present throughout southern Ontario. The geographic area of both surveillance components combined was more representative than either passive or enhanced-passive surveillance in isolation; but was restricted compared to the overall distribution of raccoons in Ontario. Regression analyses produced statistically significant associations between the presence of CDV and host and environmental variables that were at times discordant between the two datasets. Studying the properties of these datasets will inform future passive wildlife surveillance strategies and highlights the impact that a surveillance strategy can have on the results of epidemiological analyses.

**Background:**

* Passive surveillance (PS): observer-initiated sample submission with focus aimed at determining cause of death; comprehensive necropsy and more targeted diagnostics as indicated
	+ 2007-2017, 498 raccoons tested, 48% positive on average (15% in 2008, 74% in 2015)
	+ Private organizations (53%) > government facilities (31%) > members of the public (16%)
* Enhanced PS (EPS): traditional PS with active investigator involvement (solicitation of submissions); focus on select pathogens, only relevant diagnostics performed
	+ 2014-2017, 887 raccoons tested, 56% positive on average (15% in 2014, 89% in 2015)
	+ Government facilities (62%) > private facilities (36%) > members of the public (2%)

**Key Points:**

* Raccoons were considered positive on IHC or real-time RT-PCR
	+ More likely to be positive when 3+ diagnostic tests were performed
* Overall proportion of CDV-positive raccoons was similar between the two datasets
	+ CDV+ raccoons were documented each year consistent with an endemic presence
* A limitation of both components was submissions not accompanied by history or context
* Cyclicity of CDV epidemics in raccoons has been reported, generally with a periodicity of 4 years
* Increased odds of infection in the winter-breeding season vs. rearing season in adult raccoons

**TLDR:** The number and geographic distribution of reports, proportion of yearly reports classified as CDV+, and characteristics of CDV+ raccoons differed between PS and EPS surveillance components

**Related Articles:** *None on the current ACZM reading list*

*JWD* 2020 56(4):873-883

[**Canine distemper virus in the sea otter (Enhydra lutris) population in Washington state, USA**](https://doi.org/10.7589/jwd-d-19-00008)

Thomas N, White CL, Saliki J, et al

**ABSTRACT:** Before 2001, all serosurveys for morbilliviruses in sea otters (Enhydra lutris) in California, Washington, and Alaska, US, documented a 0% seroprevalence. The first published serologic detections of morbillivirus in sea otters occurred in 2001-02 in live-captured Washington sea otters, with a documented 80% seroprevalence. We conducted a retrospective study of sea otter cases from 1989 to 2010 compiled at the US Geological Survey, National Wildlife Health Center to identify cases of morbilliviral disease in Washington sea otters and to characterize the disease using immunohistochemistry, reverse transcription (RT)-PCR, genetic sequencing, virus isolation, and serology. We identified six cases of morbilliviral disease and 12 cases of morbilliviral infection in this population of sea otters during 2000-10. Significant histologic findings included inflammation in the white and gray matter of the brain characterized by lymphoplasmacytic perivascular cuffing, neuronal necrosis, and satellitosis in gray matter and by spongiosis, myelin degeneration, spheroids, and gemistocytes in white matter. Intranuclear and intracytoplasmic viral inclusion bodies were found in neurons, Purkinje cells, and glia. Immunohistochemistry for canine distemper virus (CDV) showed positive staining in neurons, glial cells, and cell processes. A pan-morbillivirus RT-PCR with subsequent restriction endonuclease digestion or sequencing identified CDV. Virus isolation was not successful. Two sea otters with morbilliviral encephalitis showed greater antibody titers to CDV than phocine distemper virus. Histologic changes were confined to the central nervous system and resembled neurologic canine distemper in domestic dogs. Cases of sea otters with morbilliviral infection without histologic changes could represent early infections or incompletely cleared sublethal infections. We found that morbillivirus was present in the Washington sea otter population as early as 2000, and we provide a description of the pathology of canine distemper in sea otters.

**Background:**

* Morbilliviruses gained prominence when PDV decimated European harbor seals in 1988
	+ CDV epidemics occurred previously in Baikal seals in 1987 and Caspian seals in 2000
	+ PDV, although related, was found to be antigenically and genetically distinct from CDV
* Morbilliviral disease across species results in acute epithelial and lymphoid system damage, potentially followed by subacute-to-chronic neurologic disease and opportunistic infections

**Key Points:**

* This study describes the pathology of morbillivirus in sea otters and identifies CDV as the causative virus by RT-PCR, sequencing, and IHC
	+ Pathology confined to the CNS; resembled neurologic CDV infection in other species
	+ Principal diagnostic features: prominent inflammation in white & gray matter
		- Intracytoplasmic and intranuclear inclusion bodies were present
	+ Morbillivirus RT-PCR+ in kidneys of otters with neurologic lesions, and by IHC in one case
* Morbillivirus was detected in tissues from sea otters with no lesions of morbilliviral disease
* Morbilliviral disease pathology in otters differed from pinnipeds and cetaceans
	+ In those epizootics, severe systemic disease accompanied neurologic lesions
	+ Viral inclusions/antigen were readily detected within lung, lymph tissue, and other sites
* Morbillivirus was detected in 4/5 sea otters examined from the 2000 mortality event, but lesions indicative of morbillivirus disease were not found in any cases until 2004
	+ Morbillivirus was present in Washington sea otters dying during the 2000 event
	+ However, no definitive evidence that infection was associated with disease
* CDV seroprevalence declined to 10% in this population as of 2011, potentially leaving a large portion of the population again susceptible should a morbillivirus be reintroduced

**TLDR:** Morbillivirus was present in the Washington sea otter population as early as 2000 but no definitive evidence that infection was associated with disease

**Related Articles**

White CL, Lankau EW, Lynch D, Knowles S, Schuler KL, Dubey JP, Shearn-Bochsler VI, Isidoro-Ayza M, Thomas NJ. 2018. Mortality trends in northern sea otters (*Enhydra lutris kenyoni*) collected from the coasts of Washington and Oregon, USA (2002–15). *J Wildl Dis* 54:238–247.

Ramsay, Edward C., et al. "**Red pandas'(Ailurus fulgens) serological response to canarypox-vectored canine distemper vaccines**." Journal of Zoo and Wildlife Medicine 50.2 (2019): 478-481.

Abstract: Red pandas (*Ailurus fulgens*) are susceptible to canine distemper, with a number of reported vaccine-induced canine distemper cases. Canarypox-vectored recombinant canine distemper vaccines (PureVax Ferret Distemper [PFD] and Recombitek CDV [rCDV]) provide protection without inoculating a live distemper virus, but there are currently no published data regarding these vaccines' safety and efficacy in red pandas. One hundred twenty-two serum samples were collected from 50 captive red pandas and analyzed for antibodies to canine distemper. All naïve red pandas (*n* = 20) had negative titers. Naïve pandas receiving two PFD vaccinations had either negative or intermediate titers (*n* = 4). In contrast, naïve pandas receiving a series of two or three rCDV vaccinations (*n* = 14) had greater antibody responses. Red pandas vaccinated with PFD >12 mo since their last vaccination and a rCDV booster vaccination showed the highest titers observed. We recommend red pandas be administered a series of at least three recombinant vaccine (PDF or rDCV) vaccinations, followed by annual booster vaccinations.

Study:

* As of 2019- no current published data regarding PureVax (PFD) or Recombitek CDV (rCVD) safety and efficacy in red pandas- used off label
* 38 *Ailurus fulgens fulgens* (Himalayan) and 12 *Ailurus fulgens refulgens* (Chinese)
* Analyzed serum from captive red pandas by serum neutralization- underwent two fold serial dilutions- and then 100 TCID50 (Tissue Culture Infectious Dose) of CDV was added and incubated at 37 degrees C for 1 hour in 5% CO2.
* After the first incubation, canine Signaling Lymphocyte Activation Molecule (SLAM)- tagged Vero cells were added to each well and then incubated again at 37 degrees C for 3-5 days in 5% CO2
* Endpoint titers were then reported (reciprocal of the last dilution of serum to neutralize 100 TCID50 in 50% of the wells)
	+ Titers of 8-16 is intermediate
	+ Titers >/= 32 as potentially protective
* Evaluation of vx to elicit cell-mediated immunity in red pandas was beyond the scope of the study and challenge studies with virulent canine distemper cannot ethically be carried out in this endangered species

Key Points:

* Naive red pandas that received 2 or 3 PFD vaccinations developed only intermediate titers
* Naive pandas that received a series of 2 or 3 rCDV vaccinations typically had stronger responses than those seen in PFD vaccinates
* Pandas <3 yrs had negative or intermediate titers whereas Pandas >3 yrs were more likely to have protective titers (more repeated boosters vs natural exposure?)
* Usually titers only increase 1-2 fold; only 1 panda had a 4 fold increase
* No adverse effects were reported for any vaccination
* Multiple vaccinations are necessary before positive titers develop
* Initial rCDV vaccination series produced GREATER antibody titers than a series of PFD vaccinations- BUT PFD was unavailable during this study period (suspect out of date vaccines were used).
* Not all pandas showed strong responses to these booster vaccines- suggested that humoral responses to these canary pox-vectored vaccines may take much longer to develop than expected

**Take Home:** Based on this study, the authors recommend red pandas be administered an initial series of at least three canarypox-vectored CDV vaccinations, followed by annual boosters.

Georoff, Timothy A., et al. "**Review of canine distemper vaccination use and safety in north american captive large felids (panthera spp.) from 2000 to 2017.**" Journal of Zoo and Wildlife Medicine 50.4 (2020): 778-789.

Abstract: Data on canine distemper virus (CDV) vaccination were collected on 812 large felids (351 tigers, *Panthera tigris*; 220 lions, *Panthera leo*; 143 snow leopards, *Panthera uncia*; 50 leopards, *Panthera pardus*; and 48 jaguars, *Panthera onca*) from 48 institutions to assess vaccine use and safety. The documented individual vaccination events with multiple products numbered 2,846. Canarypox-vectored CDV vaccines were the most commonly used vaccines (96.3% of all vaccinations) and the Purevax® Ferret Distemper (PFD) vaccine was the most commonly used canarypox-vectored vaccine (91.0% of all vaccinations). Modified live virus (MLV) CDV vaccines were used for 3.7% of all vaccinations, and only in tigers, lions, and snow leopards. Adverse effects were reported after 0.5% (13 of 2,740) of the canarypox-vectored vaccinations and after 2.9% (3 of 104) of the MLV CDV vaccinations. This low complication rate suggests large felids may not be as sensitive to adverse effects of MLV CDV vaccines as other exotic carnivores. Serological data were available from 159 individuals (69 tigers, 31 lions, 31 snow leopards, 22 jaguars, and 6 Amur leopards, *Panthera pardus orientalis*) vaccinated with the PFD vaccine, and 66.0% of vaccinates seroconverted (defined as acquiring a titer ≥1: 24) at some point postvaccination: 24.3% after one vaccination, 55.8% after two vaccinations, 54.3% after three vaccinations, and 79.2% after four or more vaccinations. Among animals exhibiting seroconversion after the initial PFD vaccinations, 88.9% still had titers ≥12 mo and ≥24 mo after the last vaccination, and 87.5% had titers ≥1: 24 at ≥36 mo after the last vaccination. The study was unable to assess fully the safety of vaccination with either canarypox-vectored or MLV CDV vaccines during gestation because of the small number of animals vaccinated while pregnant (*n* = 6, all vaccinated with PFD).

Introduction:

* There are reports of vaccine induced CDV after vaccination with the modified live virus (MLV) CDV, although none in captive Felidae
* Study of tigers- titers after booster vaccination of Recombitek C3 were much less than the titers of a single MLV CDV vaccine
* **Goals:** summarize data on CDV vaccination of large felids, humoral immune responses after vaccination with the PFD vaccine, AND help assist practitioners in designing preventative medicine programs (for zoos and conservation programs)

Materials and Methods

* Vaccination data requested from US and Canadian zoos as well as exotic felid sanctuaries with known or probably CDV vaccination programs (163 facilities- 126 AZA zoos, 21 non AZA zoos, and 16 exotic felid sanctuaries were contact and 92- %6.4% responded)
* Dates of vaccination, vaccine products used, volume administered, route, delivery method, adverse effects (minor vs major), CDV serum neutralization titer data, signs of CDV infection in vaccinated animals, and if female (pregnancy status)
* Serology was performed at Cornell University Animal Health Diagnostics Center using serum neutralization assay
	+ Negative (<1:8)
	+ Indeterminate (1:8-1:16)
	+ Seropositive (>1:24) this was also the cut off for seroconversion
	+ Animals with ANY measurable titer was excluded from data analysis
* Aversions and seroconversion prevalence were evaluate with Fisher’s exact tests applied to contingency tables
	+ Minimum level of significant x= 0.05

Results

* 48 institutions reported CDV vaccination of Panthera spp. And 44 reported no regular CDV vaccination of ANY Panthera spp.
* 2,846 vaccination events (canarypox-vectored accounted for 2,740 96.3% and MLV vaccines were 104 3.7%) Adverse events (after those removed by anesthesia causes) was 9 (seven minor and one major- THIS DOES NOT ADD TO 9).
* 11 different vaccine products in 812 individuals (most common MLV- Puppy Dpv, PFD common canary pox vectored)
* One major adverse of a snow leopard (neurologic signs that resolved after 5 days of treatment) vaccination with an MLV CDV with multiple viral components- canine adenovirus-1 or 2 showed to significantly reduce lymphocyte responsiveness in dogs
* Adverse events were significantly different between MLV and canary pox vectored groups
* 6 cats were vaccinated during gestation- one tiger aborted and another delivered 3 septic cubs (however both creatures exhibited prior and subsequent losses not associated with vaccines)
* Majority of animals seroconverted- 66%
* A small number showed seroconversion after 1 vaccination wheres more seroconverted after the second and third- seroconversion after the 4th or more increased significantly

Discussion

* Found that canarypox vectored vaccine are safe in large Felids- no accounts of reaction
* Very few adverse events from MLV vaccinations in large felids
* Rate of adverse events after MLV was significantly higher than canarypox but LOWER than expected
* SN titers do not rise in nondomestic felids vaccinated with the PFD vaccine until after three vaccinations
* Snow leopards had the lowest rate of seroconversion whereas amur leopard and jaguars had the highest
* PFD contains 8 times more canarypox vectored canine distemper dose
* Evidence that cell-mediated immunity is an important aspect of protection in siberian polecats

Take Home: Study recommends canine distemper vaccination of captive large felids with a monovalent canarypox-vectored recombinant vaccine followed by a minimum of one or two booster vaccinations (2-4 weeks apart) as an initial series and annual vaccination afterwards. PFD being the preferred vaccine. Use of MLV CDV in large felids appears not as risky as previously described Nobivac DPv appears to be the safest MLV CDV apart from pregnant females- BUT perform at your own risk.

**GEOGRAPHIC SPREAD OF CANINE DISTEMPER IN WILD CARNIVORES IN MICHIGAN, USA: PATHOLOGY AND EPIDEMIOLOGY, 2008–18.**

Fitzgerald SD, Melotti JR, Cooley TM, Wise AG, Maes RK, O'Brien DJ.

Journal of Wildlife Diseases. 2022;58(3):562-574

Canine distemper is a widespread disease affecting both domestic and wild carnivores. This investigation of the geographic distribution, wildlife species infected, and relative prevalence rates was conducted over an **11-yr period and helps to document the disease spread, most highly infected wildlife species, and histologic lesions. Animals were collected as found dead, hunter and trapper harvested, and euthanized for displaying signs of abnormal behavior or neurologic disease**. This disease appeared to spread from the Lower Peninsula of Michigan into the Upper Peninsula, was most frequently documented in raccoons (Procyon lotor), striped skunks (Mephitis mephitis), and gray fox (Urocyon cinereoargenteus), but also involved additional wildlife species. Three unique wildlife virus strains were identified. Two of these grouped within a separate subclade of the America 2 lineage. A third strain appeared to be a unique sequence type that is not associated with any existing subclade of America 2. We recommend the combined use of routine histology and immunohistochemical staining to confirm the diagnosis, and further recommend that both the lungs and spleen be collected as the optimal tissues to utilize for surveillance purposes.

Background

* Canine distemper virus (CDV) - morbillivirus, family Paramyxovirus
	+ Affects *Ailuridae, Canidae, Felidae, Hyaenidae, Mustelidae, Procyonidae, Ursidae, Viverridae*
* IHC - gold standard for detection of CDV antigen in tissue sections
* CDV spreads through host tissues in a biphasic pattern - initially respiratory lymphoid tissue, then viremia with spread into epithelial cells in numerous tissues, and long-term persistence in nervous tissue
* H gene of CDV shows greatest genetic variation and is the preferred target for molecular analysis
* Most current distemper vaccines ar based on America 1 lineage strains, though one is America 2

Key Points

* Michigan - wild carnivores submitted dead
	+ Primarily gray fox, raccoon, striped skunk > coyotes > red fox
		- No difference by sex but skunks were more commonly adults than juveniles
	+ From 2008-2013 low # cases, confined to Lower Peninsula
	+ 2014-2018 increased number of cases and spread into Upper Peninsula
* Year and species were significant predictors of IHC positivity
* Lung- most common tissue with histo lesions and IHC positivity
	+ Mild-severe lymphoplasmacytic interstitial pneumonia
	+ Occasional intraepithelial eosinophilic inclusion bodies
	+ Rare multinucleated syncytial cells in airways and alveoli
* Brain - mild to mod lymphoplasmacytic meningitis and perivascular cuffing in Virchow-Robin space, most IHC restricted to individual neurons
* Liver - 2nd most common tissue with histo lesions, periportal lymphoplasmacytic inflammation and bile duct epithelium with cytoplasmic eosinophilic inclusion bodies that were IHC positive
* Urinary bladder, renal pelvis - occasional transitional epithelium with eosinophilic intranuclear and cytoplasmic inclusions with no inflammation and strong IHC staining
* Spleen - no histo lesions but strong IHC throughout lymphoid follicular centers
* Heart - no histo lesions, no positivity on IHC in any cell types
* Virus insulation in an IHC positive gray fox, skunk, and raccoon for RNA extraction, rt RT-PCR
	+ All three in America 2 subclade, raccoon and skunk closest to an Iowa raccoon
	+ Gray fox was separate within America 2

Conclusions

* Michigan was endemic with CDV but had an epizootic from 2014-2018 where it also spread into the Upper Peninsula, with primary reservoir hosts likely raccoons, striped skunk, and gray fox
* Recommend lung and spleen for histo and IHC
	+ Lung was most sensitive tissue for histo lesions, especially early in infection
	+ Spleen will have long-term antigen persistence and will be sensitive on IHC later in infection even without obvious histo lesions
* Three strains identified were genetically different from those present in most commercial vaccines

**TEMPORAL AND SPATIAL PATTERNS IN CANINE DISTEMPER VIRUS CASES IN WILDLIFE DIAGNOSED AT THE SOUTHEASTERN COOPERATIVE WILDLIFE DISEASE STUDY, 1975-2019.**

Taylor K, Wilson JJ, Park AW, Nemeth NM, Yabsley MJ, Fenton H, Keel MK, Gottdenker NL.

J Wildl Dis. 2021;57(4):820-830

Canine distemper is a high-impact disease of many mammal species and has caused substantial carnivore population declines. **Analysis was conducted on passive surveillance data of canine distemper (CDV)-positive wild mammal cases submitted to the Southeastern Cooperative Wildlife Disease Study, Athens, Georgia, US, between January 1975 and December 2019.** Overall, **964 cases from 17 states were CDV positive, i**ncluding 646 raccoons (Procyon lotor), 254 gray foxes (Urocyon cinereoargenteus), 33 striped skunks (Mephitis mephitis), 18 coyotes (Canis latrans), four red foxes (Vulpes vulpes), three gray wolves (Canis lupus), three American black bears (Ursus americanus), two American mink (Mustela vison), and one long-tailed weasel (Mustela frenata)**.** Raccoon and gray fox case data from the state of Georgia (n=441) were selected for further analysis. Autoregressive integrated moving average models were developed predicting raccoon and gray fox case numbers. The best-performing model for gray foxes used numbers of gray fox CDV cases from the previous 2 mo and of raccoon cases in the present month to predict the numbers of gray fox cases in the present month. The best-performing model for raccoon prediction used numbers of raccoon CDV cases from the previous month and of gray fox cases in the present month and previous 2 mo to predict numbers of raccoon cases in the present month. Temporal trends existed in CDV cases for both species, with cases more likely to occur during the breeding season. Spatial clustering of cases was more likely to occur in areas of medium to high human population density; fewer cases occurred in both the most densely populated and sparsely populated areas. This pattern was most prominent for raccoons, which may correspond to high transmission rates in suburban areas,where raccoon population densities are probably highest, possibly because of a combination of suitable habitat and supplemental resources.

Background

* CDV is an enveloped, single stranded negative sense RNA Morbillivirus
	+ Transmitted via aerosol, highly infectious, shed 60-90d post infection
	+ 2nd highest case fatality rate in dogs after Rabies.
	+ Evidence of infection in all terrestrial and some marine carnivore species. Substantial declined in African lion, Amur tiger, and black footed ferret
	+ Endemic in raccoons in Eastern US, primary reservoir for wildlife, also major COD in grey foxes in SE US

Key Points

* CDV positive by fluorescent antibody testing or IHC with characteristic histo including intranuclear and intracytoplasmic inclusions
* Highest # of cases for all species was from SE states, greatest # of cases submitted from GA.
* Greatest # of raccoon and grey fox cases from 1980-1990.
* Most raccoon and grey fox cases received during the breeding season (Mar-June). Fewest cases in nonbreeding season.
* Clustering of cases in medium to medium-high human density counties (suburbs), lower #s in highest density (cities) and lowest density (rural) human counties
* Models predicting monthly fox or raccoon distemper cases were based on past months and other species (grey foxes/raccoons) suggesting an association between the 2 species

Conclusions

* CDV is wildly distributed in the southeastern US, commonly found in raccoon and gray foxes.
* Cases were more common in breeding season and in suburbs compared to cities and rural area and cases can be predicted with a model based on past month cases in foxes and raccoons.

**Article:** McEntire, Michael, et al. "Tiger (panthera tigris) and domestic cat (felis catus) immune responses to canarypox-vectored canine distemper vaccination." *Journal of Zoo and Wildlife Medicine* 50.4 (2020): 798-802.

**Abstract:** Two methods for delivering a canarypox-vectored canine distemper vaccine to tigers (Panthera tigris) and domestic cats (Felis catus) were investigated. Eight tigers were divided randomly into two vaccination groups: subcutaneous injection or topical tonsillar application. Each tiger received 2 ml of canine distemper virus (CDV) vaccine (Merial Ferret Distemper Vaccine). Blood was collected from tigers on days 0, 21, 35 or 37, and 112 post–initial vaccination (PIV). Domestic cats were divided randomly into four treatment groups: saline injection (negative controls), low- and high-dose oral, and subcutaneous vaccinates. Blood was collected from domestic cats on days 0, 7, 21, and 28 and 165 or 208 PIV. Sera were tested for CDV antibodies by virus neutralization. All individuals were seronegative at the beginning of the study. One tiger vaccinated subcutaneously developed a titer of 32 by day 35, which reduced to 16 by day 112. Another tiger vaccinated by tonsillar application developed a titer of 8 on day 112. All other tigers remained seronegative. Cats that received saline injection or oral vaccination remained seronegative at each sampling time. Domestic cats vaccinated subcutaneously developed titers ranging from 4 to >128 by day 28, and those re-bled at day 166 had titers of 16 or 64. The disparity in response between domestic cats and tigers may be due to species differences or it may represent a dose-dependent effect. Subcutaneous vaccination with canarypox-vectored Purevax Ferret Distemper is safe and elicits persistent antibody titers in domestic cats vaccinated parenterally.

**Goal of study**

* Determine safety and efficacy of CDV monovalent canarypox-vectored recombinant vaccine (PureVax Ferret Distemper, Merial) administered parenterally and orally in tigers
* Determine if domestic cats would be a suitable model for CDV vaccine studies

**Study design/methods**

* Tiger (n=8): (1) SQ, (2) topical tonsillar
* Domestic cat (n=17): (1) saline injection, (2)  SQ, (3) low dose oral, (3) high dose oral
* Serum neutralization assay performed for CDV antibodies

**Background**

* CDV problem in captive/wild nondomestic felids i.e. wild endangered Amur tigers (Panthera tigris tigris)
* North American Tiger SSP currently recommends vaccination for CDV
	+ Live attenuated caused pregnant tiger to have litter with heart defects
	+ Canarypox vector has not caused ill effects in tigers but concern for lack of humoral response
* Oral transmucosal rabies vaccination has been effective in wild racoons
* Signaling lymphocyte activation molecule (SLAM) = receptor for CDV; conserved across felids

**Key Points**

* Poor serologic response in tigers given SQ or tonsillar PFD\*\*
* Tigers: Only 2/8 tigers developed measurable titers following vaccination (1/4 SQ and 1/4 tonsillar)
* Domestic cats: All cats (4/4) who got SQ mounted titers; none who got oral mounted titers
* Larger serologic response in SQ domestic cats > SQ  tigers
* Possible species differences or dose dependent reaction in domestic felids (10x dose/kg) vs. tigers
	+ Previous dose dependent reaction for Recombitek C3 (canarypox-vectored) in tigers and with CDV/CaV2/CPV vaccines in domestic dogs
* Comparisons to other species:
	+ Similar response in African wild dog pups comparing parenteral to oral PFD
	+ Different response in Channel Island fox in which 80% of animals produced measurable Ab responses with oral PFD
* Still unknown titer levels required for protection of CVD in tigers/non-domestic felids

**Related articles on reading ACZM list:** None on reading list

**Article:** Woodroffe, Rosie. "Modified live distemper vaccines carry low mortality risk for captive african wild dogs, lycaon pictus." *Journal of Zoo and Wildlife Medicine* 52.1 (2021): 176-184.

**Abstract:** Recently, canine distemper virus (CDV) has been linked to population declines in the endangered African wild dog (Lycaon pictus). As CDV appears able to persist in wildlife, threats to free-ranging wild dogs cannot be eliminated by vaccinating domestic dogs. Conservation managers may therefore consider CDV vaccination of wild dogs in highly threatened populations. For use in field conservation, the ideal CDV vaccine would be safe, immunogenic, and readily available in Africa. The CDV vaccine type most commonly used for domestic dogs (modified live vaccine) is available in Africa, and apparently immunogenic in wild dogs, but has been linked to fatal vaccine-induced distemper in captive wild dogs. However, alternatives are either ineffective (inactivated vaccine) or difficult to obtain in Africa (recombinant vaccine). Data from a questionnaire survey of zoo vaccination practices were therefore combined with studbook tracing to assess the safety of modified live CDV vaccine in captive African wild dogs. Among 135 wild dog pups given modified live CDV vaccine for the first time, there was a single, unconfirmed, case of potential vaccine-induced distemper. Pups given modified live vaccine survived better than those given inactivated vaccine or no vaccine. Although studbook tracing revealed higher overall pup survival at zoos which responded to the questionnaire than at zoos which did not, tracing of all pups born during a 20-yr period that lived long enough to be vaccinated (n ¼ 698 pups in 155 litters) revealed no mortality events consistent with vaccine-induced distemper. Modified live CDV vaccine thus appears to carry low mortality risks for African wild dog pups in captivity, and may warrant trials in free-ranging populations.

**Goal of Study**

* Assess safety/characterize mortality patterns of modified live CDV vaccine in captive African wild dogs to determine if it warrants investigation for use in free-ranging populations

**Study Design/Methods**

* Review of published reports (4 litters), questionnaire surveys (n=135 dogs from 22 institutions that used MLV), and studbook analyses (n=1459 pups) in years before recombinant was used

**Background**

* CDV is a threat to wild dog free-ranging populations and has resulted in population declines
* Features of CDV epidemiology in several carnivores: highly variable mortality, widespread nonlethal exposure and occasion mas mortality
* Unlike rabies, wild dog exposure to CDV is not associated with domestic dog contact →  mass vaccination of domestic dogs locally failed to prevent new wildlife infections
* Vaccines ideal for field conservation = safe, immunogenic, and readily available
	+ MLV (reports of fatalities) vs. inactivated (poor immune response) vs. recombinant (supply issues)

**Key Points**

* Reports: All published reports (4 litters) of MLV vaccine-induced distemper involved pups being given their FIRST dose in a polyvalent formulation with PARVOVIRUS (MLV or inactivated) vaccine
	+ Mortality of 95% (20/21); clinical signs by 14 days, death by 18 days post-vax
	+ Proposed factors of causation: vaccine strain (but used multiple), multivalent with parvo, genetics
* Questionnaires: Mortality 0-1.5%
	+ 1 associated death (82d old, 10d after 2nd dose) of 135 dogs vaccinated with MLV; confirmed with fluorescent Ab test,but failed to isolate virus in cell culture → suspected wild-type virus
	+ 1 other questionable death (bite wounds) → max of 2/135 deaths (1.5%); no other adverse effects
* Studbook: Apparent mortality 0% but up to 7.6%
	+ Calculated ages to evaluate vaccine-induced distemper mortality: min 45d - max 99d
		- Survival for pups at age 45-99 was higher at zoos that responded to questionnaire
	+ 53/698 pups between ages 45-99d (from 18/155 litters) reported deaths; theoretically IF all pups received MLV vaccine, and all pups died of vaccine-induced distemper → 7.6% mortality
		- These 18 litters had lower mortality within litters than published reports (42% vs. 95%)
		- No litters had brief episodes of high mortality like published cases between 45-99d old; incidence of apparent vaccine-induced distemper is 0/698 → 0%
* Many positive cases unable to rule out if vaccine-induced vs. wild type
* Wild dog pups given either no vaccine or inactivated vaccine had lower survival than those given MLV (associated with Figure 1B)\*\*
	+ Potentially due to mortality from wild type CDV, protection from other canine pathogens via multivalent vaccines used, greater attention to veterinary care
* Modified live distemper vaccines carries low mortality risk for captive African wild dogs and should be considered to be investigated for free-ranging species\*\*

**Useful figures**

