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CANINE DISTEMPER IN TERRESTRIAL CARNIVORES: A REVIEW

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Abstract: Canine distemper virus is a member of the genus *Morbillivirus* in the family Paramyxoviridae. Canine distemper has been recorded in domestic dogs for centuries. It is now recognized as a worldwide problem of carnivores and has the second highest fatality rate of any infectious disease, after rabies, in domestic dogs. The importance of this disease in nondomestic animals has become evident with vaccine-induced infections in a variety of species and large-scale epidemics in captive and free-ranging felids. To date, canine distemper has been reported in all families of terrestrial carnivores: Canidae, Felidae, Hyaenidae, Mustelidae, Procyonidae, Ursidae, and Viverridae. Veterinarians, including those working with nondomestic carnivores, should be familiar with the clinical signs, diagnosis, and clinical management of this disease.

Key words: Canine distemper virus, morbillivirus, nondomestic species, review, vaccine-induced disease.

INTRODUCTION

Canine distemper (CD) is the most important worldwide infectious disease of domestic dogs (*Canis familiaris*), and its fatality rate is second only to that of rabies.[122] CD is caused by canine distemper virus (CDV), first isolated by Carré in 1905.[30] Clinical distemper has been known for centuries.[76] In recent years, vaccine-induced infections have occurred in a variety of species,[26–28,63,74,88,94,121,123] as have large-scale epidemics in felids.[14,113] Canine distemper virus may have the most far reaching implications of any infectious agent for susceptible free-living and captive carnivores.[93] The discoveries of related viruses, such as phocine and delphine morbilliviruses,[103,127] and CDV's similarity to the measles virus suggest viral mutability and a zoonotic potential for CDV.

HOST RANGE

Although CD occurs worldwide in carnivores, much of its natural history is unknown. Evidence of CDV infection has been reported in all families of terrestrial carnivores: Canidae, Felidae, Hyaenidae, Mustelidae, Procyonidae, Ursidae, and Viverridae.[9,24,45,54,61,83,93,97,110] The red or lesser panda (*Ailurus fulgens*) and giant panda (*Ailuropoda melanoleuca*) have been included in the Ursidae for this review.[100,101,134]

Morbidity and mortality vary greatly in carnivores. The case fatality rate of domestic ferrets (*Mustela putorius furo*) approaches 100%,[39] whereas 50–70% of infected domestic dogs may remain asymptomatic carriers.[59] Fatal CDV infections have also been experimentally induced in suids and primates.[13,86,135] Natural cases of CDV-induced fatal encephalitis have been documented in a Japanese macaque (*Macaca fuscata*)[136] and collared peccaries (*Tayassu tajacu*).[11] Within the U.S., regular epidemics occur in free-ranging raccoons (*Procyon lotor*), a species that may play a role in CD epidemiology in domestic dogs in that region.[67,89,114] Conversely, in regions of the world where CDV vaccination is not widely employed (e.g., parts of Africa), domestic dogs may serve as a reservoir for free-ranging wildlife.[3,113]

ETIOLOGIC AGENT, TRANSMISSION, AND PATHOGENESIS

Canine distemper virus, a relatively large (150–250 nm) single-stranded RNA virus with a lipoprotein envelope, is a morbillivirus in the family Paramyxoviridae.[59,122] Three other well-known diseases are caused by members of the *Morbillivirus* genus: measles in primates, rinderpest in artiodactylids, and peste des petits ruminants in small ruminants. Three recently discovered viruses, phocine distemper virus in seals and cetacean morbilliviruses in porpoises and dolphins, also belong to this genus.[103,127]

The major mode of CDV transmission is through aerosolization of respiratory exudate containing virus, although other body excretions and secretions (e.g., urine) can result in infection in susceptible hosts if aerosolized. Canine distemper is highly contagious, and viral shedding may follow infection for 60–90 days.[59] Transplacental infection has been documented in domestic dogs.[77] The epidemiologic role of vertical transmission in CD and whether or not such transmission can occur in nondomestic species are unknown. Although usually short-lived in the environment, the virus can sur-

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vive at lower temperatures (e.g., 48 hr at 25°C and 14 days at 5°C)[117] and may be transmitted either by direct contact or by fomites.

Natural CD pathogenesis in domestic dogs has been well characterized and may be similar in nondomestic species. A systemic infection with viremia is often present. Central nervous system (CNS) involvement is variable and dependent on the host's immune response. Within 24 hr of entering the respiratory tracts, virus spreads in macrophages via local lymphatics to tonsils and bronchial lymph nodes. Replication of the virus occurs in the tonsils and bronchial lymph nodes 2–4 days postinfection; concurrently, low numbers of CDV-infected mononuclear cells are found in other lymphoid organs. Within 4–6 days, virus proliferates widely in lymphoid organs (e.g., spleen, mesenteric lymph nodes, Kupffer's cells in the liver, and the lamina propria of the stomach and small intestine) and spreads, probably through blood, to epithelial and CNS tissues within 8–9 days of infection. The pathogenesis within 9–14 days depends on the humoral and cell-mediated host immune response. Dogs with adequate antibody titers and cell-mediated cytotoxicity will clear the virus from most tissues with no clinical signs, whereas dogs with a poor immune response experience viral spread to many tissues. Dogs with an intermediate cell-mediated response and delayed humoral response will have most virus in epithelial tissues cleared as antibody titers rise. In these latter dogs, delayed CNS signs and hyperkeratosis of the foot pads (''hard pad disease'') may result when virus persists in uveal, neural, and integumental tissues.[7,59]

SUSCEPTIBILITY/CLINICAL SIGNS

Clinical signs of CD are influenced by virus strain virulence, environmental conditions, host age and immune status, and the infected species' identity. In all species, the respiratory, gastrointestinal, integumentary, and CNS systems are most commonly affected. Diphasic fever and general malaise are often associated with viremia. Infections, probably secondary to leukopenia, are common and may complicate the clinical course.

Canidae

Up to 70% of infections in domestic dogs may be subclinical.[59] Mild illness, with nonspecific listlessness, partial anorexia, fever, and upper respiratory tract infection, may occur. However, the acute generalized form has a high mortality rate in domestic dogs, with a 14–18-day incubation period and an initial transient fever and leukopenia 4–7 days postinfection. Clinical signs in acute generalized CD are related to the respiratory and gastrointestinal systems and include conjunctivitis, pneumonia, diarrhea (often hemorrhagic), anorexia, and severe dehydration. A neurologic manifestation of CD may occur 1–3 wk after recovery from acute generalized infection.[7,125] Additionally, neurologic distemper can occur in dogs of any age that had no or mild systemic signs and may manifest as chronic progressive neurologic dysfunction in older dogs (usually over 6 yr of age). Neurologic complications depend on viral distribution in the CNS and may include hyperesthesia, cervical rigidity, seizures, cerebellar and vestibular signs, and paraparesis or tetraparesis with sensory ataxia. Myoclonus, the involuntary twitching of muscles in a forceful simultaneous contraction (often leading to ''chewing gum'' fits), is also highly suggestive of CD.[23] Additional signs of CDV in the domestic dog include digital hyperkeratosis (hard pads) and optic neuritis, chorioretinitis, and uveitis.[51] In young dogs, juvenile cellulitis and metaphyseal bone lesions and irregularities to the surface of teeth due to enamel hypoplasia may be evident.[18,42,84]

Nondomestic canid species vary in CDV susceptibility, although clinical signs in acute generalized disease often resemble those described for the domestic dog. Natural and/or vaccine-induced CDV-associated disease has been documented in African wild dogs (*Lycaon pictus*),[1,2,4,45,87,126] Australian dingos (*Canis dingo*),[16] South American bush dogs (*Speothos venaticus*),[88] maned wolves (*Chrysocyon brachyurus*),[123] bat-eared foxes (*Otocyon megalotis*),[68,90] kit foxes (*Vulpes macrotis macrotis*),[16] raccoon dogs (*Nyctereutes procyonoides*),[16,82] coyotes (*Canis latrans*),[38,52,53] red foxes (*Vulpes vulpes*),[16,80] and gray foxes (*Urocyon cinereargenteus*).[16,63,67] CD-related mortalities have also been suspected in free-ranging wolf (*Canis lupus*) pups[71] and fennec foxes (*Fennecus zerda*).[93] All canids may be susceptible to CDV.

Felidae

Subclinical CDV infection in domestic cats (*Felis catus*) has been demonstrated experimentally,[13] and CD disease has been reported sporadically in nondomestic felids.[22,35,48,58,108,124] During a 1992 CD epidemic among 74 large captive felids, infection was histopathologically confirmed in African lion (*Panthera leo*), tiger (*Panthera tigris*), leopard (*Panthera pardus*), and jaguar (*Panthera onca*).[14] Forty-seven percent of these cats became ill and 23% died, with signs of gastrointestinal, respiratory, and CNS disease. Sixty percent of ill cats manifested CNS disease with or without preceding gastrointestinal and respiratory disease. Generalized

seizure activity, the most common neurologic abnormality, usually culminated in acute death. With rare exceptions, animals that experienced mild disease and recovered had high CDV neutralizing antibody titers, whereas those that died or were euthanatized had low or no detectable titers. Hyperkeratosis of the foot pads did not appear in any case. Histopathologic lesions identified in the lungs and the CNS differed from those in canid species (see pathology section). Only members of the genus *Panthera* died, however, several mountain lions (*Felis concolor*) demonstrated vague gastrointestinal or respiratory system signs. One clinically healthy mountain lion was shown by a CDV neutralization test to have seroconverted during the epidemic. Disease was not identified in such small felid species as bobcat (*Felis rufus*), serval (*Felis serval*), and margay (*Felis wiedii*) in this collection. A serologic survey of several other private and zoologic collections revealed CDV neutralizing antibody in a variety of healthy cats, some with a past history of gastrointestinal or respiratory system disease.[14]

In 1994, a multispecies CD epidemic of unknown origin in the Serengeti ecosystem affected 30% of a population of 3,000 African lions.[65,96,113] Many of the affected lions were emaciated, but the most frequent clinical manifestations were neurologic, including grand mal seizures and myoclonus.[113] Up to 50% of lions with clinical signs may have died. Domestic dogs (up to 30,000, many of which were unvaccinated) could have transmitted the virus to spotted hyenas (*Crocuta crocuta*), which in turn may have transmitted the disease to lions.[29,61,113] Serengeti lions are nomadic and could distribute the virus over a large range.

Hyaenidae

Fatal CD has been documented in captive hyenas and in free-ranging Serengeti hyenas.[3,21,61,97,111] However, a retrospective study involving free-ranging spotted hyenas in the Masai Mara, Kenya, showed a significant rise in CDV antibodies without clinical signs or increased mortality during a period of high domestic dog mortality associated with a CD epidemic.[3]

Mustelidae

Mustelids are among the species most susceptible to CDV disease, and the clinical presentation is similar to that seen in domestic dogs, with some exceptions. Domestic ferrets and black-footed ferrets (*Mustela nigripes*) are highly susceptible to natural CDV infection and have a fatality rate close to a 100%.[10,19,39] Fatal vaccine-induced disease has also been documented in both species.[28,55] In addition to ocular and nasal discharge, diarrhea, anorexia, seizures, and myoclonus, black-footed ferrets often have severe hyperkeratosis of the foot pads, whole body erythema, and chin and groin rash with associated pruritus.[28,133] All mustelids are probably susceptible to clinical CD. There are reports of CD in American badgers (*Taxidea taxus*),[15,56] striped skunk (*Mephitis mephitits*),[41] European mink (*Mustela lutreola*) and American mink (*Mustela vison*),[94,107,121] Eurasian badgers (*Meles meles*),[16] and European otters (*Lutra lutra*).[54,116]

Procyonidae

Natural CDV infections in raccoons[37,67,75,89,112,114] and vaccine-induced infections in kinkajous (*Potos flavus*)[74] have been documented. All procyonids are probably susceptible to CDV infection, with clinical presentations resembling those in domestic dogs.[47,91,105] Cystitis with pyuria is common,[91,105] and jaundice is sometimes associated with CDV infection in raccoons.[75] Canine distemper virus is endemic in some North American raccoon populations,[37,47,67,73,89,114] so this species may be a reservoir for nondomestic zoo animals and domestic dogs. Additionally, CD must be differentiated from rabies in individual raccoons with neurologic signs.

Ursidae

Many ursids are susceptible to CDV infection on the basis of serologic surveys,[34,43,49,83,85] and clinical CD has most commonly been documented in red pandas and giant pandas,[26,27,46,69,110] although one report of clinical disease in polar bears (*Ursus maritimus*) and *Tremarctos ornatus* neonates has been published.[115] In a serologic study of polar bears in Alaska and Russia, 35.6% of 191 samples collected from 186 bears were positive for morbillivirus antibodies on the basis of the CDV microtiter neutralization test.[49] In a separate serologic study conducted in Alaska, 14% of 480 of grizzly bears (*Ursus arctos horribilis*) were seropositive, whereas none of the 40 black bears (*Ursus americanus*) tested had antibody titers.[34] Serum neutralization tests with the Onderstepoort CDV strain resulted in seroprevalences of 16% (2/12) and 36% (4/11) in captive and free-ranging Marsican brown bears (*Ursus arctos marsicanus*), respectively, in Italy.[85] A seroprevalence study of free-ranging Florida black bears (*Ursus americanus floridanus*) found 8% of 66 bears seropositive for CDV antibodies.[43]

Clinical signs of CD, whether from natural exposure or vaccine induction, may be similar in red pandas and domestic dogs,[26,27,69,118] but some differences have been described.[46] Signs include purulent

oculonasal discharge, anorexia, diarrhea, ascending paresis, and, in some cases, terminal seizures and coma.

Canine distemper virus can be fatal to captive giant pandas[110] and can also affect captive red pandas.[110] In China, CDV antibody titers were detected in one of five captive and one of three recently rescued giant pandas.[83]

Viverridae

Two viverrid species may develop CD, the binturong (*Arctictis binturong*)[31,60,64] and the masked palm civet (*Paguma larvata*).[81] There are recent anecdotal reports of vaccine-induced CD in captive binturong (R. J. Montali, unpubl. data). In the free-ranging masked palm civet, clinical signs included dehydration, dyspnea, serous oculonasal discharge, diarrhea, local alopecia, and convulsions.[81]

DIAGNOSTIC PROCEDURES

Antemortem

In domestic dogs, acute generalized CD infection is often diagnosed by clinical signs in animals not previously vaccinated. In nondomestic species, CD may be suspected on the basis of clinical signs but must be differentiated from such other diseases with respiratory, neurologic, and/or gastrointestinal manifestations as rabies, feline panleukopenia, toxoplasmosis, canine parvovirus, lead poisoning, and bacterial enteritides. Digital, nasal, and eyelid hyperkeratoses, common in infected ferrets and mink,[39,107] are highly suggestive of infection. In raccoons, foxes, and ferrets, jaundice associated with CDV infection is occasional and unique.[24,75] Absolute lymphopenia, thrombocytopenia, regenerative anemia, decreased albumin, and increased α- and γ-globulin concentrations may be present.[59,122] Low numbers of CDV inclusions may be detected in the cytoplasm (and occasionally nuclei) of stained peripheral blood cells, especially lymphocytes. Inclusion bodies may also be detected in smears prepared from conjunctival scrapings. However, inclusion bodies are unlikely to be present in either the blood or conjunctival scrapings outside of the acute phase of infection. Interstitial or alveolar lung patterns on thoracic radiographs also support a diagnosis. Central spinal fluid (CSF) may show increased protein (>25 mg/dl) and cell count (>10 cells/μl with a predominance of lymphocytes) and increased pressure associated with inflammation. Increased anti-CDV antibody in the CSF is definitive evidence of neurologic CDV infection[71] unless the blood–brain barrier has been disrupted because CDV-specific IgG is not present in the CSF of vaccinated dogs.

Serologic tests are often unrewarding in clinical CD because most nondomestic animals die before antibody titers are measurable. However, paired sera (10–14 days apart) can be tested by viral neutralization[12] or the indirect fluorescent antibody test for a four-fold rise in antibody titer.[6] Enzyme-linked immunosorbent assays have been developed to detect serum IgG and IgM antibodies to CDV[99,109,129,130] and CDV antigen.[20,109] Detection of IgM indicates recent CDV infection unless the animal was vaccinated within 3 wk of the test. The detection of IgG is more ambiguous and can indicate either vaccination or infection.

Immunohistocytochemistry is also useful in diagnosing CD.[17,78] Immunofluorescence is usually performed on cytologic smears prepared from conjunctival, tonsilar, genital, or respiratory epithelium. Other tissues in which virus may be detected antemortem with immunocytology are blood and buffy coat smears, CSF, skin, and foot pads. Viral persistence at these sites ranges from a few days postinfection in buffy coat smears to greater than 60 days in skin and foot pads.[7,59]

It is difficult to isolate CDV by routine cell culture. Virus isolation is most successful by direct cultivation of target tissues of lymphocytes and macrophages from the infected host.[10] In cultures with no cytopathic effects after 48–72 hr, fluorescent antibody tests can detect CDV.[7,10] Polymerase chain reaction should be considered for the antemortem detection and differentiation of CD.[62]

Postmortem

Lesions of CDV infection are similar in nondomestic carnivores and in domestic dogs.[24,44,107] The most significant gross lesions are pneumonia, depletion of lymphopoietic organs, and hyperkeratosis of the nose, foot pads, and eyelids. In uncomplicated CDV infection, the only consistent pathologic finding is thymic atrophy. Common histologic findings are hyperkeratosis of the nose, foot pads, and eyelids; eosinophilic inclusion bodies in many organs (most commonly cytoplasmic but occasionally intranuclear in the CNS, urinary bladder, and bronchial epithelium); lymphoid depletion; diffuse interstitial pneumonia; and perivascular lymphoplasmacytic infiltration in areas of demyelination and neuronal degeneration of the CNS. Syncytial giant cells in the lungs and CNS white matter, anterior uvea, and lymph nodes may also be present.

In contrast to histopathologic lesions identified in the domestic dog, lungs of large felids may show diffuse alveolar type 2 cell hyperplasia with intra-

cytoplasmic and intranuclear viral inclusion bodies.[14] These cells were strongly positive for CDV antigens by immunohistocytochemical staining. This cellular response appears to be unique to large felids.[14] Additionally, feline brain histopathology may lack the typical canid pattern of demyelination with astrocytosis and vascular cuffing. Most cats have had mild, patchy CNS lesions compared with those of canids.

The lung, liver, lymph nodes, brain, and spleen of any dead animal with suspected CDV infection should be collected for viral isolation and/or PCR. Immunohistocytochemistry on formalin-fixed tissues provides definitive evidence of CDV infection.[17,78] Vaccine virus can be differentiated from street virus by differential cell culture on the basis of different target cell susceptibility.[10]

CLINICAL MANAGEMENT

Canine distemper is best prevented by vaccination.[32] Currently, the vaccines commercially available in North America contain modified live CDV that is tissue culture adapted, primate tissue Vero cells adapted, or egg adapted or a canarypox-vectored CDV, in combination with modified live virus (MLV) canine adenovirus type 2, canine coronavirus, canine parainfluenza virus, and canine parvovirus.[32,95,104] MLV vaccines derived from egg-adapted and primate tissue strains of virus have generally been safer than canine tissue culture–adapted strains for nondomestic species; most vaccine-induced CDV infections result from the latter. The Fromm-D™ vaccine (Solvay, Mendota Heights, Minnesota 55120, USA), containing an egg-adapted strain and taken off the market in 1994, was labeled for use in ferrets and safe in many nondomestic species.[66,131] The USDA-approved Fervac-D™ (United Vaccines, Inc., Madison, Wisconsin 53744, USA), an egg-adapted strain containing vaccine for use in ferrets, has induced disease in red pandas[94] and anaphylaxis in some mustelids (notably ferrets) and viverrids (R. J. Montali, unpubl. data). It should not be used in these species nor, perhaps, in other exotic carnivores. Galaxy-D™ (Solvay, currently being manufactured by Fort Dodge, Overland Park, Kansas 50501, USA for Schering-Plough, Union, New Jersey 07083, USA), a MLV tissue culture–adapted strain with simian cell substrate, has shown promise in nondomestic species and may be safe for use in some canids, procyonids, and wolf species.[105] Studies by the ad hoc American Association of Zoo Veterinarian's CDV subcommittee with Galaxy-D™ showed it to be relatively safe and efficacious in maned wolves and hybrid black-footed ferret × Siberian polecat.[95] The use of multivalent vaccines containing CDV, such as Galaxy-6-MPH-L (Solvay), should be discouraged, at least in some nondomestic species, because of possible immunosuppression and clinical disease brought about by other MLV components.[94,121]

An experimental killed vaccine, prepared with B-propriolactone–inactivated Onderstepoort strain, has good safety but variable efficacy when used in both domestic and nondomestic species,[95] but unfortunately it is available only in limited amounts to selected institutions holding such species as SSP-managed red pandas and black-footed ferrets. A subunit vaccine with CDV immune-stimulating complexes protected domestic dogs experimentally infected with CDV[40] and harbor seals (*Phoca vitulina*) exposed to phocid distemper virus-1[128] and may be useful for nondomestic species. Recombinant vaccines with vaccina,[72,120] canarypox,[104,120,132] and fowlpox[72] vectors with either CDV[104,120,132] or rinderpest virus[72] antigens have been experimentally tested in ferrets and dogs. The recombinant canarypox-vectored CDV vaccine (Merial, Ltd., Inc., Athens, Georgia 30601, USA) has been safe and efficacious and lacked interference from other canine vaccine components in initial trials and may soon be available.[104,132] However, it is presently only licensed and available as a polyvalent product[104] and cannot be recommended at this time for use in nondomestic species. A monovalent form of this canarypox-vectored CDV vaccine is being sought.[95]

Vaccination schedules for nondomestic species are based on recommendations for the domestic dog.[6,32] Domestic dogs that received colostrum as neonates should be vaccinated every 3–4 wk between 6 and 16 wk of age. Colostrum-deprived neonates should be given two vaccinations administered on a 3–4 wk interval and starting at 2 wk of age because maternal antibodies acquired in utero should be absent by 4–6 wk of age.[6]

Data on maternal antibody interference with vaccination of raccoons and ferrets suggest that a final CDV vaccine should be administered at 18–20 wk of age in raccoons and after 10 wk of age in ferrets.[57,105] This illustrates the importance of tailoring vaccination programs to a particular species' needs. Additionally, vaccination schedules may require modification during CD epidemics or periods of increased risk of exposure.

Adults should be vaccinated twice, 3–4 wk apart. Modified live CDV vaccines induce long-lived immunity in domestic dogs[50] and hybrid ferrets.[131] Consequently, the risk of adverse events, including anaphylaxis, has raised questions about the need for annual vaccination of domestic animals.[50] Yearly

vaccine boosters may be advisable in nondomestic species for which data on antibody persistence postvaccination are lacking. Assessment of the immune response (e.g., IgG antibody levels) provides a way to assess the need for booster vaccination.[130]

Vaccination of nondomestic felids is not recommended by the Felid Taxon Advisory Group, although favorable results with a monovalent recombinant form of canarypox-vectored CDV vaccine (R. J. Montali, unpubl. data) may change this. Vaccination of free-ranging potential reservoir animals (e.g., domestic dogs in Africa and raccoons in urban North American zoos) for CDV and efforts to minimize their contact with captive and wild felids may decrease the risk for CDV infection in nondomestic felids.

All CDV vaccine use for nondomestic species is extra-label except for Fervac-D™ in ferrets and Distemink™ (United Vaccines, Inc., Madison, Wisconsin 53744, USA) in mink. Veterinarians should consider obtaining signed consent forms prior to vaccinating pet ferrets and pretreating with diphenhydramine to lessen the severity of anaphylactic reactions (R. A. Yates, unpubl. data). Currently, a monovalent canarypox-vectored CDV recombinant vaccine holds the most promise for general exotic carnivore protection against CDV if it becomes licensed for ferrets and widely available.

Canine distemper virus is extremely susceptible to ultraviolet light, heat, desiccation, and common disinfectants (e.g., formaldehyde, ether, chloroform, phenolic compounds, and quarternary ammonium compounds). It is short lived in the environment but can survive at low temperatures (e.g., 48 hr at 25°C and 14 days at 5°C) for extended periods.[117] Good hygienic practices and the separation of potential virus-shedding animals from susceptible hosts should be instituted.

There is no specific therapy for animals with clinical CD. Nonspecific treatment is supportive and includes fluids, antibiotics (for secondary bacterial infections), and drugs to minimize CNS inflammation and seizure activity. The prognosis in acute generalized CD is often poor but depends on the virulence of the virus strain along with the identity, age, and immune status of the individual affected. Neurologic manifestations worsen the prognosis.

ZOONOTIC POTENTIAL/FUTURE DIRECTIONS

There is no definitive evidence of naturally acquired human CDV disease although asymptomatic experimental infection may occur.[98] However, there may be a relationship between subacute sclerosing panencephalitis (SSPE), multiple sclerosis (MS), Paget's disease, and CDV infection. Dog ownership and clinical MS are statistically correlated,[36] as are dog ownership and Paget's disease.[102] However, there is no evidence of a causal relationship between CDV and MS.[25] More evidence supports an association between measles with SSPE, although such an association is still theoretical.[33,106] Nevertheless, with the new and emerging morbilliviruses, both CDV and viruses closely related to CDV in nonhuman primates,[136] tayassuids,[11] marine mammals,[127] and nondomestic felids,[14,113] there is concern about the mutability and changing epidemiology of CD. We must be cautious when working with animals potentially infected with morbilliviruses. Potential new vaccines, including DNA (plasmid) products against these agents,[119] may hold great promise as safe and effective vaccines for exotic carnivores.

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LITERATURE CITED

1. Alexander, K. A., and M. J. G. Appel. 1994. African wild dogs (*Lycaon pictus*) endangered by a canine distemper epizootic among domestic dogs near the Masai Mara National Reserve, Kenya. J. Wildl. Dis. 30: 481–485.

2. Alexander, K. A., P. A. Conrad, L. A. Gardner, C. Parish, M. Appel, M. G. Levy, N. Lerche, and P. Kat. 1993. Serologic survey for selected microbial pathogens in African wild dogs (*Lycaon pictus*) and sympatric domestic dogs (*Canis familiaris*) in Masai Mara, Kenya. J. Zoo Wildl. Med. 24: 140–144.

3. Alexander, K. A., P. W. Kat, L. G. Frank, K. E. Holekamp, L. Smale, C. House, and M. J. G. Appel. 1995. Evidence of canine distemper virus infection among free-ranging spotted hyena (*Crocuta crocuta*) in the Masai Mara, Kenya. J. Zoo Wildl. Med. 26: 201–206.

4. Alexander, K. A., P. W. Kat, L. A. Munson, A. Kalake, and M. J. G. Appel. 1996. Canine distemper–related mortality among wild dogs (*Lycaon pictus*) in Chobe National Park, Botswana. J. Zoo Wildl. Med. 27: 426–427.

5. Appel, M. J. G. 1969. Pathogenesis of canine distemper. Am. J. Vet. Res. 30: 1167–1182.

6. Appel, M. J. G. 1977. Canine distemper. *In:* Kirk, R. W. (ed.). Current Veterinary Therapy, vol. 6, Small Animal Practice. W. B. Saunders, Philadelphia, Pennsylvania. Pp. 1308–1313.

7. Appel, M. J. G. 1987. Canine distemper virus. *In:* Appel, M. J. G. (ed.). Virus Infections of Carnivores. Elsevier Science Publishers B. V., New York, New York. Pp. 133–159.

8. Appel, M. J. G., E. P. J. Gibbs, S. J. Martin, V. Ter Meulen, B. K. Rima, J. R. Stephenson, and W. P. Taylor. 1981. Morbillivirus diseases of animals and man. *In:* Kustak, E., and C. Kurstak (eds.). Comparative Diagnosis of Viral Diseases, vol. 4, Vertebrate Animal and Related Vi-

ruses, Part B—RNA Viruses. Academic Press, New York, New York. Pp. 235–297.

9. Appel, M. J. G., and R. J. Montali. 1994. Canine distemper and emerging morbillivirus diseases in exotic species. Proc. Am. Assoc. Zoo Vet. 1994: 336–339.

10. Appel, M. J. G., S. Pearce-Kelling, and B. A. Summers. 1992. Dog lymphocyte cultures facilitate the isolation and growth of virulent canine distemper virus. J. Vet. Diagn. Invest. 4: 258–263.

11. Appel, M. J. G., C. Reggiardo, B. A. Summers, S. Pearce-Kelling, C. J. Mare, T. H. Noon, R. E. Reed, J. N. Shively, and C. Orvell. 1991. Canine distemper virus infection and encephalitis in javelinas (collared peccaries). Arch. Virol. 119: 147–152.

12. Appel, M. J. G., and D. S. Robson. 1973. A microneutralization test for canine distemper virus. Am. J. Vet. Res. 34: 1459–1463.

13. Appel, M. J. G., B. E. Sheffy, D. H. Percy, and J. M. Gaskin. 1974. Canine distemper virus in domesticated cats and pigs. Am. J. Vet. Res. 35: 803–806.

14. Appel, M. J. G., R. A. Yates, G. L. Foley, J. J. Bernstein, S. Santinelli, L. H. Spelman, L. D. Miller, L. H. Arp, M. Anderson, M. Barr, S. Pearce-Kelling, and B. A. Summers. 1994. Canine distemper epizootic in lions, tigers, and leopards in North America. J. Vet. Diagn. Invest. 6: 277–288.

15. Armstrong, W. H. 1942. Canine distemper in the American badger. Cornell Vet. 32: 447.

16. Armstrong, W. H., and C. H. Anthony. 1942. An epizootic of canine distemper in a zoological park. Cornell Vet. 32: 286–288.

17. Axthelm, M. K., and S. Krakowka. 1986. Immunocytochemical methods for demonstrating canine distemper virus antigen in aldehyde-fixed paraffin-embedded tissue. J. Virol. Monogr. 13: 215–229.

18. Baumgartner, W., R. W. Boyce, S. E. Weisbrode, S. Aildinger, M. K. Axthelm, and S. Krakowka. 1995. Histologic and immunocytochemical characterization of canine distemper–associated metaphyseal bone lesions in young dogs following experimental infection. Vet. Pathol. 32: 702–709.

19. Bernard, S. L., J. R. Gorham, and L. M. Ryland. 1984. Biology and diseases of ferrets. *In:* Fox, J. G., B. J. Cohen, and F. M. Loew (eds.). Laboratory Animal Medicine. Academic Press, New York, New York. Pp. 385–397.

20. Bernard, S. L., D. T. Shen, and J. R. Gorham. 1982. Antigen requirements and specificity of enzyme-linked immunosorbent assay for detection of canine IgG against canine distemper viral antigen. Am. J. Vet. Res. 43: 2266–2269.

21. Blair, W. R. 1907. Report of the veterinarian. N. Y. Zool. Soc. Annu. Rep. 12: 119.

22. Blythe, L. L., J. A. Schmitz, M. Roelke, and S. Skinner. 1983. Chronic encephalomyelitis caused by canine distemper virus in a Bengal tiger. J. Am. Vet. Med. Assoc. 183: 1159–1162.

23. Breazile, J. E., B. S. Blaugh, and N. Nail. 1966. Experimental study of canine distemper myoclonus. Am. J. Vet. Res. 27: 1375–1379.

24. Budd, J. 1981. Distemper. *In:* Davis, J. W., L. H. Karstad, and D. O. Trainer (eds.). Infectious Diseases of Wild Mammals. Iowa State University Press, Ames, Iowa. Pp. 31–44.

25. Burridge, M. J. 1978. Multiple sclerosis, house pets, and canine distemper: critical review of recent reports. J. Am. Vet. Med. Assoc. 173: 1439–1444.

26. Bush, M., R. J. Montali, O. Brownstein, A. E. James, and M. J. G. Appel. 1976. Vaccine-induced canine distemper in a lesser panda. J. Am. Vet. Med. Assoc. 169: 959–960.

27. Bush, M., and M. Roberts. 1977. Distemper in captive red pandas. Int. Zoo Yearb. 17: 194–196.

28. Carpenter, J. W., M. J. G. Appel, R. C. Erickson, and M. N. Novilla. 1976. Fatal vaccine-induced canine distemper virus infection in black-footed ferrets. J. Am. Vet. Med. Assoc. 169: 961–964.

29. Carpenter, M. A., M. J. G. Appel, M. E. Roelke-Parker, L. Munson, H. Hofer, M. East, and S. J. O'Brien. 1998. Genetic characterization of canine distemper virus in Serengeti carnivores. Vet. Immunol. Immunopathol. 65: 259–266.

30. Carré, H. 1905. Sur la maladie des jeunes chiens. C. R. Acad. Sci. 140: 689–690, 1489–1491.

31. Chandra, A. M. S., P. E. Ginn, S. P. Terrell, B. Ferguson, A. Adjirir-Awere, P. Dennis, and B. L. Homer. 2000. Canine distemper virus infection in binturongs (*Arctictis binturong*). J. Vet. Diagn. Invest. 12: 88–91.

32. Chappuis, G. 1995. Control of canine distemper. Vet. Microbiol. 44: 351–358.

33. Chen, T. T., I. Watanabe, W. Zeman, and J. Mealey. 1969. Subacute sclerosing panencephalitis: propagation of measles virus from brain biopsy in tissue culture. Science 163: 1193–1194.

34. Chomel, B. B., R. W. Kasten, G. Chappuis, M. Soulier, and Y. Kikuchi. 1998. Serological survey of selected canine viral pathogens and zoonoses in grizzly bears (*Ursus arctos horribilis*) and black bears (*Ursus americanus*) from Alaska. Rev. Sci. Tech. Off. Int. Epizoot. 17: 756–766.

35. Cook, R. D., and G. E. Wilcox. 1981. A paramyxovirus-like agent associated with demyelinating lesions in the CNS of cats. J. Neuropathol. Exp. Neurol. 40: 328.

36. Cook, S. D., and P. C. Dowling. 1977. A possible association between house pets and multiple sclerosis. Lancet 1: 980–982.

37. Cranfield, M. R., I. K. Barker, K. G. Mehren, and W. A. Rapley. 1984. Canine distemper in wild raccoons (*Procyon lotor*) at the Metropolitan Toronto Zoo. Can. Vet. J. 25: 63–66.

38. Cypher, B. L., J. H. Scrivner, K. L. Hammer, and T. P. O'Farrell. 1998. Viral antibodies in coyotes from California. J. Wildl. Dis. 34: 259–264.

39. Davidson, M. 1986. Canine distemper, virus infection in the domestic ferret. Compend. Contin. Educ. Pract. Vet. 8: 448–453.

40. de Vries, P., F. G. C. M. Uytdehaag, and A. D. M. E. Osterhaus. 1988. Canine distemper virus (CDV) immune-stimulating complexes (iscoms), but not measles vi-

rus iscoms, protect dogs against CDV infection. J. Gen. Virol. 69: 2071–2083.

41. Diters, R. W., and S. W. Nielsen. 1978. Toxoplasmosis, distemper, and herpesvirus infection in a skunk (*Mephitis mephitis*). J. Wildl. Dis. 14: 132–136.

42. Dubielzig, R. R., R. J. Higgins, and S. Krakowka. 1981. Lesions of the enamel organ of developing dog teeth following experimental inoculation of gnotobiotic puppies with canine distemper virus. Vet. Pathol. 18: 684–689.

43. Dunbar, M. R., M. W. Cunningham, and J. C. Roof. 1998. Seroprevalence of selected disease agents from free-ranging black bears in Florida. J. Wildl. Dis. 34: 612–619.

44. Dungworth, D. L. 1993. The Respiratory System, vol. 3, Canine Distemper Virus. *In:* Jubb, K. V. F., P. C. Kennedy, and N. Palmer (eds.). Pathology of Domestic Animals. Academic Press, Inc., New York, New York. Pp. 617–624.

45. Durchfeld, B., W. Baumgartner, W. Herbst, and R. Brahm. 1990. Vaccine-associated canine distemper infection in a litter of African hunting dogs (*Lycaon pictus*). J. Med., Series B37: 203–212.

46. Erken, A. H. M., and E. F. Jacobi. 1972. Successful breeding of lesser panda (*Ailurus fulgens* F. Cuvier, 1825) and loss through inoculation. Bijdr. Dierkd. 42: 92–95.

47. Evans, R. H. 1984. Studies of a virus in a biological system: naturally occurring and experimental canine distemper in the raccoon (*Procyon lotor*). M. S. Thesis, Southern Illinois Univ., Carbondale, Illinois.

48 Fix, A. S., D. P. Riordan, H. T. Hill, M. A. Gill, and M. B. Evans. 1989. Feline panleukopenia virus and subsequent canine distemper virus infection in two snow leopards (*Panthera uncia*). J. Zoo Wildl. Med. 20: 273–281.

49. Follmann, E. H., G. W. Garner, J. F. Evermann, and A. J. McKeirnan. 1996. Serological evidence of morbillivirus infection of polar bears (*Ursus maritimus*) from Alaska and Russia. Vet. Rec. 138: 615–618.

50. Ford, R. B., and R. D. Schultz. 2000. *In:* Bonagura, J. D. (ed.). Kirk's Current Veterinary Therapy, vol. 3, Small Animal Practice. W. B. Saunders Co., Philadelphia, Pennsylvania. Pp. 250–253.

51. Gelatt, K. N., R. D. Whitley, D. A. Samuelson, and G. Garcia-Sanchez. 1985. Ocular manifestations of viral diseases in small animals. Compend. Contin. Educ. Pract. Vet. 7: 968–976.

52. Gese, E. M., R. D. Schultz, M. R. Johnson, E. S. Williams, R. L. Crabtree, and R. L. Ruff. 1997. Serological survey for diseases in free-ranging coyotes (*Canis latrans*) in Yellowstone National Park, Wyoming. J. Wildl. Dis. 33: 47–56.

53. Gese, E. M., R. D. Schultz, O. J. Rongstad, and D. E. Andersen. 1991. Prevalence of antibodies against canine parvovirus and canine distemper virus in wild coyotes in southeastern Colorado. J. Wildl. Dis. 27: 320–323.

54. Giesel, O. 1979. Distemper in otters. Berl. Muench. Tieraerztl. Wochenschr. 92: 304. (In German.)

55. Gill, J. M., W. J. Hartley, and N. L. Hodgkinson. 1988. An outbreak of post-vaccinal suspected distemper-like encephalitis in farmed ferrets (*Mustela putorius furo*). N. Z. Vet. J. 36: 173–176.

56. Goodrich, J. M., E. S. Williams, and S. W. Buskirk. 1994. Effects of a modified-live virus canine distemper vaccine on captive badgers (*Taxidea taxus*). J. Wildl. Dis. 30: 492–496.

57. Gorham, J. R. 1999. Some experiments and field observations of distemper in mink and ferrets. Adv. Vet. Med. 41: 557–570.

58. Gould, D. H., and W. R. Fenner. 1983. Paramyxovirus-like nucleocapsids associated with encephalitis in a captive Siberian tiger. J. Am. Vet. Med. Assoc. 183: 1319–1322.

59. Greene, G. E., and M. J. Appel. 1990. Canine distemper. *In:* Greene, C. E. (ed.). Infectious Diseases of the Dog and Cat. W. B. Saunders, Philadelphia, Pennsylvania. Pp. 226–241.

60. Gross, L. J. 1948. Species susceptibility to viruses of Carré and feline enteritis. Am. J. Vet. Res. 9: 65–68.

61. Haas, L., H. Hofer, M. East, P. Wohlsein, B. Liess, and T. Barrett. 1996. Canine distemper virus infection in Serengeti spotted hyaenas. Vet. Microbiol. 49: 147–152.

62. Haas, L., S. M. Subbarao, T. G. Harder, B. Liess, and T. Barrett. 1991. Detection of phocid distemper virus RNA in seal tissue using slot hybridization and the polymerase chain reaction: genetic evidence that the virus is distinct from canine distemper virus. J. Gen. Virol. 72: 393–398.

63. Halbrooks, R. D., L. J. Swango, P. R. Schnurrenberger, F. E. Mitchell, and E. P. Hill. 1981. Response of gray foxes to modified live-virus canine distemper vaccines. J. Am. Vet. Med. Assoc. 179: 1170–1174.

64. Hamerton, A. C. 1937. Diseases due to infection. Proc. Zool. Soc. Lond. 107: 443.

65. Harder, T. C., M. Kenter, M. J. G. Appel, M. E. Roelke-Parker, T. Barrett, and A. D. M. E. Osterhaus. 1995. Phylogenetic evidence for canine distemper virus in Serengeti's lions. Vaccine 13: 521–523.

66. Harrenstien, L. A., L. Munson, E. C. Ramsay, C. F. Lucash, S. A. Kania, and L. N. D. Potgieter. 1997. Antibody responses of red wolves to canine distemper virus and canine parvovirus vaccination. J. Wildl. Dis. 33: 600–605.

67. Hoff, G. L., and W. J. Bigler. 1974. Epizootic of canine distemper virus infection among urban raccoons and gray foxes. J. Wildl. Dis. 10: 423–428.

68. Hofmeyer, G. F. B. 1956. Two hundred and eighty four autopsies at the National Zoological Gardens, Pretoria. J. S. Afr. Vet. Med. Assoc. 27: 263–282.

69. Itakura, C., K. Nakamura, J. Nakatsuka, and M. Goto. 1979. Distemper infection in lesser panda due to administration of a canine distemper live vaccine. Jpn. J. Vet. Sci. 41: 561–566.

70. Johnson, G. C., W. R. Fenner, and S. Krakowka. 1988. Production of immunoglobulin G and increased antiviral antibody in cerebrospinal fluid of dogs with delayed-onset canine distemper viral encephalitis. J. Neuroimmunol. 17: 237–251.

71. Johnson, M. R., D. K. Boyd, and D. H. Pletscher. 1994. Serologic investigations of canine parvovirus and

canine distemper in relation to wolf (*Canis lupus*) pup mortalities. J. Wildl. Dis. 30: 270–273.

72. Jones, L., E. Tenorio, J. Gorham, and T. Yilma. 1997. Protective vaccination of ferrets against canine distemper with recombinant pox virus vaccines expressing the H or F genes of rinderpest virus. Am. J. Vet. Res. 58: 590–593.

73. Karstad, L., and J. Budd. 1964. Distemper in raccoons characterized by giant-cell pneumonitis. Can. Vet. J. 5: 326–330.

74. Kazacos, K. R., H. L. Thacker, H. L. Shivaprasad, and P. P. Burger. 1981. Vaccination-induced distemper in kinkajous. J. Am. Vet. Med. Assoc. 179: 1166–1169.

75. Kilham, L, R. T. Habermann, and G. M. Herman. 1956. Jaundice and bilirubinemia as manifestations of canine distemper in raccoons and ferrets. Am. J. Vet. Res. 17: 144–148.

76. Kirk, H. 1922. Canine Distemper: Its Complications, Sequelae and Treatment. Baillere, Tindall and Cox, London, England.

77. Krakowka, S., E. A. Hoover, A. Koestner, and K. Ketring. 1977. Experimental and naturally occurring transplacental transmission of canine distemper virus. Am. J. Vet. Res. 38: 919–922.

78. Kristensen, B., and M. Vandevelde. 1978. Immunofluorescence studies of canine distemper encephalitis on paraffin-embedded tissue. Am. J. Vet. Res. 39: 1017–1021.

79. Laperle, A. 1993. Distemper chez les ratons laveurs. Med. Vet. Que. 23: 83–85.

80. Little, S. E., W. R. Davidson, E. W. Howerth, P. M. Rakich, and V. F. Nettles. 1998. Diseases diagnosed in red foxes from the southwestern United States. J. Wildl. Dis. 34: 620–624.

81. Machida, N., N. Izumisawa, T. Nakamura, and K. Kiryu. 1992. Canine distemper virus infection in a masked palm civet (*Paguma larvata*). J. Comp. Pathol. 107: 439–443.

82. Machida, N., K. Kiryu, K. Oh-ishi, E. Kanda, N. Izumisawa, and T. Nakamura. 1993. Pathology and epidemiology of canine distemper in raccoon dogs (*Nyctereutes procyonoides*). J. Comp. Pathol. 108: 383–392.

83. Mainka, S. A., Q. Xianmeng, H. Tingmel, and M. J. Appel. 1994. Serologic survey of giant pandas (*Ailuropoda melanoleuca*), and domestic dogs and cats in the Wolong Reserve, China. J. Wildl. Dis. 30: 86–89.

84. Malik, R., M. Dowden, P. E. Davis, G. S. Allan, V. R. Barrs, P. J. Canfield, and D. N. Love. 1995. Concurrent juvenile cellulitus and metaphyseal osteopathy: an atypical canine distemper virus syndrome? Aust. Vet. Pract. 25: 62–67.

85. Marsilio, F., P. G. Tiscar, L. Gentile, H. U. Roth, G. Boscaglis, M. Tempesta, and A. Gatti. 1997. Serologic survey for selected viral pathogens in brown bears from Italy. J. Wildl. Dis. 33: 304–307.

86. Matsibara, Y., Y. Morikawa, Y. Yoshikawa, K. Hagashima, and K. Yamanouchi. 1985. Encephalitis induced in non-human primates by canine distemper virus adapted to human neural cells. Jpn. J. Exp. Med. 55: 99–108.

87. McCormick, A. E. 1983. Canine distemper in African cape hunting dogs (*Lycaon pictus*) possibly vaccine induced. J. Zoo Anim. Med. 14: 66–71.

88. McInnes, E. F., R. E. Burroughs, and N. M. Duncan. 1992. Possible vaccine-induced canine distemper in a South American bush dog (*Speothos venaticus*). J. Wildl. Dis. 28: 614–617.

89. Mitchell, M. A., L. L. Hungerford, C. Nixon, T. Esker, J. Sullivan, R. Koerkenmeier, and J. P. Dubey. 1997. Serologic survey for selected infectious disease agents in raccoons from Illinois. J. Wildl. Dis. 35: 347–355.

90. Moehlman, P. D. 1983. Socioecology of silver-backed and golden jackals (*Canis misomelas* and *Canis aureus*). *In:* Eisenberg, J. F., and D. G. Kleiman, (eds.). Advances in the Study of Mammalian Behavior. Special Publication 7. American Society of Mammalogists, Lawrence, Kansas. Pp. 423–453.

91. Monson, R. A., and W. B. Stone. 1976. Canine distemper in wild carnivores in New York. N.Y. Fish Game J. 23: 149–154.

92. Montali, R. J., C. R. Bartz, J. A. Teare, J. T. Allen, M. J. G. Appel, and M. Bush. 1983. Clinical trials with canine distemper vaccines in exotic carnivores. J. Am. Vet. Med. Assoc. 183: 1163–1167.

93. Montali, R. J., G. R. Bartz, and M. Bush. 1987. Canine distemper virus. *In:* Appel, M. J. (ed.). Virus Infections of Carnivores. Elsevier Science Publishers, Amsterdam, The Netherlands. Pp. 347–443.

94. Montali, R. J., R. G. Cambre, M. Sutherland-Smith, and M. J. G. Appel. 1994. Vaccination against canine distemper in exotic carnivores: successes and failures. Proc. Am. Assoc. Zoo Vet. 1994: 340–344.

95. Montali, R. J., W. Heuschele, E. Williams, and W. Lance. 1998. Development, production and safety evaluation of canine distemper vaccines for use in exotic carnivores final report, September 10, 1998. American Association of Zoo Veterinarians Canine Distemper Virus Subcommittee, Media, Pennsylvania.

96. Morell, V. 1994. Serengeti's big cats going to the dogs. Science 264: 1664.

97. Munson, L., M. J. G. Appel, M. A. Carpenter, S. J. O'Brien, and M. Roelke-Parker. 1995. Canine distemper in wild felids. Proc. Am. Assoc. Zoo Vet./Wildl. Dis. Assoc./Am. Assoc. Wildl. Vet. 1995: 135–136.

98. Nicolle, C. 1931. La maladie du jeune age des chiens est transmissible expérimentalement a l'homme sous forme inapparente. Arch. Inst. Pasteur Tunis 20: 312–323.

99. Noon, K. F., M. Rogul, L. N. Binn, T. J. Keefe, R. H. Marchwicki, and M. J. Appel. 1980. Enzyme-linked immunosorbent assay for evaluation of antibody to canine distemper virus. Am. J. Vet. Res. 41: 605–609.

100. Nowak, R. M. 1991. Order Carnivora. *In*: R. M. Nowak (ed.). Walker's Mammals of the World, 5th ed., vol. 2. The Johns Hopkins University Press, Baltimore, Maryland. Pp. 1045–1219.

101. O'Brien, S. J., W. G. Nash, D. E. Wildt, M. E. Bush, and R. E. Benveniste. 1985. A molecular solution to the riddle of the giant panda's phylogeny. Nature 317: 140–144.

102. O'Driscoll, J. B., and D. C. Anderson. 1985. Past pets and Paget's disease. Lancet 919–921.

103. Osterhaus, A. D. M. E., R. L. de Swart, H. W. Vos, P. S. Ross, M. J. H. Kenter, and T. Barrett. 1995. Morbillivirus infections of aquatic mammals: newly identified members of the genus. Vet. Microbiol. 44: 219–227.

104. Pardo, M. C., J. E. Bauman, and M. Mackowiak. 1997. Protection of dogs against canine distemper by vaccination with a canarypox virus recombinant expressing canine distemper virus fusion and hemagglutinin glycoproteins. Am. J. Vet. Res. 58: 833–836.

105. Paré, J. A., I. K. Barker, G. J. Crawshaw, S. A. McEwen, P. S. Carman, and R. P. Johnson. 1999. Humoral response and protection from experimental challenge following vaccination of raccoon pups with a modified-live canine distemper virus vaccine. J. Wildl. Dis. 35: 430–439.

106. Payne, F. E., J. V. Baublis, and H. H. Itabashi. 1969. Isolation of measles virus from cell cultures of brain from a patient with subacute sclerosing panencephalitis. N. Engl. J. Med. 281: 585–589.

107. Pearson, R. C., and J. R. Gorham. 1987. Canine distemper virus. *In:* Appel, M. J. (ed.). Virus Infections of Carnivores. Elsevier Science Publishers B. V., New York, New York. Pp. 371–378.

108. Piat, B. L. 1950. Susceptibility of young lions to distemper. Bull. Serv. Elev. Indust. Anim. Afrig. Occid. Fr. 3: 39–40.

109. Potgieter, L. N. D., and P. A. Ajidagba. 1989. Quantitation of canine distemper virus and antibodies by enzyme-linked immunosorbent assays using protein A and monoclonal antibody capture. J. Vet. Diagn. Invest. 1: 110–115.

110. Qui, X., and S. Mainka. 1993. Review of mortality of the giant panda (*Ailuropoda melanoleuca*). J. Zoo Wildl. Med. 24: 425–429.

111. Rewell, R. E. 1947. Report of the pathologist for the year 1947. Proc. Zool. Soc. Lond. 118: 507.

112. Robinson, V. B., J. W. Newberne, and D. M. Brooks. 1957. Distemper in the American raccoon (*Procyon lotor*). J. Am. Vet. Med. Assoc. 131: 276–278.

113. Roelke-Parker, M. E., L. Munson, C. Packer, R. Kock, S. Gleaveland, M. Carpenter, S. J. O'Brien, A. Pospischil, R. Hofmann-Lehmann, H. Lutz, G. L. M. Mwamengele, M. N. Mgasa, G. A. Machange, B. Summers, and M. J. G. Appel. 1996. A canine distemper virus epidemic in Serengeti lions (*Panthera leo*). Nature 379: 441–445.

114. Roscoe, D. E. 1993. Epizootiology of canine distemper in New Jersey raccoons. J. Wildl. Dis. 29: 390–395.

115. Schonbauer, M. von, S. Kobi, and A. Schonbauer-Langle. 1984. Perinatale staupeinfektion bei drei eisbären (*Ursus maritimus*) und bei einem brillenbaren (*Tremarctos ornatus*). Verhandslungsbericht Int. Symp. Erkrankungen Zootiere 26: 131–136.

116. Scott, W. A. 1979. Use of vaccines in exotic species. Vet. Rec. 104: 199.

117. Shen, D. T., and J. R. Gorham. 1980. Survival of pathogenic virus at 5°C and 25°C. Vet. Med. Small Anim. Clin. 75: 69–70.

118. Sikarskie, J. G., and G. L. Brady. 1991. Canine distemper in a vaccinated red panda (*Ailuris fulgens fulgens*). Proc. Am. Assoc. Zoo Vet. 1991: 292–293.

119. Sixt, N., A. Cardoso, A. Vallier, J. Fayolle, R. Buckland, and T. F. Wild. 1998. Canine distemper virus DNA vaccination induces a humoral and cellular immunity and protects against a lethal intracerebral challenge. J. Virol. 72: 8472–8476.

120. Stephensen, C. B., J. Welter, S. R. Thaker, J. Taylor, J. Tartaglia, and E. Paoletti. 1997. Canine distemper virus (CDV) infection of ferrets as a model for testing morbillivirus vaccine strategies: NYVAC- and ALVAC-based CDV recombinants protect against symptomatic infection. J. Virol. 71: 1506–1513.

121. Sutherland-Smith, M. R., B. A. Rideout, A. B. Mikolon, M. J. G. Appel, P. J. Morris, A. L. Shima, and D. J. Janssen. 1997. Vaccine-induced canine distemper in European mink, *Mustela lutreola*. J. Zoo Wildl. Med. 28: 312–318.

122. Swango, L. J. 1995. Canine viral diseases. *In:* Ettinger, S. J., and E. C. Feldman (eds.). Textbook of Veterinary Internal Medicine: Diseases of the Dog and Cat. W. B. Saunders Co., Philadelphia, Pennsylvania. Pp. 398–409.

123. Thomas-Baker, B. 1985. Vaccination-induced distemper in maned wolves, vaccination-induced corneal opacity in a maned wolf. Proc. Am. Assoc. Zoo Vet. 1985: 53.

124. Truyen, U., N. Stockhofe-Zurwieden, O. R. Kaaden, and J. Pohlenz. 1990. A case report: encephalitis in lions. Pathological and virological findings. Dtsch. Tieraerztl. Wochenschr. 97: 89–91.

125. Vandervelde, M., and M. Cachin. 1992. The neurologic form of canine distemper. *In:* Kirk, R. W., and J. D. Bonagura (eds.). Current Veterinary Therapy, vol. 11, Small Animal Practice. W. B. Saunders Co., Philadelphia, Pennsylvania. Pp. 1003–1007.

126. Van Heerden, J., N. Bainbridge, R. E. J. Burroughs, and N. P. J. Kriek. 1990. Distemper-like disease and encephalitozoonosis in wild dogs (*Lycaon pictus*). J. Wildl. Dis. 25: 70–75.

127. Visser, I. K. G., M. Van Bressem, R. L. de Swart, M. W. G. van de Bildt, H. W. Vos, R. W. J. van der Heijden, J. T. Saliki, C. Orvell, P. Kitching, T. Kuiken, T. Barrett, and A. D. M. E. Osterhaus. 1993. Characterization of morbilliviruses isolated from dolphins and porpoises in Europe. J. Gen. Virol. 74: 631–641.

128. Visser, I. K. G., E. J. Vedder, M. W. G. van de Bildt, C. Orvell, T. Barrett, and A. D. M. E. Osterhaus. 1992. Canine distemper virus ISCOMs induce protection in harbour seals (*Phoca vitulina*) against phocid distemper but still allow subsequent infection with phocid distemper virus-1. Vaccine 10: 435–438.

129. Von Messling, V., T. C. Harder, V. Moennig, P. Rautenberg, I. Nolte, and L. Haas. 1999. Rapid and sensitive detection of immunoglobulin M (IgM) and (IgG) antibodies against canine distemper virus by a new recom-

binant nucleocapsid protein based enzyme-linked immunosorbent assay. J. Clin. Microbiol. 37: 1049–1056.

130. Warner, T. A. N. N. Schwarz Ben Meir, Z. Babichev, and L. E. Carmichael. 1998. Assessment of immunization response to canine distemper virus vaccination in puppies using a clinic-based enzyme-linked immunosorbant assay. Vet. J. 155: 171–175.

131. Williams, E. S., S. L. Anderson, J. Cavender, C. Lynn, K. List, C. Hearn, and M. J. G. Appel. 1996. Vaccination of black-footed ferret (*Mustela nigripes*) × Siberian polecat (*M. eversmanni*) hybrids and domestic ferrets (*M. putorius furo*) against canine distemper. J. Wildl. Dis. 32: 417–423.

132. Williams, E. S., and R. J. Montali. 1998. Vaccination of black-footed ferret × Siberian polecat hybrids against canine distemper with recombinant and modified-live virus vaccines. Proc. Annu. Wildl. Dis. Assoc. Conf. 1998: 107.

133. Williams, E. S., E. T. Thorne, M. J. G. Appel, and D. W. Belitsky. 1988. Canine distemper in black-footed ferrets (*Mustela nigripes*) from Wyoming. J. Wildl. Dis. 24: 385–398.

134. Wozencraft, W. C. 1993. Order Carnivora. *In:* Wilson, D. E., and D. M. Reeder (eds.). Mammal Species of the World, 2nd ed. Smithsonian Institute Press, Washington, D.C. Pp. 279–384.

135. Yamanouchi, K., Y. Yoshikawa, T. A. Sato, S. Katow, S. Kobune, K. Kobune, N. Uchida, and A. Shishido. 1977. Encephalomyelitis induced by canine distemper virus in non-human primates. Jpn. J. Med. Sci. Biol. 30: 241–257.

136. Yoshikawa, Y., F. Ochikubo, Y. Matsubara, H. Tsuruoka, M. Ishii, K. Shirota, Y. Nomura, M. Sugiyama, and K. Yamanouchi. 1989. Natural infection with canine distemper virus in a Japanese monkey (*Macaca fuscata*). Vet. Microbiol. 20: 193–205.

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