Network for wildlife health surveillance in Europe

Diagnosis Card

Canine Distemper

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Etiology

Canine Distemper is caused by a single-stranded, negative sense RNA virus belonging to the genus *Morbillivirus*, within the family Paramyxoviridae. This virus is related to the etiologic agents of measles, peste des petits ruminants and rinderpest and more closely to phocine distemper virus in seals, marine mammals morbilliviruses and the Morbillivirus responsible for the infection in horses (Hendra virus).

CDV genome encodes six structural proteins: phospho- (P), nucleocapsid (N), large polymerase (L), matrix (M), fusion (F) and hemagglutinin (H) proteins. Phylogenetic analyses based on the H sequence revealed at least 12 distinct lineages distributed worldwide. The hemagglutinin protein is crucial, regulating the interaction between the virus and the host cell and the subsequent cell infection and viral replication.

The virus is characterized by limited resistance in the external environment and to U.V. It is extremely susceptible to high temperatures (being inactivated at 50-60°C for 30 minutes) and drying. It is also easily inactivated by common disinfectants (chloroform, formalin, phenol, quaternary ammonium salts). Survival time increases in cold climates: at temperatures close to 0°C (0-4°C) it can survive in the environment up to several weeks. At temperatures below 0 °C the virus is relatively stable, surviving at - 65°C up to 7 years.

Affected species (wildlife, domestic animals, humans)

In the order Carnivora it has been reported in Canidae (e.g. dog, fox, coyote, wolf, jackal, dingo), Mustelidae (e.g. badger, ferret, mink, marten, polecat), Procyonidae (e.g. raccoon), Phocidae (e.g. Siberian seal), Viverridae (e.g. mongoose), Felidae (e.g. cheetah, lion, jaguar, ocelot, lynx), Ursidae (e.g. brown bear) and Hyaenidae (e.g. Hyena spp.). Carnivora represent the order most commonly and more heavily impacted by the virus, both clinically (individuals) and demographically (populations). The increased circulation of CDV in European wild animals might jeopardize endangered or vulnerable species such as wolves (*Canis lupus*), golden jackals (*Canis aureus*) and lynxes (*Lynx lynx; Lynx pardinus*) and could also become a potential danger for the domestic dog population. CDV has been also found in Artiodactyla (fam. Tayassuidae), Primates (fam. Cercopithecidue) and rodents (fam. Sciuridae).

Considering the constant expansion of the host spectrum of this virus, widely observed during the last decades, adapting to new terrestrial and aquatic animal species including seals, cetaceans and felines, it might be expected that the number of species actually susceptible is much wider than those known to date. However, the epidemiology and possible impact of the virus on individuals and populations remain difficult to assess in many cases and it might be dependent on a previous relatively recent exposure of the affected population to the virus (presence of antibodies), the animals' immune status and/or the specific virulence of the CDV strain involved.

Epidemiological characteristics and disease course

Transmission occurs mainly through inhalation, by the susceptible animal, of the virus contained in the aerosol particles shed by an infected animal. However, the oral route is also possible. For transmission to take place effectively, it is therefore necessary either exposure to the aerosol released by an infected animal or direct contact between infected individual and susceptible host (for example through sniffing

and/or licking). The virus is in fact shed by the infected animal through oculo-nasal secretions and transmission is generally favored by low temperatures (which increase the resistance of the virus in the external environment) and by high concentrations of susceptible animals (especially of young animals). In the acute phase of the disease, however, CDV is also present in feces, urine and several other tissues (for example, in nervous tissue). Following the infection, an animal can transmit the virus up to 60-90 days, although shorter times are more frequent.

Clinical signs

In the dog, for which the most data are available, the time lag between infection and the appearance of clinical signs can be very short (3-7 days). Longer incubations (> 4 weeks) are also reported in the literature.

Once inhaled, the virus localizes in local (tonsils and retropharyngeal lymph nodes) and systemic (spleen, thymus, bone marrow) lymphoid tissues where replication begins. A transient fever (with a peak between the 3rd and 6th day) accompanied by loss of appetite, slight depression, nasal and ocular secretions and tonsillitis is associated with the initial circulation of the virus. Between the 6th and 9th day of infection, the virus can reach the epithelial cells of most organs.

At this point, the evolution of the infection and the severity of the clinical picture are influenced by the virulence of the virus, the age of the animal and its immune response. If the animal is able to produce a strong immune response, it will develop a sub-acute form of the disease that will resolve relatively uneventfully. If, on the other hand, the immune response is relatively weak, the multisystemic variant of the disease, including the nervous form, will develop. Death can occur relatively quickly (2-4 weeks), in case of a relatively poor or inconspicuous immune response.

Specifically for wild carnivores, and namely for the red fox and mustelids, information on the picture and the clinical course is obviously much scarcer, by virtue of the elusiveness of these species. Most of the affected subjects in fact are found dead in the field. However, it is possible to observe in some cases, and especially in the fox, dyspnea, conjunctivitis with ocular discharge and finally nervous signs such as those described above. Nervous signs often represent an "alert" for the people, being indistinguishable from those of rabies. In free ranging animals, death could follow shortly after infection, not necessarily solely on the basis of a potential weak immune response, but also because of an obvious impairment of hunting for food because of the debilitating clinical signs of the disease, with consequent starvation and death. Finally, canine distemper virus may cause a severe immune suppression, which can last up to 7 weeks post infection, significantly compromising the chances of recover in animals not assisted during the disease, such is the case for free ranging animals.

Gross lesions

As a result of the epithelial localization, within the 10th day it is possible to highlight clinical signs referable to conjunctivitis or kerato-conjunctivitis with evident ocular discharge, respiratory (nasal secretions also purulent, cough, dyspnea, pneumonia), gastro-intestinal (diarrhea, including hemorrhagic diarrhea, vomiting) and integument associated (pustules in the dermis of the groin and inner plate of the thighs) clinical signs. This picture is often accompanied and worsened by secondary bacterial superinfections. Hypoplasia of the dental enamel and hyper-keratosis of the plantar pads and nose are typical signs of canine distemper (hard-pad disease). From the 20th day onwards, neurological signs may be present (circulating movements, changes in behavior, nystagmus, ataxia, paresis, partial or total paralysis, convulsions, myoclonus and spasms). Nervous signs can also be present on the 40th -50th day

In general, the course of the disease is variable, and also influenced by the onset of secondary infections; mortality fluctuates between 30% and 80% of those affected, and neurological sequelae are often observed in recovered animals.

Histological lesions

Histological lesions associated with canine distemper virus infection complement the gross signs described above. Classic respiratory involvement is associated with the development of an interstitial or broncho-interstitial pneumonia with commonly observed eosinophilic intracytoplasmic inclusions. The inclusions can be observed in any of the epithelial tissues affected along with cell necrosis. Bile ducts of the liver can also be affected. Additionally to the inclusions, a classic histological finding is the development of cell syncytia in the affected organs, more commonly in the lung, where their number is normally higher in canids (red fox) than in mustelids (badgers and martens). The neurological form of the disease is associated with obvious histological changes in the CNS, with either demyelinating changes (vacuolization of the white matter along with gliosis) or neuronotropic lesions with neuronal necrosis and prominent intranuclear eosinophilic inclusions, which, however, can be observed also in the glial cells. Lymphoid depletion, more evident in the spleen is another microscopic change observed in CDV infected animals.

Differential diagnosis

The neurological picture due to CDV is indistinguishable from that from rabies. Therefore, whenever it is observed, rabies should be considered. Laboratory differential diagnosis is mandatory in cases of animals showing neurological symptoms that have bitten or have been in close contact with humans, pets or livestock.

Similarly, the neurological signs show some overlapping with canine infectious hepatitis, caused by Canine adenovirus type 1. Ocular discharge, can also be observed. Again, supportive laboratory diagnostics with molecular methods (PCR) can discriminate between the two agents.

Criteria for diagnosis

The clinical picture and gross lesions are not necessarily pathognomonic and do not allow to make a conclusive diagnosis. Accordingly, a presumptive "field" diagnosis should be limited to situations of known presence/endemicity of the disease, and in such a context at least the early cases should be submitted to laboratory confirmation.

The depth and extent of laboratory diagnostics may vary according to the CDV epidemiological situation (absence, endemicity, cyclic epizootics…) and the investigative questions which need to be answered (simple disease detection, or lineage/sublineage identification).

Direct molecular diagnosis should be preferred, keeping in mind the clinical course of the disease: to maximize the probability of detection, sample should be taken from different organ systems (respiratory, digestive, urinary, nervous). Where programs for passive surveillance on wild rabies are in progress, CDV testing of the brain of carnivores found dead/diseased can be a helpful strategy for CDV monitoring but importantly, the central nervous system is affected in the later stages of the disease: accordingly, animals infected in the early phases could be frequently diagnosed as false negative.

Recommended diagnostic method(s) and preferred samples (incl. recommended amount and appropriate storage)

Laboratory diagnosis can be based on several tests, including immunofluorescence (IF) and virus isolation on cell lines, although these methods are not as sensitive as molecular testing and time-consuming. Therefore, reverse transcriptase polymerase chain reaction (RT-PCR) and real-time RT-PCR usually targeting the NP (nucleoprotein) are the recommended diagnostic approaches, being both sensitive and specific. Characterization of the various CDV lineages and distinction between field and vaccine CDV strains is based on H (hemagglutinin) gene sequencing.

Main diagnostic specimens of choice are fresh or frozen samples collected from nasal swabs, lungs, or brain. Samples can be taken also from intestine, stomach and urinary bladder.

EWDA proposed harmonized protocol (for harmonization at large scale)

RT-PCR/real-time RT-PCR targeting the NP (nucleoprotein) and/or the H (Hemagglutinin) genes for diagnostics. It is advisable to periodically perform a full length hemagglutinin gene sequencing on a selection (e.g. by species and geographical location) of the positive samples, in order to monitor genetic variation of the viral strains and evolution within and between lineages.

Laboratories that can be contacted for diagnostic support

Centre for Fish and Wildlife health (FIWI), Department of infectious diseases and pathobiology, Vetsuisse Faculty, University of Bern, Länggassstrasse 122, 3001-Bern-CH. fiwi.wilddiagnostik@vetsuisse.unibe.ch

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Recommended literature

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