

# Canine distemper virus

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# Canine distemper virus (CDV),

- Currently known as Canine morbillivirus
- family *Paramyxoviridae*, genus *Morbillivirus*
- Etiological agent of canine distemper
- CDV particles are pleomorphic, frequently spherical, enveloped
- Have non-segmented single negative-stranded RNA (ssRNA)
- CDV genome structure includes six transcription units (N-P-M-F-H-L), contribute to the formation of the eight proteins

- The CDV envelope involves:
  - fusion (F) and hemagglutinin (H) proteins
  - A membrane associate protein M
  
- H glycoprotein facilitates virus binding to host cell membrane
  
- F protein achieves the viral and the host membrane's fusion, enabling the viral RNP's entrance into the cytoplasm
  
- Based on sequence analysis of the H gene, at least seven distinct lineages of canine distemper are recognized worldwide :
  - Asia-1, Asia-2, America-1, America-2, Arctic-like, European wildlife, Europe

# Canine distemper

- Highly contagious acute febrile disease of dogs
- Edward Jenner first described the course and clinical features of the disease in 1809
- Carre demonstrated its viral etiology in 1906
- Associated with multiple cell tropism (epithelial, lymphoid and neurological)
- leads to a systemic infection including respiratory, digestive, urinary, lymphatic, cutaneous, skeletal, and central nervous system (CNS) diseases

# Host range of canine distemper virus

Includes families

- Canidae (dog, dingo, fox, coyote, jackal, wolf)
- Procyonidae (raccoon, coatimundi, panda)
- Mustelidae (weasel, ferret, fishers, mink, skunk, badger, marten, otter)
- Felidae (lions, leopards, cheetahs, tigers)

# Transmission

- Canine distemper virus is shed in all secretions and excretions
- Transmission mainly via direct contact, droplet, and aerosol
- Young dogs are more susceptible
- 4 - 6 months of age more susceptible, after puppies have lost their maternal antibody

**Virus Location**

Aerosol

Tonsils, bronchial lymph nodes

Also thymus, spleen, marrow  
retropharyngeal lymph nodes

Multiplication in lymphoid system, also  
intestinal lamina propria, Kupffer's cells

Mononuclear cells in blood  
**(Viremia)**

**Inadequate** host immunity  
(**POOR** antibody response)

Widespread invasion of all  
epithelial tissues & CNS

No antibody  
response

**Severe multi-  
systemic**

Virus persists  
in tissues

Death

Recover

Low antibody  
response

**Mild or  
inapparent**

Virus cleared (may  
remain in lungs, skin)

Recover (may shed  
virus up to 60 days)

CNS signs

**Adequate** host immunity  
(**GOOD** antibody response)

Virus may enter CNS

Good antibody  
response

**Inapparent  
illness**

Low prevalence  
of CNS signs

# Pathogenesis

- CDV is considered a multi-cell pathogen
- ability to infect three different types of host cells including epithelial, lymphoid, and neurological cells
- first replicates within mononuclear cells in the tissues of the upper respiratory tract, and it then quickly spreads to the tonsils and regional lymph nodes
- After multiplication in regional lymph nodes, the virus spreads systemically via infected B and T cells
- resulting in virus amplification and the initiation of primary viremia



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- Primary cell-associated viremia coincides with the first bout of fever and results in infection of lymphoid tissues throughout the body
- The newly infected blood mononuclear cells lead to a secondary viremia that is associated with the second fever peak
- Dissemination of the virus to distal sites- liver, skin, gastrointestinal tract, genitals, and respiratory mucosal surfaces
- results in the virus' spreading and subsequent transmission to uninfected individuals

- Infection of the central nervous system occurs relatively late in the course of infection
- Virus infects both neurons and glial cells within the CNS and may persist there for very long periods
- Occurs only in animals with delayed or insufficient immune responses
- Old dog encephalitis is apparently associated with prolonged persistence of the virus in the brain

# Clinical signs

- Depend upon the strain of the virus, the host age, immune status, and levels of environmental stress
- Dogs with mild disease
  - Fever
  - Upper respiratory tract infection
  - Listless
  - Inappetant
  - Bilateral serous ocular discharges can become mucopurulent
  - Coughing
  - Labored breathing

## In severe generalized distemper

- Infected dogs first develop a fever after an incubation period of 3-6 days
- Second febrile response-
  - Anorexia
  - serous to mucopurulent nasal discharge
  - conjunctivitis
  - depression



### Some dogs show primarily respiratory signs

- respiratory signs reflect inflammation and injury to the upper respiratory tract and large airways
- Causing a productive cough, followed by bronchitis and interstitial Pneumonia

## Others develop gastrointestinal signs

- manifested by vomiting and watery diarrhea
- The duration of disease varies, often depending on complications caused by secondary bacterial infections

## Central nervous system signs develop in some infected animals

- usually occur at 13 weeks after the onset of acute signs
- may also appear after inapparent subclinical infection
- Seizures (so-called chewing gum fits and epileptic seizures)
- cerebellar and vestibular signs
- paraparesis or tetraparesis with sensory ataxia and myoclonus

- Neurologic signs leads to a poor prognosis
- surviving dogs may have permanent central nervous system sequelae
- So-called **old dog encephalitis**- chronic and slowly progressive neurologic disease caused by canine distemper infection in adult dogs
- Hyperkeratosis of foot pads (**“hard pad disease”**) and nose also occurs in some dogs, likely as a result of epithelial damage caused by the virus

# Lesions

- Puppies with distemper develop:
- pneumonia, enteritis, conjunctivitis, rhinitis, and tracheitis
- lungs edematous, bronchointerstitial pneumonia with necrosis of the epithelium lining, thickening of alveolar walls
- Secondary bacterial bronchopneumonia common consequence

## Central nervous system:

- variable, depending on duration of infection & infecting virus strain
- demyelination, neuronal necrosis, gliosis and nonsuppurative meningoencephalomyelitis

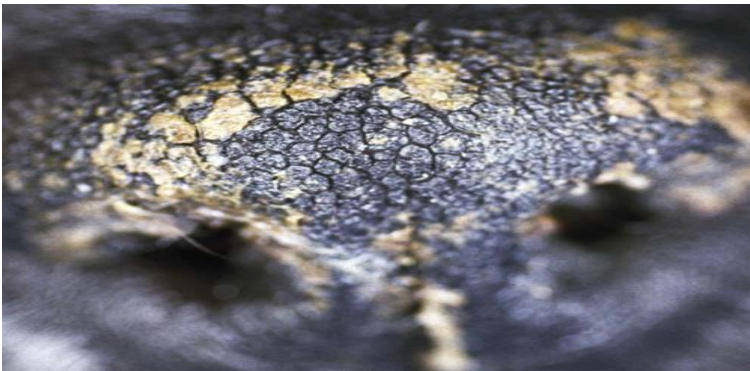
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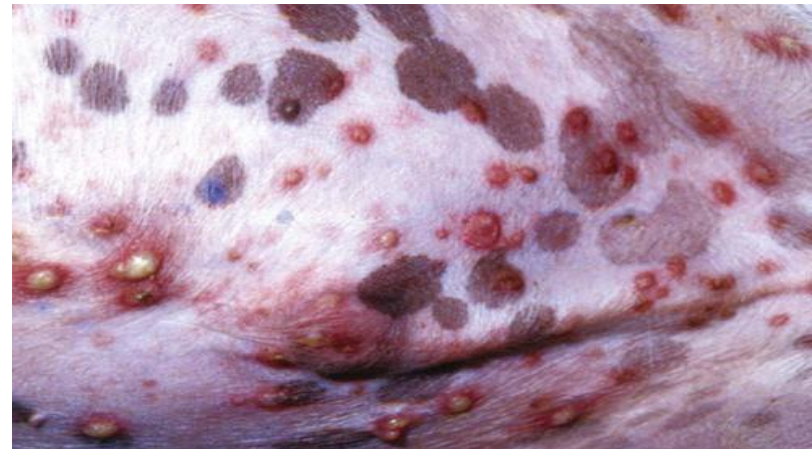
Enamel hypoplasia characterized by irregularities in the dental surface in an older dog that survived neonatal distemper



Digital hyperkeratosis ("hard pads") in a dog



Nasal hyperkeratosis in a dog with systemic distemper



Pustular dermatitis in a puppy with canine distemper



- Acidophilic inclusions may be present
- in the nuclei and cytoplasm of infected astrocytes
- in epithelial cells in the lung, stomach, renal pelvis, and urinary bladder
- Canine distemper virus infection of neonates can result in:
  - failure of enamel development of adult teeth (odontodystrophy)
  - metaphyseal osteosclerosis in long bones

## Transplacental Infection

- Young puppies infected transplacentally may develop neurologic signs during the first 4 to 6 weeks of life
- Depending on the stage of gestation at which infection occurred, abortions, stillbirths, or the births of weak puppies can occur

## Combined Infections

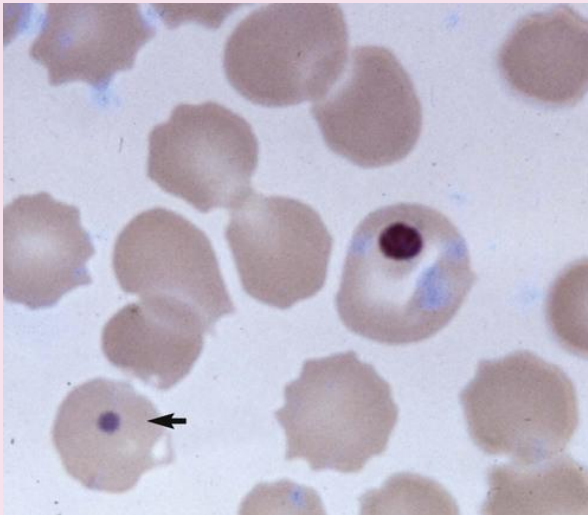
- Immunosuppression caused by or responsible for systemic CDV infection can be associated with combined opportunistic infections

# Diagnosis

- A characteristic history of a 3- to 6-month-old unvaccinated puppy with a compatible illness supports the diagnosis

## Clinical Laboratory Findings

- lymphopenia caused by lymphoid depletion
- Intracytoplasmic distemper inclusions- early phase of disease by examination of stained peripheral blood films



Distemper inclusion in an erythrocyte from a peripheral blood film

## **Radiology**

- Thoracic radiography- an interstitial lung pattern in early cases of distemper
- An alveolar pattern is seen with secondary bacterial infection and more severe bronchopneumonia

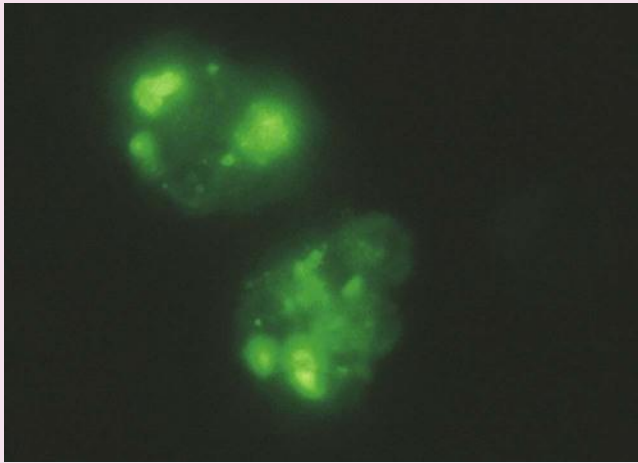
## **Cerebrospinal Fluid Analysis**

- Intracytoplasmic inclusions can be found in CSF cells
- IFN levels increased in the CSF of dogs with acute and chronic distemper encephalitis
- Increased anti-CDV antibody in CSF

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## Immunofluorescent techniques

- performed on cytologic smears prepared from conjunctival, tonsillar, genital, and respiratory epithelium
- also can be performed on cells in CSF, blood (buffy coat), urine sediment, and bone marrow



Immunofluorescent staining of CDV antigen in CSF cells

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- **Immunohistochemistry**

using fluorescent or peroxidase conjugates,  
on frozen sections of biopsy or necropsy specimens.  
CDV antigen detected in biopsy specimens of nasal  
mucosa, footpad epithelium, and haired skin of the  
dorsal neck region

Tissues collected from dogs that died from distemper  
should include spleen, tonsils, lymph nodes, stomach,  
lung, duodenum, bladder, and brain.

### Serological detection:

- by virus neutralization, ELISA or indirect immunofluorescence

### Virus isolation :

- Urinary bladder and brain are suitable postmortem specimens for virus isolation, cells from the buffy coat of heparinized blood
- Can be done on cell lines expressing the CD150 molecule
- After initial isolation, on primary dog lung cells or conventional cell lines, including MadinDarby canine kidney or Vero cells

### RT-PCR tests:

- Conjunctival swabs, blood mononuclear cells, any tissue sample that includes epithelium, and urine

# Control

- based on adequate diagnosis, quarantine, sanitation, and vaccination
- The virus relatively fragile, susceptible to standard disinfectants
- Modified live vaccines, administered usually after 12 weeks of age (maternally-derived antibody decline)

Most CDV vaccines:

- egg-adapted or avian cell culture-adapted virus (Onderstepoort strain); safer
- canine cell culture-adapted virus (Rockborn strain), post-vaccinal encephalitis occasionally