CANINE DISTEMPER

(Carre's Disease; Hard Pad Disease; Old Dog Encephalitis)

Canine distemper is a highly contagious, serious, systemic disease of dogs, caused by a **morbillivirus**. The disease is worldwide in distribution, and is characterized by a **diphasic (biphasic) fever**, leukopaenia, gastrointestinal and respiratory catarrh, and usually pneumonic and neurological complications. The disease is common in Dogs and also occurs in Wolf, Jackal and Fox. The virus is also pathogenic in ferrets, raccoons, big cats, and other animal species.

The origin of the word "distemper" is from the Middle English *distemperen*, meaning to upset the balance of the humors, which is from the Old French *destemprer*, meaning to disturb.

Canine distemper virus affects nearly all body systems. Puppies from 3-6 months old young dogs are particularly susceptible and respiratory and digestive signs predominate. Neurologic signs may occur later in the clinical course but many dogs die before these signs develop. Seizures are the most common neurologic manifestation.

Etiology:

Canine distemper virus, or CDV, is a **morbillivirus** of **Paramyxoviridae**, closely related to the viruses of measles and rinderpest. The fragile, enveloped, single-strand RNA virus. It is relatively unstable outside the host.

Spread

CDV spreads through aerosol droplets and through contact with infected bodily fluids, including nasal and ocular secretions, feces, and urine. It can also be spread by food and water contaminated with these fluids. Incubation period is **5 Days** and virus has affinity for **Lymphatic and Epithelial Tissues** (lungs, GIT, Urinary tract & Skin) and **the CNS** (including Optic nerve & Eye)

Pathogenesis

Virus is Pantropic & infects tissues of all 3 germinal layers. Following aerogenous Infection that virus infects Alveolar Macrophages and Monocytes of Respiratory system & Tonsils .After initial viral replication in **epithelium and lymphatic tissue of the respiratory tract,** the virus first appears in **bronchial lymph nodes and tonsils,** 2 days after exposure. Virus spreads through lymphatics and blood to other lymphoid tissues. It is then that the **first-round of fever / viremia** appears after 7-8th Day of incubation and ,results in infection of all lymphatic tissues (incl. tonsils, bronchial lymph

nodes), which is often accompanied by a low TLC (**Lymphocytopenia**) as well as **Thrombocytopenia**. These signs may or may not be accompanied by **Anorexia**, a runny nose, and discharge from the eye

This first round of fever recedes rapidly within 96 hours, and then a second round of fever begins around the 11-12th day and lasts at least a week. **Respiratory, Gastrointestinal and Urogenital problems tend to follow** with virus replication in these tissues, and it may become complicated with secondary bacterial infections. Virus spreads hematogenously to CNS and **Inflammation of the brain and spinal cord (poliomyelitis; encephalitis**) subsequently follows. Astrocytes and oligodendrocytes are considered target cells in CNS. Viral replication and consequent direct damage to neurons and astrocytes AND indirect damage to oligodendroglial cells result in Spongy lesions (status spongiosus), astrocyte hypertrophy and extensive demyelination of neurons. Macrophages, which are very numerous in these brain lesions, ingest immune complexes and infected cells. As a result, they release free radicals and other toxic products. It is these toxic products that damage nearby cells, especially oligodendroglia, and thus cause demyelination.

A **thickening of the footpads (Hard Pad)** sometimes develops, and **vesicular pustular lesions on the abdomen / thighs** usually develop. Neurological signs typically are found in the animals with thickened footpads from the virus

In very few dogs, which recover, the virus **remains latent** in the brain and causes "**Old Dog Encephalitis**", almost a Year later. The mechanism by which "old dog encephalitis (ODE)" develops is not clear. It is believed that the distemper virus remains suppressed in the central nervous system, and following some unknown stimulus, causes defective replication and such defective virus causes ODE.

Signs

Exposure of susceptible dogs to the virus results in **(i)** an **Acute Transient Fever**, which appears after 7-8th Day of incubation and there may be a leukopenia (especially **Lymphocytopenia**) and /or **Anorexia** at this time, which may go unnoticed. Within 96 hours, body temperature usually drops rapidly to normal levels. It remains normal up to the 11-12th Day, when it climbs again to a second peak and this **Diphasic (Biphasic) Fever Curve** is a characteristic feature of the disease.

(ii) It is accompanied by Coryza, serous nasal discharge, mucopurulent ocular discharge, purulent conjunctivitis, and bronchitis occur in varying degrees. Diffuse Interstitial Pneumonia / secondary Bronchopneumonia may occur. **(iii)** GI and Respiratory signs, typically complicated by bacterial infections, may follow and Persistent

coughing, dyspnoea, vomiting, and diarrhea is noticed. Following these systemic manifestations,

(iv) Encephalomyelitis occurs. **Classic Neurologic signs include:**

- Myoclonus (localized involuntary twitching of group of muscles) that includes (i) **Chorea / Hyperkinesia** (nervous infliction marked by muscle twitching) and (ii)"**Ties**" (spasmodic muscular contractions inv. Face/head/neck or shoulder muscles)
- Convulsions, including salivation and "**Chewing-gum Seizures**" (focal seizures involving biting movements of the mandible) movements of the jaw.

Other neurologic signs include chewing movements, excessive salivation, incoordination, circling, nystagmus (involuntary movement of the eyeball), torticollis (twisted neck), head tilt, paresis to paralysis and focal to generalized seizures. Blindness and paralysis are less common.

(v) Usually, Lymphocytopenia and Thrombocytopaenia also develop. Dogs surviving the acute phase may have **Hyperkeratosis of the footpads/digital pads** ("**Hard Pad Disease**"). Rarely, Pustular dermatitis (vesiculo-pustular lesions) are seen.

(vi) In a small number of dogs, which recover, the virus remains latent in the brain and causes "**Old Dog Encephalitis**", almost a Year later. **Chronic distemper encephalitis** (Old Dog Encephalitis, [ODE]) is a rare form of canine distemper that appears to be manifestation of chronic viral infection after years of latent brain infection. It is marked by ataxia (muscular incoordination), compulsive (irresistible) movements, such as head pressing and incoordinated hypermetria.

Lesions

In cases of acute to peracute death, exclusively respiratory abnormalities may be found. Histologically, canine distemper virus produces necrosis of lymphatic tissues, interstitial pneumonia, and cytoplasmic inclusion bodies in respiratory, urinary, and GI epithelium. Depending on the degree of secondary bacterial infection, bronchopneumonia, enteritis, and skin pustules also may be present.

(i) In the **Respiratory System**, catarrhal or mucopurulent nasopharyngitis, Microscopically, characteristic Eosinophilic Intra-Cytoplasmic / intra-Nuclear Inclusion bodies, that are round-ovoid, homogenous and sharply demarcated, and are often seen in epithelial cells associated with the exudate. Principal lesion in the **Lung** is diffuse **Interstitial Pneumonia**, but secondary bacterial infection can lead to *purulent bronchopneumonia* in which bronchi and adjacent alveoli are filled with neutrophils and tissue debris. In some cases, multinucleated giant cells form in the bronchial lining,

alveolar septa, and freely in the alveoli. This form of giant-cell pneumonia is similar to that associated with measles in humans and monkeys.

(ii) **In GIT**, the stomach and intestines contain large numbers of cytoplasmic inclusions in the lining epithelium. Apart from these inclusions, few lesions are observed.. No significant lesions occur in the liver. However, inclusions may be present in the biliary epithelium.

(iii) The **Urinary Epithelium**, particularly of the renal pelvis and bladder, contain congested vessels, and microscopically, cytoplasmic inclusion bodies. **Thymic atrophy** is a consistent postmortem finding in infected young puppies.

(iv) In the **Skin**, particularly of the abdomen, a vesicular and pustular dermatitis may occur. The vesicles and pustules are confined to the Malpighian layer of the epidermis (**Str. spinosusm & Str basale as unit**). There is usually some congestion of the underlying dermis, and occasionally lymphocytic infiltration. Cytoplasmic inclusion bodies may be present within epithelial cells of sebaceous glands. On the foot pads, extensive proliferation of the keratin layer of the epidermis (Hyperkeratosis) results in a clinically recognized lesion, which is called "hard-pad disease". However, this lesion can develop in other diseases (e.g., toxoplasmosis), and is therefore not specific for canine distemper. **Hyperkeratosis of the nose and footpads** is often found in dogs with neurologic manifestations.

(v) In the **Central Nervous System**, the virus has an affinity for the myelinated portions of the brain and spinal cord. Lesions most commonly represent extensive **chronic progressive demyelination** of CNS, a **Polioencephalomyelitis**. The structures most constantly affected are the cerebellar peduncles, the myelinated tracts of the cerebellum, and the white columns of the spinal cord.

Sharply defined holes (vacuoles) of irregular size give the affected tracts a "spongy" appearance (status spongiosa). Often, Lymphocytes in the Virchow-Robin spaces around nearby vessels and sometimes, "gitter" cells gather around areas of necrosis in white matter. **GEMISTOCYTES** (Gemistocytic astrocytes - a swollen, reactive astrocyte) are prominent in the exudate, contain intranuclear inclusions and are also characteristic. There is pyknosis, chromatolysis, gliosis, and neuronophagia in neurons.

(vi) **In** the **RETINA**, there is **Retinal atrophy** with congestion, oedema, perivascular cuffing with lymphocytes, and gliosis. **Neuritis** of the **Optic Nerve** with demyelination and gliosis is also seen.

(vii) Of particular interest in clinical diagnosis of distemper is the finding that cytoplasmic / nuclear inclusions appear in some circulating neutrophils (blood) , as well as epithelium of Respiratory, GIT, Urinary tract and skin of affected dogs.

Diagnosis

Any biphasic febrile condition in dogs with multi-systemic manifestations and neurologic sequelae justifies a clinical diagnosis of canine distemper.

Diagnosis can be made on the basis of a **(i)** history of the typical clinical disease, and **(ii)** the demonstration of characteristic lesions and **(iii)** Clinical diagnosis by **BOTH intra-cytoplasmic / intra-nuclear inclusion bodies** in bronchial, gastric and urinary epithelium and /or Peripheral Blood, mostly during the acute viremic phase only but their absence does not rule out the diagnosis of distemper, **(iv)** Immunological staining techniques, or **(v)** viral isolation and identification is preferred to confirm the diagnosis.

Distemper in dogs **should be differentiated from other systemic infections like:**

(i) Leptospirosis, (ii) Infectious Canine Hepatitis, (iii) Toxoplasmosis (for Hard pad), and (iv) Rocky Mountain Spotted Fever