Paramyxoviridae

Newcastle Disease (Ranikhet Disease), Peste des petits ruminants (PPR), Canine Distemper (CD)

Greek '**Para**'- by the side of and '**myxa**' mucus

Group V: Negative sense ssRNA viruses

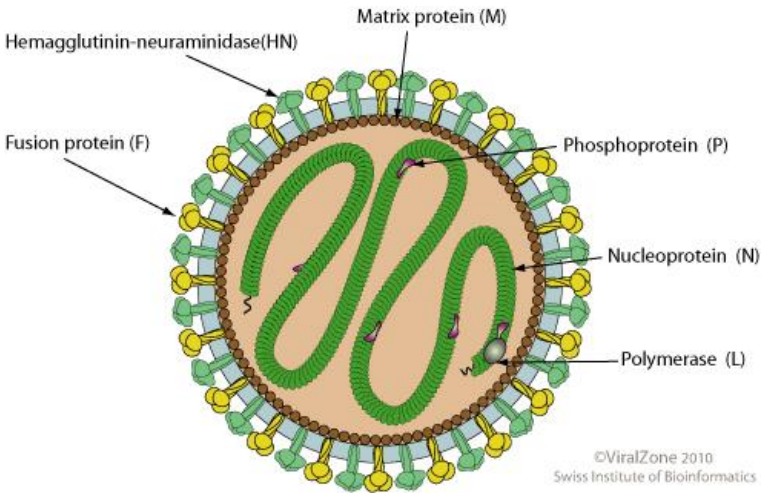
Order: *Mononegavirales*

Family: ***Paramyxoviridae***

Genus:		**Important Species**
	Aquaparamyxovirus	
	Avulavirus	*Newcastle disease virus*
	Ferlavirus	
	Henipavirus	
	Morbilivirus	*Caniner Distemper virus*
		Peste des petits ruminants virus, Measles virus
	Respirovirus	
	Rubulavirus	*Human Rubula virus* – Mumps virus

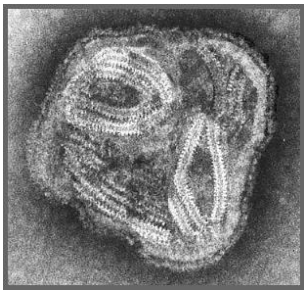
Properties of Paramyxovirus

- Virions are **enveloped**
- **Size: 150-300 nm in diameter**.
- Shape: **Pleomorphic** (**spherical as well as filamentous** forms occur).
- Covered with large peplomers
- Virion contain a "**herringbone-shaped**" **helically symmetrical** nucleocapsid
- Virion envelope contains **two viral glycoproteins Haemagglutinin & Neuraminidase**.
- Genome consists of a **single linear molecule of negative sense,single-stranded RNA**,
- **Cytoplasmic replication**, **Syncytium formation**, **intracytoplasmic and intranuclear inclusion bodies** (genus Morbillivirus)



"herringbone-shaped"

TEM of Paramyxovirus ⇨



Ranikhet Disease / Newcastle Disease

History

First seen-Java, Indonesia in 1926 and in the same year it was reported in **Newcastle, England** in 1926.
In India - First recorded by Edwards in1927 in **Ranikhet**, **Uttaranchal, India**

The virulence of ND virus varies .
Based on the virulence the NDV isolates can be divided into three groups viz.

Lentogenic (Lasota, Hitchner, England F)
Mesogenic (**R2B Mukteshwar**) &
Velogenic (Virulent ND) strain.

The **intracerebral pathogenicity index** (ICPI), is the World Animal Health Organization protocol for defining NDV pathogenicity, consists of inoculating virus into the cerebrum of one-day-old SPF (or NDV-antibody free) chickens and deriving a clinical weighted score that ranges from 0.0 to 2.0. Scores ≥0.7 classify a strain as virulent (vNDV).
Typically, ICPI values for mesogenic strains are from 0.7 to 1.5, and from 1.5 to 2.0 for velogenic strains

Physical Properties of Ranikhet Disease virus

- **Temperature**: Inactivated by 56°C/3 hours, 60°C/30
- **pH**: Inactivated by acid pH
- **Chemicals**: Ether sensitive
- **Disinfectants**: Inactivated by formalin and phenol
- **Survival**: Survives for long periods at ambient temperature, especially in faeces

Transmission Ranikhet Disease

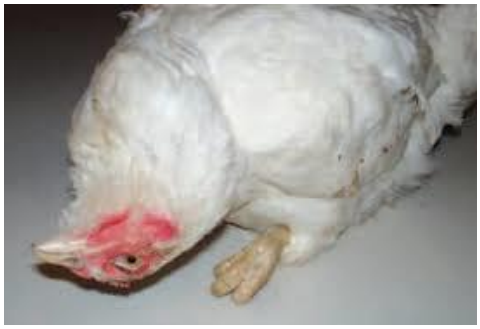
- Direct contact with faeces and respiratory discharges
- Contamination of the environment
- Feed, water
- Equipment
- Human clothing
- Contaminated or
- incompletely inactivated vaccines

Pathogenesis Ranikhet Disease

1. Virus replicates in respiratory and intestinal respiratory tract
2. Within 24 hours virus spread via blood
3. Viraemia
4. Spleen, bone marrow-other target organs proventriculus, gizzard
5. Cross brain barrier-destroy respiratory center in brain-paralysis & death.

Clinical Signs Ranikhet Disease
Incubation period : 4-6 days

Viscerotropic velogenic/Asiatic Form ND (Doyle's Form)



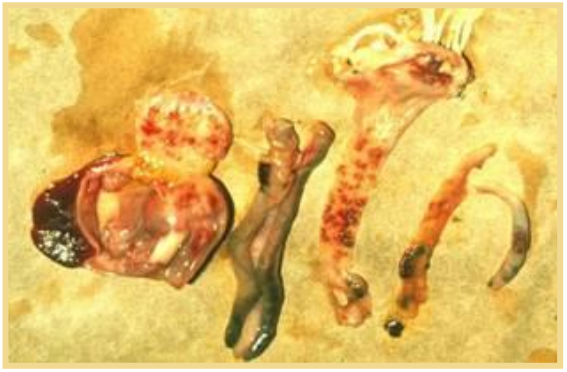
Hyperpnea,greenish blood stained diarrhea,
dehydration, tremor, torticollis and paralysis of wings or leg.
Haemorhagic lesions are prominent in the digestive tract.
Mortality is close to 90%.
Neurotropic velogenic ND (Beach's **Form)**
Severe respiratory and nervous signs predominate.
Coughing and gasping,
Head tremors, wing and leg paralysis and twisted necks.
Depression, loss of appetite and a drop in egg production also occur.
Mortality: 10% - 50% of adults .

Mesogenic ND (Beaudette's form)
Mainly respiratory signs, with coughing but no gasping.
Depression, loss of weight and decrease in egg quality and production for up to 3 weeks.
Nervous signs may develop late in the course of the disease and death rates are about 10%.

Lentogenic ND (Hitchner's Form)
Symptoms are mild or absent and include mild respiratory signs, impaired appetite and a drop in egg production.
No nervous signs occur and deaths are usually negligible.

Edema of head, especially around eyes
Greenish-dark watery diarrhea
Respiratory and neurological signs
Signs vary with species and virulence

PM lesions Ranikhet Disease
Indistinguishable from highly pathogenic avian influenza
Hemorrhagic internal lesions
-Tracheal mucosa
-Proventriculus
-Intestinal mucosa-caeco-colic jnction



Diagnosis Ranikhet Disease

1. Isolation & Identification of the agent

Samples: Tracheal and cloacal swabs (or faeces) from live birds or from pools of organs and faeces from dead birds

Serological tests: Clotted blood samples or serum

Inoculation of 9-11-day-old embryonated chicken eggs –Allantoic cavity route.

Harvest allantoic fluid after death of embryo and subject it to HI test using known antisera against **Ranikhet Disease virus.**

2. Pathogenicity assessment

Plaque test in chicken embryo fibroblast cultures

Mean death time of embryonated chicken eggs

Intracerebral pathogenicity index in 1-day-old chickens

Intravenous pathogenicity index (IVPI) in 6-week-old chickens

3.Serological tests

Haemagglutination inhibition test, ELISA .

4.Molecular detection

Reverse Transcriptase-PCR

Preventiopn and control

- Strict biosecurity measures
- All in all out strategy
- Balanced feed, Clean water
- Regular vaccination

Vaccination

Broiler– 7^{th} day, 28^{th} day (**Lasota strain**)

Layer– 7^{th} day, 28^{th} day, 9 weeks (**Mukteshwar strain**),16^{th} week (**ND Killed Vaccine**) , 40^{th} week

Breeder – 7^{th}day, 28^{th}day, 9 weeks(**Mukteshwar strain**),16^{th}week (**ND Killed Vaccine**), 40^{th}week

Booster after every 10 weeks (**ND Killed Vaccine**)

**

Canine distemper

(Hard pad disease, Diphasic Fever)

Canine distemper is a contagious and serious disease caused by a virus that attacks the **respiratory, gastrointestinal and nervous systems of puppies** and dogs.
Canine distemper is a highly contagious acute febrile disease.

Canine distemper virus (CDV) is a paramyxovirus closely related to the measles and rinderpest viruses;
Canine distemper has been known since at least 17th century and has a worldwide distribution.

1746 Well-described in by **Antonio de Ulloa**
1905 Carre demonstrated the filterable agent in disease.
1926 Laidlaw and Dunkin confirmed the causative agent.

Physical Properties of Canine distemper virus

- Virus survives heating at 55 degree C for 30 minutes.
- Inactivated at 60 degree C for 30 minutes.
- pH stability- 4.5 to 9.0
- Inactivated readily by Formalin 0.1% for 1-2 hrs., 0.5 Phenol for 48-72 hours and 0.3% Chloroform for 10 minutes
- **Eleven distinct genetic lineages of CDV are recognized** worldwide, based on phylogenetic sequence analysis of the H gene.
- These CDV lineages are known as
- America-1, America-2, Arctic, Asia-1, Asia-2, Asia-3, Asia-4, Europe-1/South America-1, Europe wildlife, Rockborn-like, and Africa-1.
- Despite genetic differences among field strains of CDV, cross-neutralization studies show only minor antigenic differences.

Transmission Canine distemper

- Puppies and dogs most often become infected through **airborne exposure** (through sneezing or coughing) to the virus from an infected dog or wild animal.
- The virus can also be transmitted by **shared food and water bowls and equipment.**
- Infected dogs can shed the virus for months, and **mother dogs can pass the virus through the placenta to their puppies**. The virus may be transmitted *in utero* and may persist in the brain.
- Contact between **wild animals and domestic dogs** can facilitate the spread of the virus. The domestic dog has largely been responsible for spreading the disease to new geographic areas and for introducing canine distemper to previously unexposed wildlife.
- As human populations expanded, **increased domestic dog contact with wild carnivores** exacerbated the risk for disease transmission

Host Canine distemper

The disease occurs in a wide variety of terrestrial carnivores including:

Canidae (dog, fox, wolf, raccoon dog),
Mustelidae (ferret, mink, skunk, wolverine, marten, badger, otter),
Procyonidae (raccoon, coatimundi),
Viverridae (palm civet),
Ailuridae (red panda),
Ursidae (bear), and large **Felidae** (lions, tigers, leopards, cheetahs), as well as a few other mammals such as Asian elephants and some primates.

Domestic and feral dogs are considered to be the **main reservoir host species**. All dogs are at risk **but puppies younger than four months old and dogs that have not been vaccinated against canine distemper are at increased risk** of acquiring the disease.

CDV is a **serious threat to endangered wildlife** and this threat is expected to increase with increased encroachment of humans (along with their dogs) into undeveloped areas of the world.

Pathogenesis Canine distemper

1. Virus enters via respiratory or alimentary passage
2. Amplification of virus in reticuloendothelial cells
3. **Viraemia** (Lymphopenia)
4. **Increase in temperature** 3-6 days post infection
5. If immune response sets in, virus fail to infect epithelial tissues and viraemia ceases. If not
6. 10-18 days post infection virus infects epithelial cells of intestine,respiratory, urogenitalskin and exocrine endocrine glands
7. Second viraemia
8. **Rise of Temperature (Diphasic Fever)**
9. Neurotropic strains invade CNS (meningeal macrophages, neurons. Recovered dogs suffer from subacute diffuce sclerosing encephalomyelitis (Old Dog Encephalitis)
10. CDV is sheded in respiratory exudates, feces, saliva, urine, and conjunctival exudates for up to 90 days after natural infection.

Clinical signs Canine distemper

- Incubation Period: 3-7 days
- Initially, infected dogs will develop **watery to pus-like discharge from their eyes**. They then develop **fever, nasal discharge, coughing**, lethargy, reduced appetite, and vomiting.
- As the virus attacks the nervous system, infected dogs **develop circling behavior, head tilt, muscle twitches, convulsions** with **jaw chewing movements** and salivation ("**chewing gum fits**"), seizures, and partial or complete paralysis.
- In cutaneous form- Appearance of rashes, vesicular lesion, pustules on the ventral aspect of abdomen and inner side of thighs and causes **footpads to thicken and harden**,

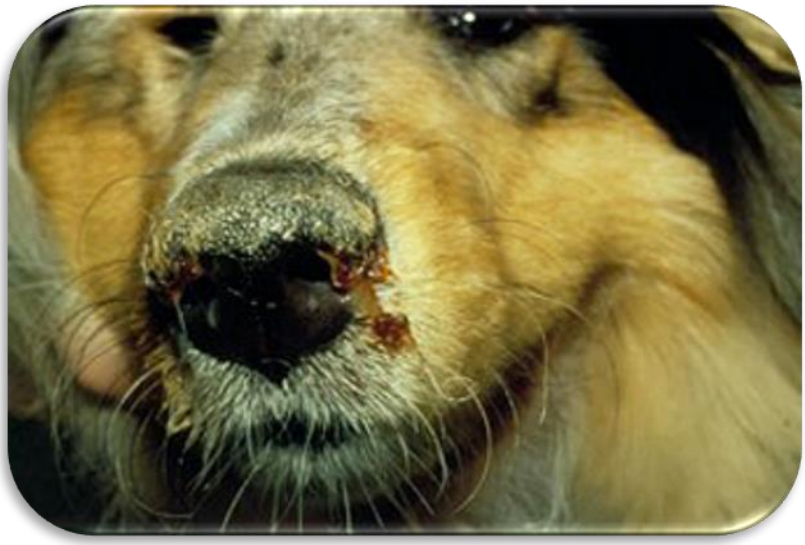
leading to its nickname "**hard pad disease**". **Nasal & Digital Hyperkeratosis**, -often found in dogs with neurological manifestations.

- In wildlife, infection with canine distemper **closely resembles rabies**.
- Distemper is often fatal, and dogs that survive usually have **permanent, irreparable nervous system damage**.

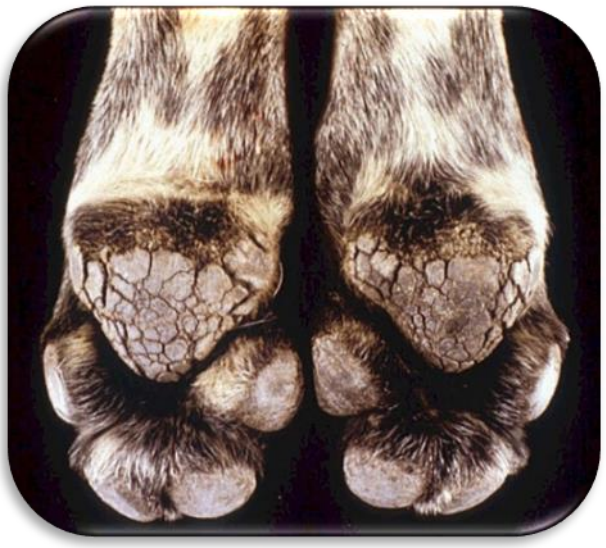
Abstract of clinical signs

- Respiratory
  - Nasal & Ocular Discharge
  - Coughing
  - Dyspnea
  - Pneumonia
- Gastrointestinal (GI)
  - Anorexia
  - Vomiting
  - "Distemper Teeth"
  - Diarrhea (May be bloody)
- Dermatological
  - Abdominal Pustules
  - Nasal & Digital Hyperkaratosis
- Ocular
  - Anterior Uveitis

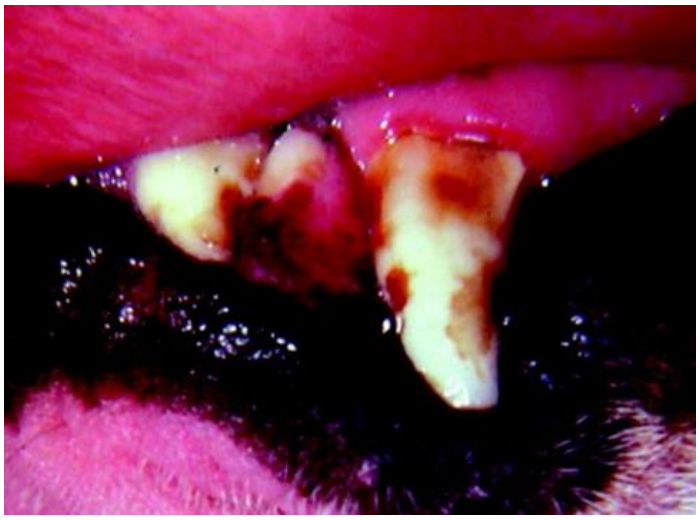
  (Inflammation of the front chamber of the eye; may cause the cornea to appear cloudy and/or cause changes in the appearance of the virus.)
  - Keratoconjunctivitis Sicca
  - Optic Neuritis
  - Retinal Degeneration
- Neurological
  - "Chewing Gum" Seizures
  - Weakness or Paralysis
  - Loss of Balance
  - Muscle Twitching
  - Hypersensitivity
  - Neck Pain
  - Behavioral Changes



Hyperkeratosis of nasal planum



Hyperkeratosis of foot pad

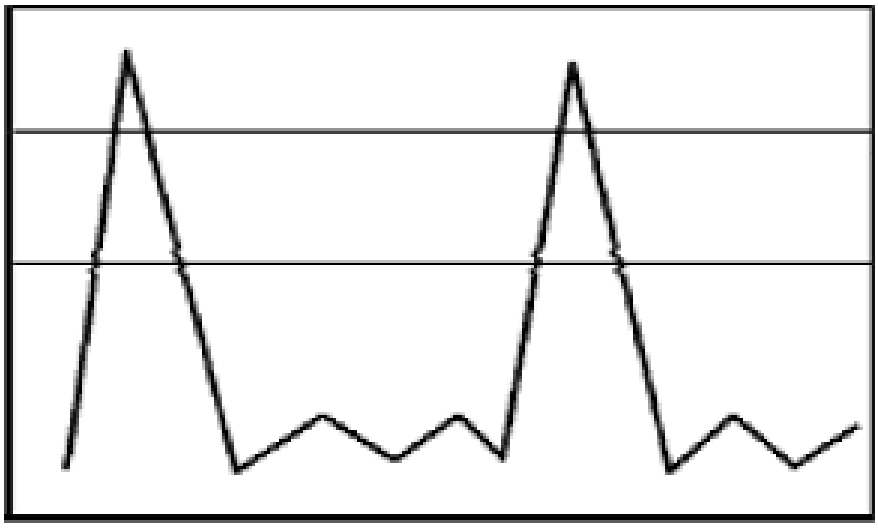


The pitted, discolored teeth that may result when young dogs are infected with distemper virus prior to the eruption of their permanent teeth.

Enamel hypoplesia

OLD DOG ENCEPHALITIS

Mucous secretion from conjuctiva
Ulceration of cornea.
Panopthalmitis-inflammation of the interior of the eye that also extends into the uvea and sclera.
Retinal atrophy of all layers.



3-4 th day High fever due to viraemia

11 th – 12th day

13 th day high fever

DIPHASIC FEVER CURVE

Diagnosis **Canine Distemper**

Material Collection:
Buffy coat cells are the most rewarding specimen for ante-mortem diagnosis of canine distemper.
6 ml of EDTA-blood from suspect distemper dogs.
If cerebral distemper is suspected, a CSF sample submitted along with serum (red top tube/clotted blood) can lead to a definitive diagnosis.

1) **Virus Isolation**: ero cells expressing canine signalling lymphocyte activation molecule (Vero.DogSLAM). Cytopathic effects (CPE) in the form of **syncytia formation** and cell necrosis were observed in 33 (20.4%) specimens within 24 h of inoculation and the presence of CDV was confirmed with the aid of the direct fluorescent antibody test and electron microscopy (EM).

2) **Immunofluorescence assay** (IFA) which looks for inclusion bodies on conjunctival scrapes, in urine sediment, in transtracheal washes and cerebrospinal fluid (with neurological signs).

3) **Blood tests (serology) look for antibodies** (titers) to distemper. It is usually necessary to take serial titers on 2 serum samples taken two weeks apart to detect rising titers as single titers do not have much diagnostic value. However, they can help to do risk assessment for exposed dogs in a shelter

4) **RT-PCR** (polymerase chain reaction) detects virus in respiratory secretions, CSF, feces, urine (depending on localization of virus). False positives are possible within 1-3 weeks of vaccination. Usually a puppy can get it's first Vaccination at 45 Days of Age..

Core Vaccination Schedule :
1st Vaccination : DHPP(Against Canine Distemper, Parvo, Hepatitis, Para Influenza) and Along with it Vaccination against leptospirosis is also given.
After 21 Days..
2nd Vaccination : Repeat Booster Dose of 1st Vaccination of DHPP and Lepto is given.
After 21 Days.
3rd Vaccination : Vaccination against Rabies is administered and 3rd Booster dose of DHPP is given. (90th Day)
After which every year the dog should be brought to the vet for an annual booster dose of Anti Rabies and DHPP Vaccination.

Vaccine	Primary Dose Puppy	Primary Dose Adult	Booster	Recommendation
Distemper	3 doses, 2-3-4 months	2 dose, 3-4 wk apart	Annual	Highly recommended for all ages

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For information

MEGAVAC®-7

single shot protection against multiple canine infectious agents

- Consistent with current Indian pharmacopoeia
- Cross-protection against CPV-2, CPV-2a and CPV-2b
- High quality, trusted efficacy and safety

Composition

- Canine Distemper Virus (Live) I.P
- Canine Contagious Hepatitis Virus CAV-2 (Live) I.P
- Canine Parainfluenza Virus (Live) I.P
- Canine Parvo Virus (Live) I.P
- Canine Contagious Hepatitis Virus (CAV-1), Inactivated I.P
- *Leptospira canicola* inactivated I.P
- *Leptospira icterohemorrhagiae* inactivated I.P

Dosage

1 mL S/C or I/M

Vaccination Regimen

- Primary Vaccination : 2 Months of age
- Booster Dose : 3 Months of age
- 2nd Booster Dose : 4 Months of age
- Re-vaccination : Annually

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* Additional information available on request

Peste des petits ruminants

Pseudo-rinderpest, Kata, Goat Plaque, Pests of Sheep & Goat, Pneumo-enteritis Complex
Goat Catarrhal Fever

Peste des petits ruminants (PPR), is an acute contagious disease caused by a Morbillivirus of Paramyxoviridae family. It affects small ruminants, especially goats, which are highly susceptible, and occasionally wild animals.

Resembles rinderpest in cattle.

PPR is characterised by severe pyrexia, which can last for 3-5 days, erosive lesions, which occur in the mouth, diarrhoea and pneumonia, serous ocular and nasal discharges. At necropsy, characteristic 'zebra markings' may occur in the large intestine, but is not a consistent finding.

Etiology
PPR disease is caused by Genus Moribillivirus of Paramyxoviridae family.
The **PPR virus is antigenically similar to RP virus,CD virus & Measle virus**.

Susceptible Host - ***Peste des petits ruminants***

1. Goat (markedly evident)
2. Sheep (less susceptible)
3. White tail deer (less susceptible)
4. Cattle (subclinical)

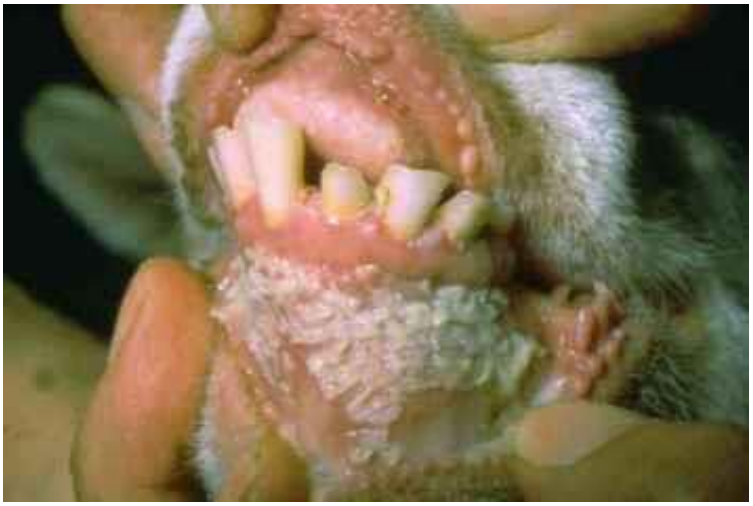
Transmission primarily through

-Direct contact
-Contaminated food
-Water
-Beddings & other appliances.
-Secretion & excretions from affected animal

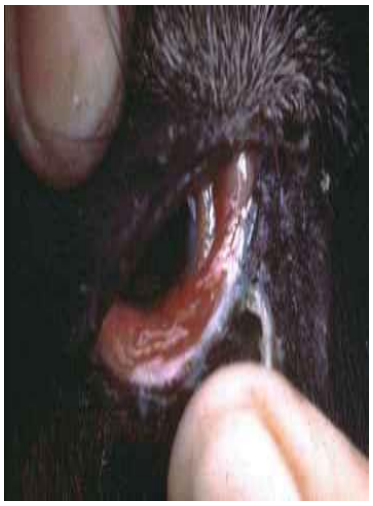
Clinical Signs ***Peste des petits ruminants***
Incubation period is 3-10 days.

Acute form :

Sudden rise in body temperature (40-41°C),
Restlessness, dull coat, dry muzzle,loss of appetite,
Serous **nasal discharge becoming mucopurulent** and resulting, at times in a profuse catarrhal exudate leads to respiratory distress,
Small areas of necrosis on the visible nasal mucous membrane,
Necrotic stomatitis with halitosis is common,
Severe non-haemorrhagic diarrhoea
Bronchopneumonia evidenced by **coughing is a common feature**
Abortion,
Dehydration, emaciation, dyspnoea, hypothermia and death within 5-10 day.

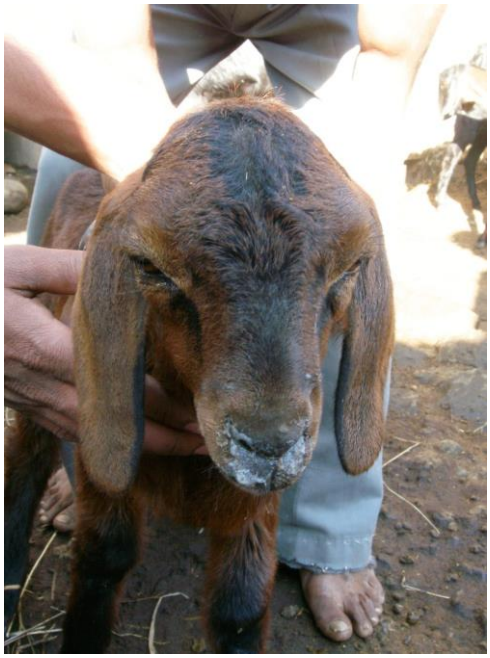


'Bran' like deposits on inner aspect of lower lip



Congestion, ocular discharge

Diarrhoea



Nasal Discharge

Lesions ***Peste des petits ruminants***

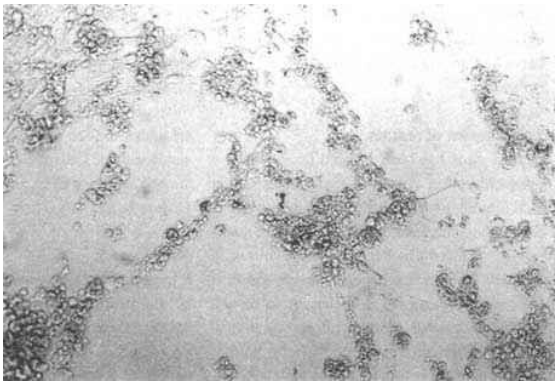
- Emaciation, conjunctivitis, errosive stomatitis inside the lower lips and the free portion of the tongue '**Bran like deposits**' on oral mucosa
- Lesions on the hard palate, pharynx and upper third of the oesophagus in severe cases
- Small streaks of haemorrhages and errosions in the first portion of the duodenum and the terminal ileum
- Extensive necrosis and sometimes severe ulceration of Peyer's patches
- 'Zebra stripes' of congestion in the posterior part of the colon
- Small erosions and petechiae on the nasal mucosa, turbinates, larynx and trachea
- Bronchopneumonia
- Congestion, enlargement and oedema of most of the lymph nodes

Differential diagnosis of *Peste des petits ruminants* from

Contagious caprine pleuropneumonia
Rinderpest
Bluetongue
Pasteurellosis
Contagious ecthyma
Foot and mouth disease
Heartwater
Coccidiosis
Mineral poisoning

Diagnosis

1. Virus isolation and identification
Primary lamb kidney cells or VERO cell line
The CPE produced by PPRV can develop within 5 days
Cell rounding and aggregation culminating in syncytia formation in lamb kidney cells.



In Vero cells, it is sometimes difficult to see the syncytia. If they exist, they are very small. However, in stained, infected Vero cells, small syncytia are always seen.

Syncytia are recognised by a circular arrangement of nuclei giving a 'clock face' appearance. Cover-slip cultures may give a CPE earlier than day 5. There are also intracytoplasmic and intranuclear inclusions.

Material Collection - *Peste des petits ruminants*
Swabs of the conjunctival discharges and from the nasal, buccal and rectal mucosa.
Whole blood collected on heparin (blood and anticoagulant should be mixed gently) .
Lymph nodes, especially the mesenteric and bronchial nodes, Spleen , large intestine and lungs.

Note- Samples should be transported under refrigeration. Never use 50% GPB for collection or transport, when opting for Paramyxovirus isolation.

2. Virus neutralization Test
3. Electron microscopy
4. Amplification by RT-polymerase chain reaction (RT-PCR) : Virus RNA detection using PPR-specific cDNA probes / primers.

5. Identification of the agent :
Viral Antigen detection -

Agar gel immunodiffusion
Counter immunoelectrophoresis
Indirect fluorescent antibody test
ELISA, Immunohistopathology

6. Serological tests :

Competitive ELISA
Counter immunoelectrophoresis
Agar gel immunodiffusion
Immunodiffusion inhibition test

Prevention and control ***Peste des petits ruminants***

Strict sanitation & hygienic measures to be adapted in flock.
Quarantine measures should be followed.

Rinderpest vaccine is commonly used
A homologous PPR vaccine (Sungri strain) is available and is preferable.
Both vaccines give strong immunity. Immunity lasts for 3 years. First age of vaccination at the age of 4 months.

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