## Paramyxoviridae

Viruses classified in the Family Paramyxoviridae (G. para = alongside; myxo = mucus) are pleomorphic, enveloped viruses, that are single negative-sense RNA. The family has four genera: paramyxovirus, morbillivirus, rubulavirus, and pneumovirus. The viruses grouped in the genus "Paramyxovirus" contain **Neuraminidase**, whereas viruses in the other genera do not.

Those in the genus "morbillivirus" are antigenically related and induce similar diseases. The principal members of this family are listed in Table below:-

Table. Diseases caused by Paramyxoviridae

**Paramyxoviruses**
- Mumps
- Parainfluenza - 1 (human, swine)
- Parainfluenza - 2 (human, canine)
- Parainfluenza - 3 (human, bovine, ovine)
- Parainfluenza - 4 (human)

**Morbilliviruses**
- Measles
- Canine distemper
- Rinderpest
- Peste-des-petits-ruminants (PPR)
- Equine morbilli virus

**Rubulaviruses (newly k.a. Avulaviruses) : have both**
- Avian paramyxovirus - 1 - Newcastle disease (Ranikhet disease)
- Avian paramyxoviruses (type 2-9)

**Pneumoviruses**
- Respiratory syncytial virus (human)
- Respiratory syncytial virus (bovine)
- Avian pneumovirus
- (Turkey rhinotracheitis, TRT)
- Swollen head syndrome (SHS) of chickens

# RANIKHET DISEASE
# NEW CASTLE DISEASE (NCD)

(Commonly known as: "Ranikhet Disease in India" and "avian pneumo-encephalitis")

Newcastle disease or Ranikhet Disease is caused by paramyxovirus type 1 (PMV-1), that are of genus **Rubulavirus** or **Avulaviruses**. These have both hemagglutinin and neuraminidase activities. It is a rapidly spreading disease of domestic poultry and other birds, characterized by rapid onset, respiratory signs, and nervous manifestations; and variable mortality.

The first outbreaks of Newcastle disease were recorded in 1926, in Java, Indonesia. The name "Newcastle disease" was coined by Doyle who first investigated it among fowls in *Newcastle-on-Tyne*, England. **In India**, the disease was first recorded at Ranikhet region, in Kumaon hills (Almoda, District Nainital, U.P.), by Edward in 1927; hence the name "Ranikhet disease" and till date is the most important viral disease of poultry.

Chickens are highly susceptible to disease; turkeys do not tend to develop severe signs. Disease in variable severity is also seen in Game birds (pheasants, partridges, quail and guinea fowl); Pssitacine birds (like parrots), Passerine birds (order Passeriformes), gulls (order Charadriiformes), owls (order Strigiformes), pelicans (order Pelecaniformes) and also the Wild birds and waterfowl

**CAUSE / ETIOLOGY:**

Newcastle disease is caused by a group of closely related viruses i.e. paramyxovirus type 1 (PMV-1) serotype of Genus Rubulavirus. Paramyxovirus type-1 are pleomorphic, enveloped viruses, that are single-straded, negative-sense RNA genome of negative polarity.

Considerable antigenic variation exists between different strains of NDV. (The term "strain" is generally used to mean a well-characterized isolate of the virus). A striking feature of NDV strains and isolates is their ability to cause quite distinct signs and severity of disease, even in the same host species.

Based on the disease produced in chickens, NDV shave been placed in **Five Pathotypes**:

1. **Viscerotropic velogenic**: The NDVs cause a highly virulent form of the disease, wherein acute septicemic form with haemorrhagic lesions mainly in proventriculus and diphtheritic ulcerations in intestines are characteristically present in the intestinal tract.
2. **Neurotropic velogenic**: These NDVs cause high mortality as it is also highly virulent, however following respiratory and nervous signs.
3. **Mesogenic**: These NDVs have moderate virulence and causes pneumo-encephalic form of disease with low mortality, having a prolonged course.
4. **Lentogenic**: These respiratory NDVs cause mild or inapparent respiratory infection.
5. **Asymptomatic**: The enteric NDVs cause inapparent enteric infection (intestinal).

However, such groups should be regarded only as a guide as there is always some degree of overlap and some viruses cannot easily be placed in a specific pathotype.

Surface Projections (Spikes)

The ND virus particles have typical projections or "spikes" covering the surface. These are inserted into the envelope.

They are of two types:

1) The longest (about 8 nm) consists of single glycoprotein (HN) with which both haemagglutination and neuraminidase activities are associated.
2) The smaller spikes are formed by the F (fusion) glycoprotein. These are associated with host-cell fusion-the ability of the virus envelope to fuse with cell membranes, allowing insertion of virus genetic material into the host cell, and to cause fusion of infected cells, resulting in the characteristic cytopathic effects or syncytial formation.

**SPREAD**

- Direct contact with secretions of infected birds; principally via ingestion (faecal/oral route) and inhalation
- Fomites: feed, water, implements, premises, human clothing, boots, sacks, egg trays/crates, etc.
- Survival of agent is prolonged by presence of faeces; as in soiled egg shells
- Hatching chicks may be infected through egg for some NDV strains;
- Movement of live birds, contaminated vehicles, fomites, and poultry products (such as unfumigated eggs, dead birds and faeces for fertilizer), from affected premises are also source of spread.

The spread from bird to bird depends on the organs in which the virus multiplies. Birds showing respiratory disease shed the virus in aerosols (droplets) of mucus, which may be inhaled by susceptible birds. Viruses which are restricted to intestinal replication may be spread by ingestion of contaminated faeces, either directly or in contaminated food or water, or by inhalation of small infective particles produced from dried faeces. Viruses transmitted by the respiratory route may spread extremely rapidly, whereas viruses excreted in the faeces and transmitted by the orallfaecal route may spread extremely slowly. A key to the successful spread of the virus is its ability to survive in the dead host or excretions.

**PATHOGENESIS**

The initial step is attachment of the virus to host-cell receptors. This is mediated by the HN glycoprotein. Attachment at the replication site is followed by fusion of the virus membrane with the cell membrane which is brought about by fusion (F) glycoprotein.

Thus, the nucleocapsid complex enters the cell. Intracellular virus replication takes place entirely within the cytoplasm. The F glycoprotein is synthesized as a non-functional precursor, $F_0$, which requires cleavage (a split, division) to $F_1$ and $F_2$ by host proteases for the production of infective viral particles. The HN of some strains of NDV may also require post-translational cleavage (i.e., after the HN molecule has been formed). This cleavage plays a crucial role in the molecular basis of its pathogenicity, as discussed below.

Cleavage Site

During the replication of virus, it is necessary for the precursor glycoprotein $F_0$ to be cleaved to $F_1$ and $F_2$ for the progeny virus particles to be infective. This post-translation cleavage (i.e., split after the $F_0$ molecule has been formed) is mediated by host cell proteases.

If cleavage fails to take place, non-infectious virus particles are produced. Trypsin is capable of cleaving $F_0$ for all strains of NDV. *in vivo* treatment of non-infectious virus by trypsin, also restores its infectivity.

There is fundamental difference in the amino acid sequences at the cleavage site between viruses of low virulence (lentogenic) and virulent viruses (velogenic or mesogenic). It was found that viruses of low virulence have only a single basic amino acid **arginine** at the cleavage site, whereas virulent viruses contain **multiple (additional) basic amino acids** at the site of cleavage. It was also revealed that the susceptibility of the $F_0$ molecule by host proteases depends on the number of basic amino acids at the cleavage site. Trypsin-like enzymes can

cleave if only a single amino acid is present at the cleavage site, whereas other host proteases require multiple (additional) basic amino acids.

Thus, mechanism controlling the pathogenicity of Newcastle disease virus is interesting and resembles that for avian influenza. The presence of additional basic amino acids in virulent strains means that cleavage can be brought about by proteases present in a wide range of host tissues and organs, but in lentogenic viruses (i.e., in viruses of low virulence), cleavage can be caused by only those proteases that recognize the single amino acid **arginine**, i.e., by trypsin-like enzymes, such as are present in the respiratory and intestinal tracts.

So, since viruses-of-low-virulence, they cannot be cleaved elsewhere, no infective virus is produced at other places. Therefore, their growth and pathogenicity are limited to the respiratory and digestive tracts. On the other hand, the virulent viruses, because they possess additional amino acids at the cleavage sites in the $F_0$ molecule, can be cleaved by many other proteases found throughout the body. The virulent viruses thus invade and replicate in many tissues and organs, resulting in the production of infective virus throughout the body, generalized disease, and death.

The virus has affinity for vascular endothelium and lymphoid tissues. Damage/necrosis of endothelial cells, hydropic swelling of media of vessel wall, hyaline changes in capillaries etc lead to various lesions in respiratory and enteric forms.

## SIGNS

- The clinical signs vary considerably with the pathotype of the infecting virus.
- In addition, the species of bird, the immune status, age, and conditions under which they are reared also greatly affect the clinical signs, while the presence of other organisms may greatly aggravate even the mildest forms of disease.

The highly virulent (velogenic) viruses may produce peracute infections, where the first indication of disease is sudden death. Typically, signs such as depression, prostration (lying down), diarrhoea, swelling of periorbital area or entire head (facial oedema) and nervous signs may occur, with mortality reaching 100%.The appearance of shell-less or soft-shelled eggs, followed by complete cessation of egg laying, may be an early sign in adult fowl. Respiratory symptoms with laboured breathing; coupled with expulsion of tenacious mucus is also seen.

The moderately virulent (mesogenic) viruses usually cause severe respiratory disease. This is followed by nervous signs, with mortality up to 50% or more. In laying hens, there may be a marked drop in egg production which may last for several weeks.

The viruses of low virulence (lentogenic) may cause no disease, or mild respiratory distress for a short time. However, the presence of other organisms, such as avian pneumovirus, infectious bronchitis, and vaccine strains of NDV, or poor management may cause disease similar to that seen with more virulent virus.

## LESIONS

### GROSS LESIONS

As with clinical signs, the gross lesions and the organs affected depend on the strain and pathotype of the virus.

The presence of haemorrhagic lesions in the intestine has been used to distinguish viscerotropic velogenic (VVND) viruses from neurotropic velogenic (NVND) viruses. Those prominent are HEMORRHAGES (focal; not very diffuse) in **Proventriculus**; around the orifices of proventricular glands (considered pathognomonic), in **caecal follicles (caecal tonsils)**, small intestine and in the **Cardiac fat** and serous membrane covering **Xiphisternum**. These lesions include haemorrhage in the **mucosa of the proventriculus**, **enlarged and necrotic caecal**

**tonsils**, **ulceration / hemorrhages of Peyer's patches**, necrosis and haemorrhage in **intestinal lymphoid aggregates**, and **splenic necrosis on the capsular surface**. **Laryngeo-Tracheitis** associated hemorrhages may also be seen.

Gastrointestinal catarr with focal diphtheritic lesions in mucosa on pharynx, oesophagus and intestines are also noticed.

Usually, gross lesions are not observed in the central nervous system, regardless of the pathotype. Gross changes are not always present in the respiratory tract. Viruses causing respiratory disease may induce haemorrhagic lesions and marked congestion of trachea. **Airsacculitis** (airsacs being cloudy and congested) and **thickening of the airsacs with catarrhal or caseous exudates** is often observed.

Laying hens reveal egg yolk in the abdominal cavity. The ovarian follicles are often flaccid (lacking firmness) and degenerate, and may even show **haemorrhagic stigmata (i.e., spots**). Haemorrhage and discoloration of the other reproductive organs may occur.

## MICROSCOPIC LESIONS

Microscopic lesions are as varied as the clinical signs and gross lesions.

Lesions in the vascular system, necrosis of endothelial cells associated with hyperaemia, oedema, and haemorrhage in many organs and tissues is observed. Regressive changes in the lymphopoietic system consist of disappearance of lymphoid tissue.

Necrotic lesions are found throughout the **spleen**. Marked degeneration of the medullary region is seen in the **bursa**. The **haemorrhagic-necrotic lesions in the intestinal tract** develop in lymphoid aggregates. Focal necrotic lesions also seen in **muscles**.

Lesions in the upper respiratory tract may be severe and related to the degree of respiratory distress. Lesions may extend throughout the length of the **trachea**. **Cilia may be lost within 2 days** of infection. In the mucosa, congestion, oedema, and dense cellular infiltration of lymphocytes and macrophages may be seen. Oedema, cell infiltration, and increased thickness and density of the **airsacs** may occur.

Lesions in the central nervous system are those of non-purulent encephalomyelitis with neuronal degeneration, foci of glial cells, perivascular infiltration of lymphocytes, and proliferation of endothelial cells. Lesions usually occur in the cerebellum, medulla, mid brain, brain stem and spinal cord, but rarely in the cerebrum.

### Zoonotic Significance

Although Newcastle disease virus can produce a transitory (of brief duration) **conjunctivitis** in laboratory workers or vaccination teams, if exposed to large quantity of virus.

## DIAGNOSIS

- None of the clinical signs or lesions can be regarded as specific/ pathognomonic. At best, they are only suggestive of the disease.
- Serological Tests: detect presence of specific antibodies in the serum but gives little information on the infecting strain of the ND virus, so has limited diagnostic value. Serological tests include single radial immunodiffusion, agar gel precipitin, virus neutralization (VN) in chick embryos, and plaque neutralization.
- ELISA has become popular, especially as part of flock screening procedure.
- Currently, the **Haemagglutination Inhibition test** (HI test) is most widely used. NDV may be confirmed by HI test using specific NDV antiserum. Can enable differentiation and grouping of NDV isolates, by using a group of monoclonal antibodies.

- At present the only sure method of diagnosis, which allows identification of the strain, is **isolation of the virus** and its characterization. Sampling from live birds should consist of both cloacal swabs(or faeces) and tracheal swabs, regardless of the clinical signs. From dead birds, intestines, intestinal contents and tracheas should be taken, together with affected organs and tissues.

**DIFFERENTIAL DIAGNOSIS**:

- ✓ Fowl cholera
- ✓ Highly pathogenic avian influenza
- ✓ Laryngotracheitis
- ✓ Fowl pox (diphtheritic form)
- ✓ Psittacosis (psittacine birds)
- ✓ Mycoplasmosis
- ✓ Infectious bronchitis
- ✓ Aspergillosis