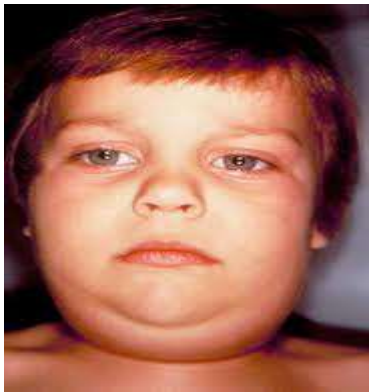
RNA VIRUSES

PARAMYXOVIRIDAE

Family Characteristics

The Paramyxoviridae include some of the great and ubiquitous disease-causing viruses of humans and animals, including one of the most infectious viruses known (**measles virus**), some of the most prevalent viruses known (**parainfluenza viruses**, **mumps virus**, **Rinder pest**, **Canine distember** and **respiratory syncytial virus**), **a virus that has been targeted by the World Health Organization(WHO) for eradication (measles virus), viruses that have a major economic impact on poultry and animal rearing (Newcastle disease virus and rinderpest virus).**

mumps virus



Classification

The family Paramyxoviridae is classified into two subfamilies the Paramyxovirinae and the Pneumovirinae.

The **Paramyxovirinae** contains five genera:

1- **Respirovirus** which cause (Human parainfluenza virus1and 3).

2- **Rubulavirus** which included, Mumps virus, Para influenza virus 2,4a, 4b.

3- **Avulavirus** (Members of this genus include the Newcastle disease virus)

4-**Morbillivirus**:- which included, rinderpest virus, Canin distember virus and measles virus.

5- **Henipavirus** which included Hendra virus (HeV) and Nipah virus (NiV)

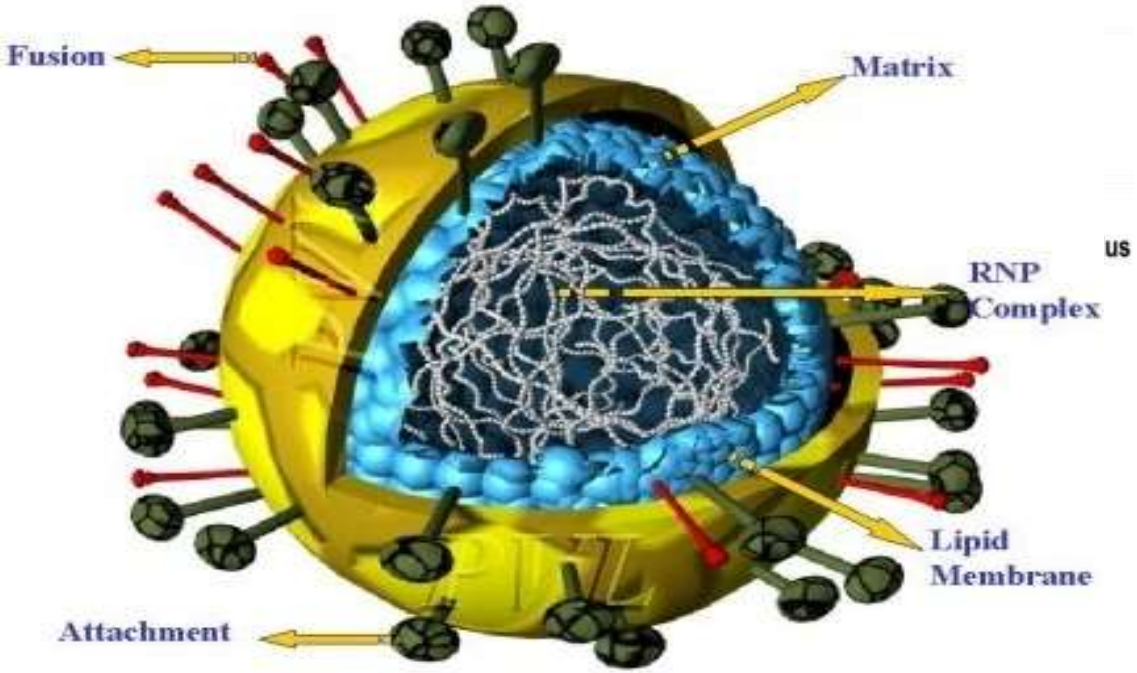
The Pneumovirinae contains two genera:

1- **Pneumovirus**:- which included Human respiratory syncytial virus (HRSV), bovine syncytial respiratory virus (BRSV), Caprine respiratory syncytial virus, Ovine respiratory syncytial virus and *Rodentia* = *Pneumonia virus of mice*.

2- **Metapneumovirus**:- which include Avian metapneumovirus cause Turkey rhinotracheitis virus.

Morphology and Structure

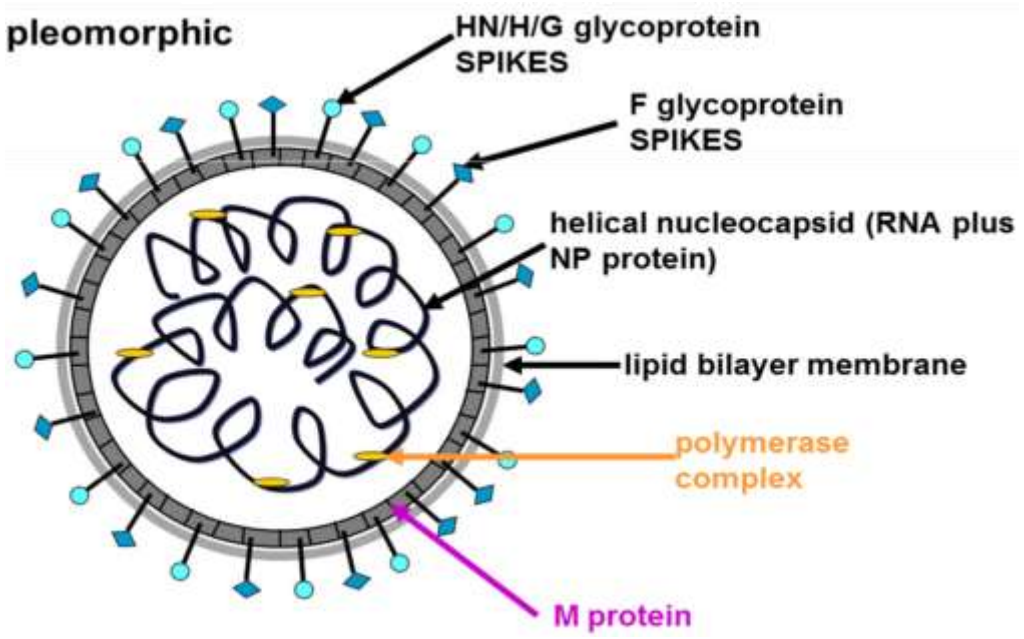
- Nonsegamented single- stranded RNA of negative sense, unsegmented and replicated entirely in the cytoplasm, their genomes are 15 to 19 kB in length.
- Paramyxoviridae are generally spherical, 150 to 350 nm in diameter, but can be pleiomorphic in shape, and filamentous forms can be observed.



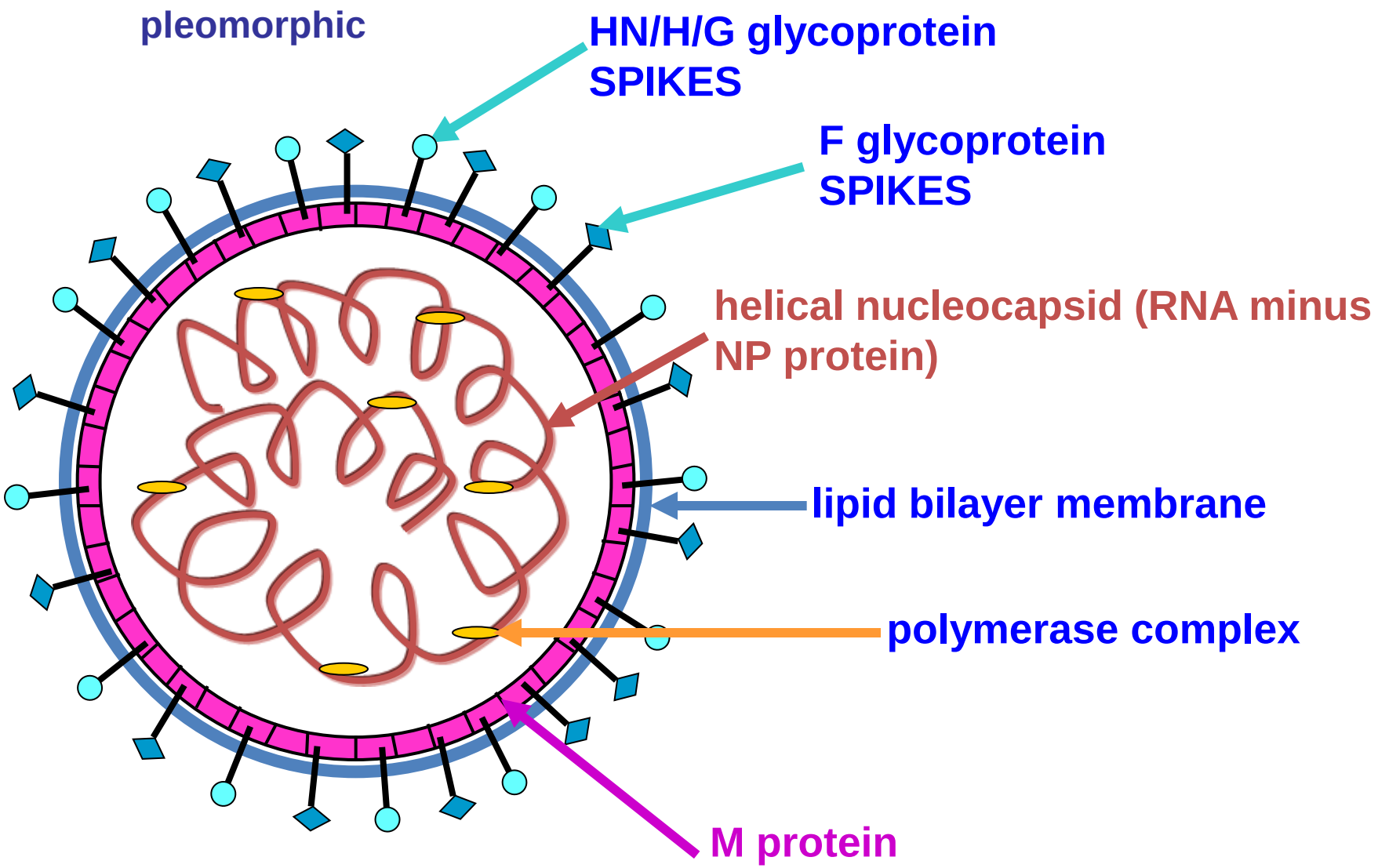
•Structral units of capsid protein called nucleocapsid surrounded the RNA genome to give a helical symmetry with a zipper like appearance by negative staining.

• The envelope is composed of a lipid bilayer which contains matrix protein.

• A lipid envelope containing two surface glycoproteins which comprise separate spikes (fusion glycoprotein (F) and a second glycoprotein variously called hemagglutinin-neuraminidase (HN) surrounds the virions



PARAMYXOVIRUSES

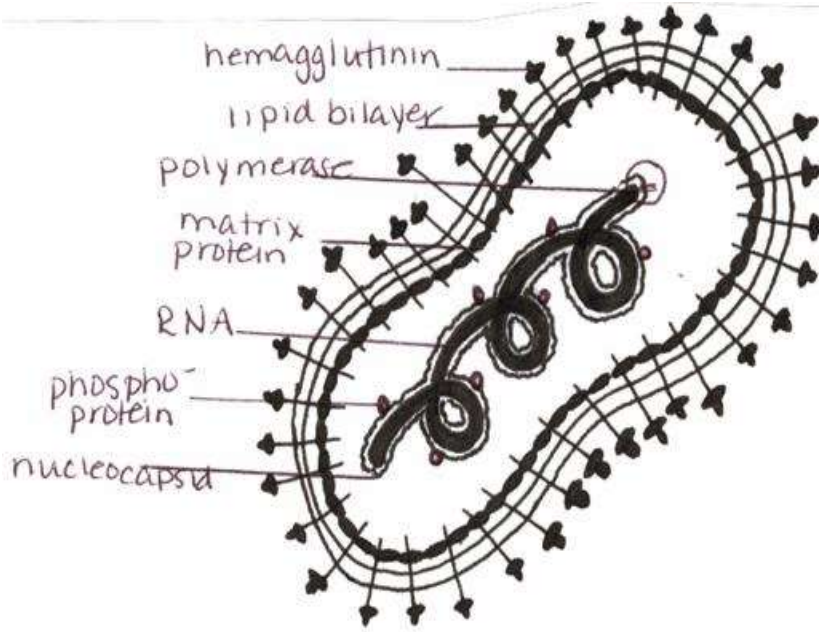


The envelope of paramyxoviruses contains 2 glycoproteins, **HN and F**, that form spikelike projections from the surface of the viral membrane. These glycoproteins are involved in the early interactions between virus and cell. **The larger glycoprotein, HN, has neuraminidase and hemagglutinating activities and is responsible for virus adsorption.**

The other glycoprotein, F, is involved in virus-induced cell fusion and hemolysis and in virus penetration through fusion of viral and cell membranes. The membrane-fusing activity of Ihe **F protein** is activated by proteolytic cleavage of a precursor (Fo) by a host enzyme to yield 2 disulfide-linked polypeptides (F_1 and F_2). Only then can viral replication begin.

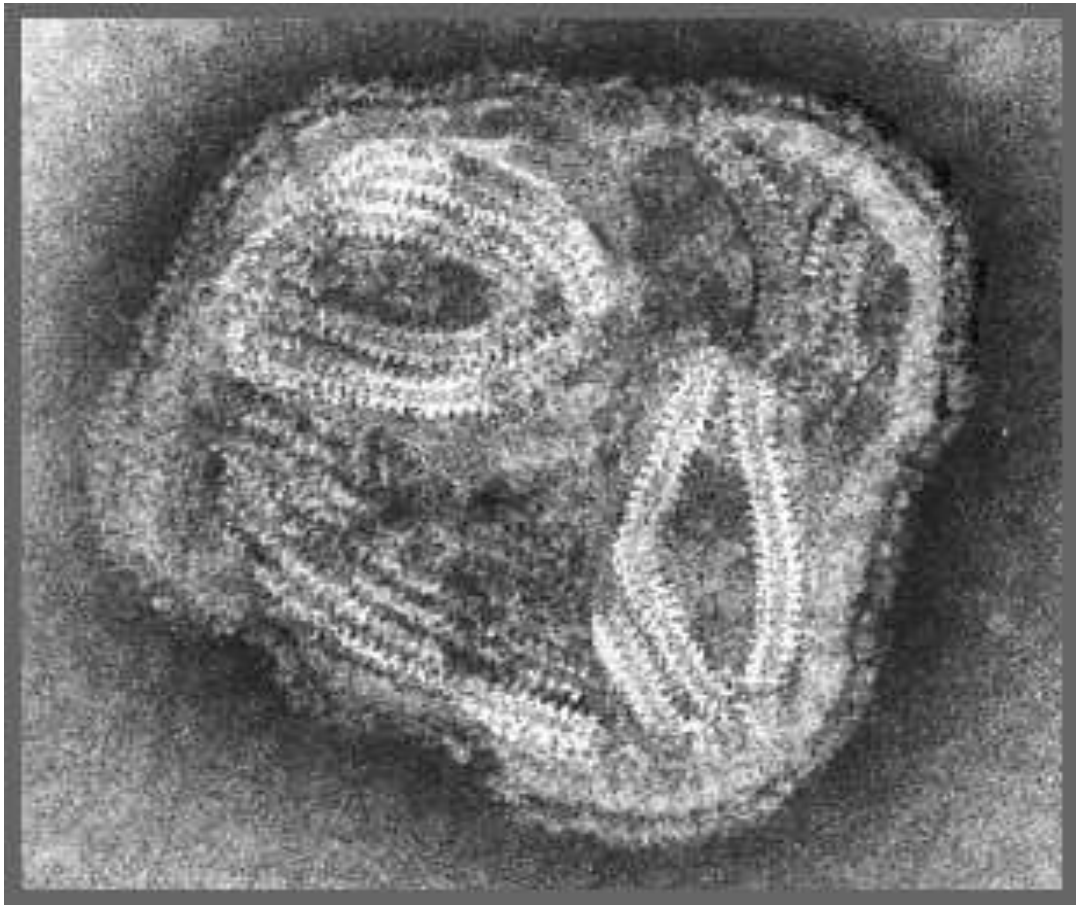
Physico-chemical Properties

- Heat labile
- pH stable
- Withstand drying



- The hemagglutinin, the hemolysin, and the infectivity of the virus are destroyed by heating at 56 °C for 20 minutes.

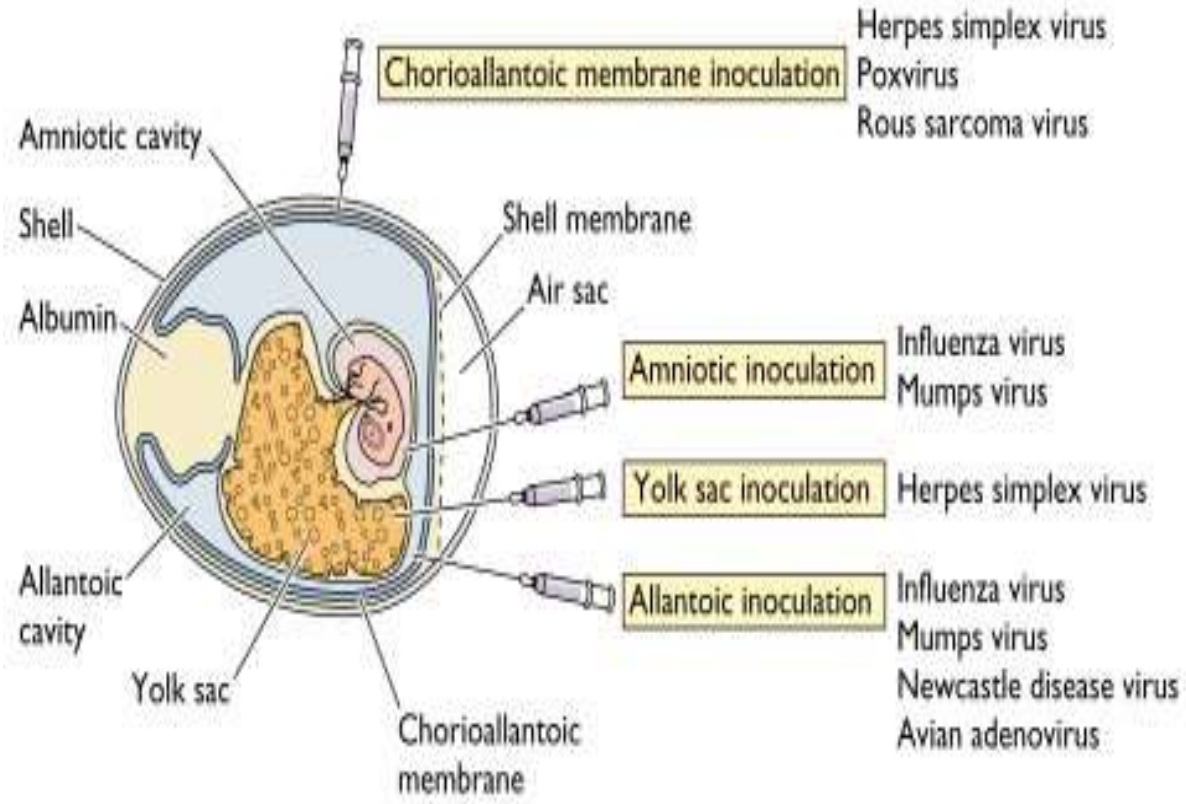
STRUCTURE-PARAMYXOVIRUSES



The virus grows readily in embryonated eggs and in cell culture. Passage in embryonated eggs reduces pathogenicity for humans, and this method was used to obtain a vaccine strain. Mumps virus growing in cell culture produces multinucieated giant cells (syncytia).

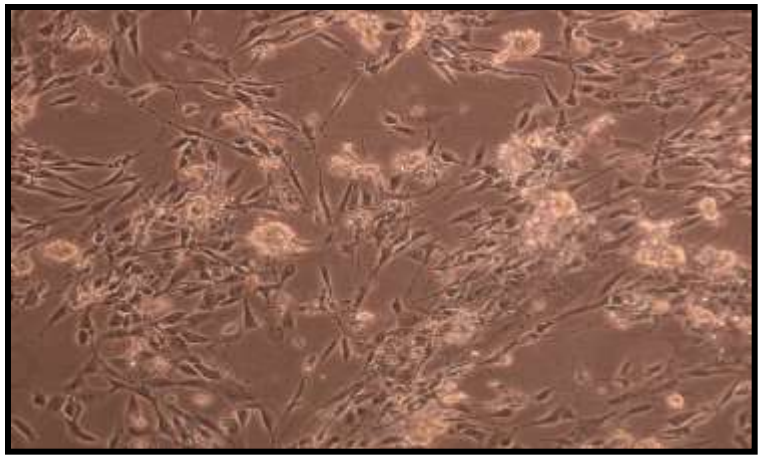
Cultivation and Cytopathic Effect

Virions grow in eggs and TC.



Cultivation and Cytopathic Effect

- Can be detected in TC by CPE, Cytoplasmic Inclusion body formation and syncytium.
- Haemadsorption by guinea pig cells can be used to detect cells infected by the virus.



Host Range

Man:- Can be infected with Mumps, Parainfluenza(PI) 2, 4a, 4b, Measles, Respiratory syncytia virus, Newcastle disease virus of poultry (conjunctivitis).

Cow:- Can be infected with Rspiratory syncytial virus, PI-3, Rinderpest virus.
Sheep, goats, Pigs:- PI-3, Rinderpest virus
Dog:- PI-5, Canine distember virus (CDV).
Horse:- PI-3(rarely).
Mouse:- Pneumonia virus of mice.
Mouse and Hamster:- PI-5 which is also called Simiun virus-5
Bird:- Newcastle disease virus in chickens, Turkeys, Pheasant, Duck, Psittacine and Pigeons.

Cell Tropism In-Vivo

- All replicate in the upper respiratory tract epithelium.
- Some others replicate outside the respiratory tract (lymphoid cells, neurons, enteric cells and endothelial cells of blood vessels and bladder.

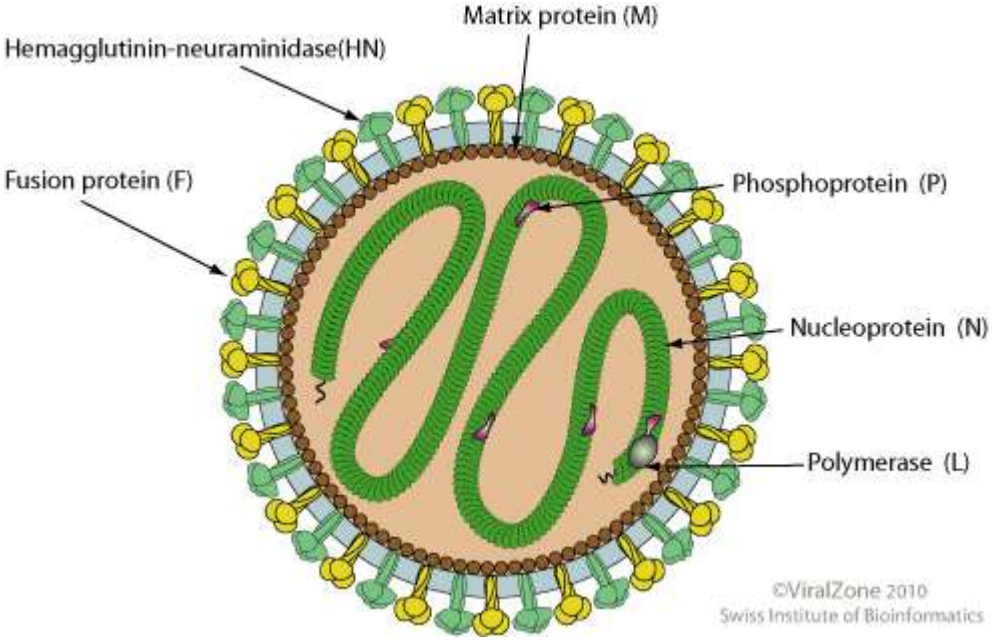
Genus/ Avulavirus:-

Species Newcastle disease virus (NDV

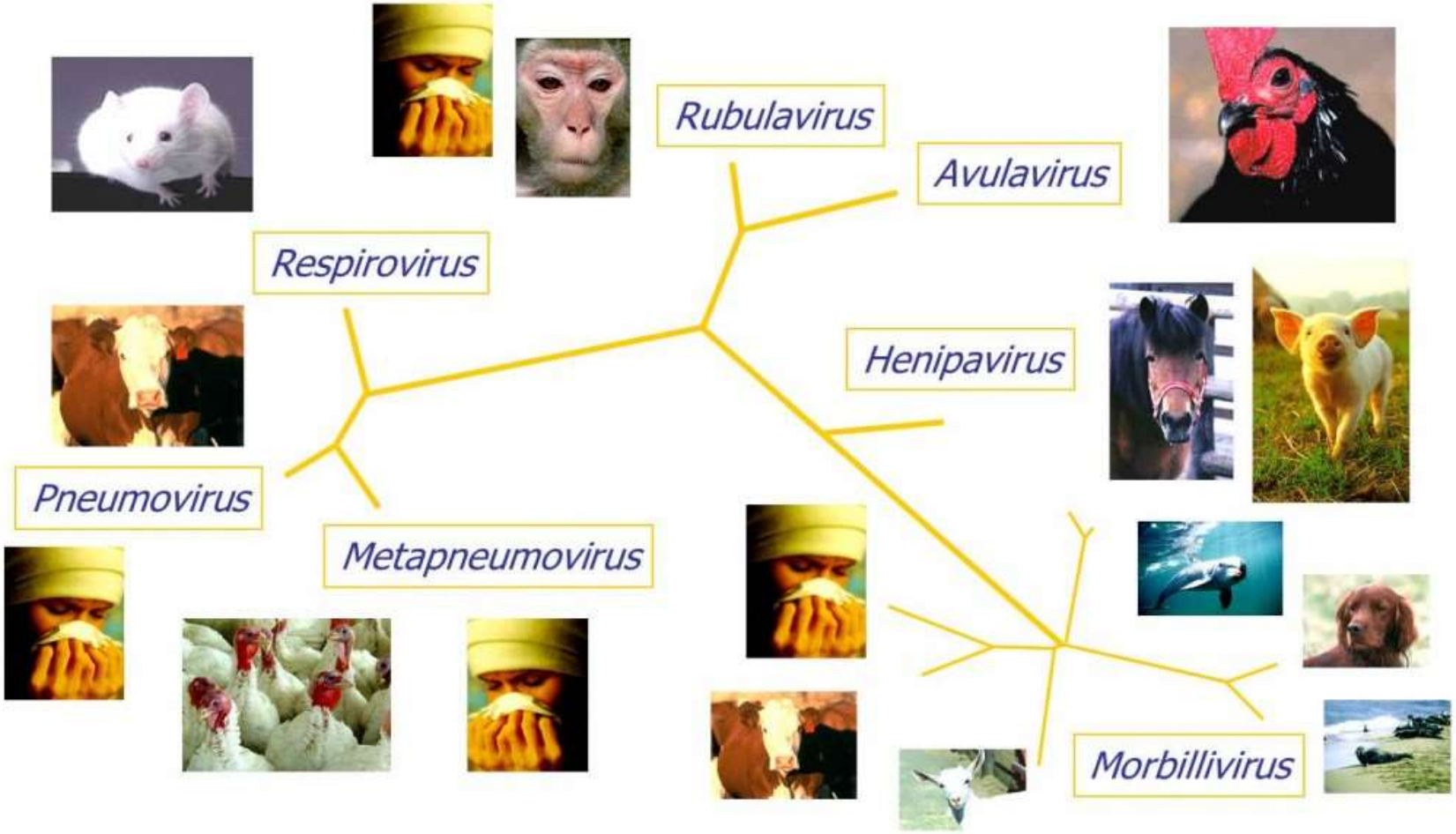
NDV:- Is a contagious disease caused by virulent avian paramyxovirus in the genus *Avulavirus.* There are ten serotypes of avian paramyxoviruses designated APMV-I to APMV-10 and ND virus (NDV) has been designated APMV-1.

The disease affected a wide range of avian species including Chickens, Turkey, Pigeons. Ducks and Geese are less susceptible.

Avulavirus



The Virus: Enveloped with HN and F spikes.
The isolates cross react with each other.
The virus easily grows in cell culture and eggs.



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The **Pneumovirinae** contains two genera:
1- **Pneumovirus**:- which included (HRSV), (BRSV) and (PVM).
2- **Metapneumovirus**:- which include Avian metapneumovirus cause Turkey rhinotracheitis virus.

Pathogenesis

- Virus spreads by ingestion or inhalation.
- The virus replicates in epithelial cells of R. T and intestinal tract, then spread by blood to spleen and bone marrow and then from later to lung, intestine and CNS, the spared depended on the strain virulence.

Isolates can be divided into:

a-Lentogenic: which are a virulent that remain localized causing subclinical infection (Hitchners form).

b-Mesogenic: Causing mild disease with mortality about 25% confined to young birds (Beudette's form).

c-Viscerotropic Velogenic: This isolates causing severe fatal disease characterized by hemorrhagic intestinal lesions(Doyle's form) and high mortality rate may reach 100%.(fowl pest).

d- **Neurotropic Velogenic** : This isolates causing acute disease characterized by nervous and respiratory signs with high mortality (Beach's form).

Immunity and Epidemiology

- T cells and HI abs developed in birds infected with lentogenic strains.
- Presence of many strains may cause failure of vaccination.
- It is advisable to make vaccine from local strains.
- Transmission is by aerosol or ingestion.
- Excretion occurs for 2 months from recovered birds.
- Transmission between farms is possible.

CLINICAL SIGNS AND LESIONS

Incubation period(I.P) 5 days

The clinical signs depend on virulence of viral strain. Tissue tropism, age and immune system status of the host.

1-prostration and depression in the birds.

2- Ruffled feathers.

3- Greenish white diarrhoea.

4-The head turned to one side, a condition known as torticollis.

5-Paralysis of the legs, wings or other neurological signs.

6-Other typical characteristics of the disease include: rapid spread; death within 2-3 days.

7- On necropsy, typical lesions are mucus in the trachea, and usually haemorrhages in the intestine, particularly in the proventriculus.


Cornell University


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5 days. PI with Viscerotropic Velogenic NDV
Clinical Description
• Necrosis of lymphoid tissue at the cecal tonsils, as seen here, and throughout the intestinal walls is used to help distinguish viscerotropic from neurotropic strains of Newcastle disease in the field.
Cornell University/PIADC

Diagnosis:-

1- CLINICAL SIGNS AND LESIONS

For a definitive diagnosis of ND, both virus isolation and laboratory characterization are necessary.

2- SEROLOGICAL DIAGNOSIS

The presence of specific antibodies against the ND virus indicates that the bird has been infected by the virus. In practice, a high antibody titre is indicative of a recent infection. Two methods are used to measure antibody titres: the **haemagglutination inhibition (HI)** test, and **the enzyme-linked immunosorbent assay (ELISA)**. For both, it is necessary to collect blood samples from the chickens.

3- VIRUS ISOLATION

The definitive diagnosis of ND is done through isolation and identification of the virus. Tracheal and cloacal swabs are good sources of virus for isolation from living birds without having to kill them. Virus can also be isolated from homogenised organs from dead birds, chosen to reflect the clinical signs. Nine-day-old embryonated fowls' eggs are injected with 0.1 mL of the suspension into the allantoic cavity and returned to incubation. The eggs are candled twice daily. As dead eggs occur, they are chilled, together with d all eggs after 5-7 days incubation, are chilled at 4°C at which point the allantoic fluid is then harvested and tested for its ability to haemagglutinate chicken red blood cells. Diagnosis is based on the inhibition of haemagglutination by specific anti-NDV serum. This proves infection of the bird by the virus, but does not indicate whether the virus is a pathogenic or avirulent strain.

Detection of virulence of isolates by:

1- Detection of Mean death time (MDT) by inoculation of embrionated egg and , if the virulent strain kill the embryo less than 60 hours.(velogenic strain).

The mesogenic strain kill the embryo in (60-90) hours.

The lentogenic more than 90 hours.

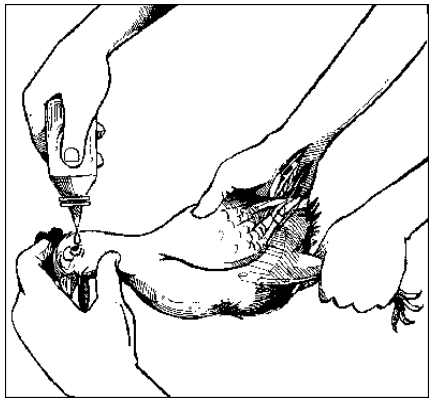
2-Detection of intracerebral pathogenecity index. Inoculation chicken one day old in brain, if kill after 24 hours is mean virulent isolate.

3- Determination intravenous pathogenecity index(IVP) , inoculation in I/V of 6 weeks chicken, more death more virulent.

Control

No tretment

•Restriction of eggs and chicken importation.
•Psittacine birds are quarantined for 35 days under vet. Supervision.
•In new outbreaks, cleaning, and disinfection are essential and movement must be restricted.
•Vaccination with lentogenic strains at 7 days old and repeated in 21 days old.
•Vaccination is done by aerosol or drinking water.
•-One age group per farm ('all in-all out') breeding is recommended; disinfection between groups during outbreaks.



Vaccination:-

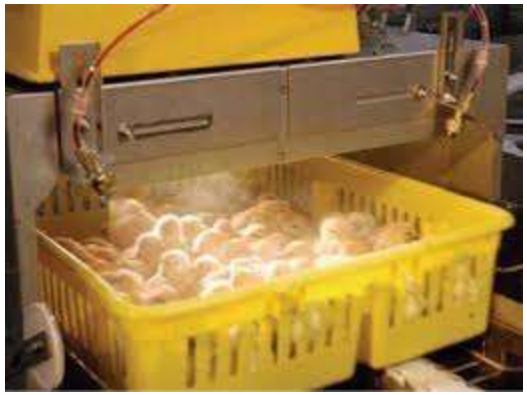
One of the most important considerations for any vaccination programmed is the type of vaccine to be used, the immune and disease status of the birds to be vaccinated, the level of maternal immunity in young chickens and the level of protection required in relation to any possibility of infection with field virus under local conditions.

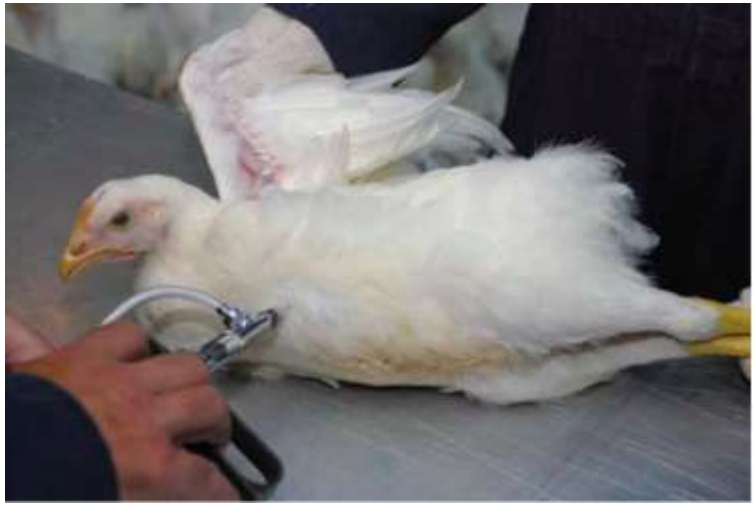
Bird must be vaccinated with lentogenic strain (e.g. Hitchner-B1, Lasota, V4, NDW, I2 and F) at 7 days old chicks and repeated of 21 days old.

Live virus vaccines administered to birds by incorporation in the drinking water, or

as a coarse spray, or by intranasal or conjunctival instillation; some mesogenic strains are given by wing-web intradermal inoculation.

Inactivated vaccines tend to be more expensive than live vaccines application entails handling and injecting individual birds prepared from allantoic fluid that has had its infectivity inactivated by formaldehyde incorporated into an emulsion with mineral oil, and is administered intramuscularly or subcutaneously.





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Genus: Pneumovirus

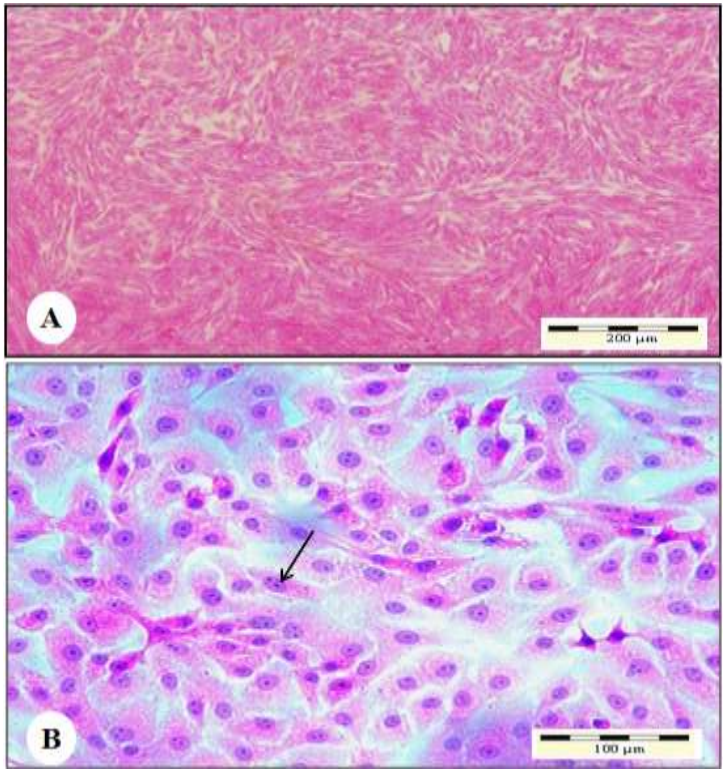
- Respiratory syncytial Virus is the only important member of the genus

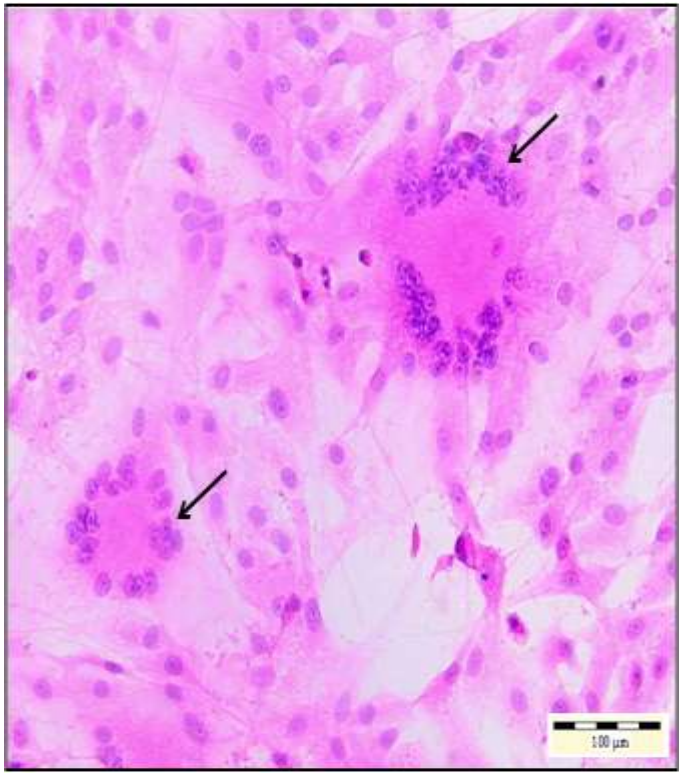
Bovine Respiratory Syncytial Virus

Host: cattle, humans ; ferrets experimentally infected.

(**BRSV**):- is a respiratory condition in cattle. It replicates in nasal epithelium and then disperses throughout the upper respiratory tract to the bronchial tree. Here, syncytia form and further spread into the bronchioles occurs.

Outbreaks of RSV associated disease usually occur associated with winter housing and also during periods of stress such as mixing of calves and transport. The causative agent is an RNA virus classified as a pneumovirus in the paramyxovirus family and is a major cause of respiratory disease in young calves. This virus was named for its characteristic cytopathic effect—the formation of syncytial cells


A
200 µm
B
100 µm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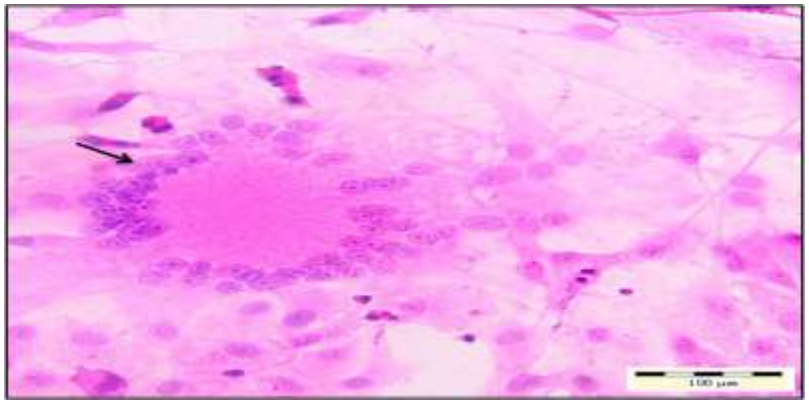
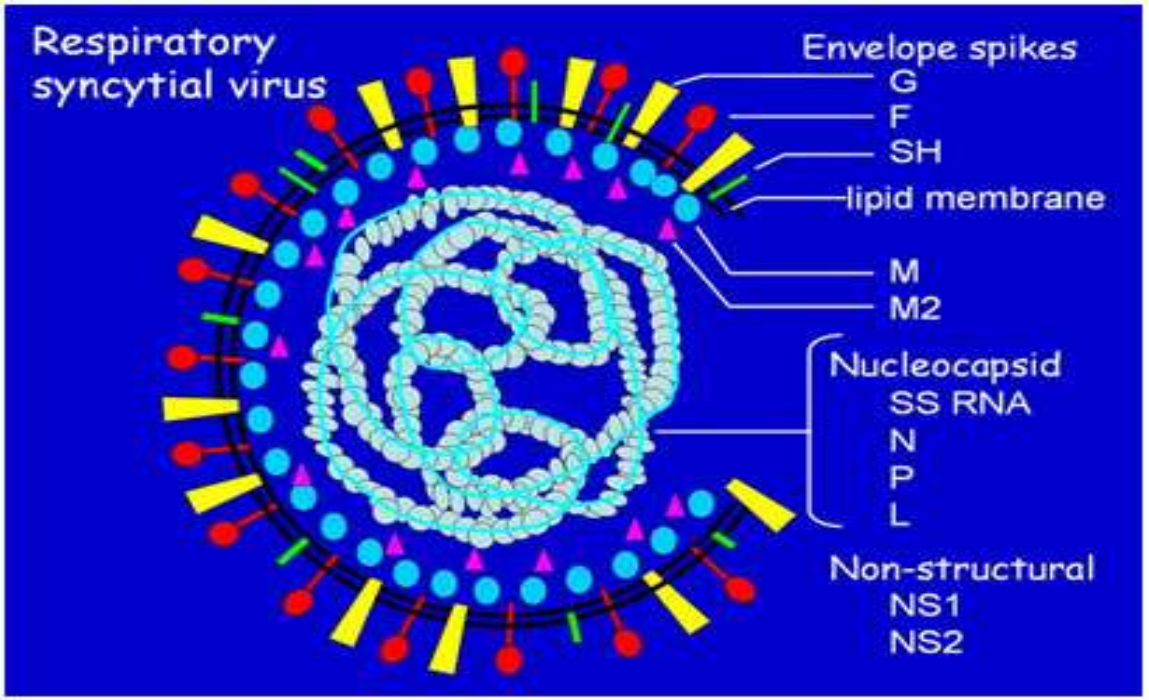


Virus:

*Morphology is the same of other genus of Paramyxoviridae.

*No active hemagglutinins or neurominidase.

*CPE CC by syncytial with formation of intacytoplasmic IB.



Pathogenesis and Clinical Signs

- Aerosol transmission (The main sources of infection are cows already infected with this respiratory disease. It has been suggested therefore that the virus is transferred from an infected cow to an unaffected cow via aerosols droplets.
- Replication in the nasal epith, and upper respiratory tract and bronchial tree.

The clinical sings characterized by:

1- Pyrexia of (104-108°F [40-42°C]) occurs 3-4 days after exposurfe. with increase respiratory rates, anorexia, serous nasal discharge, dry muzzle.

2- Decreased feed intake (anorexia), depression and malaise.

3- Rhinitis, lead to serous nasal discharge, Trachitis and increased respiratory rate.

4- Presence of secondary bacterial infection causes extensive bronchopneumonia.

- Three of 5 calves developed fevers of 40"C.

Immunity and Epidemiology

- CF and VN abs appear within 10 days of infection.
- The protection after infection is not life long.
- Subclinical infections may be important in spreading the disease.
- Virus is prevalent in most countries.

Diagnosis and Control

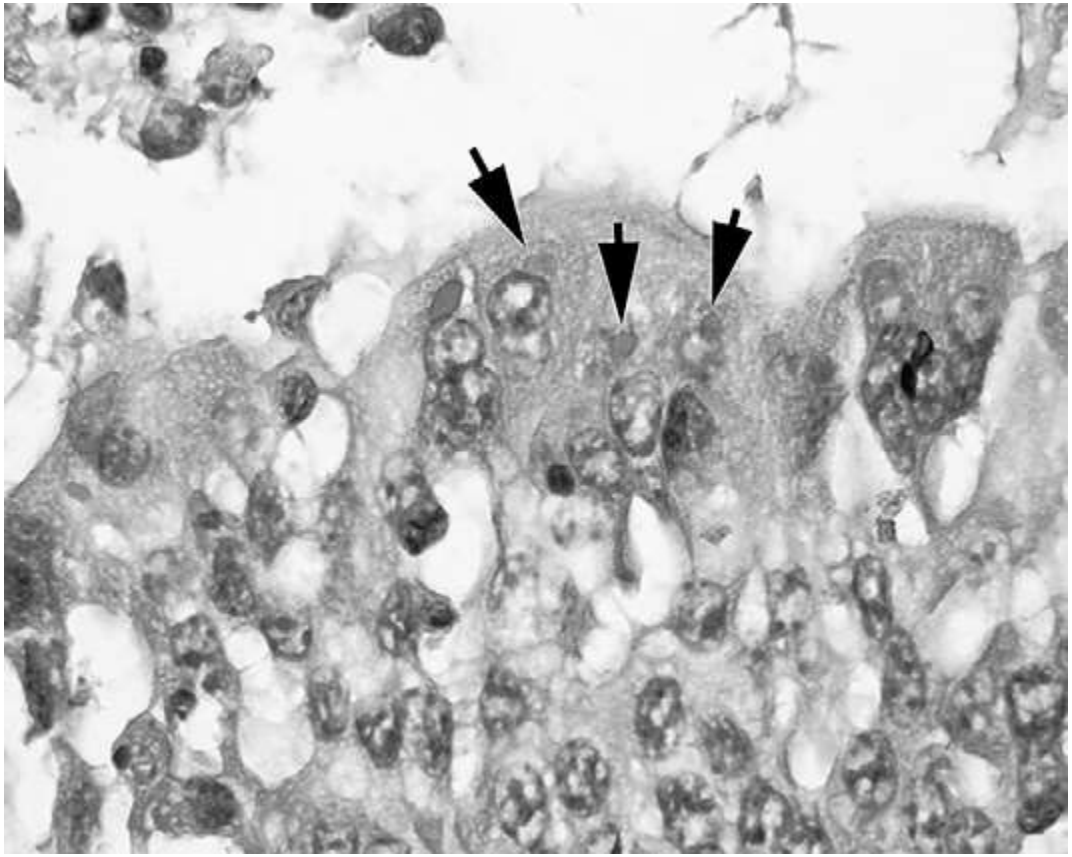
Diagnosis

A variety of tests have been used to identify BRSV in field specimens collected during outbreaks of respiratory disease. Initially, identification of the virus was by virus isolation and recognition of cytopathic effect in the cell culture.

- 4 folds rise in CF or VN abs is the usual confirmation, using paired sera from several animals.
- IF test on nasal scraping cells of infected calves.
- RT-PCR is becoming more popular as a means of identification of BRSV in clinical cases.

Control

- Management of calves.
- Isolation of infected animals.
- Live vaccines administered parenterally (abnormal route). Inactivated vaccine can be used.
- Vaccines do not prevent infection but may reduce or eliminated the severity



Morbillivirus Genus

Canine Distember virus

The disease is most commonly associated with domestic animals such as dogs and ferrets, although it can infect wild animals as well as.

Is a highly contagious, systemic, viral disease of dogs seen worldwide. Clinically, it is characterized by a fever, leukopenia, and frequently pneumonic and neurologic complications.

Host: Dog, Ferret and Mink.

Virus: Morphology and CPE typical to that of the genus paramyxovirus. The virus can be adapted to grow on CAM producing opacity and oedema. Only one antigenic strain is recognised.

The virus, a single-stranded negative RNA, can cause systemic infection in the host carnivore.

Puppies from three to six months old are particularly susceptible. CDV spreads through aerosol droplets and through contact with infected bodily fluids, including nasal and ocular secretions, feces, and urine, six to 22 days after exposure

Pathogenesis and Clinical Signs

- **Aerosol infection.**
- **Upper respiratory tract and tonsils is primary site of replication.**
- **Lymphocyte and macrophage infection leads to leukopnea and lymphodenitis and secondary pyrexia.**

Clinicl Signs:-

a-Mucopurulent nasal and ocular discharge.

b-Interstitial pneumonia.

c-Vomiting and diarrhoea.

d-Inco-ordination or muscle tremors which may progress to paralysis and coma.

e-virus can cross the placenta.

Clinical Signs

F-Squamous epithelium of the nares and pads become infected giving rise to increased sensitivity and hyperketosis so called hard-pad.

Clinical Signs

Typically, canine distemper virus affects the lymphatic system, nervous system, lungs, gastrointestinal tract, urinary tract, eyes and skin of the animal and,

as a result,,,,,,,,,,,,,,,,,,,,,,

Animals generally present with a range of neurological signs, **respiratory signs**, gastrointestinal signs (vomiting, diarrhea), **ocular signs and skin signs**..

Canine distemper affected animals will also present with non-specific signs of illness: fever, lethargy, inappetence and dehydration.

Immunity and Epidemiology

- **Maternal abs are transferred via colostrum and prevent puppies up to 8 weeks or 12 weeks.**

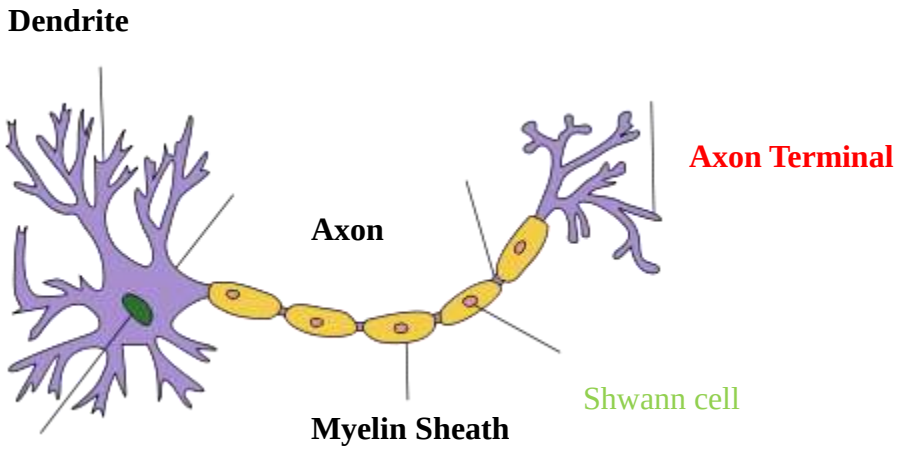
  Mortality varies may be up to 20%.

CNS infection leads to 90% mortality.

Diagnosis

- **Clinical symptoms.**
- **Nasal or conjunctival smears or lymphocytes can be subjected to IF test.**
- Histopathological exam of brain tissues showed **demyelination** in the cerebellar area.
- Virus isolation and Identification.

Myelin is a dielectric (electrically insulating) material that forms a layer, the **myelin sheath**, usually around only the axon of a neuron. It is essential for the proper functioning of the nervous system. It is an outgrowth of a type of glial cell. The production of the myelin sheath is called myelination.



Control

. **Treatments** are directed at limiting secondary bacterial invasion, supporting fluid balance, and controlling nervous manifestations.

- **Vaccination** with **inactivated** vaccine followed by **virulent** virus vaccine.
- Most vaccines are live attenuated in eggs and TC such is modified live virus (**MLV**).
- Successful immunization of pups with canine distemper modified live virus (MLV) vaccines depends on the lack of interference by maternal antibody.
- **Polyvalent vaccines(more than one strain)** can be used.
- Measles can be used as a vaccine.

sRinderpest Viru

cattle plague

- **Rinderpest:-** Rinderpest (**RV**) was an acute to subacute **contagious viral disease of ruminants and pigs that could cause morbidity and mortality rates in excess of 90%.**
- **Host**: Cattle, domesticated buffalo and some species of wildlife can be infected naturally.

  Rabbits, mice, hamesters and chicks embryos can be infected experimentally.

The classical form of rinderpest is one of the most lethal diseases of cattle, and can have a catastrophic effect.

Virus: A member of the genus Morbillivirus of the family Paramyxoviridae. Typical of the group **paramyxovrus** in **morphology** and **CPE** in cell culture. The virus is an enveloped, negative-sense single-stranded RNA virus. Despite its extreme lethality, the virus is particularly fragile and is quickly inactivated by heat.

Pathogenesis and Clinical Signs

1- Highly infectious virus is excreted on aersol in nasal and ocular exudates and in saliva and faeces.

2- Primary replication occurs in epithelium of lymphoid cells of the orophorynx followed by viremia.

3- Incubation period 3-10 days. The secondary localization of the virus in the alimentary tract and respiratory tract.

4- Diarrhoea and dysentery.

5- Salivation.

6- Exudative dermatitis.

Immunity and Epidemiology

1- VN Abs appears 6 days after oneset of clinical symptoms.

2- Colstrol Abs protects calves for 10-11 days if suckling vaccinated cow.

-

3- Cattle plaque (rinderpest) is worldwide distribution.

-

Diagnosis and Control

Diagnosis

1-AGD test on samples from lymph nodes or small intestine.
2-Virus isolation on calf kidney cells.
3-CF and ELISA can be used.
4-Clinical disease is characterised by an acute febrile attack within which prodromal and erosive phases can be distinguished

Stage of pathogenesis

1-Prodromal period lasts approximately 3 days: affected animals develop a pyrexia of between 40 and 41.5°C together with partial anorexia, depression, reduction of rumination, constipation, lowered milk production, increase of respiratory and cardiac rate, congestion of visible mucosae, serous to mucopurulent ocular and nasal discharges, and drying of the muzzle

2- **Erosive phase** with development of necrotic mouth lesions at height of fever: flecks of necrotic epithelium appear on the lower lip and gum and in rapid succession may appear on the upper gum and dental pad, on the underside of the tongue,

necrotic material works loose giving rise to shallow, nonhaemorrhagic mucosal erosions

• Gastrointestinal signs appear when the fever drops or about 1–2 days after the onset of mouth lesions

Control

Slaughter of infected and in contact animals, along with incineration, disinfection and movement restriction may be made in controlled systems of husbandary.

In enzootic areas mass vaccination is practised. All susceptible ruminants must be vaccinated .

Originally virus passaged in rabbits, goats or eggs was given as live or inactivated vaccine. Currently the vaccine used is freeze dried virus which has been attenuated by repeated passage in calf kidney cells. It is highly protective under adequately organised systems of husbandry and animal movement.