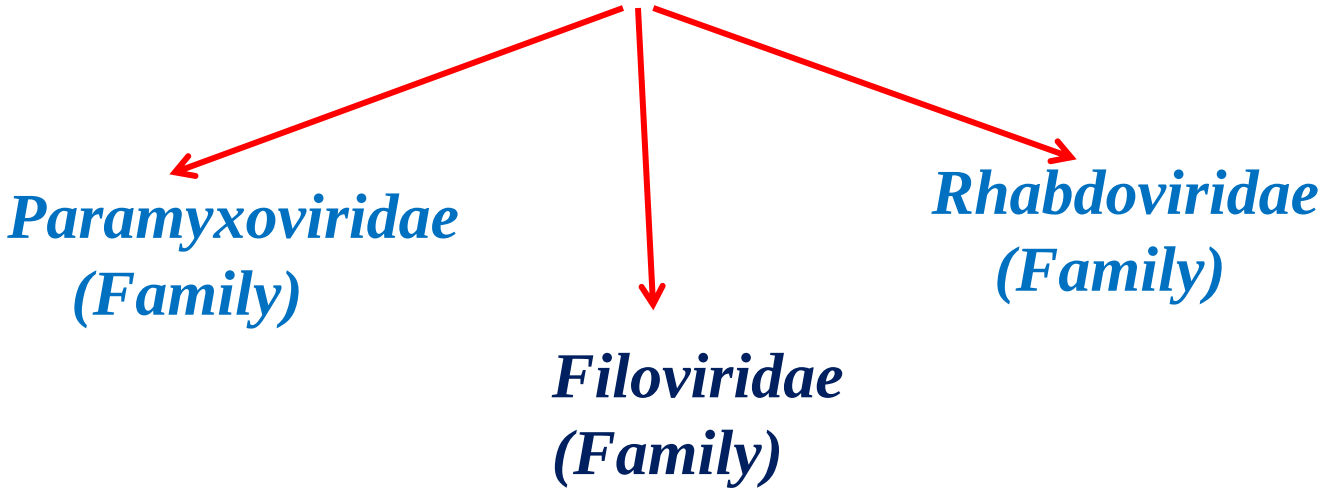
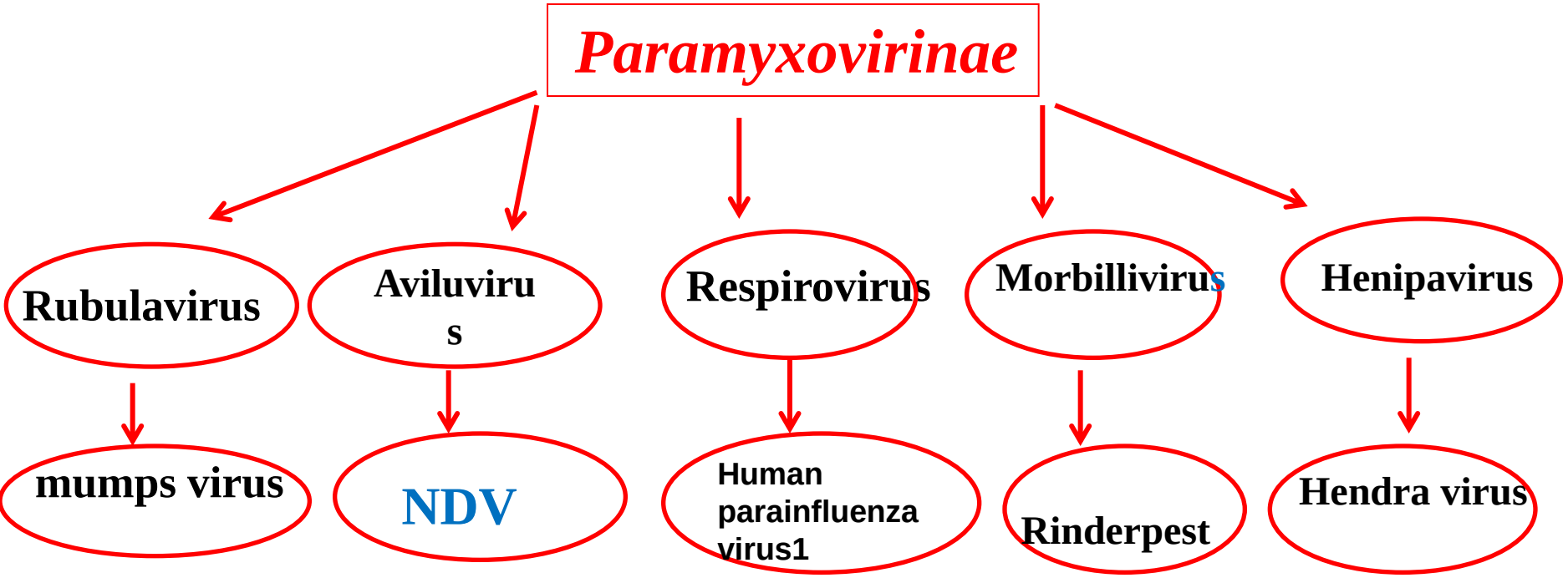
POULTRY DISEASES

Newcastle Disease

Mononegavirales (order)

Single-stranded, nonsegmented, negative-sense RNA viruses showing helical capsid symmetry




Paramyxovirinae
Rubulavirus
Aviluviru
s
Respirovirus
Morbillivirus
Henipavirus
mumps virus
NDV
Human
parainfluenza
virus1
Rinderpest
Hendra virus

INTRODUCTION

Definitions and Synonyms

ND has been termed pseudo-fowl pest, pseudo-poultry plague, avian pest, avian distemper, and avian pneumoencephalitis.

Newcastle disease (ND), caused by ND virus (NDV), which is an **Avulavirus of the family Paramyxoviridae**. There are nine avian paramyxovirus serotypes designated APMV-1 to APMV-9. Of these, Newcastle disease virus, which is APMV-1, remains the most important pathogen for poultry, but APMV-2, APMV-3, APMV-6, and APMV-7 also cause disease in poultry. The disease is one of the most important encountered in the poultry industry.

NDV is a highly fatal viral disease affecting most species of birds. NDV has been a devastating disease of poultry, it is causing heavy economic losses to the poultry industry and in many countries the disease remains one of the main problems affecting existing or developing poultry industries. The disease can vary from clinically in apparent to highly virulent forms, depending on the virus strain and the host species.

The first reported ND outbreak occurred in 1926 in Java (Indonesia).

Doyle (1935) named the disease “Newcastle disease” after the outbreak in Newcastle-upon-Tyne in Great Britain 1927.

This was to avoid giving a scientific name that may be confused with other disease entities.

In Iraq the Newcastle disease virus isolate in 1979 (Ag 79) and (Al-shekly 81).

Beard and Hanson classified the disease **into 5 forms** or pathotype based on clinical signs in chickens, strain causes, mortality rate and bird age, which included:

1) **Doyle's form, which is an acute, lethal infection of all ages of chickens. Hemorrhagic lesions of the digestive tract are frequently present, and this form of disease has been termed viscerotropic velogenic Newcastle disease (VVND).**

2) **Beach's form, which is an acute, often lethal infection of chickens of all ages. Characteristically, respiratory and neurological signs are seen, hence the term neurotropic velogenic (NVND).**

3) Beaudette's form that appears to be a less pathogenic form of NVND in which deaths usually are seen only in young birds. Viruses causing this type of infection are of the mesogenic pathotype and have been used as secondary live vaccines.

4) Hitchner's form, represented by mild or inapparent respiratory infections caused by viruses of the lentogenic pathotype, which are commonly used as live vaccines.

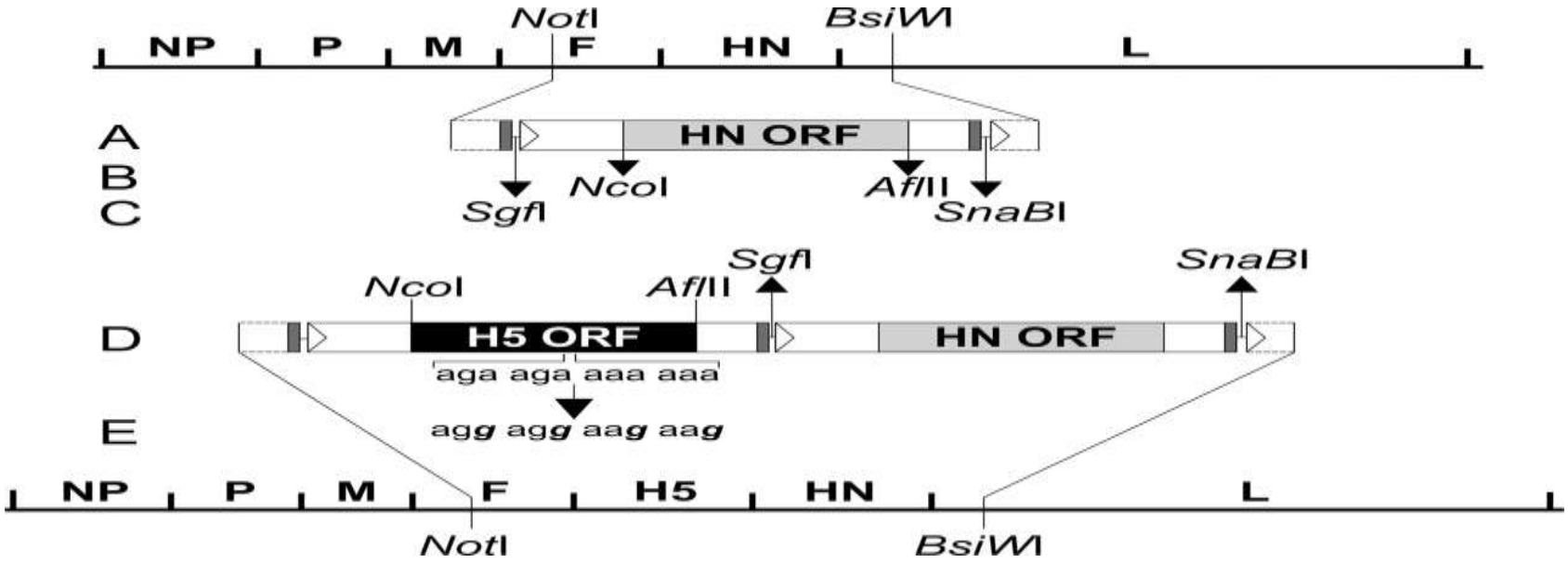
5) Asymptomatic-enteric form, which is chiefly a gut infection with lentogenic viruses causing no obvious disease. Some live commercial vaccines are of this pathotype

ETIOLOGY

Classification

Newcastle disease is a severe infectious disease of birds caused by Newcastle disease virus (NDV), or avian paramyxovirus type 1 (APMV-1). NDV is classified in the genus *Avulavirus* of the family *Paramyxoviridae* and has a single-stranded, negativesense.

RNA genome consisting of six genes in the order 3´-NP-P-M-F-HN-L-5´which encode the six structural proteins. Three of these are associated with the lipid envelope of the virion: the haemagglutin-neuraminidase(HN) and fusion glycoproteins(F) are attached in the membrane and appear as spikes on the virion surface, the matrix protein (M) is peripherally attached to the inner surface of the envelope. The remaining three proteins are associated with genomic RNA to form the viral nucleocapsid, these are the nucleocapsid protein(N), the phosphoprotein(P) and the large protein(L).


NotI
BsiWI
NP
P
M
F
HN
L
A
B
C
HN ORF
SgfI
NcoI
AflII
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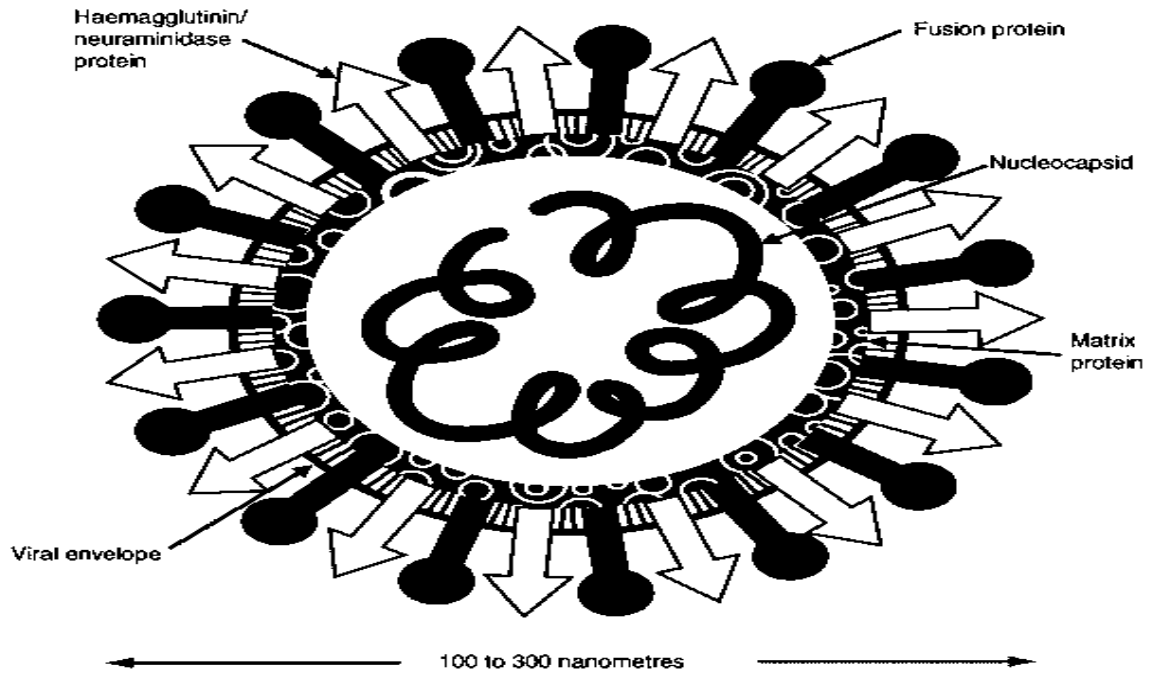
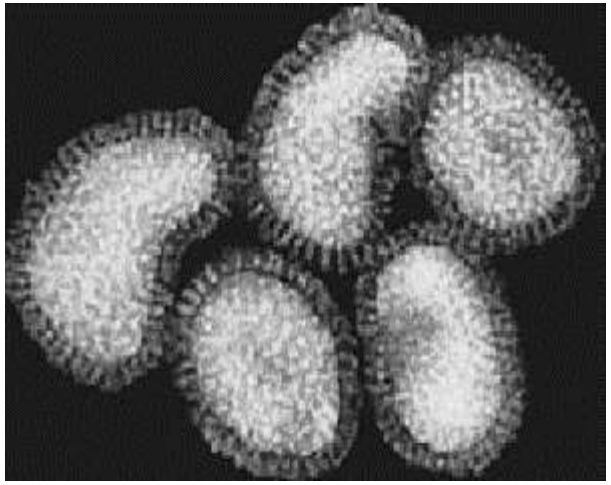
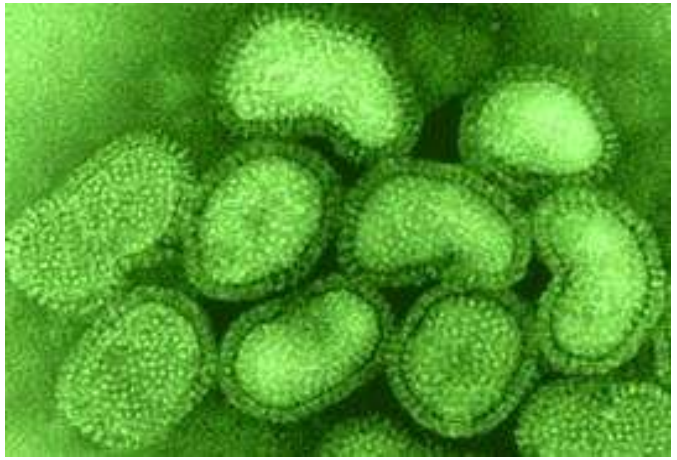
D
E
H5 ORF
aga aga aaa aaa
agg agg aag aag
H5
NotI
BsiWI


Haemagglutinin/
neuraminidase
protein
Fusion protein
Nucleocapsid
Matrix
protein
Viral envelope
100 to 300 nanometres

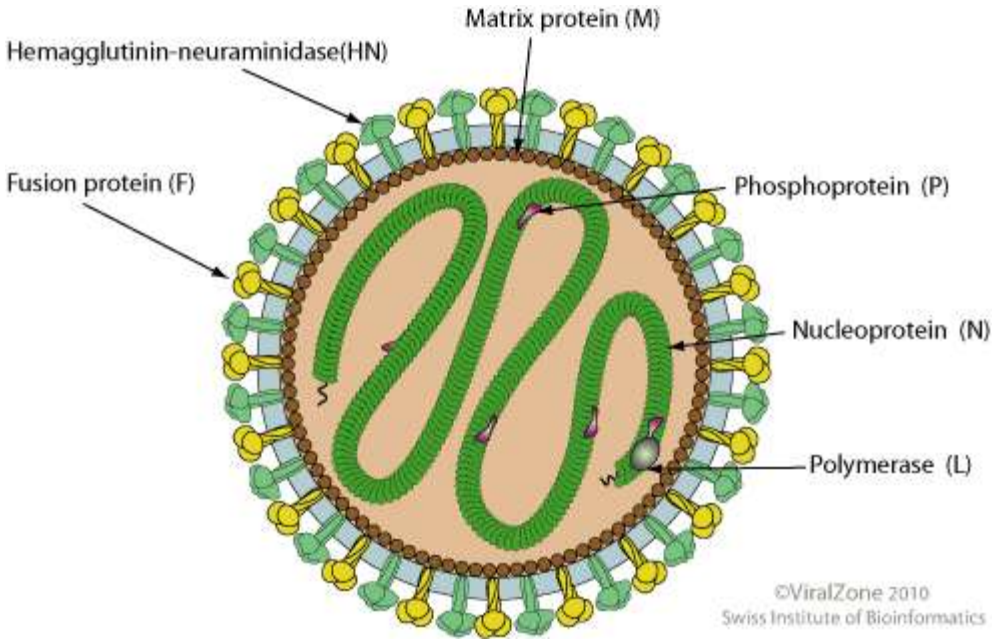
Morphology

Negative contrast electron microscopy of NDV reveals very pleomorphic virus particles typical of members of the *Rubulavirus* genus. Generally spherical and **150 to 350 nm in diameter**. The surface of the virus particle is covered with projections about 8 nm in length. In most electron micrographs, the “herring bone” nucleocapsid, about 18 nm across and showing helical symmetry.





Avulavirus


Matrix protein (M)
Hemagglutinin-neuraminidase(HN)
Fusion protein (F)
Phosphoprotein (P)
Nucleoprotein (N)
Polymerase (L)
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Swiss Institute of Bioinformatics

Classification

1-Viscerotropic velogenic (Dolye's form or vvNDV)

2-Neurotropic velogenic (Beach's form)

3-Mesogenic (Beaudette's form)

4-Lentogenic (Hitchner's form)

5-Asymptomatic/ avirulent enteric form of infection

Classification

1-Viscerotropic velogenic (Dolye's form or vvNDV):

Clinical Signs:

1-With extremely virulent viruses, the disease may appear suddenly, with high mortality occurring in the absence of other clinical signs. Mortality=50-100% (usually 90%)

3- More often death in 4-8 days preceded by weakness and prostration.

4-Edema of head, wattles and tissues around eyes.

5-Increased rate of breathing.

6-During course of infection, greenish diarrhea, sometimes blood stained.

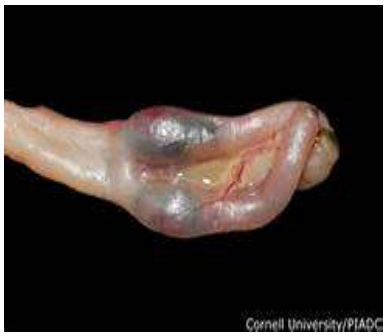
7-CNS signs closely follows the respiratory signs including Clonic spasms, muscular tremors, twisted heads and stargazers, Torticollis and opisthotonus appear in birds that survive the initial phase of disease.

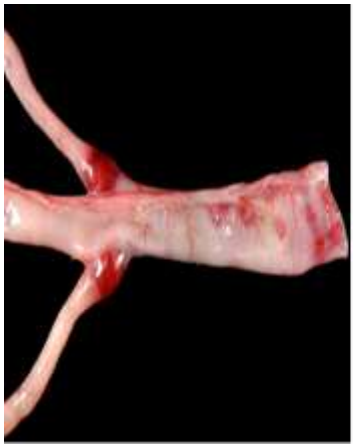
8-Also paralysis of legs and occasionally the wing may occur.

Gross Lesion

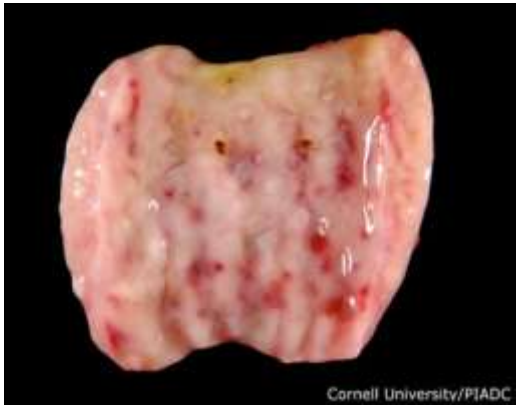
1-Only velogenic strains produce significant gross lesions, the gross lesions are dependent on the strain and pathotype of the infecting virus.

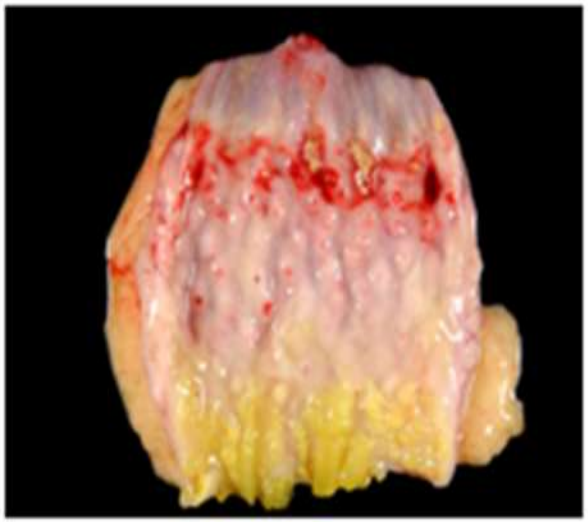
2-Dark red, purplish haemorrhagic and necrotic lesions, especially the digestive tract and intestinal wall (jejunum, ileum, and posterior half of duodenum) result from the necrosis of the intestinal wall or lymphoid tissues including Peyer's patches and cecal tonsils. Lesion vary in length from a few mm to 15 mm or more. The latter may bulge outwardly or inwardly to the extent, that the lumen is constricted. Lesion may appear bleb like due to edema.

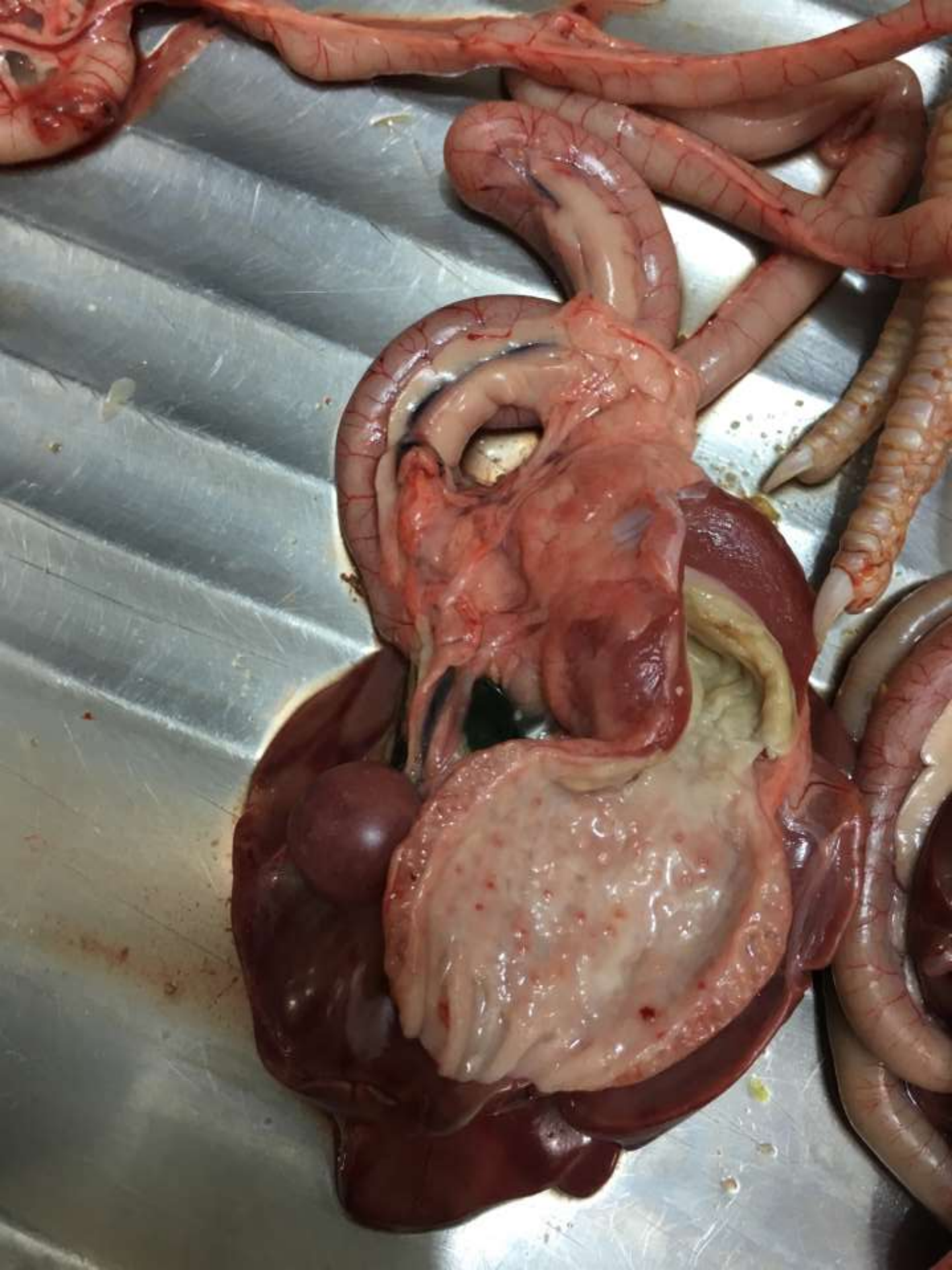


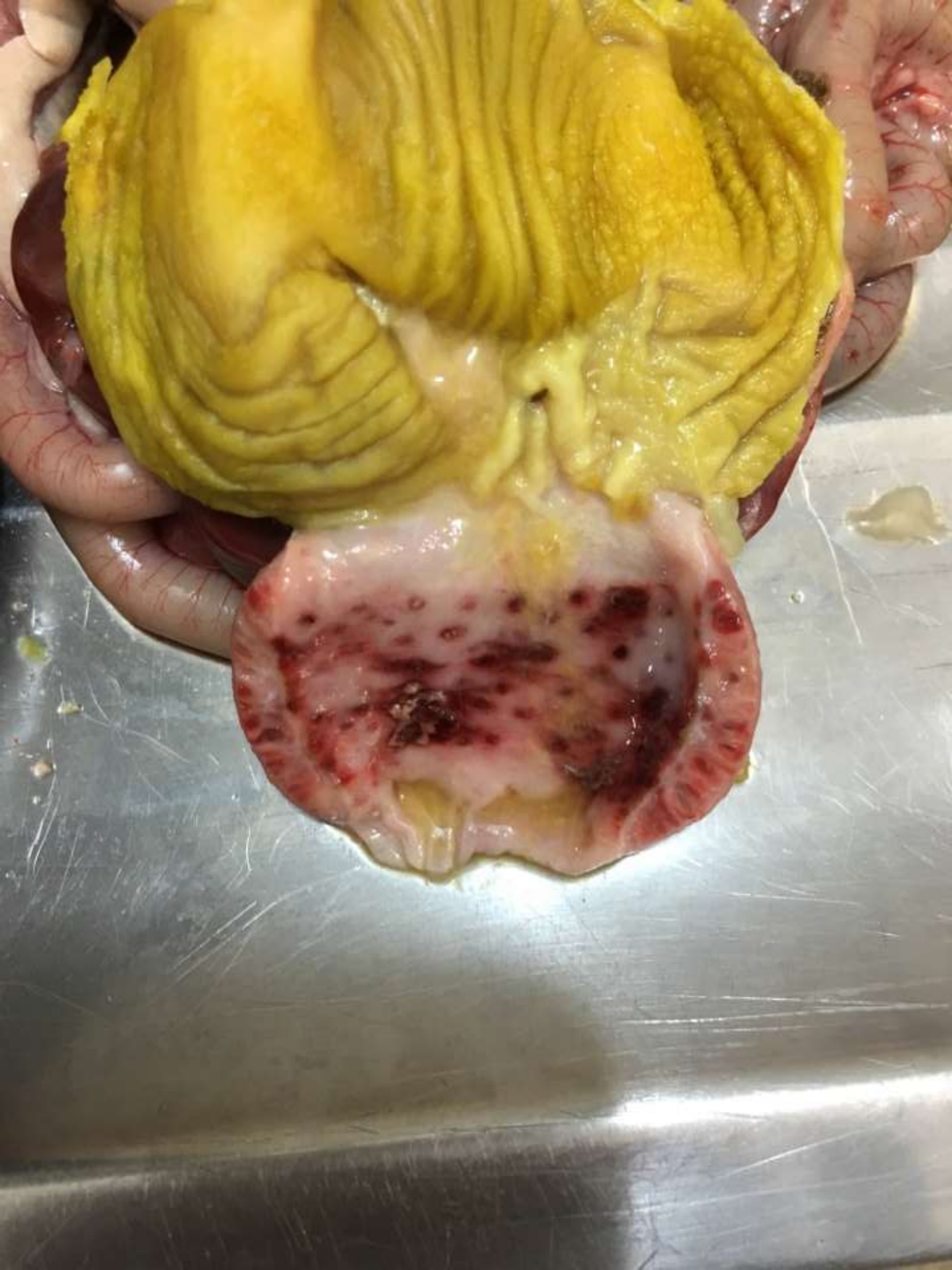


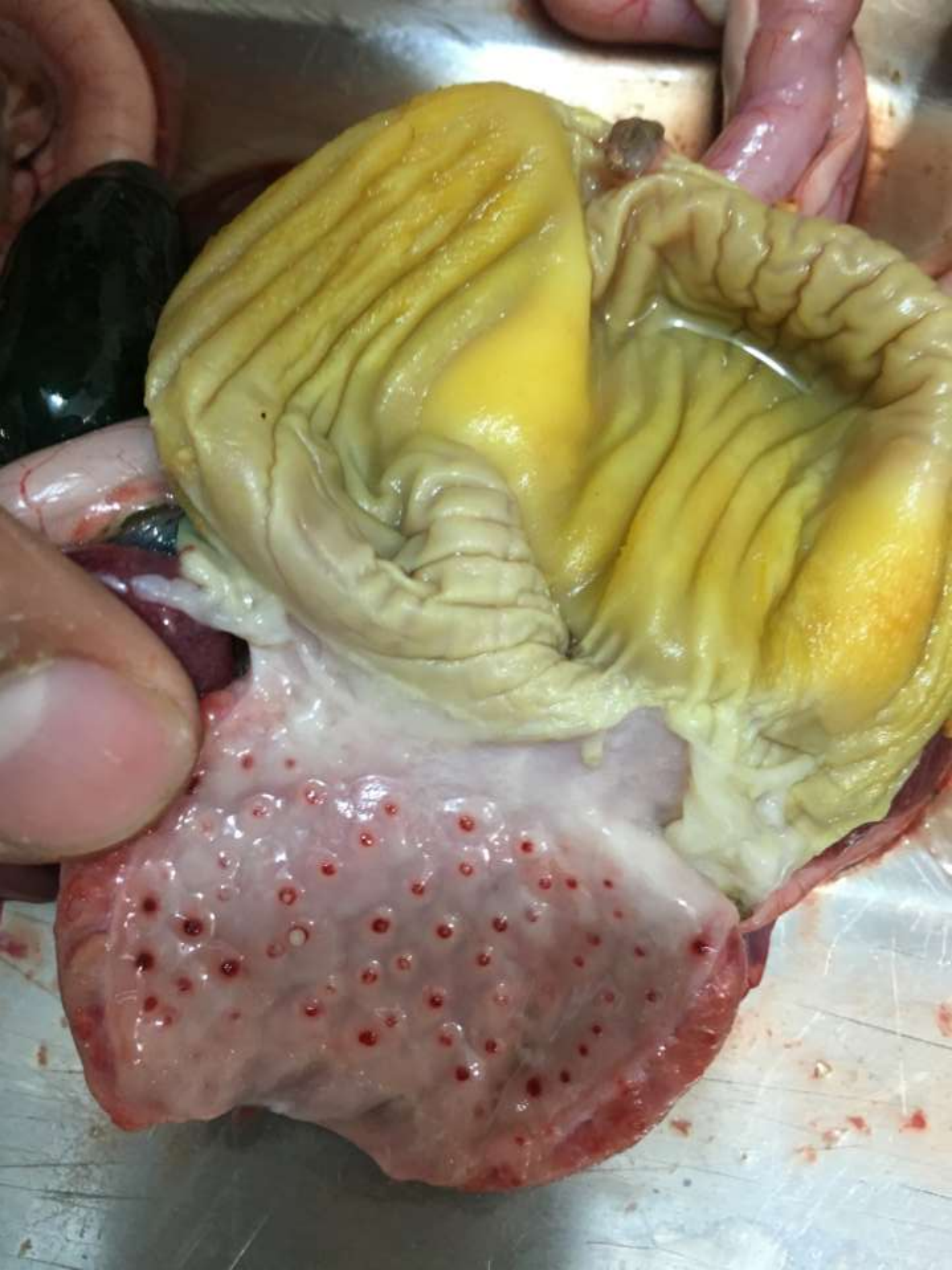
3-Petechiae and small ecchymoses on the mucosa of the proventriculus.

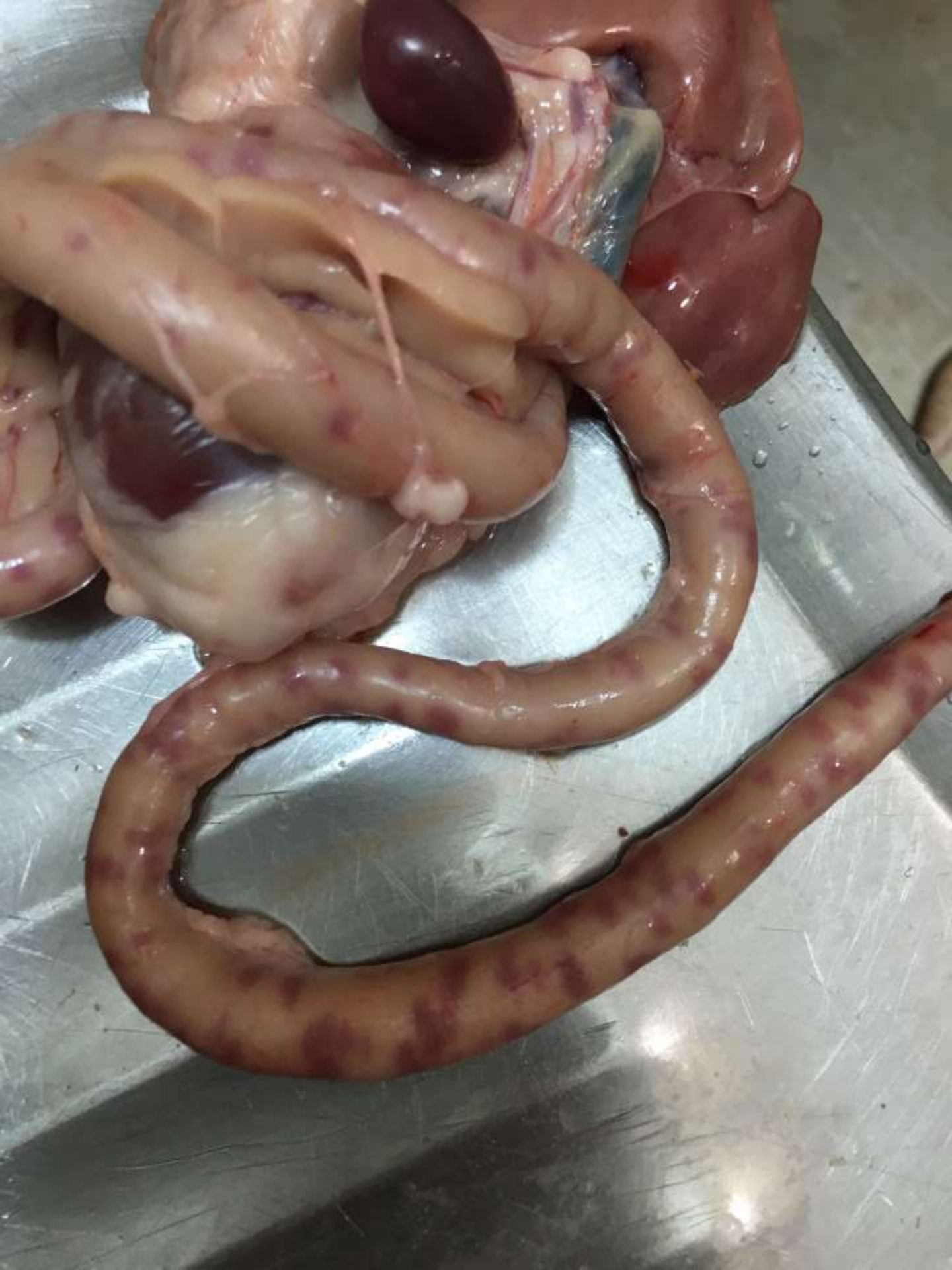












2-Neurotropic velogenic (Beach's form)

Clinical signs:

1-Mortality:50-100% (lmmature chickens 90%. Adult birds 10-50%)

2-Respiratory distress, coughing and gasping.

3-Decline or cessation of egg production.

4-Nervous signs may appear within a day or two, such as paralysis of legs or wings and torticollis.

Gross lesions:
Catarrhal exudates in nasal passages, larynx and trachea.
Occasionally. Haemorrhages in the trachea. Thickened membranes of one or more air sac sometimes with catarrhal or caseous exudates.
Airsacculitis may be present even after infection with relatively mild strains and thickening of the air sacs with catarrhal or caseous exudates is often observed in association with secondary bacterial infections.
Most problems in commercial poultry are caused by vaccinal strains acting as stressors causing secondary infection such as E. coli airsacculitis.

Mesogenic (Beaudette's form):

Clinical signs:

1-Mortality up to 50%. Are considered of intermediate virulence. Infection is typically systemic

2-Acute respiratory distress (coughing but rarely gasping).

3-Egg production declines or ceases for 1-3 weeks.

4-Egg quality is affected with rough or soft shelled, and some birds never returned to normal production.

5- Rarely symptoms of the nervous system can develop, but mortality is usually low following infection, except in very young and susceptible bird.

6-Birds never returned to normal production.

Gross lesions:
Respiratory lesions similar to those describe above.

Lentogenic (Hitchner's form): Mild or subclinical respiratory infection.

Clinical sings:

isolates do not usually cause disease in adults, if occur can lead to nonapparent to mild respiratory or gastrointestinal disease in adult chickens. When replication is limited to the gastrointestinal tract, the infection is often classified as asymptomatic enteric due to lack of respiratory symptoms.
In young, fully susceptible birds develop more serious respiratory disease problems that can lead to death due to increased susceptibility to secondary infection.

With no gross lesions.

Asymptomatic/ avirulent enteric form of infection: Subclinical enteric infection

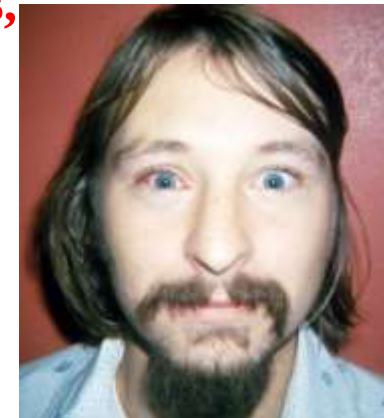
Economic Significance

The global economic impact of vND is huge. No other poultry virus comes close in terms of the economic impact, and it may represent a bigger drain on the world's economy than any other animal virus.

In developed countries with established poultry industries, not only are outbreaks of vND extremely costly, but control measures, including **vaccination, represent a continuing loss to the industry.**

The economic impact of vND is not only measured **in direct commercial losses**, but in some countries, **also in the effect it has on human health**.

NDV is a recognized human pathogen in its own right, clinical signs in human infections have been included, eye infections, usually consisting of **unilateral or bilateral reddening, excessive lachrymation, edema of the eyelids, conjunctivitis and subconjunctival haemorrhage**.



Biologic Properties of NDV

Hemagglutination Activity

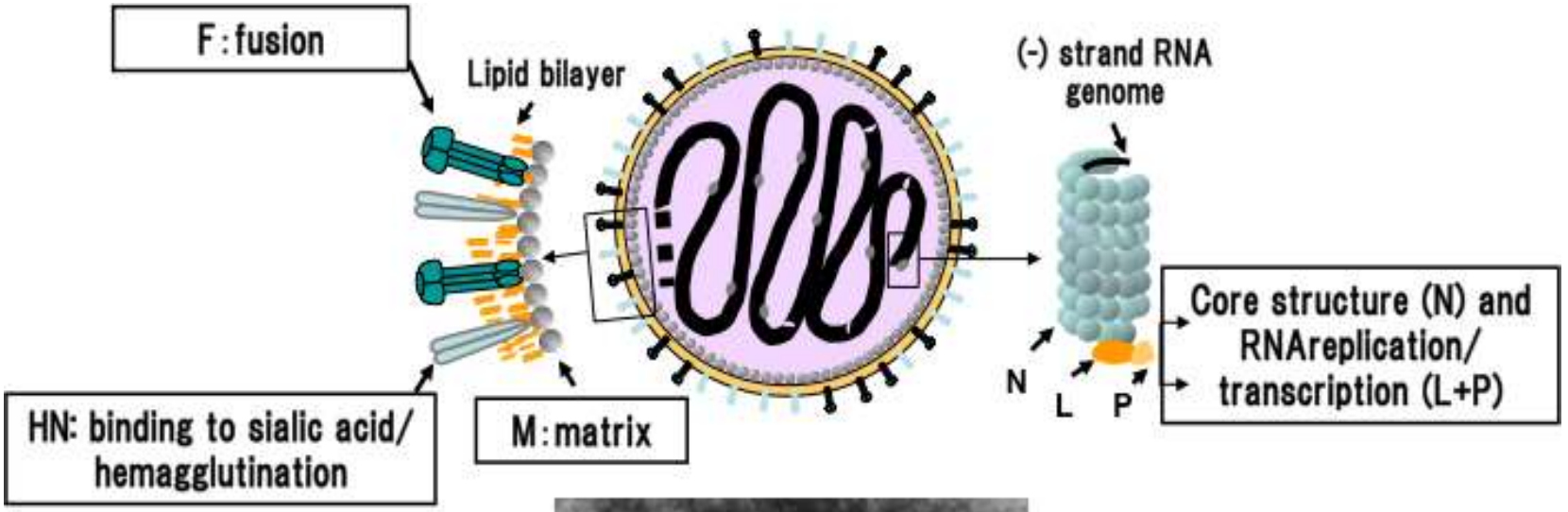
The ability of NDV and other avian paramyxoviruses to agglutinate red blood cells (RBCs) is due to the binding of the hemagglutininneuraminidase (HN) protein to receptors on the surface of the RBCs. This property and the specific inhibition of agglutination by antisera have proven to be powerful tools in the diagnosis of the disease.

Neuraminidase Activity

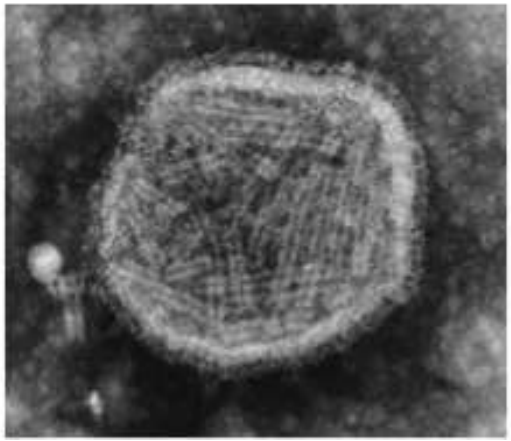
The enzyme neuraminidase is also part of the HN molecule. An obvious consequence of the possession of this enzyme is the gradual elution of agglutinated RBCs. The exact function of the neuraminidase in virus replication is unknown, but it seems likely that neuraminidase removes virus receptors from the host cell which prevents the reattachment of released virus particles and virus clumping.

Cell Fusion and Hemolysis

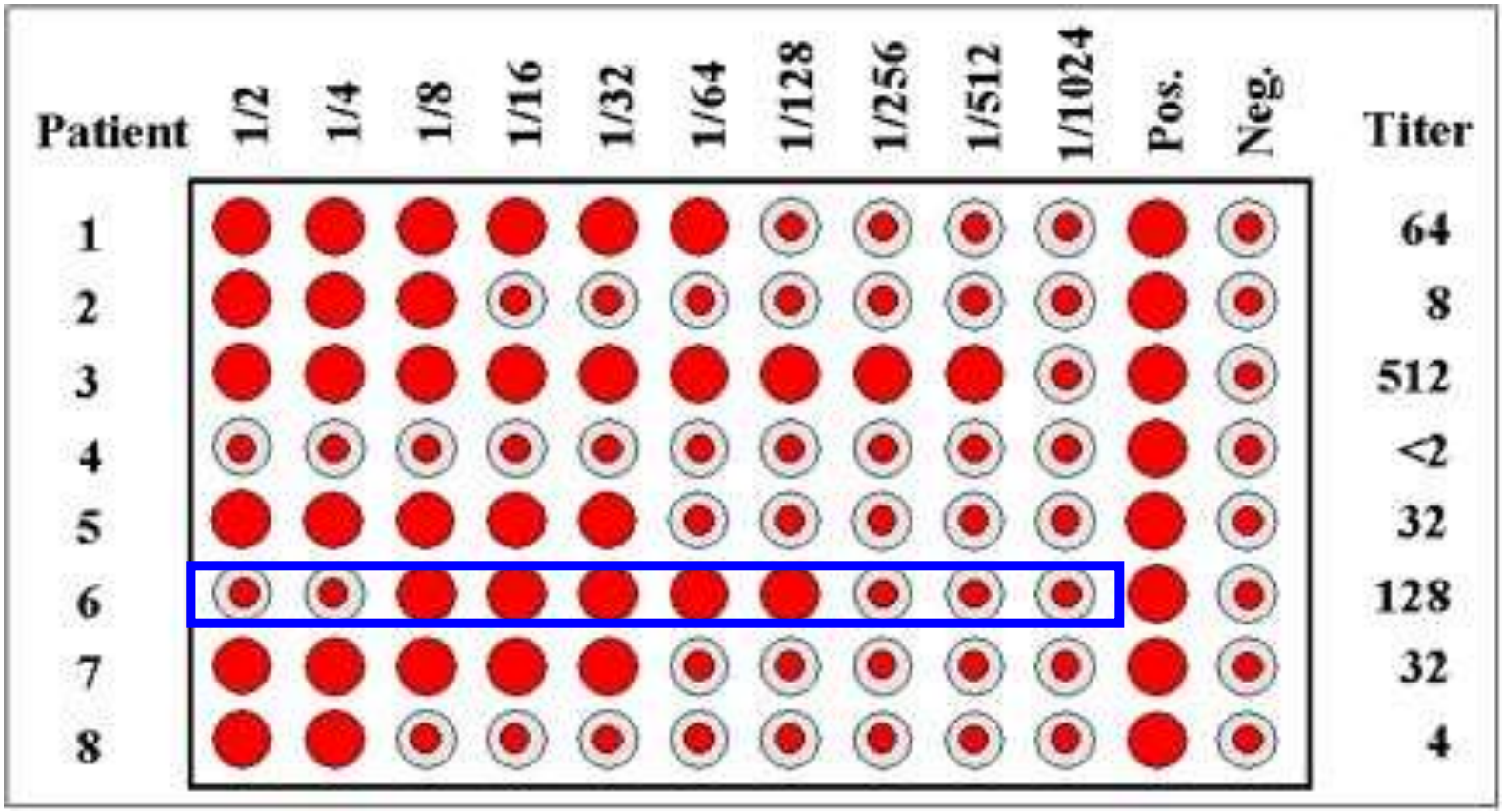
Attachment at the receptor site during replication is followed by fusion of the virus membrane with the cell membrane, which may result in the fusion of two or more cells. The rigid membrane of the RBCs usually results in lysis from the virus membrane fusion.



envelope



Ribonucleotide-protein complex (RNP)


Patient
1/2
1/4
1/8
1/16
1/32
1/64
1/128
1/256
1/512
1/1024
Pos.
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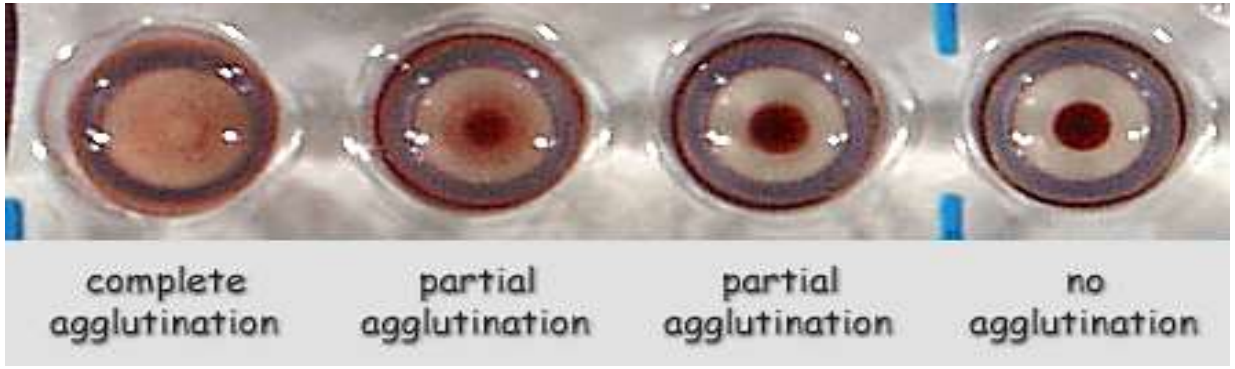

complete agglutination
partial agglutination
partial agglutination
no agglutination

Viral replication

The initial step is attachment of the virus to cell receptors, mediated by the **HN polypeptide**.

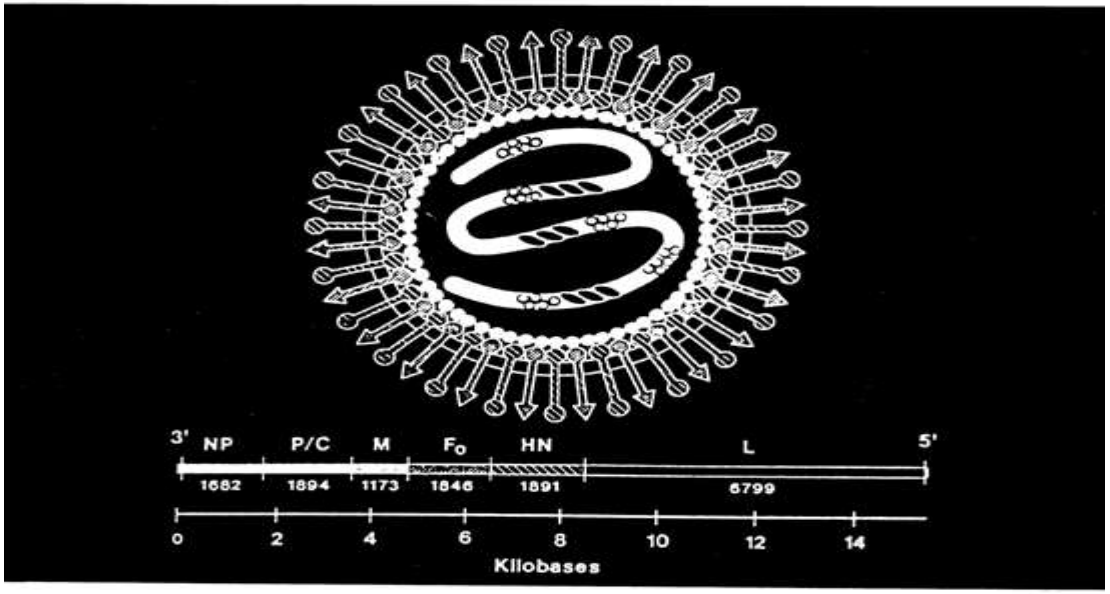
Fusion of the viral and cell membranes is brought about by action of the fusion (F) protein, and, thus, the nucleocapsid complex enters the cell.

Intracellular virus **replication takes place entirely within the cytoplasm.**

Because the virus RNA has negative sense, the viral RNA-directed RNA-polymerase (transcriptase) must produce complementary transcripts of positive sense that may act as messenger RNA and use the cell's mechanisms, enabling the translation into proteins and virus genomes .

The NDV replication cycle is the most rapid of all paramyxoviruses, replacing host protein synthesis with viral protein synthesis within 6 hours while producing maximal yields of viruses within 12 hours post infection

a



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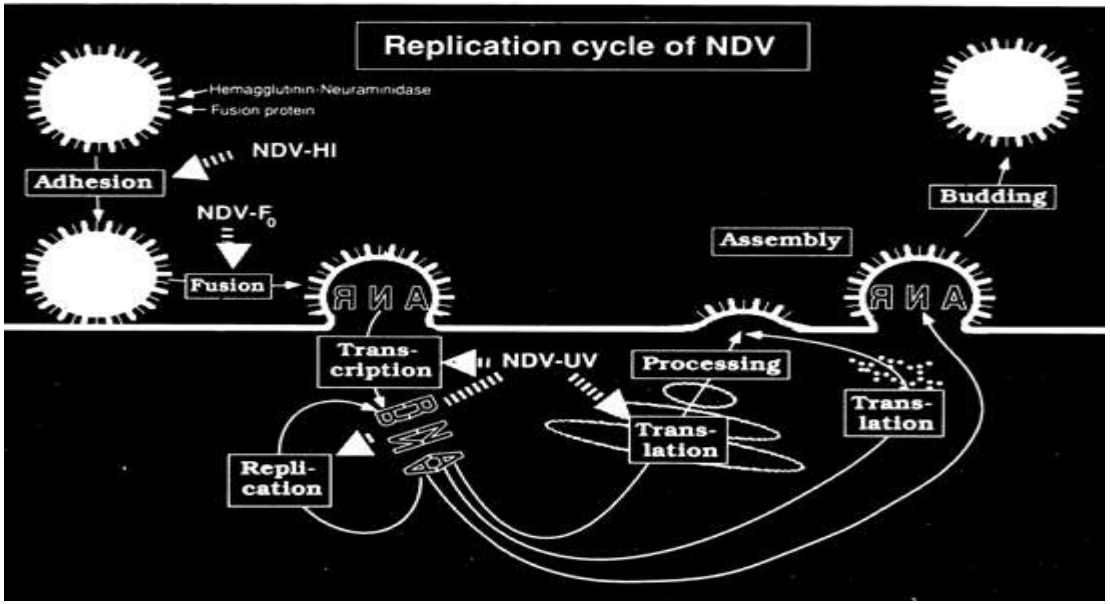


Physico-Chemical properties

The infectivity of NDV and other avian may be destroyed by physical and chemical treatments such as **heat, irradiation (UV).**
NDV tolerated 56°C for 30 minutes but got inactivated within 45°C, The virus remain active at PH 4 and 9 up to 24 hours, but lost its viability at PH 1 and 13 within six hours and the virus remain active following exposure of ultraviolet light for 45 minutes.

Laboratory Host Systems

1-Animals: NDV can infect and multiply in a range of nonavian as well as avian species following laboratory infection. The chicken, however, remains the most readily available and frequently used laboratory animal.


2- Chicken Embryos: All avian paramyxoviruses replicate in embryonated chicken eggs. Because of their availability their sensitivity for virus growth and the high titers to which viruses grow in them, they are generally used for virus isolation and propagation.

3-Cell Cultures: Newcastle disease virus strains can replicate in an enormous range of cells. The growth of the virus in cell culture characterized by cytopathic effects (CPE) lead to formation of syncytia with subsequent cell death.

Strain Classification

Strains of NDV could be conveniently grouped according to their severity as

1-Velogenic 2-Mesogenic 3- Lentogenic

Lentogenic - mild - kills embryos in > 90 hours.

Mesogenic - moderate - kills embryos in 60-90 hours.

Velogenic - highly virulent neurotropic or viscerotropic - kills embryos in < 60 hours

Velogenic strains are now officially designated as Exotic Newcastle Disease (END),

Lentogenic & mesogenic are used as vaccine strains.

Hitchner: B1 - B1 - milder

La Sota: B1 - La Sota - more virulent.

The most widely used tests are the intracerebral pathogenicity index (ICPI) in day-old chicks and the intravenous pathogenicity index (IVPI) in 6-week-old chickens.

Important distinction is made between viscerotropic velogenic NDV and other strains and virulence, by swabbing the cloaca of four 6- 8 week old individually with infective allantoic fluid. If the birds develop clinical signs and die, the virus is classified as velogenic.

viscerotropic velogenic NDV

Pathogenicity

The virulence of NDV strains varies greatly with the host.
Chickens are highly susceptible while ducks tend to show no clinical symptoms.
Waterfowl are considered a natural reservoir for NDV.
In chickens, the pathogenicity of ND virus depends on multiple factors including: **host species**, **age, immune status**, **secondary infections**, **stress**, **environmental conditions**, **the amount of virus transmitted**, and the route of transmission but **most importantly the strain of the infecting virus.**

Pathogenesis

Cleavage of the F protein during viral replication in the host plays a major role in the virulence of the virus. Velogenic and mesogenic strains of NDV are able to replicate systemically **due to the active state of the F protein**. Unfortunately velogenic NDV and mesogenic NDV, strains cannot be differentiated based on their amino acid sequences at the F protein cleavage site.

Due to the lack of several basic amino acids in **low virulent strains**, the F protein must be cleaved by secretory trypsin-like proteases which are limited to the mucosal membranes in the respiratory and gastrointestinal tracts, Low virulent strains are not able to replicate systemically due to the limited availability of these trypsin-like proteases.

In general, the younger chicken infected with the more acute disease. With virulent viruses in the field, young chickens may experience sudden deaths without major clinical signs; however, in older birds the disease may be more prolonged and with characteristic clinical signs.

Transmission

The primary route of transmission is either **by ingestion of fecal contaminated material or inhalation of droplets** containing the organism from one bird to another.

Viral replication in the respiratory tract of infected birds allows for spreading of the virus during nasal discharge and easily spreads the virus through the flock.

In naturally occurring infections, large and small droplets containing virus will be liberated from infected birds as a result of replication in the respiratory tract or as a result of dust and other particles, including feces. During the course of infection of most birds with NDV, large amounts of virus are excreted in the feces.

Ingestion of feces results in infection; this is likely to be the main method of bird-to-bird spread for a virulent enteric NDV.

Vertical transmission (i.e., passing of virus from parent to progeny via the embryo) **remains controversial**.

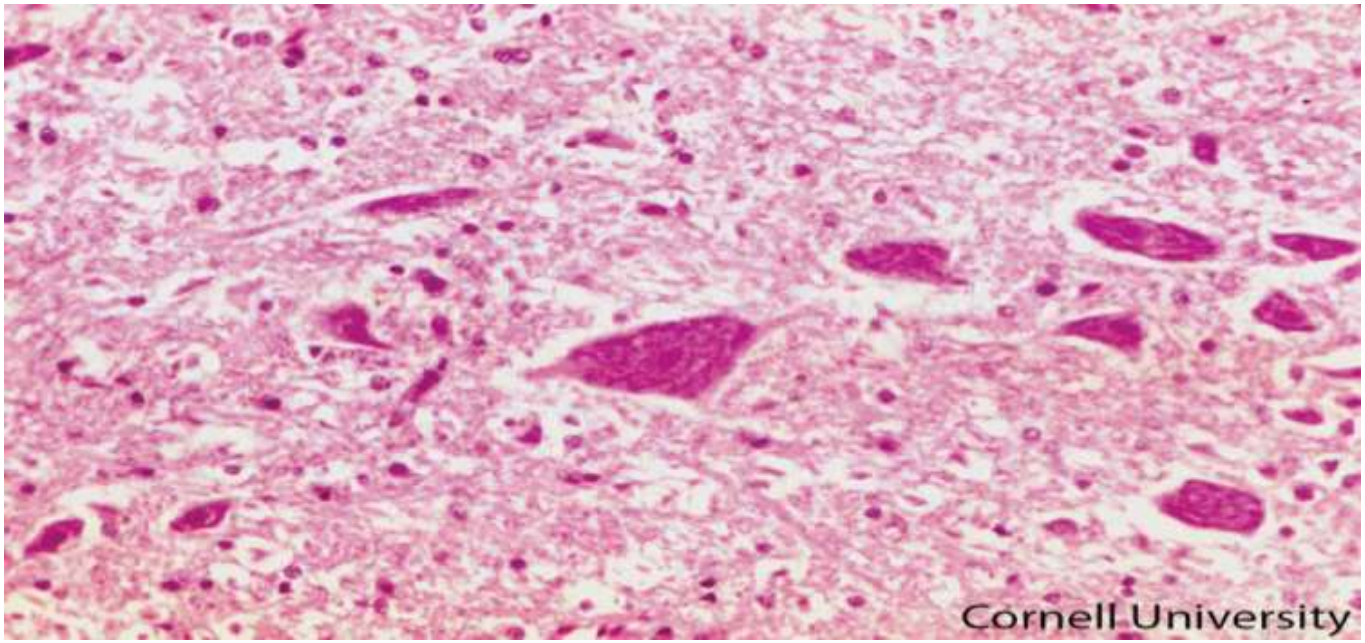
Infected embryos have been reported during naturally occurring infections of laying hens with virulent virus, but this generally results in the death of the infected embryo during incubation.

Cracked or broken infected eggs may serve as a source of virus for newly hatched chicks.

Histopathologic lesions

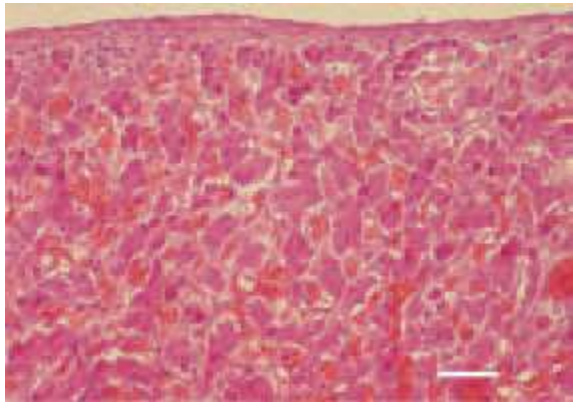
Changes following NDV infections are related to the virulent pathotypes.

1- Lesions seen in nervous system characterized by nonpurulent encephalomyelitis with neuronal degeneration, foci of glial cells, perivascular infiltration of lymphocytes, and hypertrophy of endothelial cells. Lesions usually are seen in the cerebellum, medulla, mid brain, and spinal cord but rarely in the cerebrum .



2- Hyperplasia of the mononuclear phagocytic cells in various organs, especially the liver.

3- Necrotic lesions are found throughout the spleen. Focal vacuolation and destruction of lymphocytes may be seen in the cortical areas and germinal centers of the spleen and thymus.



4- The intestinal tract showed Hemorrhage and necrosis of mucosal.
5- Following aerosol exposure to NDV, The cilia may be lost within two days of infection, the mucosa of the upper respiratory tract appeared congestion, with edema, and dense cellular infiltration of lymphocytes and macrophages.
6- Changes in female reproductive organs included atresia of follicles with infiltration of inflammatory cells and the formation of lymphoid aggregates.

Diagnosis:

None of the clinical signs or lesions of vND may be regarded as pathognomonic, and the wide variation in disease with virus strain, host species, and other factors means that at best, these can serve as only a suggestion of infection with NDV.

Laboratory diagnosis

Samples

Samples should be collected from recently dead birds or moribund birds that have been killed humanely.

Dead birds: oro-nasal swabs; lung, kidneys, intestine, spleen, brain, liver and heart tissues.

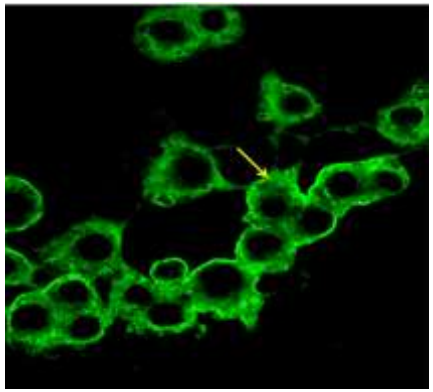
Live birds: tracheal and cloacael swabs (visibly coated with faecal material) from live birds.

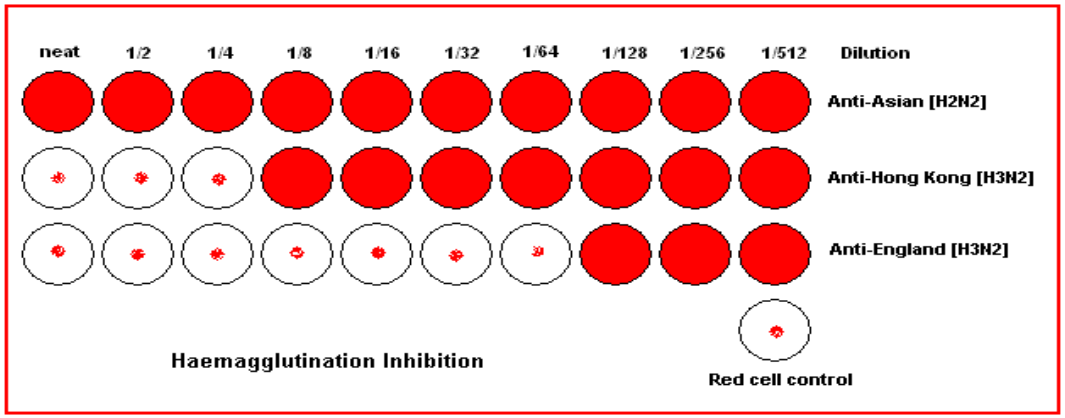
Serological tests

Haemagglutination , haemagglutination inhibition tests, Virus Neutralization test**,** Fluorescent Antibody test most widely used and detects antibody response to virus glycoprotein.

Enzyme-linked immunosorbent assay (ELISA): as whole virus is antibody to all of the virus proteins.

PCR detection of NDV





Differential Diagnosis

Infectious bronchitis and avian influenza – may cause respiratory disease and egg production problems in chickens and turkeys that closely resemble APV(NDV) infection.

Laryngotracheitis showed respiratory signs, avian encephalomyelitis showed neurological signs and Vitamin E & selenium deficiency – shows neurological signs.

A number of bacteria and *Mycoplasma* species can cause disease signs very similar to APV infection

Only by isolating or identifying APV in the affected birds can a clear distinction be made.

Control and Prevention

No treatment

Vaccination

Ideally, vaccination against vND would result in immunity against infection and replication of the virus.

The most important considerations for any vaccination programme is:

1- The type of vaccine to be used,

2- **The immune and disease status of the birds to be vaccinated**,

3-**The level of maternal immunity in young chickens.**

Live Vaccines

Live vaccine divide into two groups, lentogenic and mesogenic, the mesogenic vaccines fall within the current of virus responsible for vND. They are used only in countries where vND is endemic and are suitable for secondary vaccination of birds because of their virulence.

Conventional live virus vaccines: 2 groups:

1-Lentogenic vaccines (e.g. Hitchner-B1, La Sota, V4, NDW, F(Asplin))

2- Mesogenic vaccines (e.g. Roakin, Mukteswar and Komarov).

Most live virus vaccines grown in allantoic cavity of **embryonated fowl eggs**; **some mesogenic** strains have been adapted to a variety of **tissue culture systems.**

Live virus vaccines administered to birds by incorporation **in the drinking water**, **delivered as a coarse spray**, **or by intranasal or conjunctival** instillation.

Some mesogenic strains are given by wing-web intradermal inoculation.

Vaccine is applied in fresh drinking water at concentrations carefully calculated to give each bird a sufficient dose.

Drinking water application must be carefully monitored as the virus may be inactivated by excessive ambient heat, impurity in the water, and even

the type of pipes or vessels used to distribute the drinking water. To some extent, virus viability can be stabilized bv the addition of dried skim milk powder to the drinking water.

Spray and aerosol vaccination

Mass application of live vaccines by sprays and aerosols is also very popular due to the ease with which large numbers of birds can be vaccinated in a short time.

It is important to achieve the correct size of particles by controlling the conditions under which the aerosol is generated.

Coarse sprays of large particles do not penetrate deeply into the respiratory tracts of birds and give less reaction, so these may be more suitable for the mass application of vaccine to young birds.

Spray and aerosol vaccination are the preferred methods for vaccination against respiratory infectious diseases.

Coarse spray generators can be hand-held or knapsack sprayers or are integrated in spraying cabinets for 1-day-old chickens.

Inactivated vaccines

Tend to be more expensive than live vaccines, application and handling need to injecting individual birds.

Prepared from allantoic fluid that has had its infectivity inactivated by formaldehyde or beta-propiolactone, incorporated into an emulsion with mineral oil, and is administered intramuscularly or subcutaneously; each bird thus receives a standard dose.

Advantage of no subsequent spread of virus or adverse respiratory reactions, virulent and avirulent strains are used as seed virus; from a safety control perspective.

Much larger amount of antigen is required for immunization than for live virus vaccination.(No virus multiplication takes place after administration)

Vaccination Programs

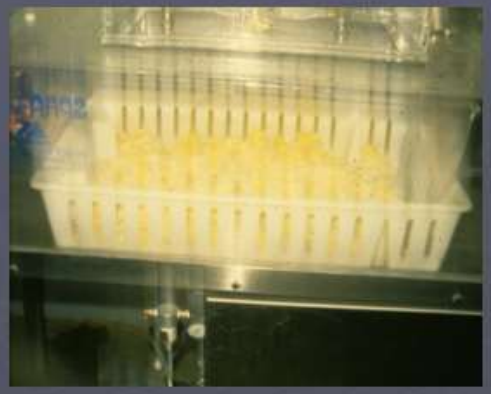
Vaccination programs and vaccines may be controlled by government policies. They should always be adapted to go with the availability of vaccine, maternal immunity, use of other vaccines, presence of other organisms, size of the flock, climatic conditions, past vaccination history, and cost.

Timing of vaccination of broiler chickens can be especially difficult due to the presence of maternal antibodies.

Because of their short life, broiler chickens are sometimes not vaccinated in countries where there is a low risk of ND.

Vaccination of laying hens always requires more than one dose of vaccine to maintain immunity throughout their lives.

Vaccination Cabinet

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