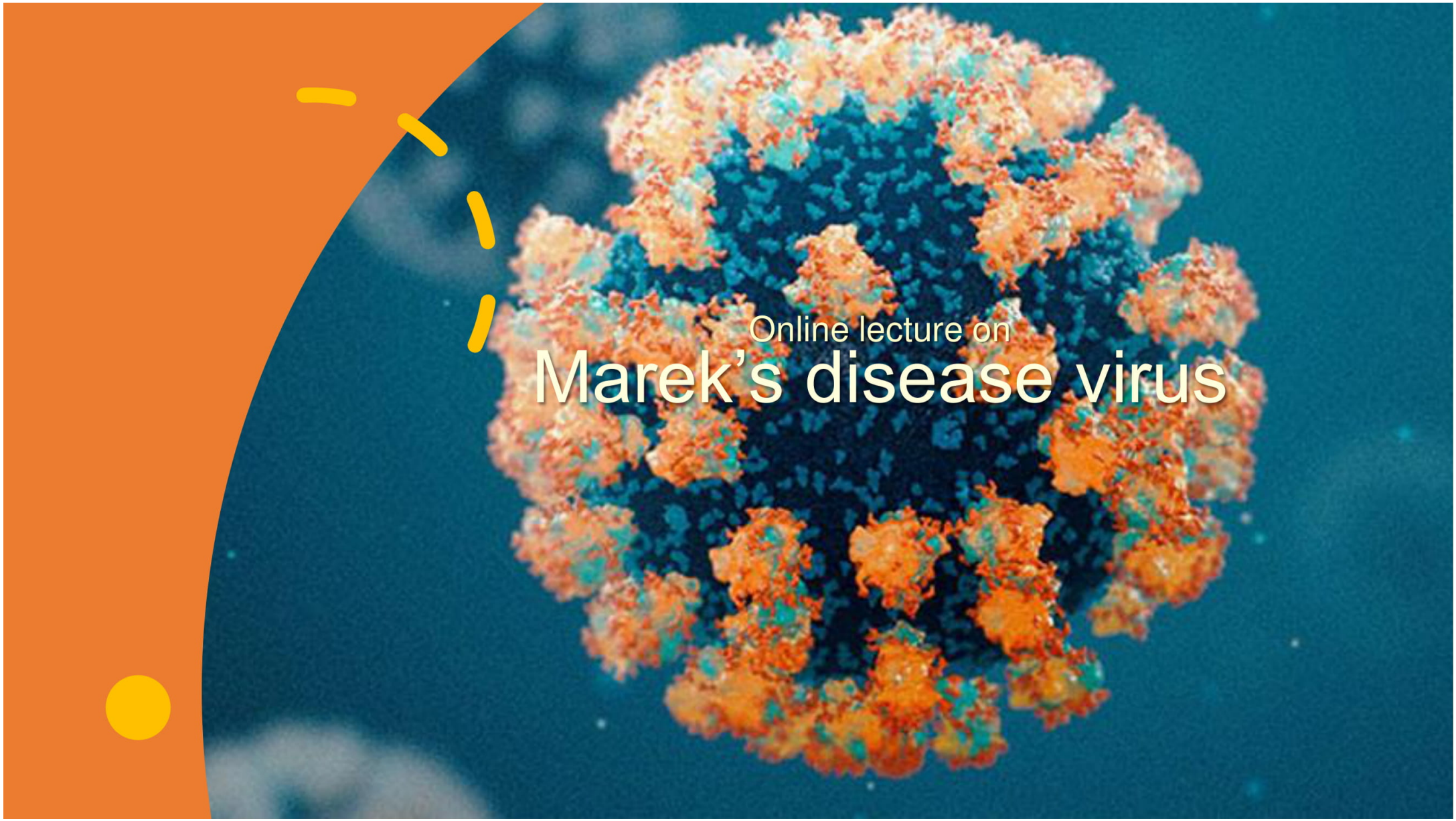
Online lecture on
Marek’s disease virus

VMC 605: Systematic Animal Virology

Marek's disease virus

Prepared by

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Department of Veterinary Microbiology
Bihar Veterinary College
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Taxonomy

- Order: *Herpesvirales*
- Family: *Herpersviridae*
- Subfamily: *Alphaherpesvirinae*
- Genus: *Mardivirus* (Marek's disease like viruses)
- Species: Gallid Herpesvirus 2 (GaHV-2) /Marek's disease virus (MDV)

Gallid herpesvirus

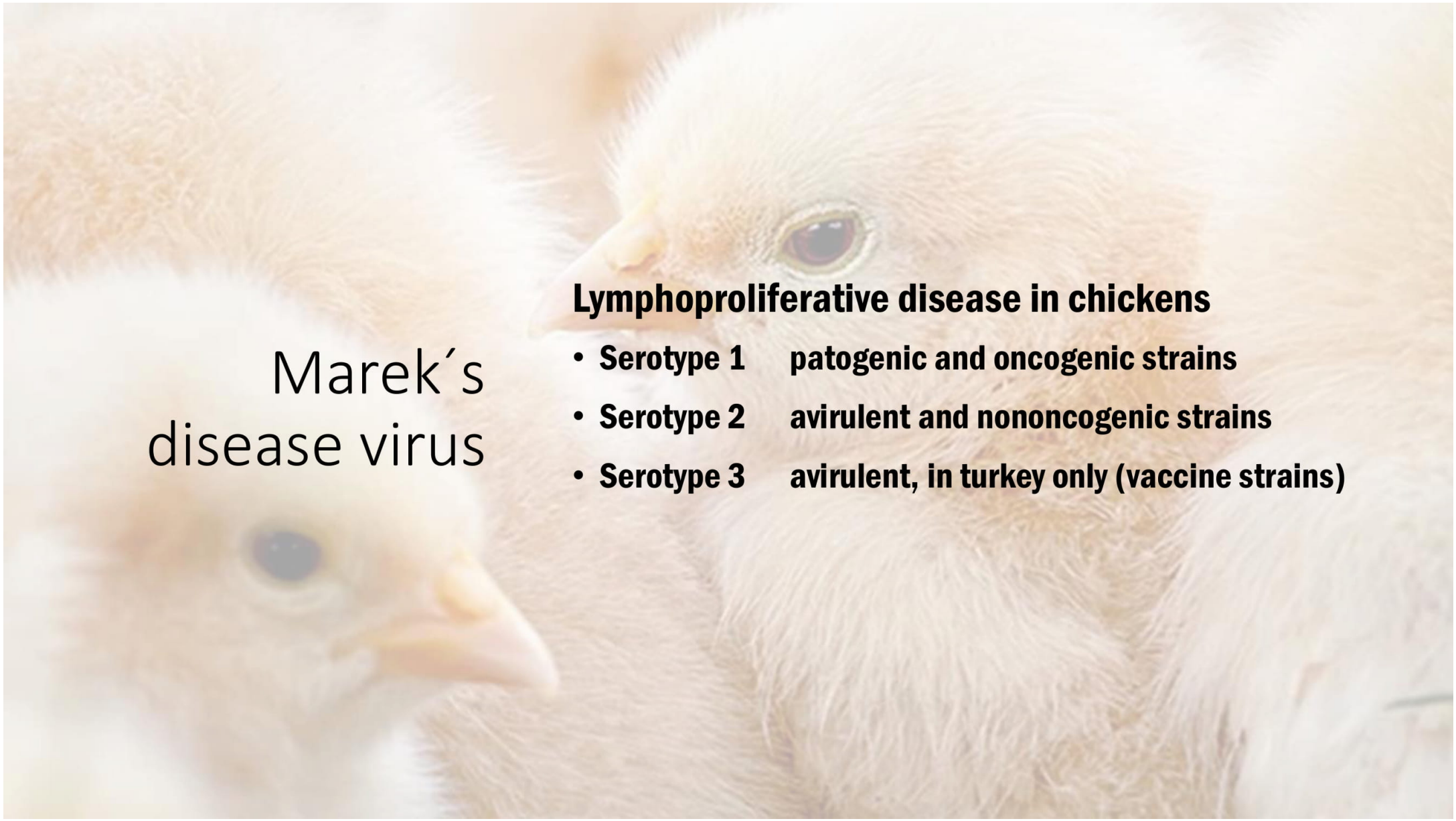
- 4 other species:
  - Gallid herpesvirus 3 (GaHV-3)
  - Meleagrid herpesvirus 1 (MeHV-1) - commonly known as herpesvirus of turkey (HVT),
  - Anatid herpesvirus 1
  - Columbid herpesvirus 1.
  - GaHV-3 and HVT infect domestic fowls like MDV, but are not pathogenic.

Vaccine strain of GaHV

- All the currently used vaccines are live vaccines derived from the three viral strains:
- HVT FC126 strain
- GaHV-3 SB-1 strain
- GaHV-2 CVI988/Rispens strain
- HVT and SB-1 vaccines are heterologous vaccines
- Rispens vaccine is homologous vaccine

Classification

International Committee on Taxonomy of Viruses (ICTV, 2011)



Marek´s disease virus

Lymphoproliferative disease in chickens

- **Serotype 1** **patogenic and oncogenic strains**
- **Serotype 2** **avirulent and nononcogenic strains**
- **Serotype 3** **avirulent, in turkey only (vaccine strains)**

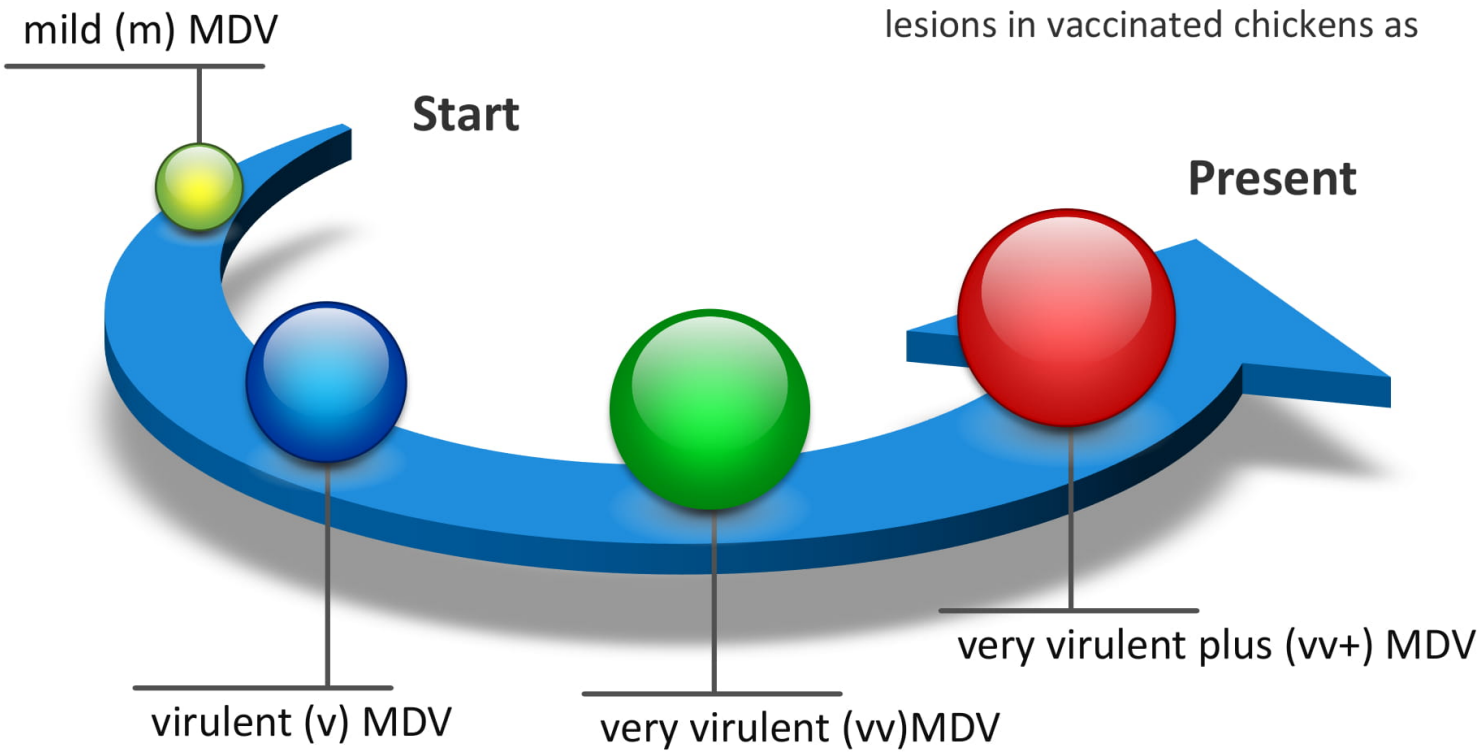
Serotypes

Serotype 1 Viruses ("hypervirulent")	Serotype 2 Viruses	Serotype 3 Viruses(HVT)
Viruses grow best in duck embryo fibroblast or chicken kidney cell	✓ Viruses grow best in chicken embryo fibroblast	~ • Viruses grow best in chicken embryo fibroblast.
Virus grows slowly	✓ Virus grows slowly	~ • Virus grows rapidly
Produce small plaques	✓ Produce medium plaques	~ Produce large plaques
Include all the oncogenic strains and their attenuated forms	✓ Non-oncogenic viruses isolated in chickens	~ Non-oncogenic viruses isolated in turkey; herpesvirus of turkey or HVT

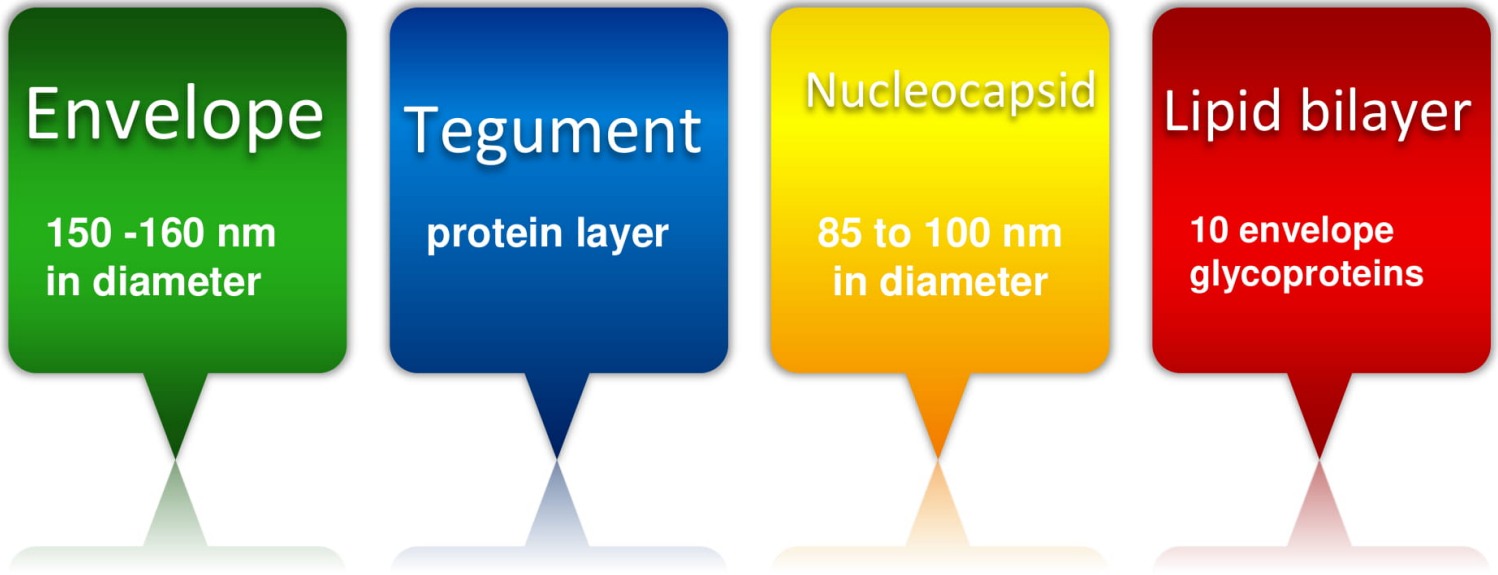
Serotype 1 MDV strains are further classified

Basis of classification

- Four pathotypes based on induction of lymphoproliferative lesions in vaccinated chickens as



MDV characteristics:



Sample subtitle

- Lipid bilayer in which about 10 envelope glycoproteins

Sample subtitle

- Comprising of more than 15 proteins

Sample subtitle

- Viral genome (linear, double standard DNA molecules of approximately 160 – 180 kbp)

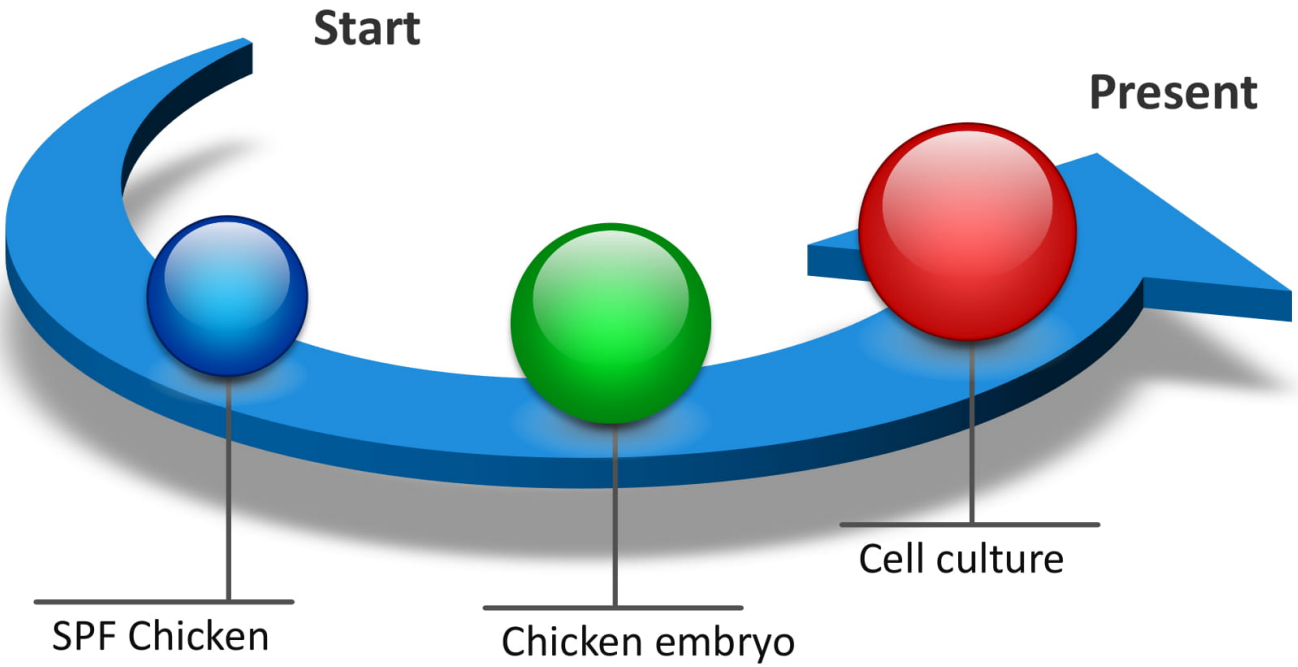
Sample subtitle

- (glycoprotein B (gB), gC, gD, gH, gI, gK, gL and gM) are anchored

Cultivation of virus

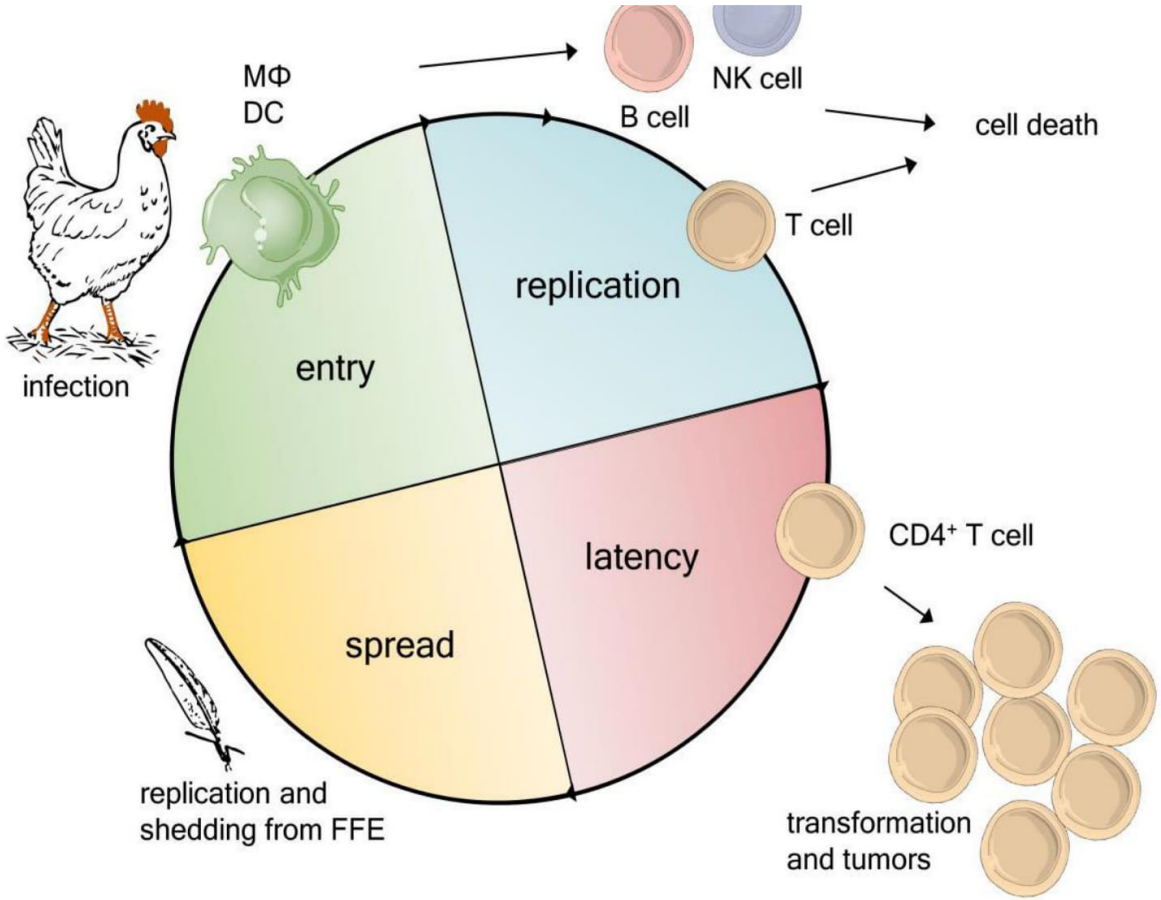
Host system

- For isolation of virus
- Development of vaccine
- Diagnosis



Marek's disease virus (MDV) infection

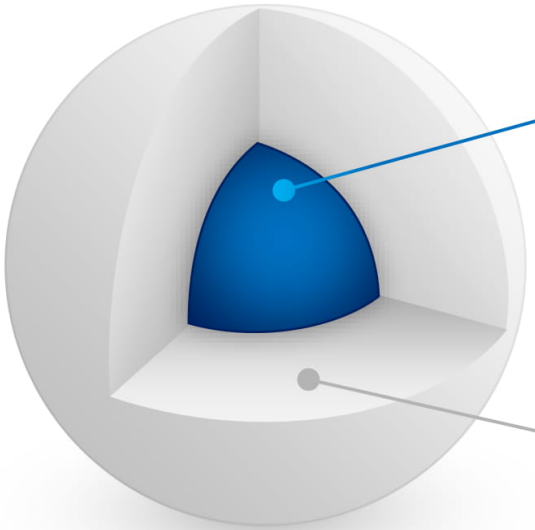
- Inhalation of infectious dust.
- Mononuclear phagocytes transfer the virus to lymphoid organs - spleen, thymus, and bursa - virus lytically replicates in lymphocytes.
- MDV is able to establish latency in infected t cells.
- Latently and/or lytically infected t cells transport the virus to the skin and feather follicle epithelia (FEE)
- Cell free MDV is generated
- MDV can transform latently infected T-cells, resulting in deadly lymphomas.



THE DISEASE

- MD is a neoplastic and neuropathic disease of poultry caused by a highly contagious, cell-associated herpesvirus. MD virus (MDV)

Route



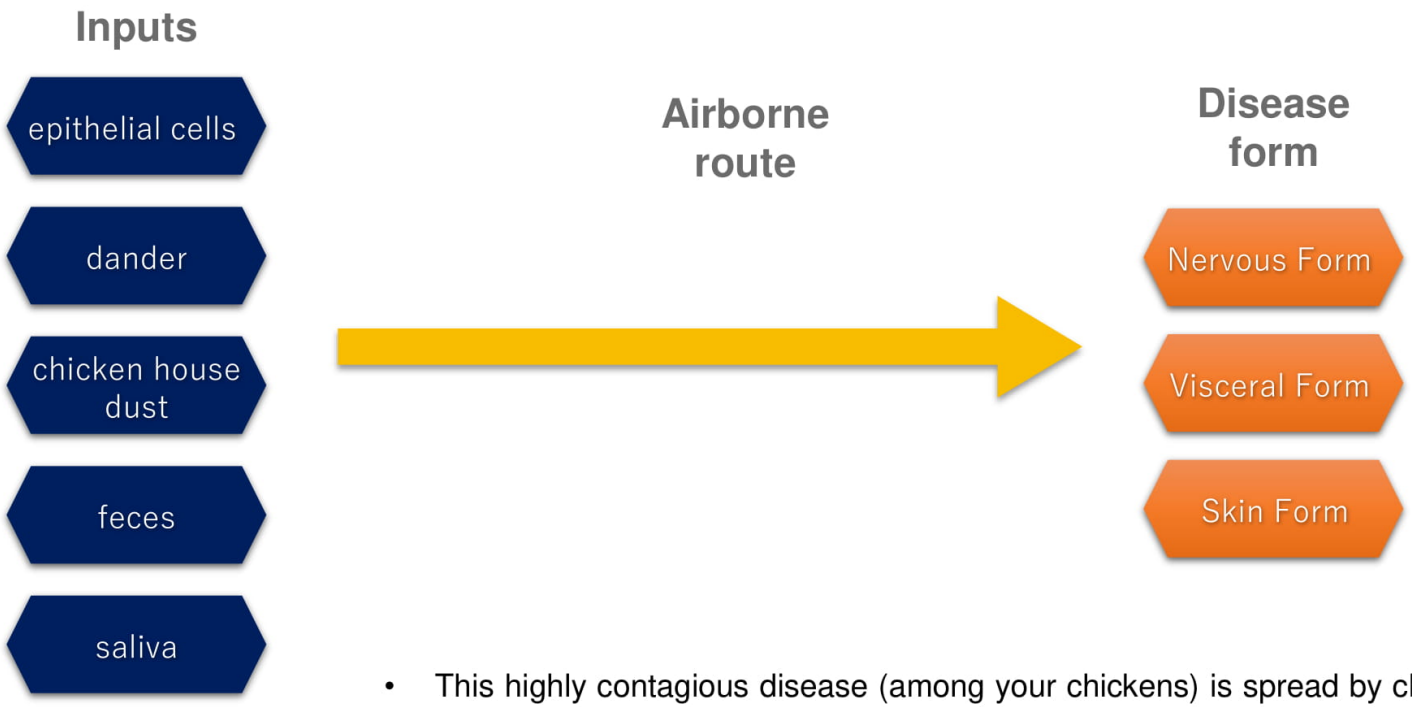
Route of infection

Natural route of MDV infection is via respiratory tract

Spread

Following inhalation of infectious cell-free MDV present in dander shed from feather follicles.

Transmission



- This highly contagious disease (among your chickens) is spread by chicken dander (dust) through inhalation
- This condition increases the risk of other diseases as the immune system is compromised
- It can also spread rapidly through contact with other contaminated chickens in the flock
- Dander from other wild birds, the wind, human shoes can all spread the disease
- It can be spread through environmental factors such as an infected enclosure MD can survive in the soil where chickens are kept for at least five months Diagnosis of Marek's

Transmission

- Marek's disease virus is shed in dead skin and feather follicle epithelial cells, where enveloped infectious virions egress from the body that contribute to the dust found in chicken houses, this disease is spread horizontally but, it is not spread vertically from chicken to egg
- MDV is spread easy by bird-to-bird contact, and contact with infected dust and dander and indirect contact with infected chickens, premises litter, and chopped feathers and airborne route to the environment and to other chickens

Steps of Pathogenesis

Pathogenesis

MDV-1 causes lytic infection of lymphoid cells, mainly B cells that last for up to six days after infection. Then, this cytolytic infection induces the activation of T cells, and MDV establishes latency in a part of the activated CD4+ T cells at 1–2 weeks after infection

Infected chickens show no clinical signs, but cellular immunity is continually inhibited by apoptosis of CD4+ T cells, CD8-down regulation in CD8+ T cells, decrease in the responsiveness to the stimulation through T cell receptor (TCR) in CD4+ and CD8+ T cells and MHC class i-down regulation at 2–3 weeks after infection

Immunosuppression and tumor development.
MDV-1 transforms a few latently infected CD4+ T cells, and develops malignant lymphomas. The main targets for the transformation by MDV-1 are CD4+ T cells, suggesting that latent infection in this T cell subset is intimately related to the subsequent transformation by MDV-1

Pathogenesis

i. MDV reaches the lymphoid organs within 2–3 days after infection.

ii. In the lymphoid organs, infection of lymphocytes is assisted by splenic ellipsoid-associated reticulum cells

iii. A productive, cytolytic, infection is shortly established in the lymphoid organs

iv. The initial target cells for the cytolytic infection are B lymphocytes

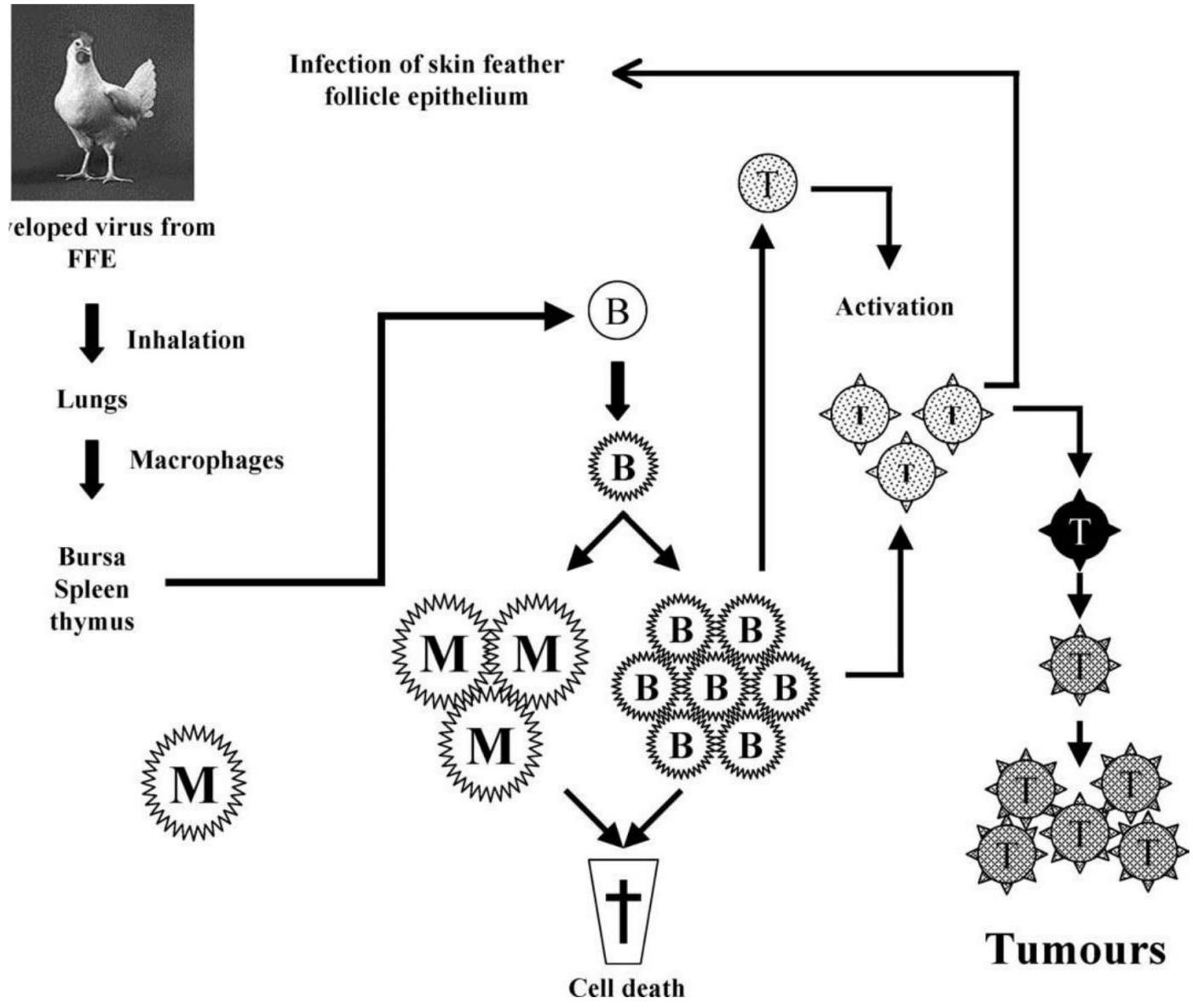
v. The necrosis of B cells in the lymphoid organs elicits an immune response and the subsequent recruitment of numerous inflammatory cells, especially macrophages, T and B lymphocytes and some heterophils.

vi. Activated T cells can also support productive infection but in most cases, infection becomes latent after T cells are infected

vii. The switch from cytolytic infection to latency occurs very fast and by 7–8 days, there is minimal evidence of cytolytic infection in the lymphoid organs.

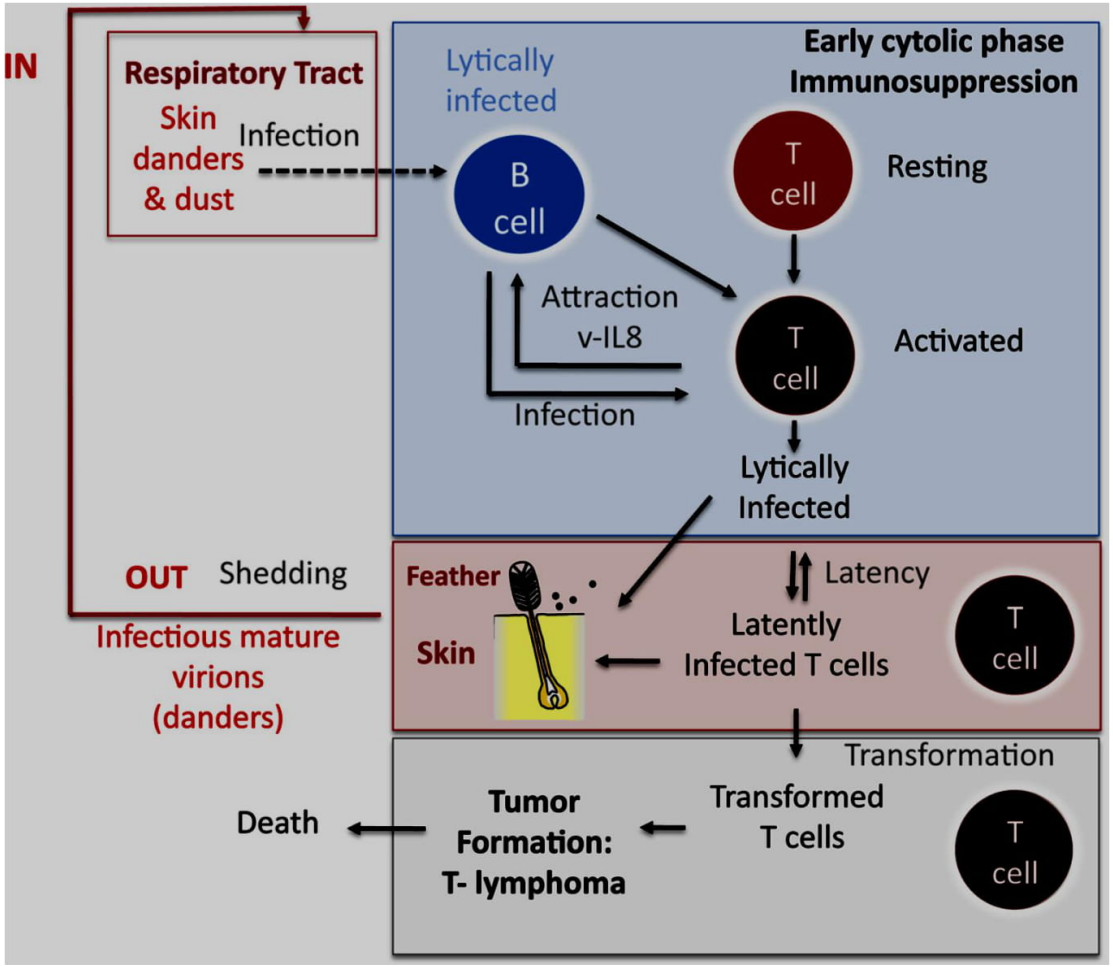
viii. Latent infection can be detected by 7–8 days post-infection not only in lymphoid organs but also in peripheral blood lymphocytes. Latently infected peripheral blood lymphocytes probably are the disseminators of MDV to other tissues of the chickens. As early as 6 days post-infection, MDV can be detected in the brain, peripheral nerves and eye

ix. A second wave of cytolytic infection is detected in most tissues of epithelial origin by the end of the second week after infection.


veloped virus from FFE
Inhalation
Lungs
Macrophages
Bursa
Spleen
thymus
Infection of skin feather follicle epithelium
B
B
T
Activation
T
T
T
T
T
T
T
T
T
T
T
T
M
M
M
M
B
B
B
B
B
B
B
Cell death
Tumours

Pathophysiology of Marek's disease

- Marek's disease virus (MDV) enters into the chicken
- through the respiratory tract. MDV has a tropism for B- and T-lymphocytes as well as for the feather follicle epithelium, from which MDV is
- shedded into the environment. Feathers, skin danders and dust are the major source of MDV infectious materials and the basis of horizontal
- bird-to-bird transmission in field conditions.



Clinical findings

- Based on its clinical symptoms MDV is divided in to two forms *viz*,.

i. **Early mortality syndrome (EMS)** - EMS results in high mortality of young chicks infected with virulent MDV showing the symptoms of depression and comatose prior to death.

ii. **Transient paralysis (TP).**

- TP, is further divided into two forms

    a) classical form

    b) acute form

Classical form- *most common*

Classical Marek's (neurolymphatosis), also known separately as **neural** and **visceral** forms.

- Paralysis of one or both legs, and sometimes wings.
- Torticollis of nerves controlling the neck are affected.
- Vagal involvement will lead to dilatation of the crop and/or gasping
- Going off of food or inability to “connect” with food when trying to eat.
- Difficulty breathing, darkening comb
- Lymphomas / Neoplasms (cancerous tumours) throughout the chicken
- Weight loss, “wasting”, depression
- Loose, watery, and/or bright green stool

Ocular Marek's (ocular lymphatosis)

- Discoloration of the iris.
- Deformity of the pupil.
- Pupil with no reaction to light changes
- Partial or complete blindness("grey eye") in one or both eyes, accompanied by distortion of the pupils, depigmentation (silver or grey eyes) and iritis were observed in several paralysed chickens.

Cutaneous Marek's

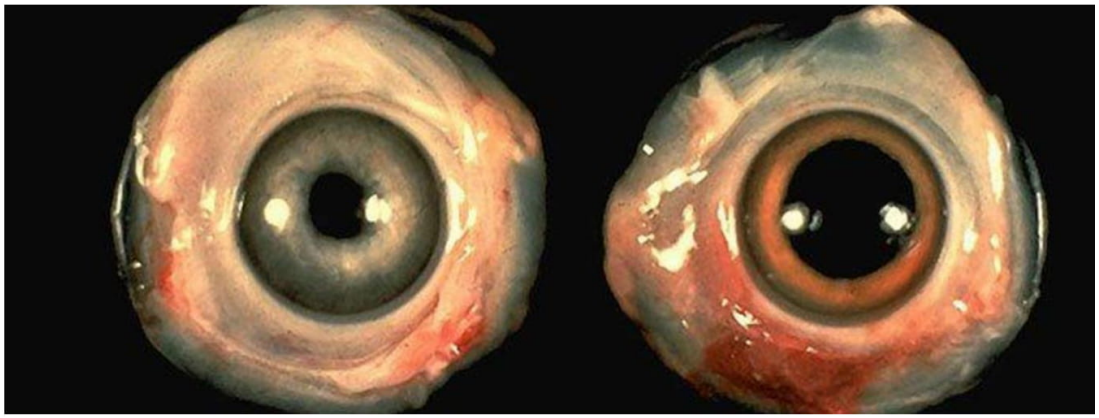
- **Lesions or deformities at the feather follicles**.
  - This may be minor to severe and can range from large bumpy nodules to crusty looking lesions. They may be rounded or hard.

Indications of nervous form

- Neck, -wings or legs include torticollis,
- Drooping of the wings, paresis of the legs or wings on one side or both,
- Inward curving of the toes, weakness of the legs and a squatting position which are regarded as were observed.

Characteristic respiratory symptoms

- Gasping which may indicate disturbances of the vagus were also found.
- Symptoms in the neck or wings were usually associated with the symptoms in the legs.
- At the begining, respiratory symptoms appear, and a sudden onset of paralysis became aware by a difficulty or inability in walking.
- Partial or complete blindness in one or both eyes, accompanied by distortion of the pupils, depigmentation (silver or grey eyes) and iritis were observed in several paralysed chickens.
- Depression, some show anaemia, emaciation, diarrhoea and excretion of green faces. Drooping of the wings is found frequently. In most of the cases, paralytic symptoms of the legs are not conspicuous, and only a few showed abnormal reflex and sensation.



BACKYARD
CHICKEN COOPS

MAREK'S
CHECK YOUR CHOOK

Diagnosis

- Clinical signs
- Gross & histopathology
- Isolation & identification of virus
- Molecular characterization of MDV

Leg paralysis

Marek's disease virus (MDV) infected White Leghorn (WLH) birds showing paralysis

Experimentally MDV infected broiler birds showing complete paralysis

Flaccid neck

Swelling of wattle

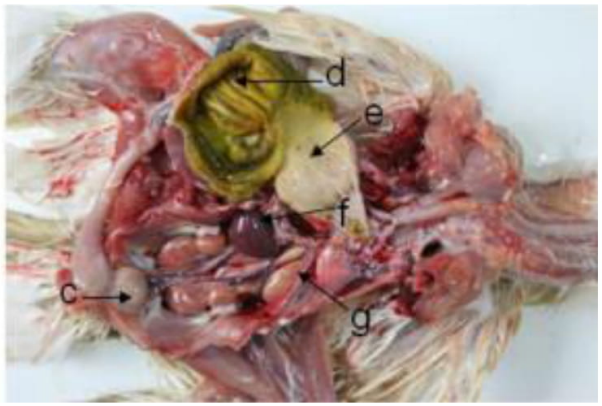
BACKYARD
CHICKEN COOPS

MAREK'S
CHECK YOUR CHOOK


MAREK'S IS transmitted
BY PARTICLES IN THE AIR
BACKYARDCHICKENCOOPS.COM.AU


Manifest itself in
three different ways:
• 1. Nervous (neurological) – paralysis of the legs/wings,eye lesions.
• 2. Visceral – tumours of the organs and muscles.
• 3. Cutaneous – tumours of the skin and feather follicles.

depression, with birds standing around looking ‘off colour’. This could be followed by lame or paralysed birds. Mortality may occur with no symptoms at all or there may be paleness, loss of appetite, diarrhoea and dehydration, gasping, or blindness.



(**a**) yellow degeneration diffusely in liver edge;

(**b**) rough and uneven in liver surface;

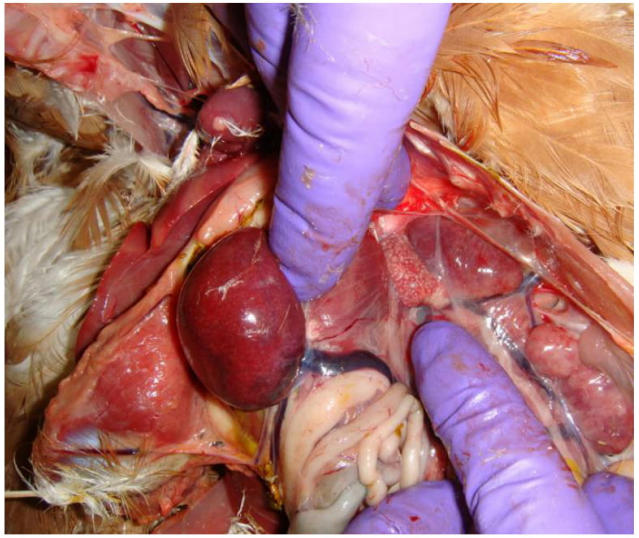
(**c**) bursa of Fabricius swelling;

(**d**) muscular stomach swelling;

(**e**) glandular stomach swelling;

(**f**) lots of white diffused nodule in the swelled spleen;

(**g**) kidney swelling and pale in color.



Visceral form

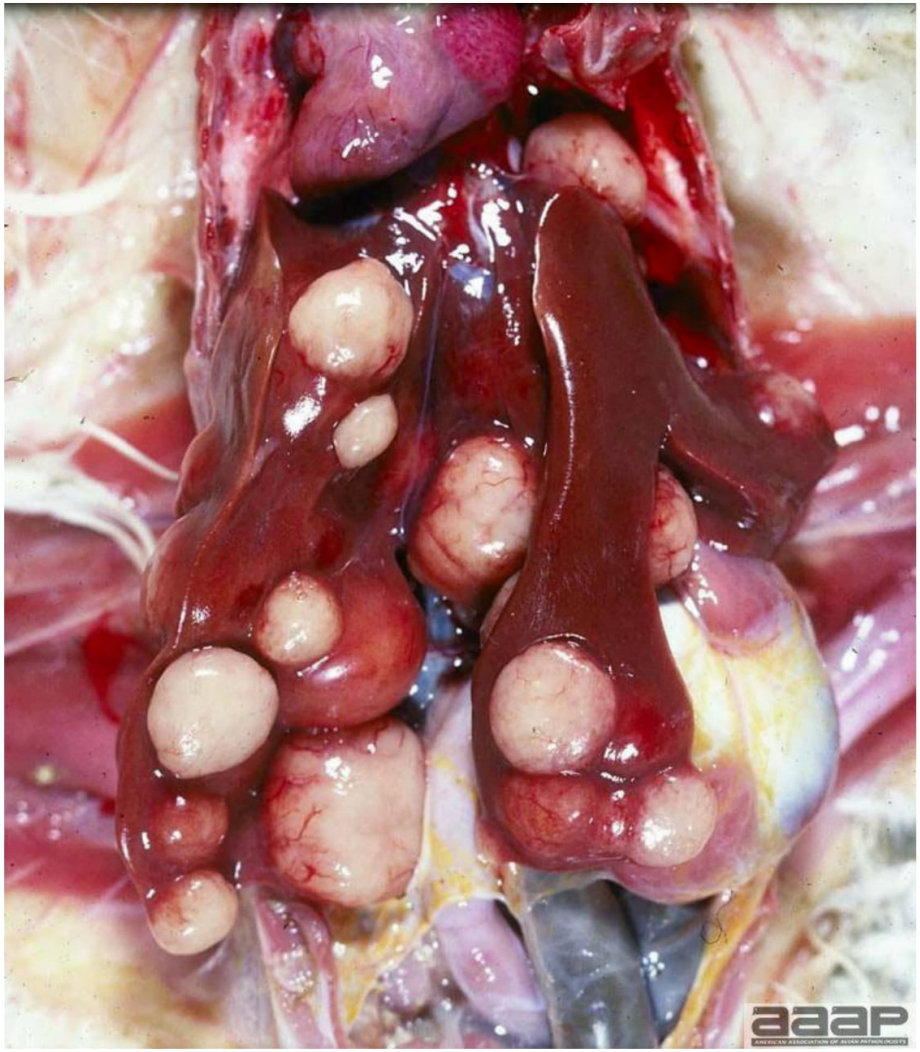
Tumors in liver

Visceral form

Tumors in liver

Visceral form

Visceral tumour



Visceral form

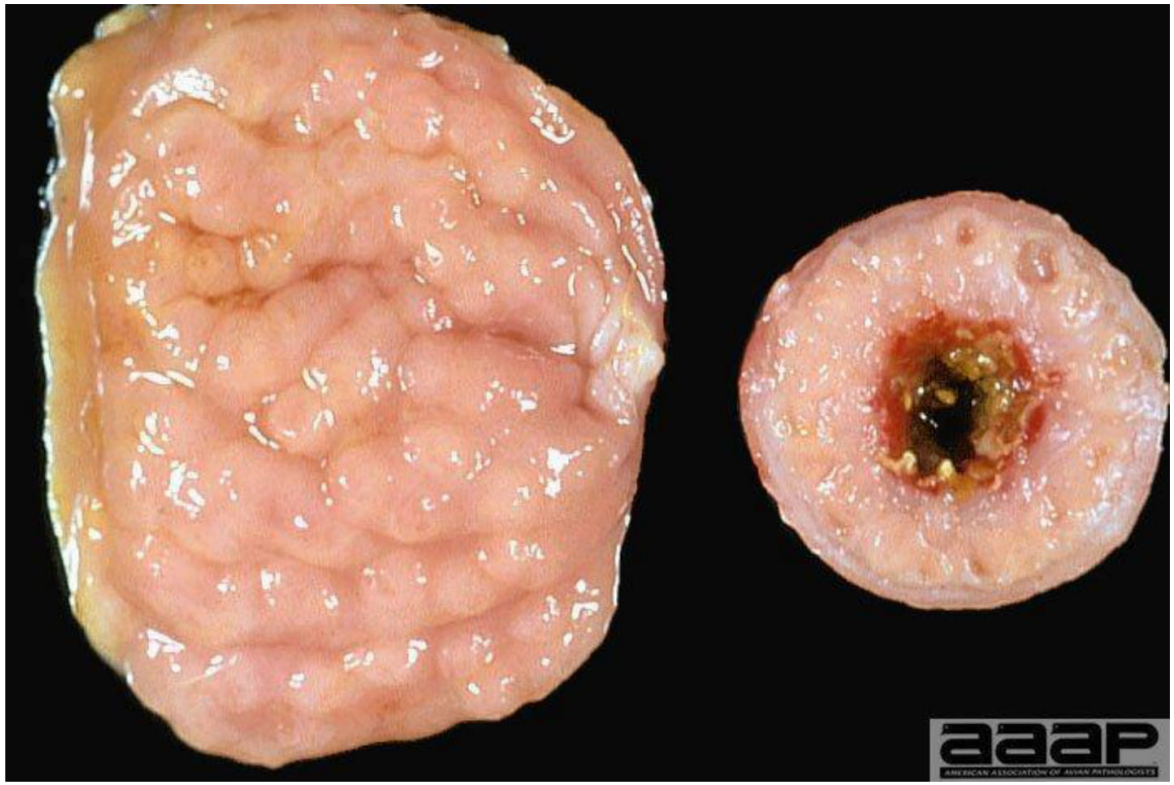
Heart tumour

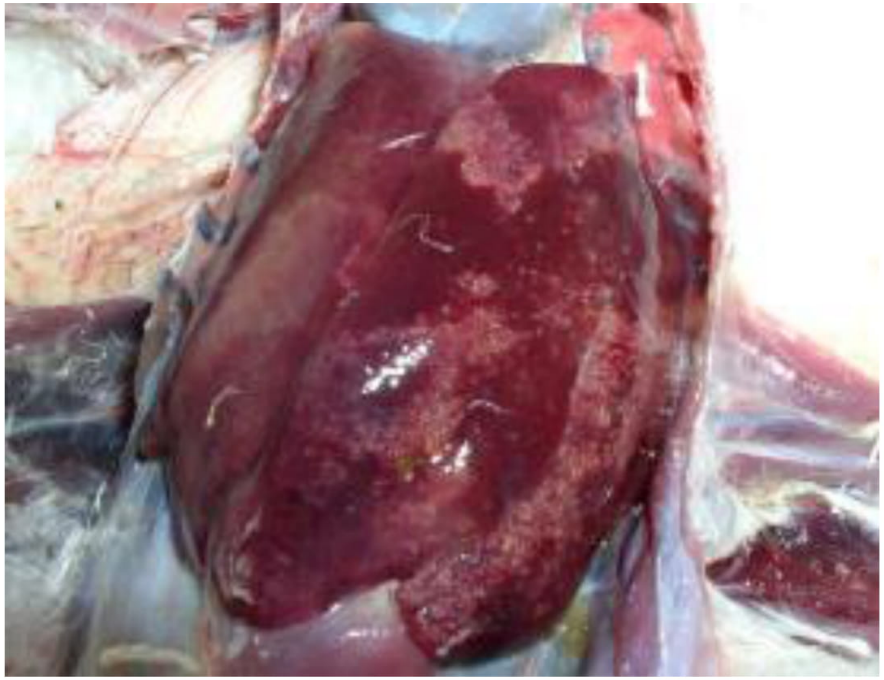
Visceral form

Kidney tumour

Visceral form

Proventriculus tumour





Liver showing multiple, miliary, coalescing white foci of lymphoid tumours.

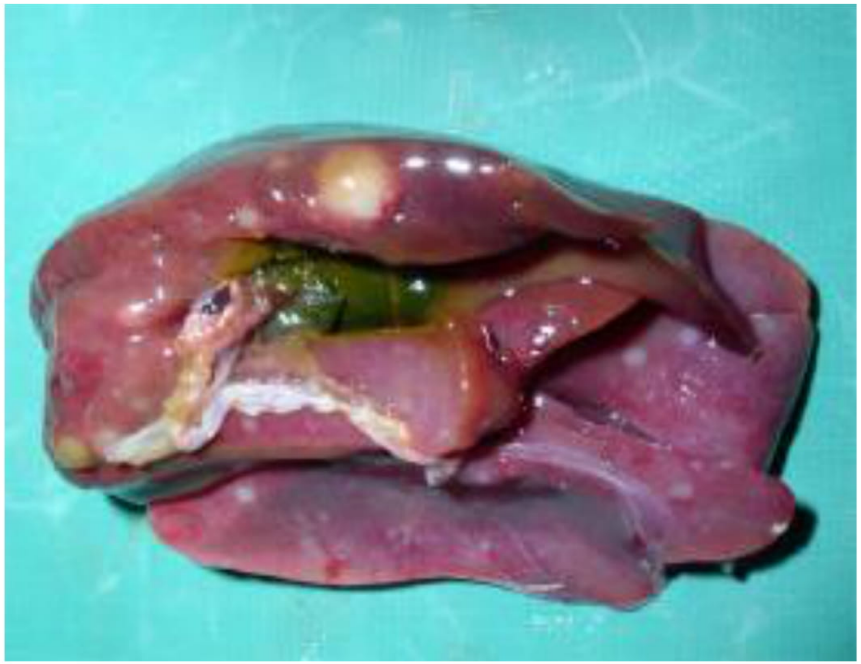
Liver showing solid, grayish white neoplastic lymphoid areas

Congestion, enlargement and thickening of proventriculus

Spleen showing diffuse enlargement with varied size, neoplastic lymphoid areas.

Liver showing round-oval grayish white lymphoid tumours.

Liver showing multifocal, military-moderate sized lymphoid foci on the surface.



Liver showing a solid lymphoid growth along with multiple grayish white foci.

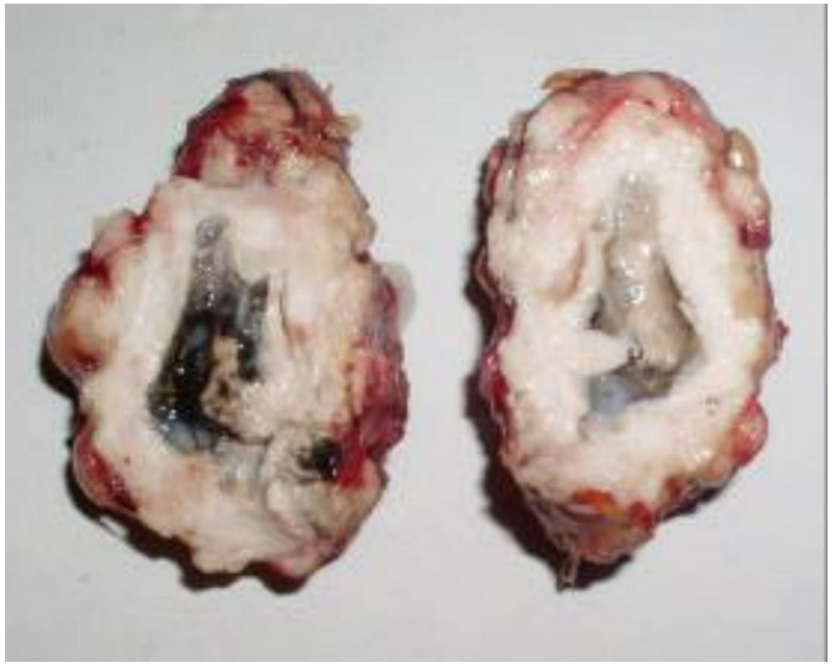
Liver – multifocal grayish white lymphoid areas visible on the surface.

Proventriculus – thickened mucosal surface showing areas of necrosis

Pearl- like, grayish white lymphoid growths visible on the surface of proventriculus and gizzard.

Grayish white lymphoid growths seen on the surface of caecal wall and mesentery.

Ovary showing grayish white, large, neoplastic lymphoid growth.



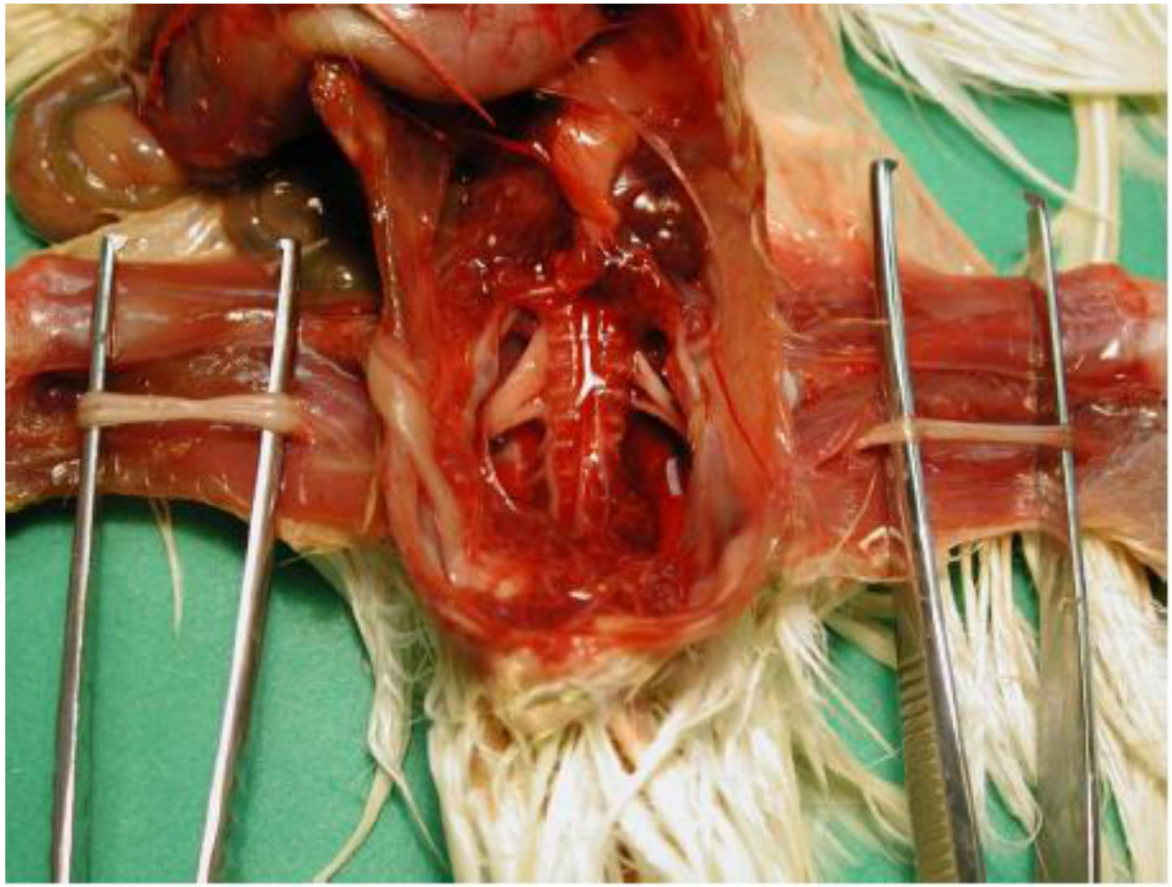
Cut surface of ovarian tumour showing central area of necrosis.

Heart showing diffuse enlargement with grayish white lymphoid areas.

Ovary showing multiple, sessile, pearl- like lymphoid nodules.

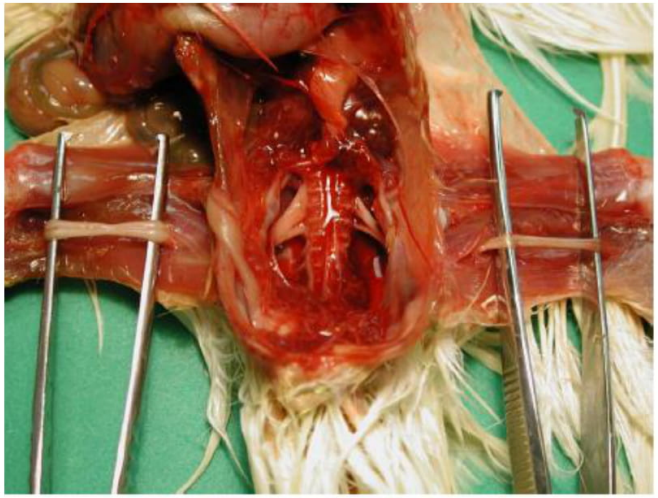
Marek's disease, peripheral nerve enlargement, chicken

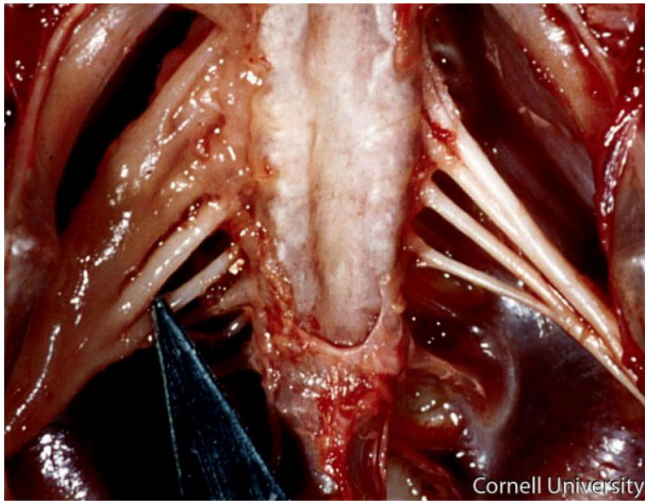
Unilateral enlargement of sciatic nerve and sacral plexus in a chicken with Marek's disease.

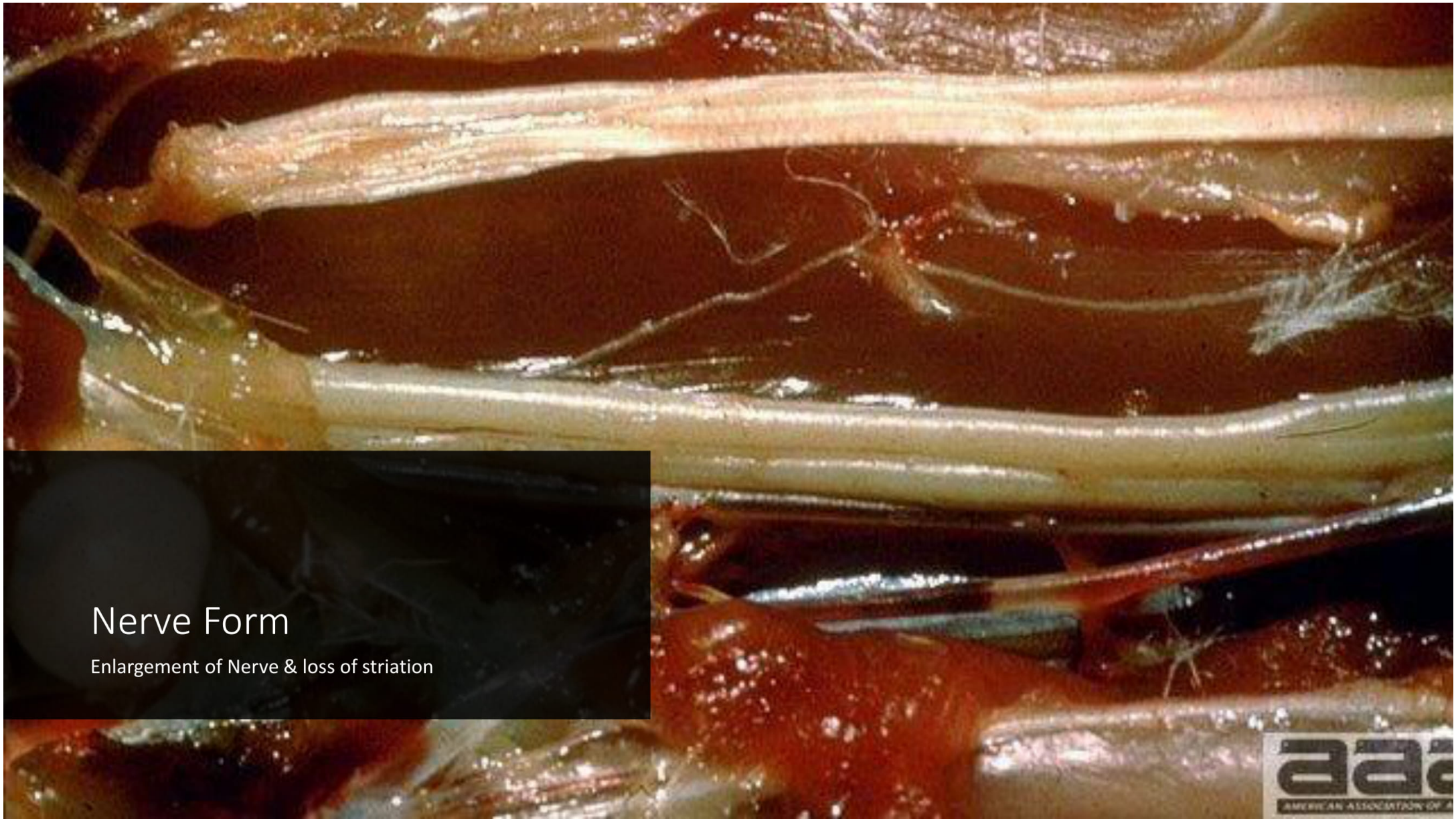


Marek's disease, peripheral nerve enlargement, chicken

Unilateral enlargement of sciatic nerve and sacral plexus in a chicken with Marek's disease.

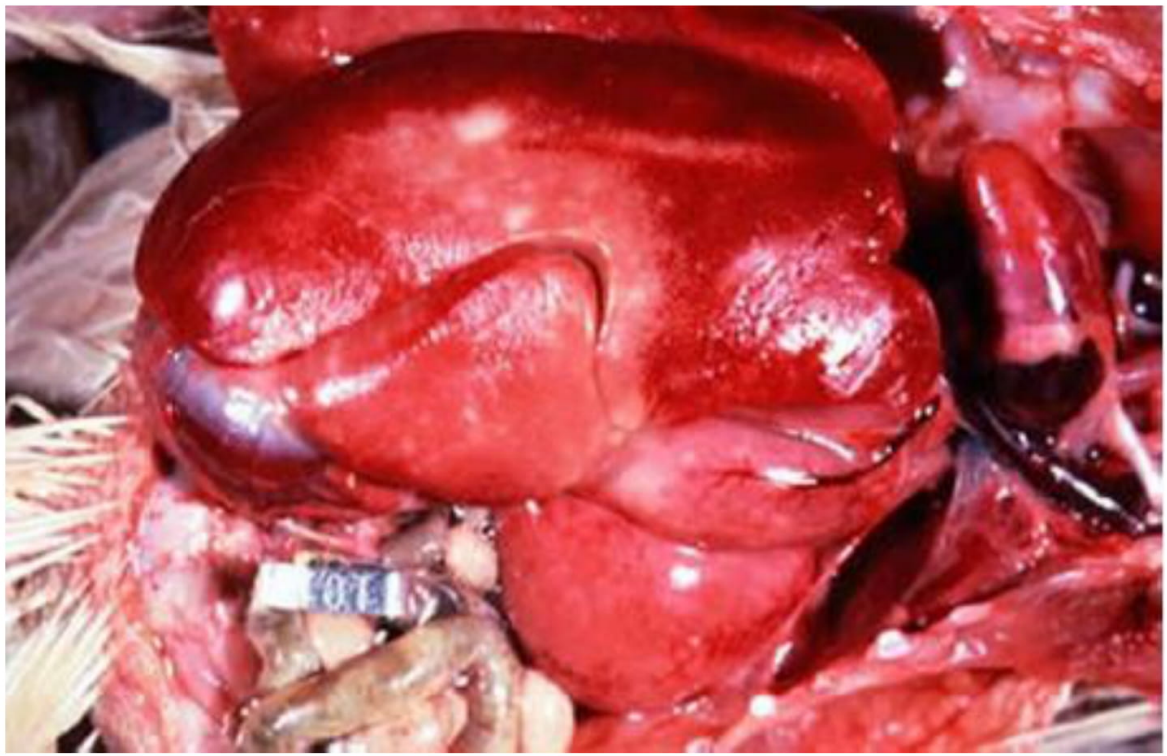





Nerve Form
Enlargement of Nerve & loss of striation

Marek's disease, liver and spleen involvement, chicken

Enlarged and mottled liver and spleen in a chicken with Marek's disease.



Marek's disease, skin involvement, chicken

Skin involvement in a chicken with Marek's disease.

Ulcer in feather follicle

Skin Form

Enlarged feather follicle

Skin Form

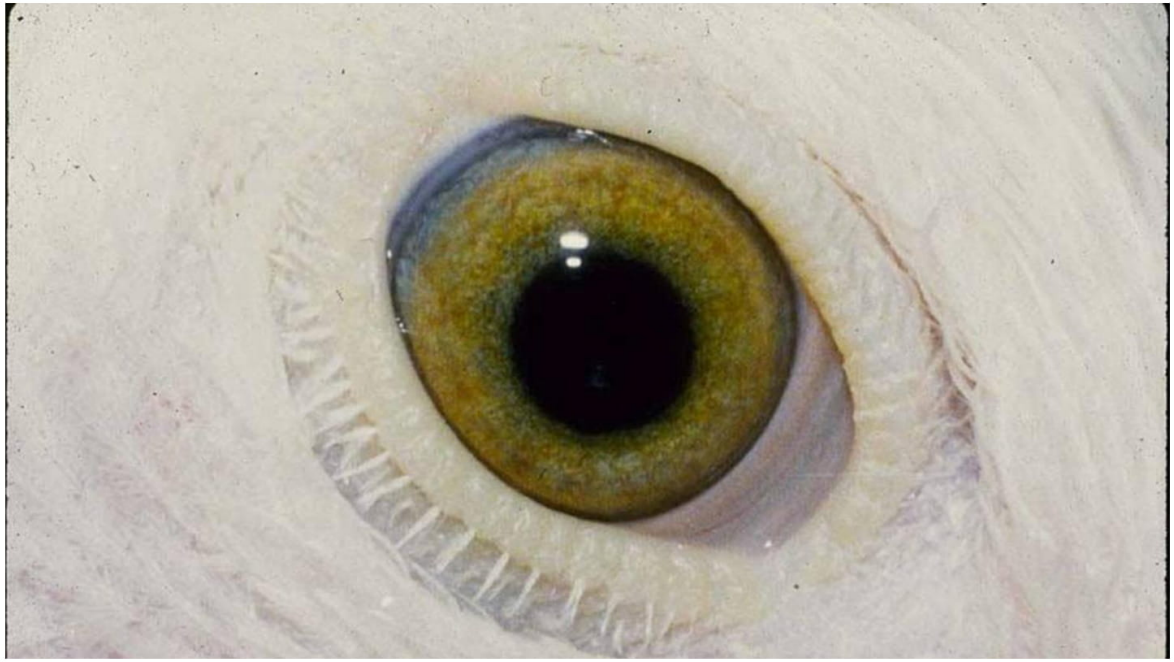
Enlarged feather follicle

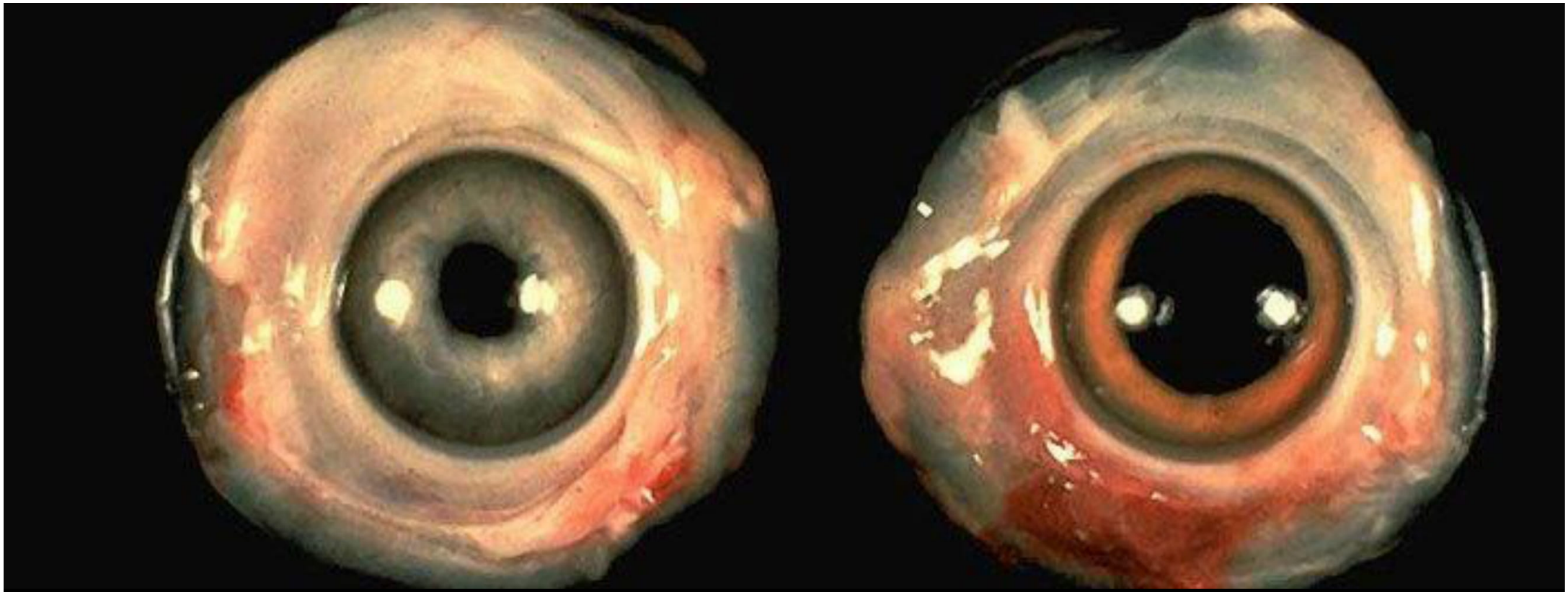
Ocular form:
involvement of eye

- Eye involvement with neoplastic cell infiltration into the iris, resulting in an irregular pupil, in a chicken with Marek's disease.

Occular form

Infiltration of iris



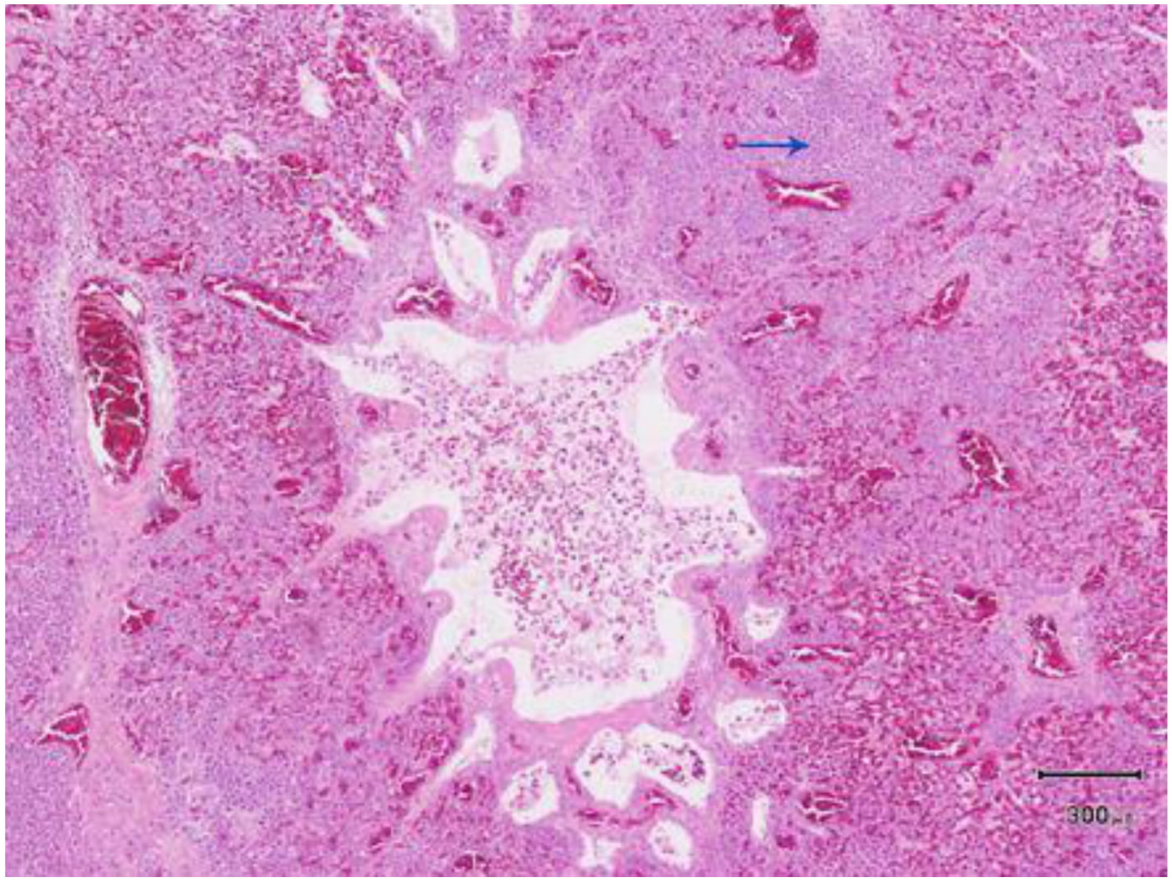


Occular form

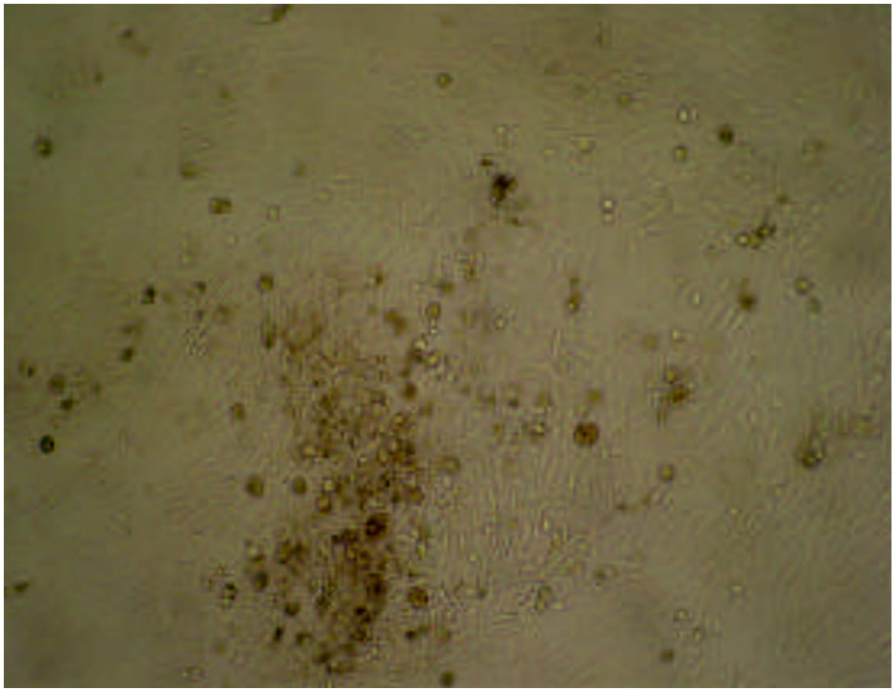
Discolouration of iris

Lung

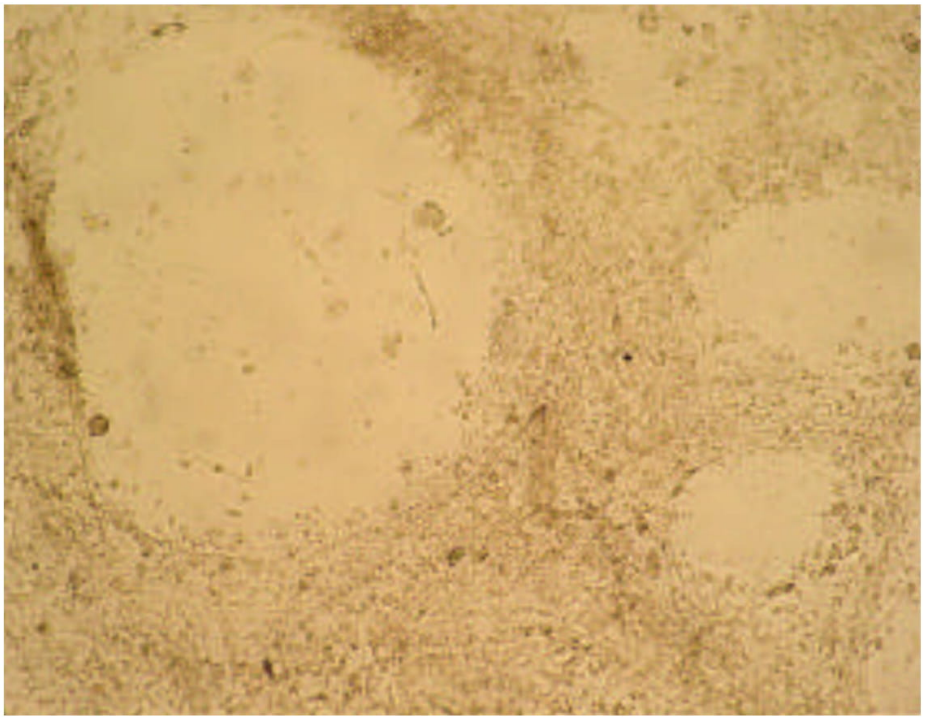
- The majority of the pulmonary parenchyma, including the respiratory atria, is diffusely infiltrated and effaced by a pleomorphic neoplastic round cell population (arrow). Mucus and cellular remains are present within a large airway. Haematoxylin and eosin stain. Bar, 300 µm



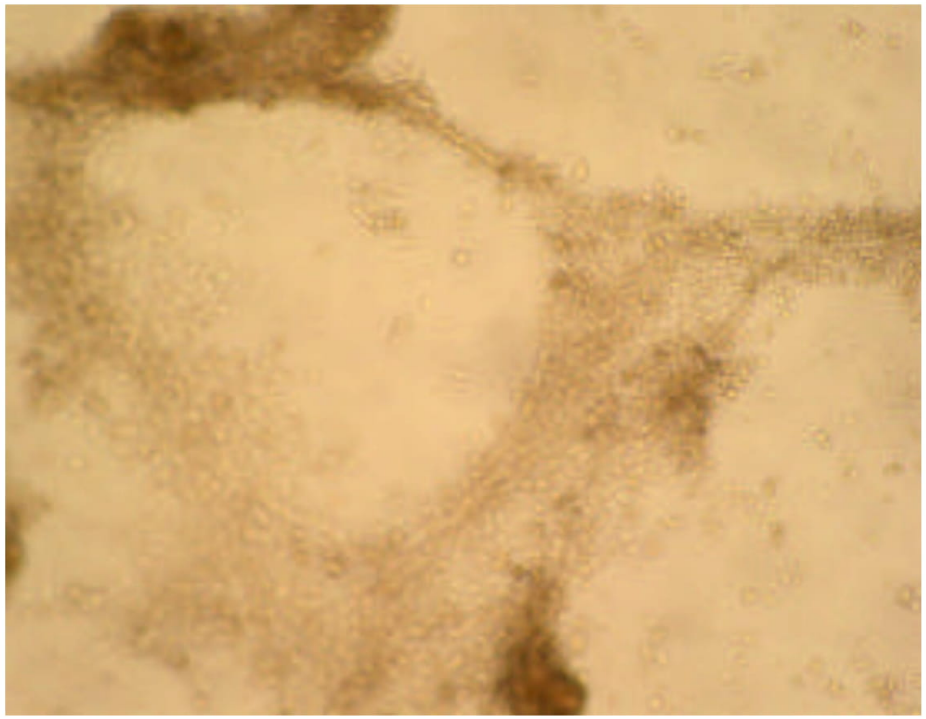
Normal CEF: Chicken Embryo Fibroblast (CEF) confluent monolayer.



Infected CEF : Clumping of infected cells leading to clear plaque formation



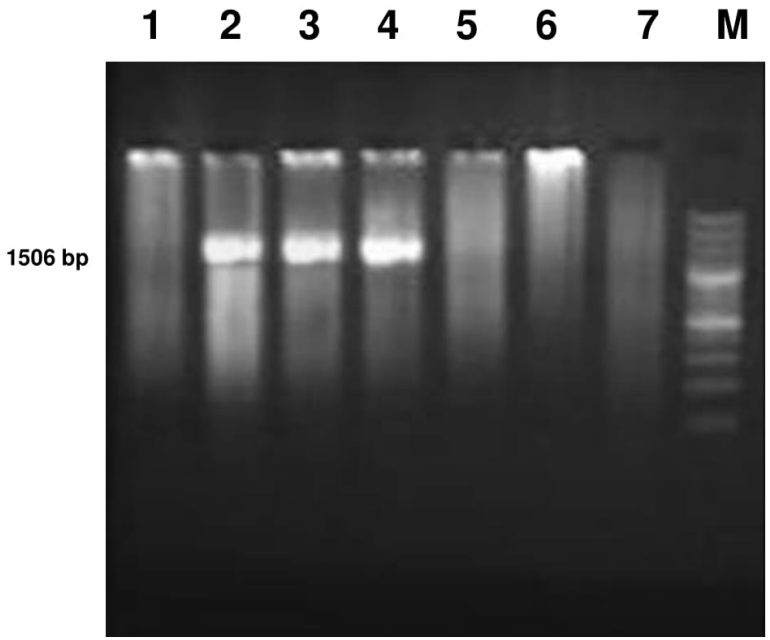
CEK : Size of the empty space progressively increased in size while days advanced.



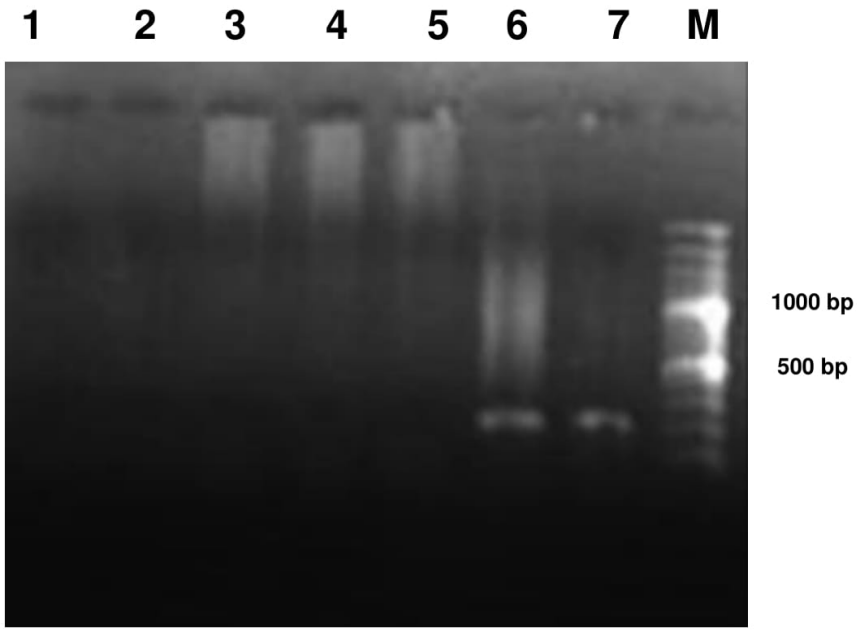
CEK : Detachment of infected cells lead to large empty spaces

CPE on CEK cell due to GaHV infection

AGPT : Clear white precipitation band was observed between the two wells.



1. Glycoprotein C (gC) gene
2-4 : 1506 bp product
M : 100 bp plus (MBI Fermentas)



3. Lymphoid Leucosis (LL) Subgroup A
6 – 7 : 224 bp product
M : 100 bp plus (MBI Fermentas)


CHICKS SHOULD BE vaccinated
WHEN THEY ARE 1 DAY OLD

Prevention:

- *Vaccination:* Vaccines are extremely effective (90%+) in the prevention of Marek's disease.
- There are three serotypes:
  - Serotype 1 which is available commercially as attenuated virulent or attenuated mildly virulent,
  - Serotype 2 vaccines which are naturally non-pathogenic strains of MDV, or
  - Serotype 3 "Herpes Virus Turkey (HVT) which are effective against virulent MDV but less effective against very virulent MDV.
- *Bivalent and Trivalent Vaccines:* Synergistic effect and good protection can be achieved by combining the serotype vaccines 1,2, or 3 as bivalent or trivalent vaccines.
- These have become standard for the layer chick hatcheries, administered subcutaneously at hatching.
- Broiler chicks are given vaccine *in ovo* at the time of egg transfer.

ACKNOWLEDGEMENT

The images and part of the content has been taken from www.google.com .The contributors are duly acknowledged

Thank you