

VMC 321: Systematic Veterinary Virology

Marek's disease virus

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Taxonomy

- Order: *Herpesvirales*
- Family: *Herpesviridae*
- 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
 - Columbidae 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

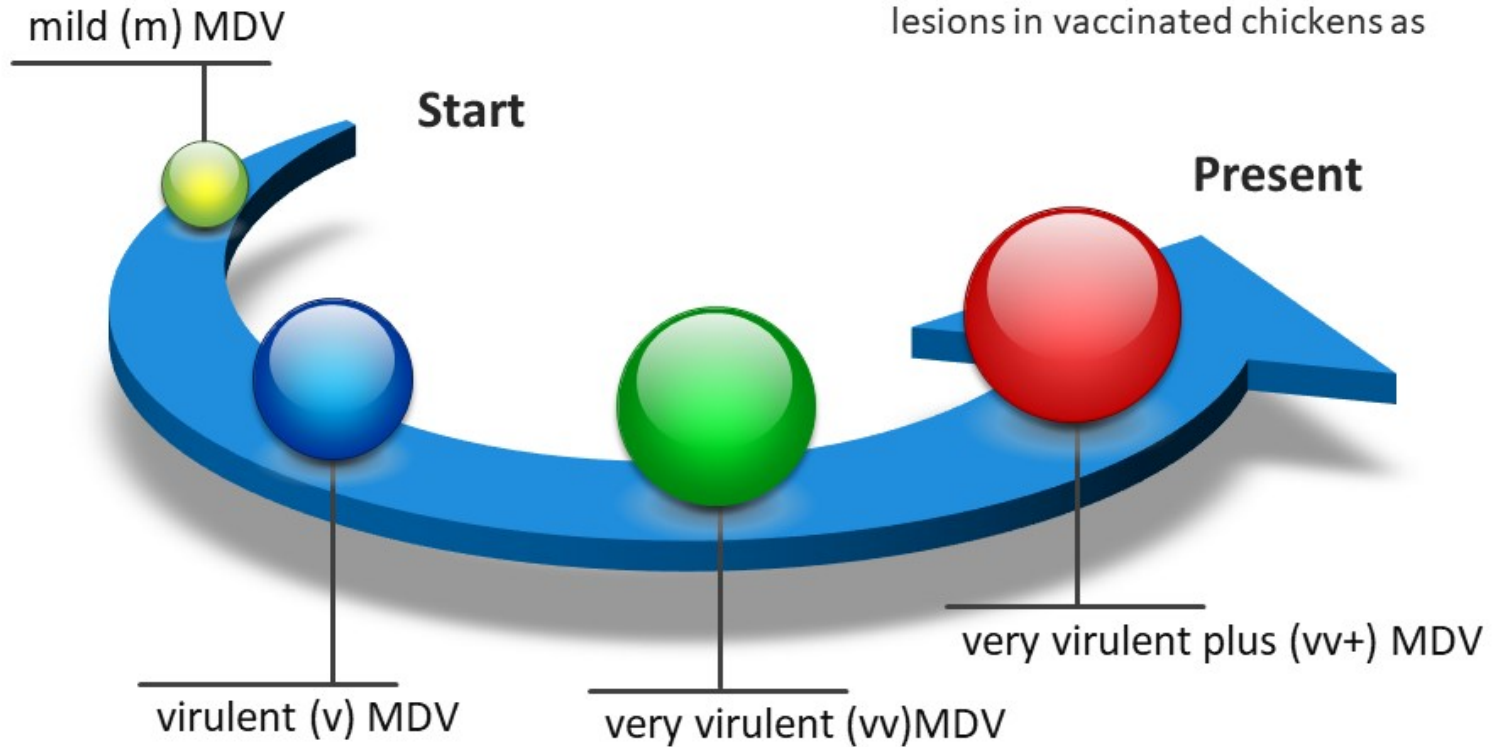
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Serotype 1 MDV strains are further classified

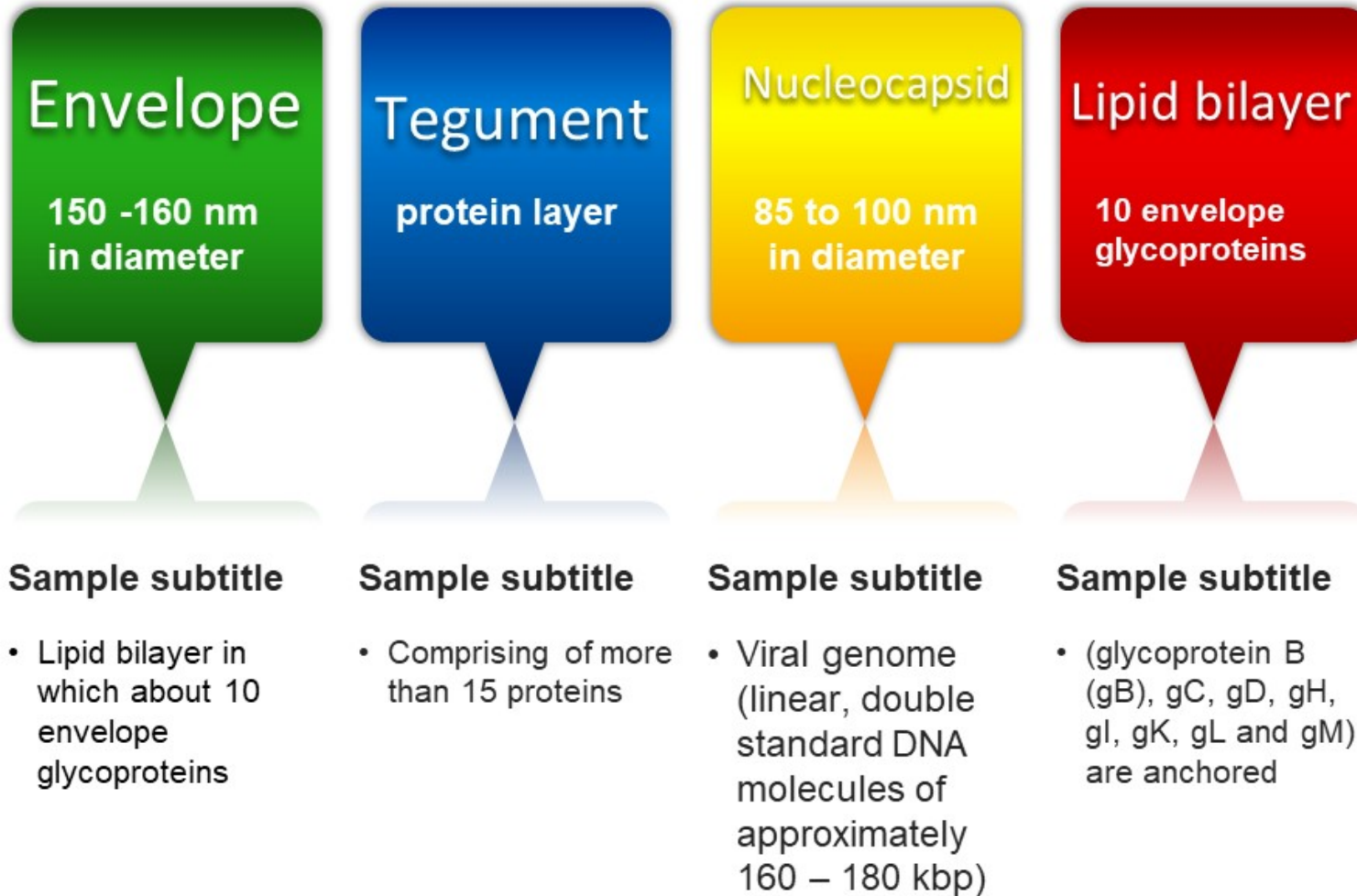
Basis of classification

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



- Serotype 1 MDV strains are further classified into four pathotypes **based on induction of lymphoproliferative lesions** in vaccinated chickens as
 - mild (m) MDV,
 - virulent (v) MDV,
 - very virulent (vv)MDV,
 - very virulent plus (vv+) MDV

MDV characteristics:



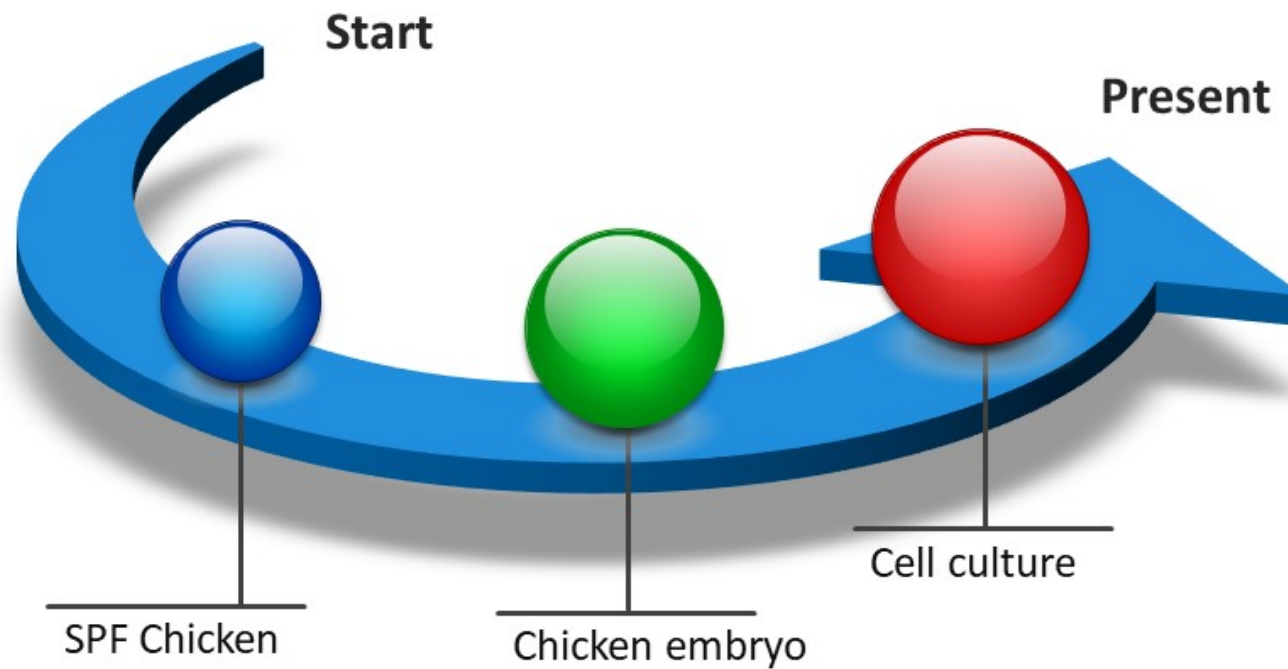
MDV characteristics:

- Complex architecture including the following:
 - (i) enveloped particles 150 -160 nm in diameter
 - (ii) a central hexagonal nucleocapsid (85 to 100 nm in diameter) containing the viral genome (linear, double standard DNA molecules of approximately 160 – 180 kb)
 - (iii) a protein layer termed tegument, comprising more than 15 proteins
 - (iv) a lipid bilayer in which about 10 envelope glycoproteins (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



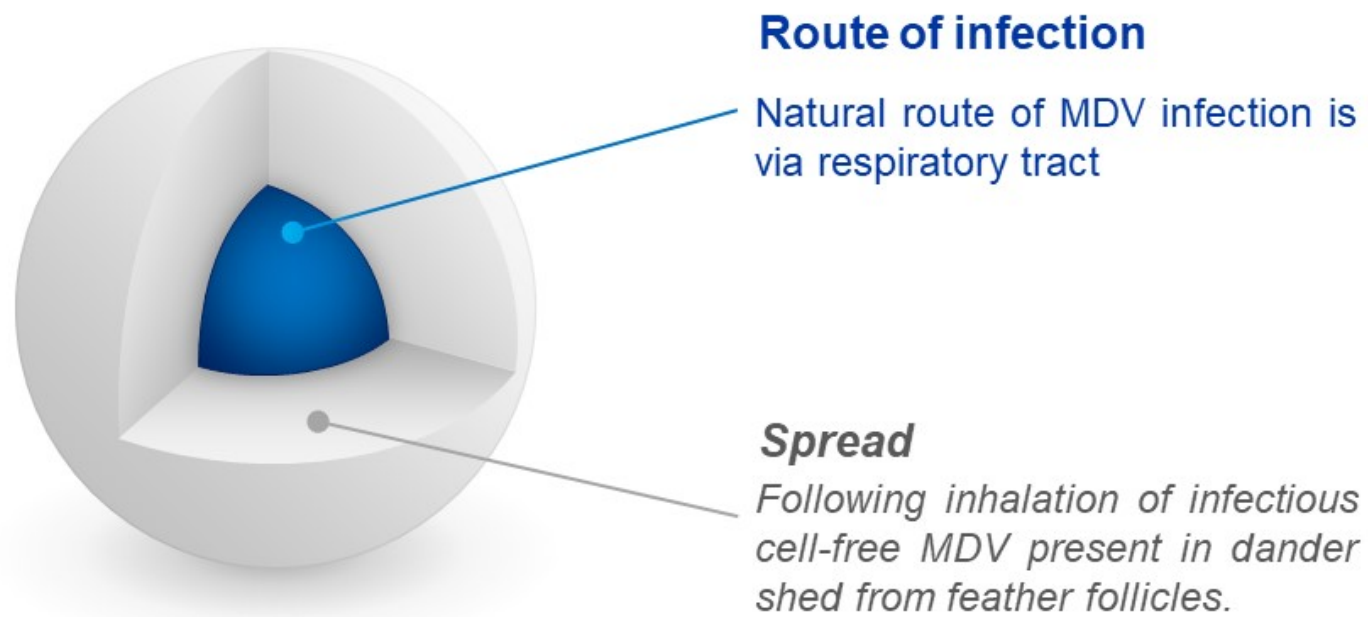
THE DISEASE

Marek's disease

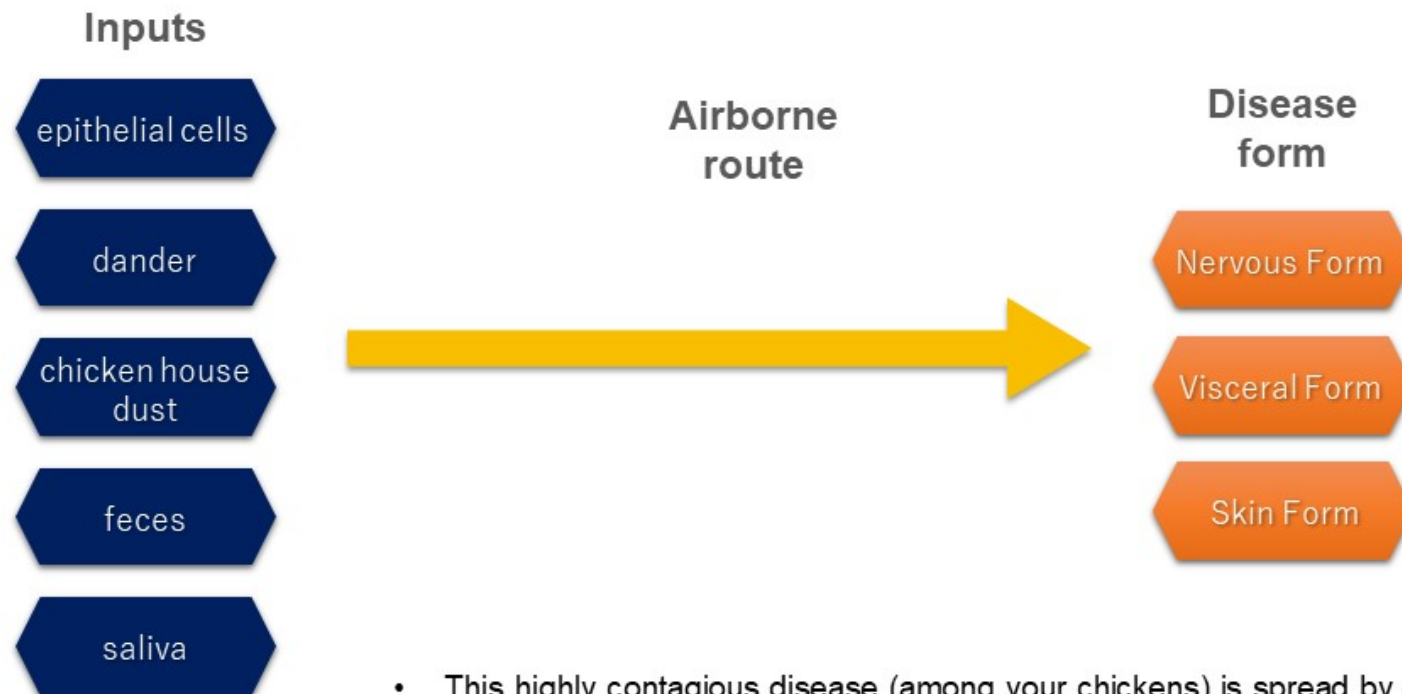
- **Preferred Scientific Name:** Marek's Disease
- **Other Scientific Names-** "range paralysis; neural lymphoma; skin leucosis; neurolymphomatosis gallinarium "fowl paralysis" or "neurolymphomatosis,"
- **International common name:** Marek's Disease
- **English: English acronym:** MD

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

Route



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

Route of infection:

- The natural route of MDV infection is via respiratory tract following inhalation of infectious cell-free MDV present in dander shed from feather follicles.

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



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Pathogenesis

- i. Early cytolytic phase:**
- ii. Latent phase:**
- iii. Secondary cytolytic phase**

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.



Developed virus from
FFE

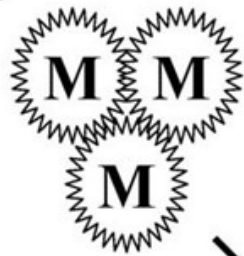
Inhalation

Lungs

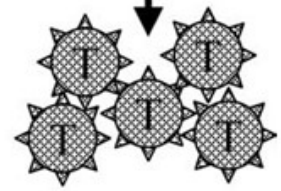
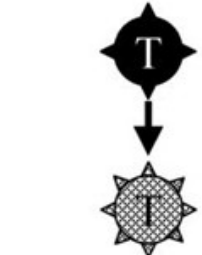
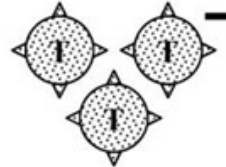
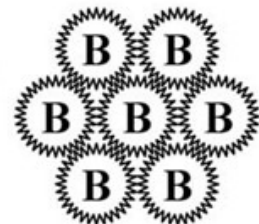
Macrophages

Bursa
Spleen
thymus

Infection of skin feather
follicle epithelium

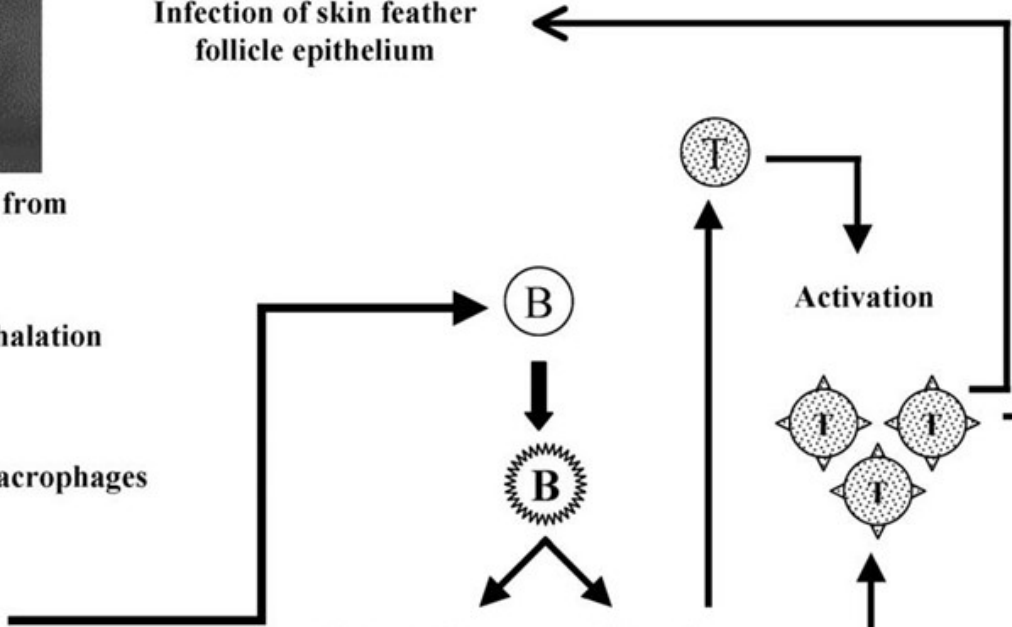


Cell death



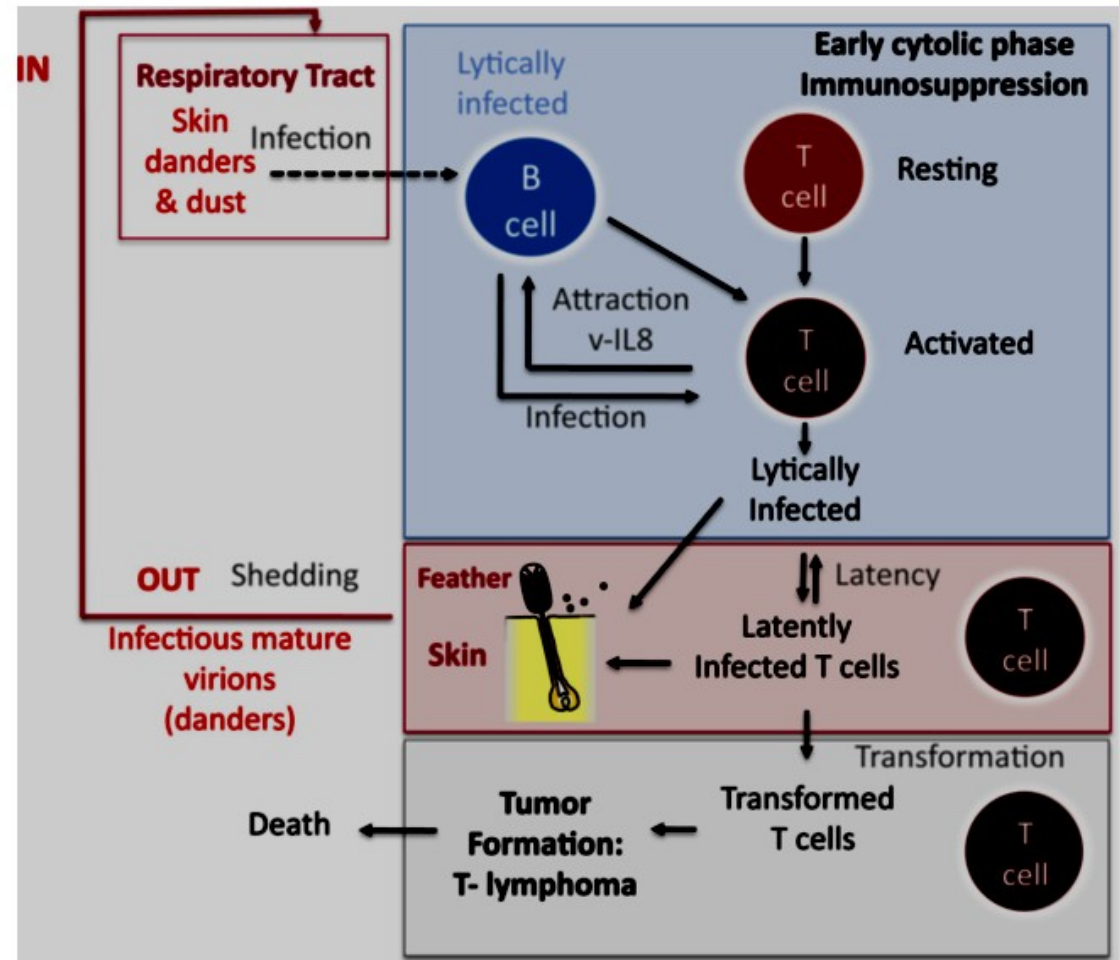
Tumours

Activation



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.



Early cytolytic phase:

- 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

Latent phase:

- 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

Secondary cytolytic phase

with 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

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 (nerolymphatosis), 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 tumors) 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 beginning, 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 faeces. 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.

Diagnosis

Clinical signs

Gross & histopathology

Isolation & identification of virus

Molecular characterization of MDV

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