

Fowl Paralysis in Poultry

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[DOI:10.5281/ScienceWorld.17496501](https://doi.org/10.5281/ScienceWorld.17496501)

Marek's disease (MD), commonly known as Fowl Paralysis is a lymphoproliferative disease of chicken caused by MD herpes virus (MDV) and is characterized by lymphoma formation in visceral organs, muscles, skin and lesions in peripheral nerves (Calnek and Witter, 1991). It is named after Jozsef Marek, a Hungarian Veterinarian. Feather follicle cells are the important source of infection and infected dander is readily disseminated in premises and inhaled by susceptible birds (Schat and Nair, 2008). MDV causes infiltration of lymphocytes in peripheral nerves, iris, skin and visceral organs resulting into development of tumours in visceral organs and immune suppression. In MDV infection, clinical signs include anorexia, weight loss, paralysis of legs, wings and neck, grey eye, vision impairment, blindness, skin lesions and poor performance. MDV causes huge economic losses to the poultry industry because it is an immunosuppressive disease which increases susceptibility to other infections (Shambhu *et al.*, 2022). MDV is currently distributed worldwide including India. Waterfowls act as reservoir of MDV for other avian species since they are involved in transmission of the virus without showing any clinical signs (Vahid and Monire, 2018). Turkey is an unusual host for MDV. Chickens are the most important natural host for Marek's disease virus (MDV), a highly cell-associated but readily transmitted alpha herpes virus with lymphotropic properties of gamma herpes viruses. Quail and turkeys can also be infected, especially when they are raised in proximity to chicken farms. Turkeys are also commonly infected with turkey herpesvirus (HVT), an avirulent strain related to Marek's disease virus that is commonly used

as a Marek's disease vaccine in chickens. Although Marek's disease has been reported in other birds, such as pheasants and peafowl, mammals appear to be refractory to the infection. Marek's disease is one of the most ubiquitous avian infections; it is identified in chicken flocks worldwide. Every flock, except for those maintained under strict pathogen-free conditions, is presumed to be infected. Although clinical signs of disease are not always apparent in infected flocks, a subclinical decrease in growth rate and egg production may be economically important.

Etiology:

Marek's disease is caused by an [alpha herpes virus](#) commonly known as "Marek's disease virus" (MDV). It is caused by Marek's disease virus (MDV) serotype 1 of the family Herpesviridae, subfamily Alpha Herpesvirinae, genus *Mardivirus* and species *Gallid herpesvirus 2* (Hirai, 2001). MDV is a strictly cell associated virus except in feather follicle epithelium, where the cell free virus is produced. Within the genus *Mardivirus* are three closely related species previously designated as three serotypes of Marek's disease virus:

- *Gallid alphaherpesvirus 2* (MDV serotype 1) represents all virulent Marek's disease virus strains and is further divided into pathotypes, designated as mild (m), virulent (v), very virulent (vv), and very virulent plus (vv+).
- *Gallid alphaherpesvirus 3* (MDV serotype 2) and *Meleagrid alphaherpesvirus 1* (turkey herpesvirus, MDV serotype 3) represent avirulent virus strains isolated from chickens and turkeys, respectively, and are commonly used as vaccines against Marek's disease.

Transmission and Epidemiology:

- **Inhalation of Dander and Dust:** The primary mode of transmission is the inhalation of contaminated dust and dander from infected poultry houses (Fenner *et al.*, 1993).
- **Feather Follicles:** Infected birds shed the virus from their feather follicles, creating a reservoir of the infectious agent.
- **Environmental Contamination:** MDV can remain infectious in the environment for months, particularly in dust and dander found in previously infected poultry houses.
- **Contaminated Surfaces:** People, equipment, and clothing can carry the virus, leading to indirect contact with healthy birds.
- **Aerosol Transmission:** The virus can spread through the air, making it a highly contagious and rapidly spreading disease within a flock.



Key Aspects of Transmission

- **Infected Birds:** Any chicken carrying the virus can shed it for a long period, even if they don't show clinical signs of the disease.
- **Environmental Persistence:** The virus's ability to survive in the environment, especially at room temperature, facilitates the continuous spread of the disease.
- **Contagious Nature:** Once introduced into a flock, the virus spreads quickly, leading to widespread infection, especially in unvaccinated birds.

Marek's disease is highly contagious and readily transmitted among chickens. The virus matures into a fully infective, enveloped form in the epithelium of the feather follicle, from which it is released into the environment. It may survive for months in poultry house litter or dust. Dust or dander from infected chickens is particularly effective in transmission. Once the virus is introduced into a chicken flock, regardless of vaccination status, infection spreads quickly from bird to bird. Infected chickens continue to be carriers for long periods and act as sources of infectious virus. Shedding of infectious virus can be decreased, but not prevented, by prior vaccination. Live, attenuated MDV strains vary greatly in their transmissibility among chickens; the most highly attenuated are not transmitted. Marek's disease virus is not vertically transmitted. Unlike virulent strains of Marek's disease virus, which are highly contagious, turkey herpesvirus is not readily transmissible among chickens (although it is easily transmitted among turkeys, its natural host).

Pathogenesis of Marek's Disease:

Currently, four phases of infection with Marek's disease are recognized:

1. **Early cytolytic infection (productive-restrictive):** MDV enters the host through the respiratory tract via inhalation of contaminated dust. The virus replicates in lymphocytes, primarily within lymphoid organs like the spleen, thymus, and bursa. This initial phase is characterized by viral replication and can cause inflammation and immune responses. During this phase, there's a brief period of immunosuppression, affecting both T and B cells.
2. **Latent infection:** MDV can establish latency in infected T cells. Latency is characterized by the virus residing in the cell without actively replicating. Latently infected T cells can be activated and transformed into cancerous cells.
3. **Lymphoma Development (Proliferative Phase):** Latently infected T cells can undergo neoplastic transformation, leading to the development of tumors



(lymphomas). These lymphomas can occur in various organs, including the nerves, muscles, and visceral organs.

4. **Immunosuppression:** MDV can also cause immunosuppression, making the host more susceptible to other infections. This immunosuppression is often associated with the late cytolytic phase of the disease.

Viral Shedding: Infected chickens shed the virus through feather dander, which can then be inhaled by other birds, continuing the cycle of infection. The feather follicle epithelium is a major site of viral replication and shedding.

Second phase of cytolytic, productive-restrictive infection coincident with permanent immunosuppression. Proliferative phase, involving nonproductively infected lymphoid cells that may or may not progress to the point of lymphoma formation. Productive infection may occur transiently in B lymphocytes within a few days after infection with virulent Marek's disease virus strains and is characterized by antigen production, which leads to cell death. Because few if any virions are produced, this has also been termed a restrictive-productive infection. Productive infection also occurs in the feather follicle epithelium, in which enveloped virions are produced.

Latent infection of activated T cells is responsible for the long-term carrier state. No antigens are expressed, but virus can be recovered from such lymphocytes by cocultivation with susceptible cells in tissue cultures. Some T cells, latently infected with oncogenic MDV strains, undergo neoplastic transformation. These transformed cells may multiply to form characteristic lymphoid neoplasms.

Symptoms & Lesions:

Birds infected with MDV can be carriers and shedders of the virus for life. Newborn chicks are protected by maternal antibodies for a few weeks. After infection, microscopic lesions are present after one to two weeks, and gross lesions are present after three to four weeks.

Six syndromes are known to occur after infection with Marek's disease. These syndromes may overlap.

1. **Classical Marek's disease / Neurological form:** Asymmetric paralysis of one or more legs, wings, or the neck (Athletic Posture). Difficulty standing or uncoordinated movement. Head tremors. Enlarged nerves are one of the most consistent gross lesions in affected birds. Various peripheral nerves, but particularly the vagus, brachial, and sciatic, become enlarged and lose their striations.



2. **Acute Marek's disease / Visceral Signs (Tumors):** is an epidemic in a previously uninfected or unvaccinated flock, causing depression, paralysis, and death in a large number of birds (up to 80%). The age of onset is much earlier than the classic form; birds are four to eight weeks old when affected. Infiltration into multiple organs/tissue is observed. Tumors in various organs, including the liver, spleen, kidneys, gonads (ovaries), heart, and lungs. Enlargement of these organs due to tumor growth. Diffuse or nodular lymphoid tumors may be observed in various organs, particularly the liver, spleen, gonads, heart, lung, kidney, muscle, and proventriculus. The cloacal bursa (bursa of Fabricius) is only rarely tumorous and more frequently is atrophic.
3. **Ocular lymphomatosis:** Lymphocytic infiltration of the eye's iris, leading to a grey color. Irregular pupil shape or size, resulting in partial or total blindness.
4. **Cutaneous Signs (Skin):** Round, firm lesions at feather follicles. Enlarged feather follicles (commonly termed skin leukosis) may be noted in broilers after defeathering during processing and are a cause for condemnation (Fenner *et. al.*, 1993)
5. **Atherosclerosis** is induced in experimentally infected chickens. (Fabricant and Fabricant, 1999).
6. **Immunosuppression** is impairment of the T-lymphocytes resulting from Marek's disease, preventing a competent immunological response against pathogenic challenge, with the affected birds become more susceptible to disease conditions such as coccidiosis and *Escherichia coli* infection.—(Islam, 2002)—Furthermore, without stimulation by cell-mediated immunity, the humoral immunity conferred by the B-cell lines from the Bursa of Fabricius also shuts down, thus resulting in birds that are totally immunocompromised.

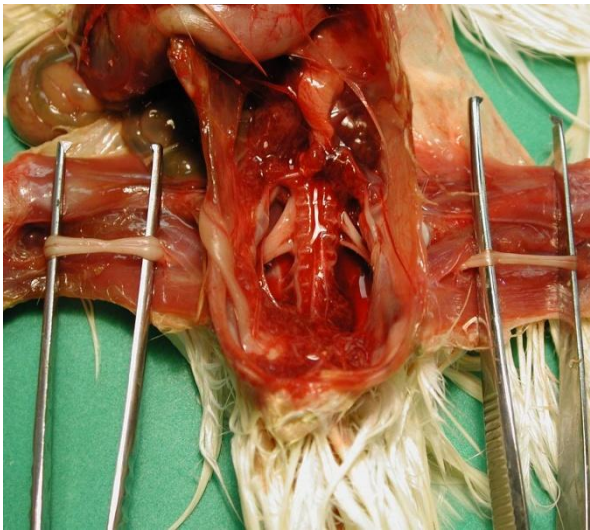
General Signs are Depression and lethargy, Weight loss and muscle wasting, Reduced appetite and Anemia. Histologically, the lesions consist of a mixed population of small, medium, and large lymphoid cells plus plasma cells and large anaplastic lymphoblasts. These cell populations undoubtedly include tumor cells and reactive inflammatory cells. When the cloacal bursa is involved, the



Marek's disease, leg paresis



tumor cells typically appear in interfollicular areas.



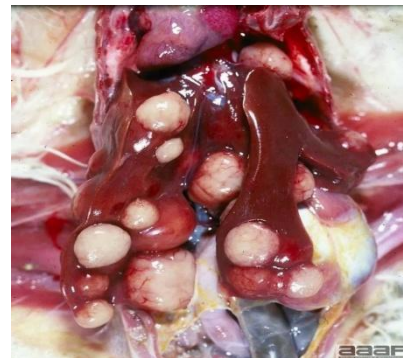
Marek's disease, peripheral nerve enlargement



Marek's disease, skin involvement



Marek's Disease affected left eye



Liver tumors seen with Marek's Disease

Diagnosis:

Diagnosis of lymphoid tumors in poultry is complicated due to multiple etiological agents capable of causing very similar tumors. It is not uncommon that more than one avian tumor virus can be present in a chicken, thus one must consider both the diagnosis of the disease/tumors (pathological diagnosis) and of the virus (etiological diagnosis). A step-wise process has been proposed for diagnosis of Marek's disease, which includes:

1. History, epidemiology, clinical observations and gross necropsy;
2. Characteristics of the tumor cell, and;
3. Virological characteristics

The demonstration of peripheral nerve enlargement along with suggestive clinical signs in a bird that is around three to four months old (with or without visceral tumors) is highly suggestive of Marek's disease. Histological examination of nerves reveals infiltration of



pleomorphic neoplastic and inflammatory lymphocytes. Peripheral neuropathy should also be considered as a principal rule-out in young chickens with paralysis and nerve enlargement without visceral tumors, especially in nerves with interneuronal edema and infiltration of plasma cells.

The presence of nodules on the internal organs may also suggest Marek's disease, but further testing is required for confirmation. This is done through histological demonstration of lymphomatous infiltration into the affected tissue. A range of leukocytes can be involved, including lymphocytic cell lines such as large lymphocyte, lymphoblast, primitive reticular cells, and occasional plasma cells, as well as macrophage and plasma cells. The T cells are involved in the malignancy, showing neoplastic changes with evidence of mitosis. The lymphomatous infiltrates need to be differentiated from other conditions that affect poultry including lymphoid leukosis and reticuloendotheliosis, as well as an inflammatory event associated with hyperplastic changes of the affected tissue.

Key clinical signs as well as gross and microscopic features that are most useful for differentiating Marek's disease from lymphoid leukosis and reticuloendotheliosis include:

1. Age: Marek's disease can affect birds at any age, including <16 weeks of age;
2. Clinical signs: Frequent wing and leg paralysis;
3. Incidence: >5% in unvaccinated flocks;
4. Potential nerve enlargement;
5. Interfollicular tumors in the bursa of Fabricius;
6. CNS involvement;
7. Lymphoid proliferation in skin and feather follicles;
8. Pleomorphic lymphoid cells in nerves and tumors; and
9. T-cell lymphomas.

In addition to gross pathology and histology, other advanced procedures used for a definitive diagnosis of Marek's disease include immunohistochemistry to identify cell type and virus-specific antigens, standard and quantitative PCR for identification of the virus, virus isolation to confirm infections, and serology to confirm/exclude infections.

The World Organisation for Animal Health (OIE) reference laboratory for Marek's disease is Avian Viral Oncogenesis group (led by Professor Venugopal Nair OBE) at The Pirbright Institute, UK.

PCR blood testing can also detect Marek's disease, and proper testing can differentiate between a vaccinated bird with antibodies and a true positive for Marek's disease. Standard criteria are often sufficient for a presumptive diagnosis; however, advanced criteria are needed



for a definitive diagnosis. Immunohistochemical testing can be used to confirm that tumors are composed of predominant T-cell populations or expressing specific MDV antigens.

MATSA stands for Marek's disease tumor-associated surface antigen, a surface glycoprotein found on lymphocytes in chickens infected with Marek's disease virus (MDV) or turkey herpesvirus (HVT) (Powell & Rennie, 1984). It appears during the virus infection and is used as a marker to identify infected or cancerous lymphoid cells, even before the characteristic tumors of Marek's disease become evident. Early research aimed to use MATSA as a target for immune responses, but later studies suggested that the cell-mediated immunity against Marek's tumors is directed against other antigens.

Key Characteristics

- **Location:** It is a surface antigen located on lymphoid cells, including lymphocytes and lymphoblastoid cells.
- **Association:** It is associated with tumors in Marek's disease and also appears on lymphoid cells from non-oncogenic MDV infections and HVT-infected birds.
- **Appearance:** MATSA can be detected early in the infection, before tumors are visible, in various lymphoid tissues of infected birds.
- **Nature:** It is a glycoprotein and has been studied using various biochemical methods.

Significance of MATSA

- **Diagnostic Marker:** MATSA serves as a marker for the presence of MDV or HVT infection in lymphoid cells, helping to diagnose the disease.
- **Immune Target:** It was initially investigated as a potential target for the chicken's cell-mediated immune response against Marek's tumors.
- **Antigenic Target:** While MATSA is present on Marek's cells, later studies indicated that cell-mediated immunity against these tumors may be directed against other, as yet undefined, antigens, not solely MATSA.

There is a quantitative association between viral load and Marek's disease tumors; most tumor-bearing chickens have high viremia titers and usually positive results of PCR assay. Thus, the demonstration of high quantities of virus, viral DNA, or viral antigens in tumor cells and the exclusion of other relevant tumor viruses should be sufficient for a specific diagnosis of Marek's disease.

Prevention & Control of Marek's Disease in Poultry:

- Vaccination
- Biosecurity
- Breeding for genetic resistance



Common Misperceptions about Marek's Disease

1. **Mix turkeys and chicks together to prevent Marek's Disease so the chickens will be exposed naturally to turkey herpes virus.** This is not correct! Not only will the chickens not get Marek's Disease protection, but turkeys might be exposed to other common chicken diseases such as Mycoplasma and Blackhead.
2. **Don't vaccinate birds so that the survivors will become resistant.** Genetic disease resistance takes decades to develop and so far, has not been successful with Marek's Disease. If it were successful, one would think the commercial chicken genetic companies would have developed resistant chickens by now.
3. **Only vaccinate a few birds and the vaccine will leak and protect the other chickens.** This is incorrect. Every bird needs to get a full dose of vaccine **before** they become exposed to the actual disease-causing virus. This is the only way to achieve protection.
4. **Don't vaccinate birds because this vaccine is dangerous and might make the chickens ill.** If careful mixing of the vaccine in a sanitary manner is not followed, the birds may get a bacterial infection. Wash hands, use a sterile needle, and avoid touching the needle with hands or any soiled object. Use only commercial vaccines. The companies making these vaccines are testing for potency and making sure the vaccine does not become contaminated with other diseases.

Vaccination is the central strategy for the prevention and control of Marek's disease, along with strict sanitation to decrease or delay exposure and breeding for genetic resistance.

The most widely used vaccines include the following:

- Turkey herpesvirus (HVT, naturally avirulent *Meleagrid alphaherpesvirus* 1)
- SB-1 or 301B/1 (naturally avirulent *Gallid alphaherpesvirus* 3)
- CVI988/Rispens (attenuated *Gallid alphaherpesvirus* 2)

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