

Marek Disease in Poultry

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Marek disease is a highly contagious viral disease of poultry characterized by T-cell lymphomas and peripheral nerve enlargement. Standard criteria used for diagnosis include history, clinical signs, gross necropsy, and histopathology. Although no treatment is available, current vaccines are highly protective.

Chickens are the most important natural host for Marek disease virus (MDV), a highly cell-associated but readily transmitted alphaherpesvirus with lymphotropic properties of gammaherpesviruses. Quail can be naturally infected, and turkeys can be infected experimentally. However, severe clinical outbreaks of Marek disease in commercial turkey flocks, with mortality from tumors reaching 40%–80% between 8 and 17 weeks of age, were reported in France, Israel, and Germany. In some of these cases, the affected turkey flocks were raised in proximity to broilers. Turkeys are also commonly infected with turkey herpesvirus (HVT), an avirulent strain related to Marek disease virus that is commonly used as a Marek disease vaccine in chickens. Other birds and mammals appear to be refractory to the disease or infection.

Marek 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 disease is not always apparent in infected flocks, a subclinical decrease in growth rate and egg production may be economically important.

Etiology of Marek Disease in Poultry

Marek disease virus is a member of the genus *Mardivirus* within the subfamily Alphaherpesvirinae. Within the genus *Mardivirus* are three closely related species previously designated as three serotypes of Marek disease virus. *Gallid alphaherpesvirus* 2 (MDV serotype 1) represents all virulent Marek 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 disease.

Transmission and Etiology of Marek Disease in Poultry

Marek 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 reduced, but not prevented, by prior vaccination. Unlike virulent strains of Marek disease virus, which are highly contagious, turkey herpesvirus is not readily transmissible among chickens (although it is easily transmitted among turkeys, its natural host). Attenuated Marek disease virus strains vary greatly in their transmissibility among chickens; the most highly attenuated are not transmitted. Marek disease virus is not vertically transmitted.

Pathogenesis of Marek Disease in Poultry

Currently, four phases of infection with Marek disease in vivo are recognized:

1. Early cytolytic infection (productive-restrictive)

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2. Latent infection
3. Second phase of cytolytic, productive-restrictive infection coincident with permanent immunosuppression
4. 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 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 longterm 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 Marek disease virus strains, undergo neoplastic transformation. These transformed cells, provided they escape the immune system of the host, may multiply to form characteristic lymphoid neoplasms.

Clinical Findings of Marek Disease in Poultry

Marek disease, leg paresis, chicken



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The **incidence of Marek disease** is quite variable in commercial flocks and depends on:

- strain and dose of virus
- age at exposure
- maternal antibody
- host gender and genetics
- strain and dose of vaccine virus
- several environmental factors, including stress

In addition to lymphoid neoplasms, Marek disease virus **can also induce** other clinically distinct disease syndromes, including:

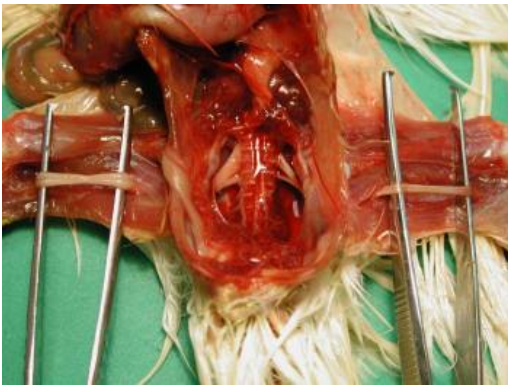
- transient paralysis
- early mortality syndrome
- cytolytic infection
- atherosclerosis
- persistent neurologic disease

Typically, affected birds show only depression before death, but a transient paralysis syndrome has been associated with Marek disease; chickens become ataxic for periods of several days and then recover. This syndrome is rare in immunized birds. Death is usually the result of paralysis, rendering the birds unable to reach food and water.

Lesions

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Marek disease, peripheral nerve enlargement, chicken



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Marek disease, skin involvement, chicken



COURTESY OF DR. JEAN SANDER.

Marek disease, eye involvement, chicken



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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. Diffuse or nodular lymphoid tumors may be seen in various organs, particularly the liver, spleen, gonads, heart, lung, kidney, muscle, and proventriculus. Enlarged feather follicles (commonly termed skin leukosis) may be noted in broilers after defeathering during processing and are a cause for condemnation. The bursa is only rarely tumorous and more frequently is atrophic. 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 bursa is involved, the tumor cells typically appear in interfollicular areas.

Diagnosis of Marek Disease in Poultry

- Standard criteria: history and clinical signs, gross pathology, and histopathology
- Advanced criteria: immunohistochemistry, standard and quantitative PCR, virus isolation, serology

For the diagnosis of Marek disease, it is critical to diagnose the tumors and not the infection because Marek disease is considered ubiquitous within commercial poultry flocks. Usually, diagnosis is based on enlarged nerves and lymphoid tumors in various viscera. The absence of bursal tumors helps distinguish this disease from [lymphoid leukosis](#), although the presence of bursal tumors does not exclude Marek disease. Marek disease can develop in chickens as young as 3 weeks old, whereas lymphoid leukosis typically is seen in chickens >14 weeks old. [Reticuloendotheliosis](#), **although rare, can easily be confused with Marek disease**, because both diseases can feature enlarged nerves and T-cell lymphomas in visceral organs.

Standard criteria are often sufficient for a presumptive diagnosis, but advanced criteria are needed for a definitive diagnosis. Immunohistochemistry can be used to confirm tumors are composed of predominant T-cell populations or expressing specific MDV antigens. There is a quantitative association between viral load and Marek disease tumors; most tumor-bearing chickens have high viremia titers and are usually PCR positive. 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 disease.

Control of Marek Disease in Poultry

- There is no effective treatment for Marek disease
- Prevention methods include vaccination, biosecurity, and genetic resistance

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

The most widely used vaccines include:

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

HVT vaccine has seen rapidly increased use as a backbone in recombinant vaccines featuring the insertion of genes from other poultry viruses, such as [Newcastle disease virus](#), [infectious bursal disease virus](#), or [infectious laryngotracheitis virus](#). These recombinant vaccines offer protection against both Marek disease virus and the inserted virus. Bivalent vaccines consisting of HVT and either the SB-1 or 301B/1 strains of *Gallid alphaherpesvirus* 3 have been used to provide additional protection against challenge with virulent Marek disease virus isolates. The most protective commercial vaccine currently available appears to be CVI988/Rispens, an attenuated Marek disease virus strain that is also commonly mixed with HVT at vaccination.

Vaccines are administered at hatch or *in ovo* to embryos at the 18th day of incubation. *In ovo* vaccination is now performed by automated technology and is widely used for vaccination of commercial broiler chickens, mainly because of reduced labor costs and greater precision of vaccine administration.

Proper handling of vaccine during thawing and reconstitution is crucial to ensure that adequate doses are administered. Cell-associated vaccines are generally more effective than cell-free vaccines, because they are neutralized less by maternal antibodies. Under typical conditions, vaccine efficacy is usually >90%. Since the advent of vaccination, losses from Marek disease have been reduced dramatically in broiler and layer flocks. However, disease may become a serious problem in individual flocks or in selected geographic areas (eg, the Delmarva broiler industry). Of the many causes proposed for these excessive losses, early exposure to very virulent virus strains appears to be among the most important.

Key Points

- Marek disease is a highly contagious neoplastic disease characterized by T-cell lymphomas and peripheral nerve enlargement.
- Leg paralysis is a common clinical sign.

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- Presumptive diagnosis can be made based on history, clinical signs, gross pathology, and histopathology.
- Vaccines are highly protective and should be used in combination with good biosecurity.

For More Information

- [Marek Disease in the OIE Terrestrial Manual](#)
 - [Tumor Diagnosis Manual](#) available from the AAAP
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