MAREK'S DISEASE

Marek's disease (MD) is a neoplastic highly contagious disease of domestic chickens caused by an *alphaherpesvirus* known as Marek's disease virus (MDV) or *Gallid alphaherpesvirus 2* (GaHV-2) that characterized by mononuclear cellular infiltrates in peripheral nerves and various other organs and tissues including iris and skin. Disease forms are subdivided into visceral, neural, ovarian, ocular and cutaneous forms. Also, acute disease due to virulent MDV and the skin form which is common in broilers.

Etiology:

Marek's disease virus (MDV) is a DNA cell-associated *alphaherpesvirus*. Dander, litter, and feathers from infected chickens are infectious. The infectivity of such materials was retained for 4-8 months at room temperature and for at least 10 years at 4°C. Virus infectivity was inactivated by a variety of common chemical disinfectants. Within the genus *Mardivirus*, closely related but distinct species of viruses are grouped together. These include:

- Serotype 1 MDV (*gallid herpesvirus* type 2), which includes all the pathogenic strains of MDV as well as the attenuated strains such as CVI988
- Serotype 2 MDV (*gallid herpesvirus* type 3)
- Serotype 3 *herpesvirus* of turkey (HVT, *meleagrid herpesvirus* type 1).

Natural and experimental host:

1. Chickens are susceptible as natural host, while baby chicks (newly hatched) show clinical signs under field condition.
2. Cell cultures as DEF: serotype 1 induces plaques 5-14 days on primary isolation and 3-7 days after adaptation.
3. ECE is used for propagation by CAM inoculation producing pocks.
4. Lymphoblastoid cells can be used for propagation.

Transmission:

1. Direct and indirect contact.
2. Inhalation (air-borne) of epithelial cells of the keratinizing layer of the feather follicles.
3. No vertical transmission but egg shell contamination.

Incubation period:

1. It is difficult to determine the incubation period under field conditions.
2. Outbreaks sometimes occur as early as 3-4 weeks, but serious outbreaks occur 8-9 weeks of life.
3. In laying types chicks occurs between 16-30 weeks.

Signs:

Clinical signs associated with MD can occur in chickens from 4 weeks of age, signs are most frequently seen between 12 and 24 weeks of age and sometimes later. The following are some of the characteristics of the different forms of the disease.

1. **Classical form** (**Neural)** In this form of the disease, with mainly neural involvement, mortality rarely exceeds 10-15%, occurring over a few weeks or many months. The most common clinical sign is partial or complete paralysis of the legs and wings. The signs can vary from bird to bird depending on the involvement of the different nerves. When the nerves controlling the neck muscles are affected, signs such as bending of the head or torticollis are seen. Similarly, the involvement of the vagus nerve can result in the paralysis and dilation of the crop. Such birds may also show symptoms of gasping and respiratory distress.

2. **Acute form**: In this form of the disease, where there is usually formation of lymphomas in the visceral organs, the incidence of the disease is frequently between 10 30% and in major out- breaks can go up to 70%. Apart from generalized manifestations such as depression, weight loss, anorexia and diarrhea, the clinical signs are less marked. Mortality can increase rapidly over a few weeks, and then cease, or can continue at a steady or falling rate over several months.

3. **Skin form:** Probably; it is the most important cause of condemnation in broiler chickens, usually are associated with feather follicles meanly can be detected in slaughter house

Necropsy:

Classical (chronic) form:

The characteristic lesions including is the enlargement of one or more peripheral nerves. The most commonly affected nerves are the brachial and sciatic plexus and nerve trunks, coeliac

plexus, abdominal vagus and intercostal nerves. The affected nerves are grossly enlarged and often two or three times their normal thickness. The normal cross striated and glistening appearance of the nerves is lost: they have a grayish or yellowish appearance and are edematous. Localized or diffuse enlargement causes the affected portion to be 2-3 times normal size.

Acute (atypical) form: Visceral lymphomas are common in more virulent forms of the disease. Visceral tumors can occur in the absence of gross nerve lesions. MD lymphomas in most viscera (ovary, lung, heart, mesentery, kidney, liver, spleen, bursa, thymus, adrenal gland, pancreas, proventriculus, intestine, iris, skeletal muscle, and skin) appear as diffuse enlargements, sometimes to several times the normal size, and a diffuse white or grayish discoloration is often present. Lymphomas may also occur as focal, nodular growths of varying size; nodules are white or gray in color and are firm, and the cut surface is smooth. The proventriculus becomes thickened and firm as a result of focal leukotic areas within and between the glands

Ovary: The immature ovary are observed as small to large grayish translucent areas. Mature ovaries may retain function, even though some follicles are tumorous. Marked involvement is indicated by a cauliflower-like appearance.

Skin: The nodular lesions may involve few scattered follicles, or they may be numerous and coalesce to form a distinct whitish nodule, especially in dressed carcasses, may become scablike with brownish crust formation in extreme cases.

Eye (ocular): changes include loss of pigmentation in the iris ("gray eye") and irregularity of the pupil, both the result of mononuclear infiltration of the iris. (Fig. 15.9C). Conjunctivitis, occasionally with multifocal hemorrhages and corneal edema, can be observed. it was found that all field isolates induced ocular lesions in nonvaccinated or HVT-vaccinated chickens; rates ranged from 5-100%.

The cytolytic infection: chickens may die without gross lesions except severe bursal and thymic atrophy. Some chickens also develop a transient splenomegaly. The splenomegaly is a nonneoplastic response to viral replication because it is induced by both virulent and avirulent serotype I strains as well as serotype 2 and 3 strains.

Transient Paralysis (CNS Syndromes): lesion in transient paralysis was vasculitis, which resulted in vasogenic brain edema. The edema and vasculitis were expressed coordinately

with clinical flaccid paralysis and resolved in 2-3 days. Other, apparently unrelated, brain lesions (perivascular cuffing, lymphocytosis, and gliosis) could be observed after clinical recovery or in infected but clinically normal birds.

Vascular syndromes are manifested principally by occlusive atherosclerosis . Susceptible P-line chickens inoculated with the CU2 isolate of MDV developed grossly visible fatty atheromatous lesions in large coronary arteries, aortas, major aortic branches, and other arteries.

Blood: Blood leukocyte counts may be elevated, largely because of increased numbers of large lymphocytes and lymphoblasts the. Majority of leukemic cells are T cells. Bone marrow changes in MD have variously been reported to include multiple tumor nodules.

lymphodegenerative syndromes, related to intense cytolytic infections of lymphoid organs, usually are characterized by severe atrophy of the bursa of Fabricius and thymus.

DIAGNOSIS:

Diagnosis of MD procedures include both pathological by identification of the nature of the tumor and virological methods to identify the presence of infection are isolation of the virus, demonstration of viral DNA or antigens in tissues as well as detection of antibody.

MDV can be detected by isolating the virus from the infected tissues. Materials commonly used for the isolation of the virus are puffy coat cells from heparinized blood samples, or suspensions of lymphoma and spleen cells. As MDV is highly cell-associated, feather follicles from which cell-free MDV can be extracted and for virus isolation. it is essential that the suspensions contain viable cells. These cell suspensions are inoculated into monolayer cultures of chick kidney cells or duck and chicken embryo fibroblast. Evidence of MDV replication in the culture can be seen as plaques, which appear in 3- 4 days.

Molecular biological techniques such as polymerase chain reaction (PCR) tests have been used widely to differentiate between the oncogenic and vaccine strains.

Diagnosis can also be made by detection of viral antigens or nucleic acids by immuno-fluorescence and immunohistochemical methods using polyclonal and monoclonal antibodies.

Serology: The presence of antibodies to MDV in birds from about 4 weeks of age is an indication of infection. Antibodies detected in birds before that age are likely to represent maternally derived antibodies and are not considered evidence of active infection.

Differential Diagnosis:

Acute MD tumors must be differentiated from Lymphoid leukosis, REV in chickens. Nerve enlargements can be induced by REV, riboflavin deficiency. Other diseases that may present confusing gross lesions or paralytic signs are myelocytomatosis (myeloid leukosis), myeloblastosis, erythroblastosis, carcinoma of the ovary, various other nonviral neoplasms, tuberculosis, histomoniasis, genetic gray eye, Newcastle disease, avian encephalomyelitis, and joint infections or injuries.

Prevention and Control:

Because of the highly contagious nature of MDV and its ability to survive for long periods, both within the host and in the environment, eradication of the disease is difficult. Control of the disease is based mainly on preventive vaccination, with improved management methods and use of genetically resistant birds.

1. Management measures or effective biosecurity measures must be followed to delay and lessen the seriousness of the disease. Young chicks should be reared in isolation from older flocks for the first 2-3 months, when. An all-in/all-out referred option for the whole site. This would make it possible to break the infection cycle by disinfection when the houses are empty. Removal of used litter and disinfection of buildings are important aspects of disease control, especially in view of the possibility of selection for pathogens with increased virulence. Furthermore, placing the chicks in an environment heavily contaminated with virus before they have developed a solid immunity can lead to vaccination breaks. Strict biosecurity is also necessary to prevent the introduction of new MDV strains into a farm. Because insects could act as reservoirs of infection, treatment of premises with insecticides is desirable.

2. Vaccination: Vaccination represents, Live virus vaccines are still the cornerstones of disease control programs. These are usually administered to day-old chicks at hatching to provide protection against the natural challenge the chicks are exposed to early in life from the infected poultry house environment. With the introduction of in ovo immunization

methods, an increasing number of birds are vaccinated by this route. MD vaccines are highly effective, often achieving over 90% protection under commercial conditions. Commercially available vaccines have been derived from all the three serotypes and are usually administered at the minimum recommended dose of 1000 plaque-forming units (pfu) per chick.

a. Serotype 1 vaccines Commercial vaccines developed from the members of this species include the attenuated HPRS-16 and the CVI988/Rispens strain of MDV vaccine. The CVI988/ Rispens strain is able to induce protection against the challenge from more recently isolated vvMDV and vv MDV pathotypes.
b. Serotype 2 vaccines Naturally nonpathogenic strains of MDV belonging to serotype 2 are widespread among poultry. Vaccines derived from these strains are protective against many virulent pathotypes but less so against very virulent strains. Cell-associated serotype 2 vaccines incorporating SB-1 and 301B/1 strains are available.
c. Serotype 3 vaccines FC-126 strain of HVT is widely used commercially in many countries, highly effective against virulent MDV strains, availability as cell-free and cell-associated forms and its low cost but is less effective against some of the very virulent pathotypes.
d. Polyvalent vaccines: The concept of polyvalent vaccine evolved from the demonstration of protective synergism, where the protection was greater with a combination of two vaccines than with individual components. The bivalent vaccines that are available commercially include the combinations of HVT with either HVT and SB-1 strains as CVI988/Rispens or 301B/1 strains.
e. Recombinant vaccines: Recombinant DNA technology potentially offers several advantages for the development of superior vaccines with very little residual pathogenicity. The fowl pox virus and HVT expressing the glycoprotein B (gB) gene of serotype 1 MDV offered significant levels of protection against MDV.

3. Selection for genetic resistance:

Genetic resistance to MD is well documented and susceptible and resistant lines can be developed by progeny testing. Two distinct genetic loci that play a major role in controlling resistance have been identified. The best characterized association is the one between the chicken major histocompatibility complex (MHC) and resistance to MD, the most notable being the association with the B21 allele. This association develops early in life and is accompanied by reduced numbers of infected T cells. A second type of

resistance associated with non-MHC genes is provided by the observation that RPL line 6 and 7 chickens, which are both homozygous for the same MHC allele, differ markedly in MD susceptibility.