

Neoplastic diseases



Economic importance

- Mortalities and cost of prevention
- Widespread
- Genome integration into host cell
- Occurrence of latent infections
- Effect on international trade



Marek's disease



Outline

- Introduction
- Causative agent(s)
- Economic Impact
- Transmission
- Clinical Signs
- Diagnosis and Treatment
- Prevention and Control



Introduction

- Contagious lymphoproliferative neuropathic disease of primarely chickens caused by highly cell-associated but readily transmitted alphaherpesvirus
- Chickens are the most important natural host
- Quail and turkeys can be infected



Introduction

- Other birds and mammals appear to be refractory to the disease or infection.
- One of the most ubiquitous avian infections; it is identified in chicken flocks worldwide.
- Although clinical disease is not always apparent in infected flocks, a subclinical decrease in growth rate and egg production may be economically important.



Etiology

- Family *Herpesviridae*:
 - Subfamily Alphaherpesvirinae
 - 3 serotypes:
 - Serotype 1 (pathogenic or oncogenic strains) divided into pathotypes:
 - Mild (m), virulent (v), very virulent (vv), and very virulent plus (vv+).
 - Serotype 2(non-pathogenic strains)
 - Serotype 3 non-pathogenic turkey herpesvirus (HVT)
- (chicken and tiurkey avirulent strains commonly used as vaccines)**



Host

- Chickens are the main natural host
- Other hosts include
 - Turkeys
 - Quail
- The disease has global distribution in poultry-producing regions



Transmission

- Highly contagious
- The virus matures into a fully infective, enveloped form in the epithelium of the feather follicle
- Dust or dander from infected chickens is particularly effective in transmission.
- Infected chickens continue to be carriers for long periods



Pathogenesis

- 4 phases of infection in vivo are recognized:
 1. Early productive-restrictive virus infection causing primarily degenerative changes
 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 progress to the point of lymphoma formation.



Pathogenesis

- Productive infection may occur transiently in:
 - B lymphocytes (nonenveloped virions)
 - Feather follicle epithelium (enveloped virions).
- Latent infection occur:
 - T cells
 - Cause long-term carrier state.
 - Some T cells undergo neoplastic transformation.



Clinical signs

- The incidence of Marek's disease depends on
 - strain and dose of virus
 - age at exposure
 - maternal antibody
 - host gender and genetics
- Incubation period from few weeks to several months



Clinical signs

- Forms of the disease
 - **Classical or neural form:** paralysis of wings and legs
 - **Acute form** with more virulent strains with lymphomatous lesions in organs and high mortalities
 - **Transient paralysis** for 24-48 hrs
 - **Early mortality syndrome** an early acute cytolytic disease. Typically, affected birds show only depression before death even before any lesion development





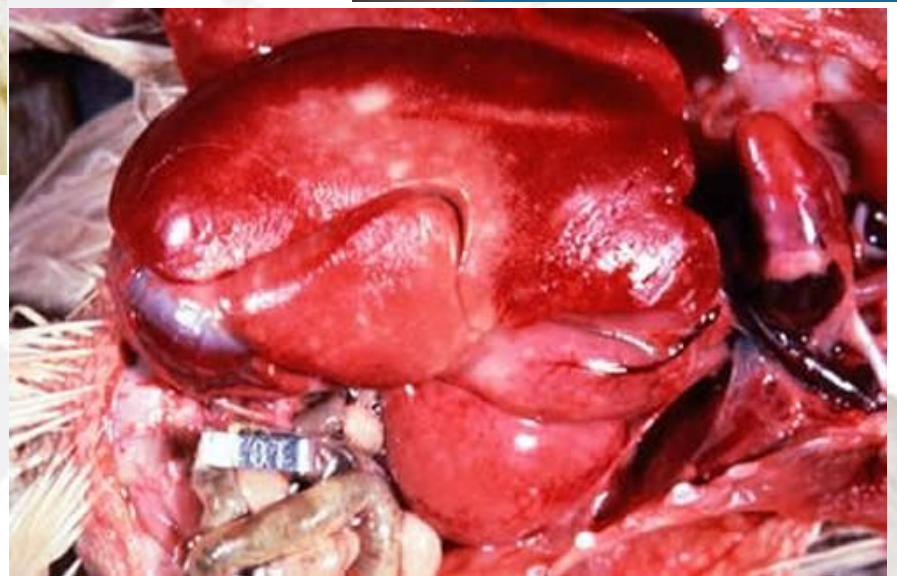
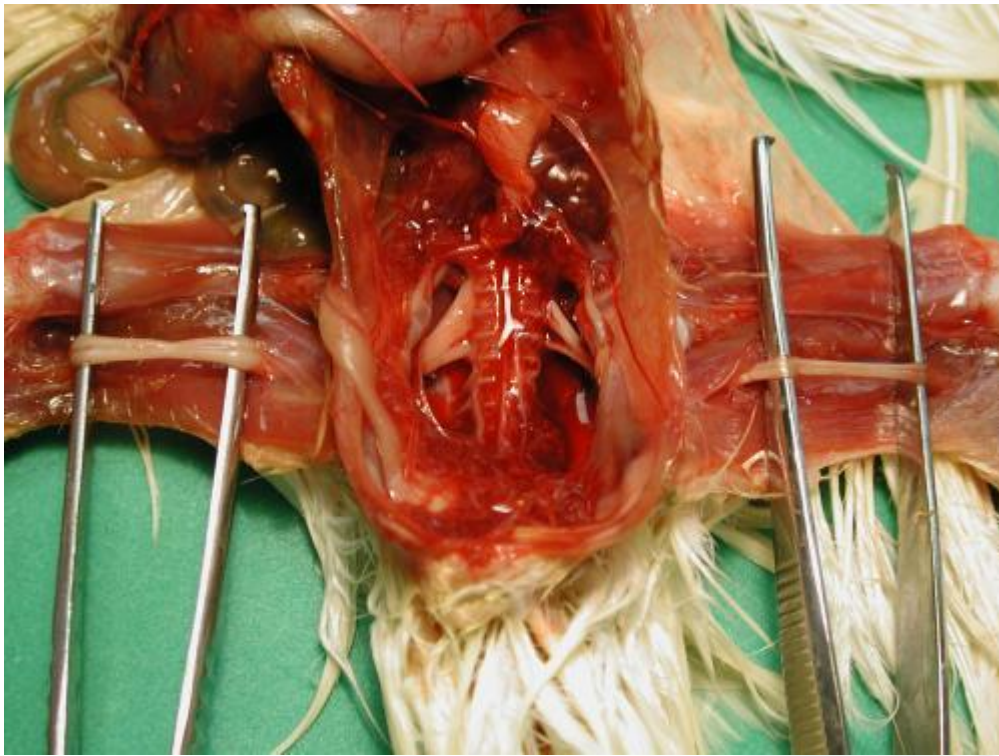
- Classical form:
 - Enlargement and loss of striations peripheral nerves (vagus, brachial, and sciatic)
 - Small soft grey tumors may seen in ovaries, kidneys and liver
- Acute form:
 - Diffuse or nodular lymphoid tumors in various organs
 - Peripheral nerves may be involoved
 - Enlarged feather follicles
 - Eye involovment (fish eye)



- Common in all forms:
 - The bursa and thymus are atrophic.
 - Histologically: mixed population of small, medium, and large lymphoid cells plus plasma cells and large anaplastic lymphoblasts.



Postmortem lesions



Postmortem lesions



Diagnosis

- **Clinical signs and lesions:**
- Enlarged nerves and lymphoid tumors in various viscera.
- The absence of bursal tumors helps distinguish this disease from lymphoid leukosis
- Marek's disease can develop in chickens as young as 3 wk old
- Histology
- Histochemistry and PCR, respectively.



Prevention and control

❑ Biosecurity:

- Improve management and hygiene
- The efficacy of vaccines can be improved by strict sanitation to reduce or delay exposure
- Breeding for genetic resistance



□ Vaccination:

- Turkey herpesvirus (HVT) vaccine,
- Used for recombinant vaccines offer protection against both Marek's disease virus and the inserted virus.
- Bivalent vaccines (HVT + either the SB-1 or 301B/1 strains of serotype 2) provide additional protection
- The most protective commercial vaccine is CVI988/Rispens+HVT at vaccination.
- In ovo vaccination 18th day of incubation.
- Proper handling of vaccine is critical



Prevention and control

□ Vaccination:

- Cell-associated vaccines are generally more effective than cell-free vaccines
- Vaccines administered at hatching and require 1–2 wk to produce an effective immunity, so biosecurity is very important



Avian Leucosis



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Introduction

- Several different leukemia-like proliferative disease of haemopoietic system including:
 - Lymphoid leucosis the commonest form involving B-cells
 - ▶ extravascular lymphoblasts
 - Erythroid leucosis uncommon sporadic cases with involving erythrocytes ▶ intravascular erythroblastosis
 - Myeloid leucosis
 - Myeloblastic myeloid leucosis ▶ myeloblast tumor cells
 - Myelocytic myeloid leucosis ▶ well differentiated myelocytes (involving skeleton)



Introduction

- Subclinical infection assoc. with egg production and quality problems.
- In recent years this control program has expanded, and infection has become infrequent or absent in certain commercial flocks.



- Family *Retroviridae*:
 - Genus Alpharetrovirus
 - 6 subgroups:
 - A, B, C, D , E&J
 - A and B are most prevalent
 - J assoc. with myloid neoplasms
 - E non-oncogenic endogenous viruses
 - C and D are rare
 - All strains of avian leukosis virus are oncogenic.



Host& transmission

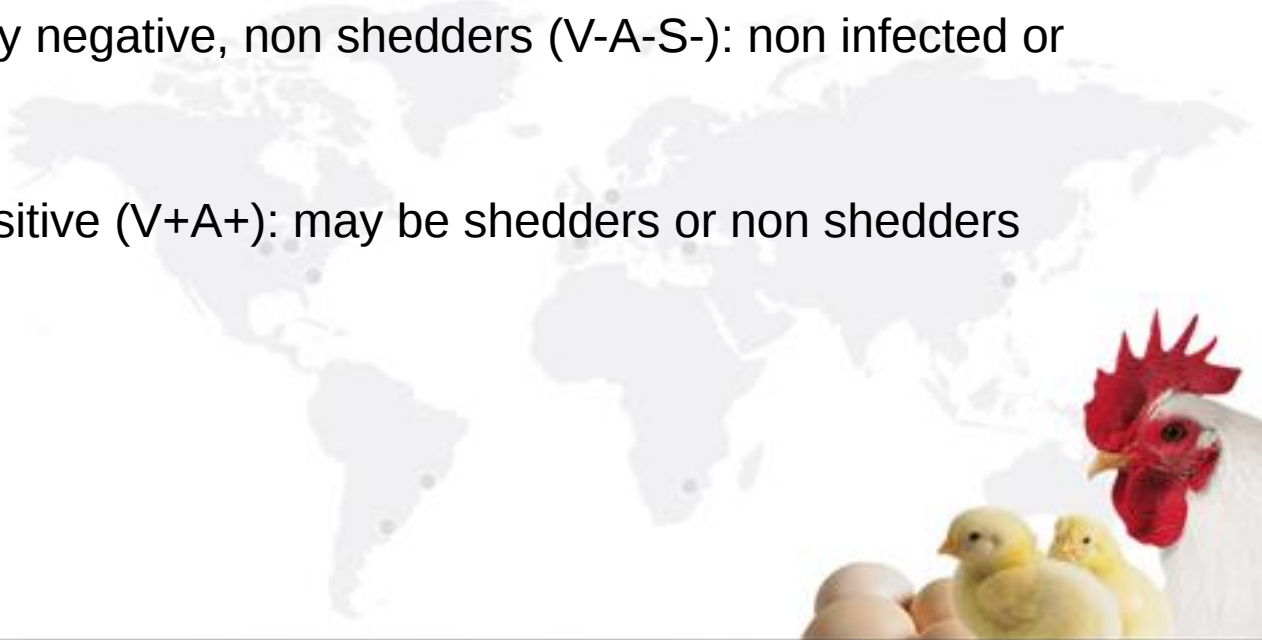
- Chickens are the natural host
- Other hosts; pheasants, partridges, and quail.
- Transmission:
 - Vertical: small portion of birds (no antibodies) ► transmit virus to contacts
 - Horizontal infection by direct or indirect contact
- The earlier the infection, the more likely it is to lead to tolerance, persistent viremia, and tumors.



Host& transmission

FOUR classes of avian leukosis virus infection in the flock can be seen :

1. Tolerant viremic, antibody negative shedders (V+A-S+): vertical infected birds and early infection ► more susceptible to neoplasms (MINOR)
2. Non-viremic, antibody positive, non shedders (V-A+S-) and shedders (V-A+S+): infected birds by contact after hatching (MAJORITY)
3. Non-viremic, antibody negative, non shedders (V-A-S-): non infected or genetically resistant
4. Viremic, antibody positive (V+A+): may be shedders or non shedders



Clinical signs & lesions

1- Lymphoid leukosis

- Almost caused by ALV A&B
- Few general signs (diarrhea, dehydration, emaciation).
- Diffuse, nodular or miliary enlargement of liver
- Nodular tumors of bursa
- Tumors of spleen and other organs

2- Erythroid leucosis

- Rare
- Few general signs (diarrhea, dehydration, emaciation).
- Sometimes Diffuse enlargement of liver and spleen
- Bright cherry red liver, spleen and bone marrow



Clinical signs & lesions

1- Myeloblastic Myeloid leukosis

- Sporadic disease of adult broiler breeders
- Few general signs (diarrhea, dehydration, emaciation).
- Diffuse enlargement of liver and spleen (yellowish grey granular)
- Immature myeloblasts

2- Myelocytic myeloid leucosis

- Sporadic disease of adult broiler breeders
- Few general signs (diarrhea, dehydration, emaciation).
- Myelocytomas involve skeleton
- Well differentiated myelocytes





Diagnosis

- **Clinical signs and lesions:** are most important
- lymphoid leucosis in various organs.
- Presence of bursal
- leucosis can develop in chickens as young as 14 wk old
- Histology
- Virus isolation, serology and PCR, are useless.



❑ Biosecurity:

- Improve management and hygiene
- Breeding for genetic resistant breeds
- Eradication from primary breeding stocks is the most effective means
- Vaccination for tumor prevention has not been promising.



Comparison of marek's vs leucosis

Principal gross and microscopic features of importance in the differential diagnosis of the leukoses and Marek's disease lymphoma

Feature	Lymphoid leukosis	Erythroid leukosis	Myeloid leukosis (myeloblastosis)	Myeloid leukosis (myelocytomatosis)	Marek's disease lymphoma
Liver	Greatly enlarged; diffuse, miliary or nodular tumours; moderately firm	Moderately enlarged; diffuse infiltration; cherry-red colour; soft	Greatly enlarged; diffuse infiltration; mottled; granular surface; firm	Often yellowish white nodular or diffuse tumours	May be moderately to greatly enlarged; miliary or nodular tumours; firm
Spleen	Usually enlarged; diffuse, miliary or nodular tumours; soft	Often enlarged; cherry-red; smooth; very soft	Often enlarged; diffuse tumour; mottled; smooth; soft	Often nodular or diffuse tumours	Often atrophic; may be enlarged; usually diffuse tumours
Bursa of Fabricius	Usually enlarged; nodular tumours	No changes	Sometimes tumorous	No changes	May be diffusely enlarged
Bone marrow	Often tumorous; diffuse or focal	Semi-liquid; cherry-red	Diffuse, reddish-grey tumour infiltration	Usually diffuse yellowish-grey tumour infiltration	No changes
Blood	Occasionally lymphoblastic leukaemia	Erythroblastic leukaemia; immature erythrocytes; anaemia; thin buffy coat	Myeloblastic leukaemia; thick buffy coat	Myelocytic leukaemia; thick buffy coat	May be lymphocytosis or lymphocytic leukaemia
Cytology and histopathology	Lymphoblasts; mainly extravascular infiltrations	Erythroblasts; intravascular	Myeloblasts in intravascular and extravascular locations	Myelocytes in intravascular and extravascular locations	Pleomorphic, sometimes blastic, lymphoid cells in perivascular locations
Other organs and tissues often grossly involved	Kidneys, ovary	Kidneys; may be haemorrhages in muscles	Kidneys, ovary	Kidneys, ovary, thymus, surface of bones (sternum, ribs, skull)	Nerves, kidneys, ovary, proventriculus, heart, muscle, skin, iris



