

BASICS

DEFINITION

Lymphoid neoplasia in chickens and related species is most often due to Marek's disease (MD), lymphoid leukosis (LL), or reticuloendotheliosis (RE), all of which are caused by viruses. These viruses are common in chicken flocks (especially MD virus), and it can be difficult to differentiate between these viral etiologies due to their similar clinical signs.

PATHOPHYSIOLOGY

- MD – caused by Marek's disease virus (MDV), an alphaherpesvirus initially affecting B lymphocytes but later predominantly involving T lymphocytes, horizontally transmitted by the respiratory route from the inhalation of infected dust or skin/feather dander. Numerous strains of serotype 1 exist and their virulence varies, with recent emergence of more virulent strains. Serotypes 2 and 3 are not oncogenic. Incubation period from time of infection to time of clinical signs can range from a few weeks to several months.
- LL – caused by lymphoid leukosis virus (LLV), an alpharetrovirus predominantly involving B lymphocytes, vertically (through the egg) or horizontally transmitted (oculonasal, oral, respiratory or skin, via feces, saliva or skin dander). Disease is most commonly due to a virus of subgroup A or B, less commonly subgroup J. Also can be transmitted as a contaminant of live vaccines (MDV, fowl pox) produced in chicken embryo cells or tissues. Incubation period from time of infection to time of clinical signs can range from a few weeks to several months.
- RE – caused by reticuloendotheliosis virus (REV), a gammaretrovirus involving B or T lymphocytes, vertically or horizontally transmitted. Mosquitoes can transmit REV. Also can be transmitted as a contaminant of live vaccines (MDV, fowl pox) produced in chicken embryo cells or tissues. Incubation period from time of infection to time of clinical signs can range from 2 weeks to several months.

SYSTEMS AFFECTED

- Cardiovascular
 - MD – atherosclerosis
- Gastrointestinal
 - Diarrhea, hepatomegaly
- Hemic/Lymphatic/Immune
 - MD – immunosuppression due to thymic and bursal atrophy
 - LL – Leukemia is not typically seen, thus the term "leukosis" is used. Commonly affects the bursa of Fabricius.
 - RE – immunosuppression is considered one of the most important effects of infection; stunted growth can be due to immunosuppression
- Musculoskeletal
 - MD, RE - Stunted growth

- Neuromuscular
 - MD can include paralysis due to T cell infiltration and demyelination of peripheral nerves, typically the sciatic nerves and less often the nerves of the wings or neck. MD less commonly causes a transient paralysis of 1-2 days due to encephalitis.
- Ophthalmic
 - MD - Iris abnormalities due to lymphocyte infiltration (gray discoloration, unequal PLR's, misshapen iris); blindness
- Renal/Urologic
 - MD – glomerulopathy due to immune complex deposition
- Reproductive
 - Decreased egg production and quality, reproductive tract tumors
- Skin/Endocrine
 - MD - Enlarged/swollen feather follicles visible in skin
 - RE - Abnormal feathering (“nakanuke”)

GENETICS

MD - Genetic resistance to MD is present in some lines of birds.

INCIDENCE/PREVALENCE

- MDV and LLV are considered to be ubiquitous in chicken flocks, and REV is considered common.
- LL – incidence of neoplasms in infected flocks is usually only 1-2%, although losses of up to 20% can occur.
- RE – clinical disease is rare, but losses from mortality or condemnation at slaughter in affected flocks can be as high as 20%.

GEOGRAPHIC DISTRIBUTION

Worldwide

SIGNALMENT

- Species –
 - Chickens – MD, RE, LL
 - Turkeys – MD, RE
 - Pheasants – MD, RE
 - Partridges - RE
 - Prairie chickens – RE
 - Peafowl - RE
 - Quail – MD, RE
 - Ducks – RE
 - Geese – MD, RE
- Breed Predilections –

- MD – Genetic resistance to MD is present in some lines of birds
- Mean Age and Range –
 - MD - ≥4 weeks old, most commonly at 10-24 weeks of age
 - LL – ≥14 weeks old, with most mortalities at 24-40 weeks of age. Generally, resistance to infection increases with age.
 - RE – stunted growth can be noticed as early as 1 month of age; lymphomas typically occur at ≥15 weeks of age, depending on bird species
- Predominant Sex –
 - MD, LL – females are more likely to develop tumors than males

SIGNS

- General Comments – any of the 3 viruses can cause lethargy, diarrhea, inappetence, emaciation, dehydration, depressed egg laying, stunted growth
- Additional Historical Findings –
 - Lameness or weakness – MD
 - Regurgitation – MD
 - Blindness – MD
 - Head tilt – MD
 - Labored respirations – MD
 - Stunted growth – ME, RE
- Physical Examination Findings –
 - Unilateral leg paralysis or crop stasis due to lymphocyte infiltration into peripheral nerves (sciatic nerve plexus, sciatic nerve, GI tract), sometimes called “fowl paralysis” or “range paralysis” - MD
 - Iris abnormalities due to lymphocyte infiltration (gray discoloration, unequal PLR’s, misshapen iris)
 - Enlarged/swollen feather follicles visible in skin – MD
 - Abnormal feather development, with adhesion of the barbs to a localized section of the shaft (“nakanuke”) - RE
 - Abdominal distention – MD, LL

CAUSES

- Inhalation of skin/feather dander from infected birds – MD
- Vertical transmission from hen – LL, RE
- Vertical transmission from rooster – RE
- Horizontal transmission from infected birds – MD, LL, RE

RISK FACTORS

- LL – incidence may be reduced by the presence of infectious bursal disease virus
- MD – high-protein diets or selection for fast growth rate may increase susceptibility

- MD – concurrent infection with other immunosuppressive viruses will usually exacerbate disease (infectious bursal disease virus, chicken infectious anemia virus, REV)

DIAGNOSIS

DIFFERENTIAL DIAGNOSIS

All 3 viruses should be considered in the differential diagnosis list, as well as other neurological or visceral diseases, e.g. ovarian adenocarcinoma.

CBC/BIOCHEMISTRY/URINALYSIS

- RE – Anemia is sometimes seen
- LL, MD – leukemia is rarely seen

OTHER LABORATORY TESTS

- Antibody titer measurement (ELISA or virus neutralization) is available for all 3 viruses, but since the viruses all occur commonly, evidence of exposure for a particular virus does not necessarily confirm the etiology of observed clinical signs. Viral antibodies present in birds <4 weeks old are likely to have been maternally derived. Viral antibodies against LLV in day-old chicks indicate the presence of exposure in the hen, therefore the chick may be congenitally infected and could spread the infection to other chicks. Individual birds without antibodies in a known infected flock may have “tolerant infection” and be viremic shedders of LLV or REV. Samples for antibody detection include plasma, serum, or egg yolk (LLV).
- Viral detection by virus isolation, PCR tests or ELISA are available for all 3 viruses, but as above, evidence of infection does not confirm etiology. Samples for testing include buffy coat cells from heparinized whole blood (MDV, LLV), oviduct swabs (LLV), cloacal swabs (LLV, REV), egg albumen (LLV, REV), embryo tissue (LLV), meconium (LLV), feces (LLV, REV), oral swabs (LLV), semen (LLV, REV), or suspensions of splenic, feather tip or lymphomatous tissue (MDV, LLV).

IMAGING

N/A

DIAGNOSTIC PROCEDURES

Antemortem diagnostic tests are unlikely to be informative as to a specific etiologic diagnosis.

PATHOLOGIC FINDINGS

- Various gross findings can be seen, depending on the phase of disease:
 - Swelling and loss of striations in peripheral nerves, especially the sciatic nerves, less frequent in adult birds than in young birds – MD, less striking in RE
 - Hepatomegaly – LL, MD, RE
 - Diffuse, miliary or nodular tumors in liver – LL, MD, RE

- Splenomegaly – LL, MD, RE
 - Splenic atrophy - MD
 - Diffuse, military or nodular tumors in spleen – LL, MD (usually diffuse), RE
 - Spleen is soft in texture – LL
 - Bursal enlargement – LL, MD
 - Bursal atrophy – MD, RE
 - Nodular tumors in bursa – LL, RE
 - Thymus atrophy - RE
 - Diffuse or focal tumors in bone marrow – LL
 - Normal bone marrow – MD
 - Intestinal thickening and annular lesions – RE
 - Vessel thickening (atherosclerosis) - MD
 - Kidney involvement – LL, MD
 - Ovarian involvement – LL, MD
 - Proventricular involvement – MD
 - Heart involvement – MD
 - Muscle involvement – MD
 - Feather follicle involvement – MD
 - Skin lesions on head and mouth - RE
 - Abnormal feathering (“nakanuke”) - RE
 - Iris involvement - MD
 - Leukemia, although uncommon – LL (lymphoblastic), MD (lymphocytic)
 - If lymphomas are found in ducks, geese, pheasants or quail, REV is a likely cause rather than MDV or LLV.
- Various microscopic findings can be seen in cytologic or histopathologic exam, depending on the phase of disease:
 - Extravascular infiltrations of lymphoblasts – LL, RE
 - Perivascular infiltrations of pleomorphic lymphocytes, sometimes blastic – MD
 - Brain edema – MD
 - Glomerulopathy due to immune complexes – MD
 - Immunoproliferative lesions in feather pulp - MD

TREATMENT

APPROPRIATE HEALTH CARE

Treatment has been unsuccessful for birds clinically affected by any of these viruses; symptomatic infections become fatal.

NURSING CARE

N/A

ACTIVITY

N/A

DIET

N/A

CLIENT EDUCATION

When obtaining new chickens, clients should choose those that were vaccinated against MDV as day-old chicks.

SURGICAL CONSIDERATIONS

N/A

MEDICATIONS

DRUG(S) OF CHOICE

Treatment has been unsuccessful for birds clinically affected by any of these viruses; symptomatic infections become fatal. However, in one study, chickens fed a diet containing the cortisol-reducing drug metyrapone showed regression or lack of Marek's disease tumors compared to a control group. Nonsteroidal anti-inflammatory drugs may temporarily improve the quality of life of affected birds.

CONTRAINDICATIONS

N/A

PRECAUTIONS

N/A

POSSIBLE INTERACTIONS

N/A

ALTERNATIVE DRUGS

See "drug(s) of choice" section above.

FOLLOW-UP

PATIENT MONITORING

N/A

PREVENTION/AVOIDANCE

- MD – Vaccination is 90% effective, either *in ovo* (day 18 of incubation) or on the day of hatch, using a product containing turkey herpesvirus as well as another MD virus (often CV1988-Rispens). Vaccination can prevent some lymphoma formation and clinical disease, but does not prevent superinfection by especially virulent MDV strains. Vaccine-induced immunity takes 2 weeks to develop, so vaccinated chicks should be kept away from infection sources the first 2 weeks of life. Re-vaccination of an adult bird does not cause harm, but may be unnecessary since nearly all birds will have become naturally exposed by this time.
- LL, RE – Vaccines are not commercially available, therefore eradication from a flock depends on breaking the vertical transmission cycle from dam to chicks (eliminating dams and roosters that are infected), and prevention of reinfection of chicks. Although roosters do not transmit LLV via semen to embryos, they can be a venereal source of infection for hens. Hatched chicks can be reared in isolation in small groups and tested for viremia and viral antibodies from approximately 8 weeks of age to verify virus-free status.
- MD - Genetic resistance to MD is present in some lines of birds and can be a useful component of prevention.
- RE – Reduction of insect vectors (mosquitoes)
- Hygiene, including removal of used litter and disinfection. MDV is long-lived outside a host, retaining infectivity for 4-8 months at room temperature or for at least 10 years at 4°C. LLV and REV only survive for a few hours outside of a host. The most effective types of disinfectants for these viruses are chlorine-releasing agents and iodophors; chlorhexidine is ineffective. Freezing and thawing will degrade LLV and REV, as will high temperatures (>50°C.) or pH extremes (<5 or >9). MDV requires more extreme pH's (<3 or >11) or temperatures (>60°C.) for inactivation than LLV or REV.
- Biosecurity, preventing introduction of new viral strains to a bird enclosure (especially for MDV)
- Minimization of stress, especially in newly-hatched chicks (to encourage development of immunity) and around the time of onset of egg production

POSSIBLE COMPLICATIONS

N/A

EXPECTED COURSE AND PROGNOSIS

Symptomatic infections with any of these 3 viruses invariably become fatal.

MISCELLANEOUS

ASSOCIATED CONDITIONS

- LL – fowl glioma
- MD - atherosclerosis

AGE-RELATED FACTORS

LL – congenitally infected chicks are an important source of infection for other chicks in the hatchery and during the brooding period.

ZOONOTIC POTENTIAL

Although seropositivity has been seen in humans, there is no direct evidence of disease potential in humans for MDV, LLV or REV.

PREGNANCY/FERTILITY/BREEDING

Poor egg production, egg size, fertility, hatchability and chick growth rate

SYNONYMS

- MD – fowl paralysis, range paralysis, polyneuritis, neurolymphomatosis gallinarum, acute leukosis, early mortality syndrome, Alabama redleg, gray eye
- LL – big liver disease, lymphatic leukosis, visceral lymphoma, lymphocytoma, lymphomatosis, visceral lymphomatosis

SEE ALSO

N/A

ABBREVIATIONS

LL – Lymphoid leukosis

LLV – Lymphoid leukosis virus

MD – Marek's disease

MDV – Marek's disease virus

RE – Reticuloendotheliosis

REV – Reticuloendotheliosis virus

INTERNET RESOURCES

Dinev, Ivan. 2014. Virus-induced neoplastic diseases: Marek's disease. Accessed on July 27, 2014. Available at: <http://www.thepoultrysite.com/publications/6/diseases-of-poultry/201/virusinduced-neoplastic-diseases-mareks-disease>

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http://www.merckmanuals.com/vet/poultry/neoplasms/overview_of_neoplasms_in_poultry.html

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Suggested Reading

Nair, Venugopal, Karel A. Schat, Aly M. Fadly, and Guillermo Zavala. 2013. Chapter 15: Neoplastic Diseases. In: Diseases of Poultry, 13th edition (e-book). Swayne, David E., John R. Glisson, Larry R. McDougald, Lisa K. Nolan, David L. Suarez, and Venugopal Nair (eds.). Wiley-Blackwell, Hoboken, NJ. Pp. 513-604.

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