



Diagnostic Exercise

From The Davis-Thompson Foundation*

Case #: 95 Month: April Year: 2018

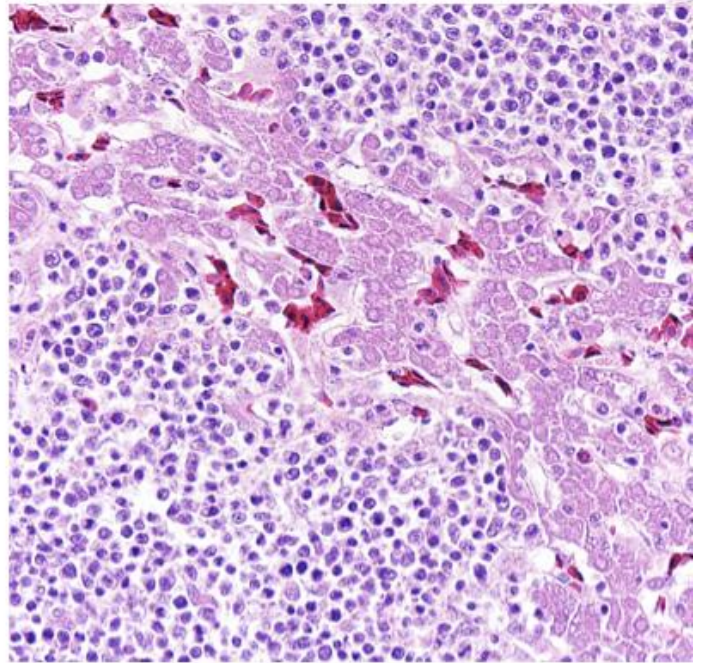
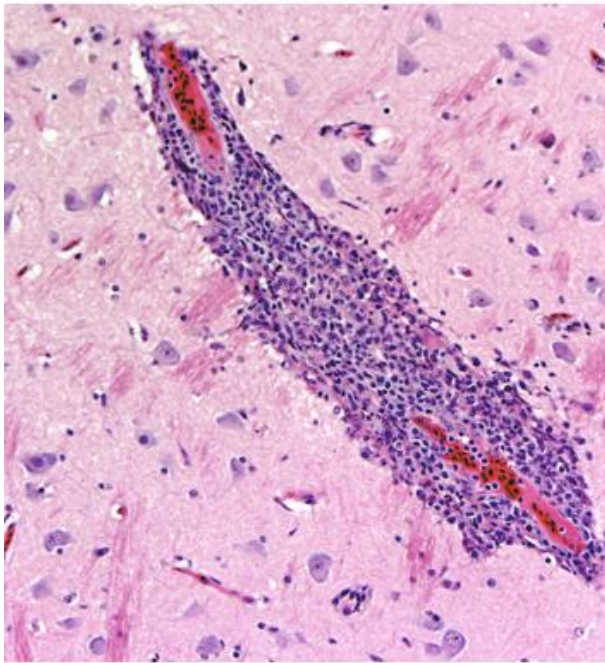
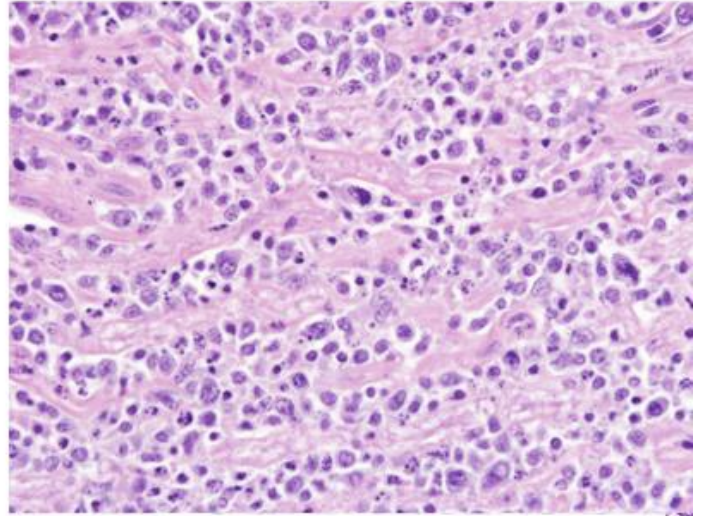
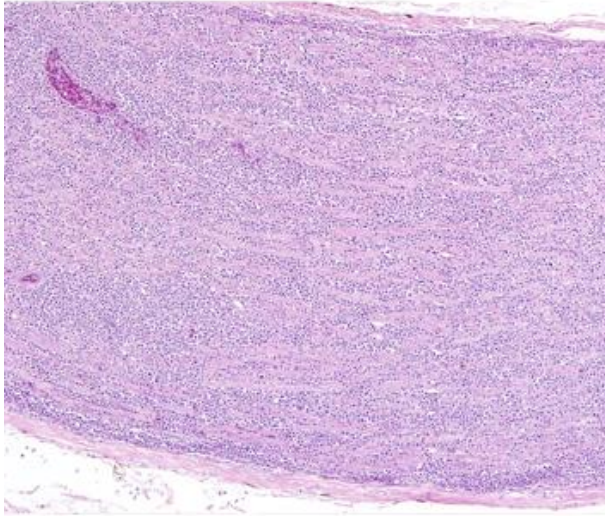
Answer Sheet

Title: *Chicken, backyard flock, multiple tissues (CNS, PNS, liver, kidney, ovary) Marek's disease.*

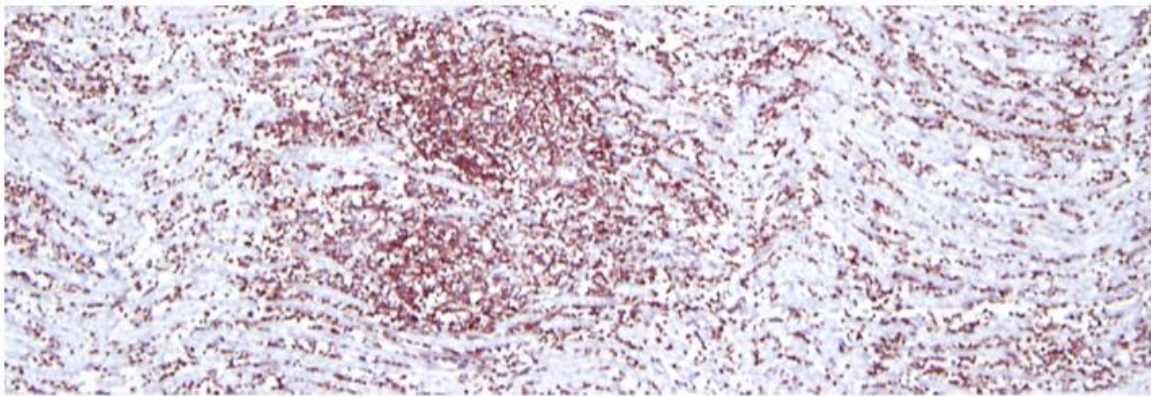
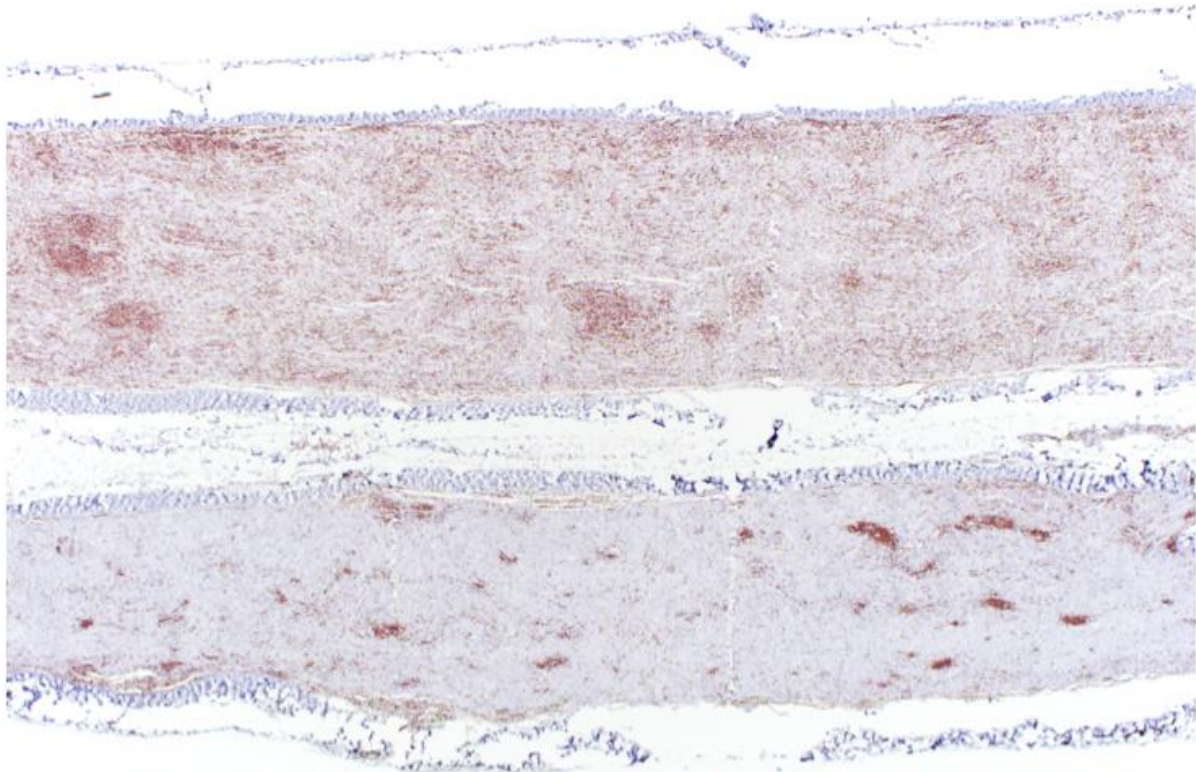
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Morphologic diagnosis: disseminated lymphoid (T-cell) neoplasia represented by pleomorphic lymphocytes infiltrating the peripheral nerves brain/meninges, liver, and kidneys (consistent with marek's disease).

Microscopic findings: The following sections were examined with an H&E stain: brain, peripheral nerves, skeletal muscle, heart, trachea, air sacs, lung, liver, spleen, kidneys, ovary, oviduct, esophagus, crop, proventriculus, ventriculus, pancreas, and intestines. Perivascular to diffuse sheets of pleomorphic lymphocytic infiltration of the peripheral nerves was observed. Thick layers of similar pleomorphic lymphocytes cuffed vessels of the brain/meninges. The neoplastic cells mostly formed nodules that obliterated the kidney and liver parenchyma. Using immunohistochemistry, neoplastic lymphocytes in the peripheral nerves were determined to be CD3 immunopositive T-cells.



Histologic description: 4X and 40X: Perivascular to diffuse sheets of pleomorphic lymphocytic infiltration and invasion of the peripheral nerves (sciatic). Thick layers of similar pleomorphic lymphocytes cuffed vessels of the brain/meninges. In other organs (cerebrum (upper), liver (lower) pictured here) a pleomorphic lymphocytic infiltration surrounds vessels, and randomly infiltrates the parenchyma.



4X, 20X, sciatic nerve: immunohistochemistry, CD3 (T cell)

Discussion: T-Rex demonstrated characteristics of Marek's disease. This preliminary diagnosis was made based on the severe disseminated lymphoid neoplasia in characteristic locations such as the peripheral nerves and visceral tissues.

Marek's disease is a commonly encountered and highly contagious disease of primarily domestic chickens (*Gallus gallus*) and less commonly in turkeys, pheasants, and quail (Nair 2005). Understanding the etiology and pathology of Marek's disease is imperative with it causing an approximate 1 billion US dollar annual loss in the global poultry industry (Nair 2005). The infectious agent of Marek's disease is an alphaherpesvirus appropriately named "Marek's disease virus" (MDV). Marek's disease was first described in 1907 by Dr. Jozsef Marek as a mild paralytic syndrome with endemic distribution (Marek 1907; Nair 2005). Modern MDV has since evolved into a worldwide highly contagious neoplastic disease of four manifestations: cutaneous, neural, ocular, and visceral, or a combination thereof (Savage and Darre 2008) with the following signs:

- Cutaneous: inflamed feather follicles and bumps on the skin;
- Neural: progressive paralysis of a pelvic limb due to swelling of the sciatic nerve, weight loss, difficulty breathing, and diarrhea resulting in death;
- Ocular: grey colored iris, anisocoria, and blindness;
- Visceral: lymphocytic infiltration/tumors in the visceral organs (ovary, spleen, liver, kidneys, lungs, heart, proventriculus, and adrenals) and skeletal muscle.

MDV infection can additionally result in either an acute or chronic form depending on the viral pathotype and host genetic susceptibility (Witter et al. 2005). Infection occurs through inhalation of dust containing dander from infected birds, which is then transported by macrophages from the lungs to the lymphoid tissues of the spleen, thymus, and bursa (avian organ for B-cell development). At these tissues, MDV targets lymphocytes where B-cells go through an initial lytic infection resulting in tissue atrophy and eventual immunosuppression. From here, the specific strain will determine the outcome of the infection where MDV-1 is oncogenic and MDV-2 and MDV-3 (HVT) are non-oncogenic. If a highly virulent strain, macrophages will undergo a lytic infection process, resulting in monocytosis and lesions in the central nervous system (esp. brain) demonstrating histologically apparent mononuclear infiltration and perivascular cuffing. Low virulence strains will switch to a latent phase of infection in T-cells, which will transform into neoplastic lymphomatous tumors in visceral organs, while affected immune tissues regenerate. Both strains will result in shedding of extracellular viral particles through feather follicle epithelium (Nair 2005).

Control of MDV is focused towards vaccination against the highly pathogenic MDV-1 using immunizations of MDV-2 and MDV-3 strains (Mete et al. 2016; Nair 2005, 2013). Vaccination against MDV is commonly performed by large hatcheries and the poultry meat and egg industry. In contrast, the emerging backyard poultry culture practices vaccination on a much lower rate with less biosecurity concern (Mete et al. 2013; Whitehead and Roberts 2014; Elkhoraibi et al. 2014). The combination of an expansive poultry production and backyard poultry economy in California has created a "hot zone" for potential biosecurity breaks and a

need for continued research and support (Metz et al. 2013; Stinson and Metz 2013; Metz et al. 2016).

Preliminary diagnosis of Marek's disease can be made through gross and histologic examination. At gross necropsy the following may be observed: multifocal white to tan nodules throughout the parenchyma of visceral organs including the ovary, spleen, liver, kidneys, lungs, heart, proventriculus, adrenals and skeletal muscle; thickening of peripheral nerves; and/or grey coloration of the iris (Metz et al. 2016; Savage and Darre 2008; Nair 2005). Histologic sections of MDV-infected tissues will have pleomorphic lymphocytic infiltration, which results in the destruction of the parenchyma (Nair 2005; Metz et al. 2016; Gornatti Churria et al. 2017).

For a definitive diagnosis of Marek's disease, molecular techniques have to be performed, with a preference for quantitative real-time polymerase chain reaction (RT-PCR) (Nair 2005; Gimeno 2008; Biggs and Nair 2012), in conjunction with gross and histologic findings. Ancillary testing ruled out salmonellosis, secondary bacterial infections, and avian influenza.

References and Recommended literature:

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*The Diagnostic Exercises are an initiative of the **Latin Comparative Pathology Group (LCPG)**, the Latin American subdivision of The Davis-Thompson Foundation. These exercises are contributed by members and non-members from any country of residence. Consider submitting an exercise! A final document containing this material with answers and a brief discussion will be posted on the CL Davis website (http://www.cldavis.org/diagnostic_exercises.html).

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