# “Duchess’s Distressing Dilemma”

Lauren Scott

Mississippi State University

College of Veterinary Medicine

Class of 2022

Clinicopathologic Conference

November 19th, 2021

Advisor: Jennifer Beam, DVM

## Introduction

The following case will outline a common neurologic disease of ruminants. Suppurative central nervous system diseases in small ruminants commonly results in meningoencephalitis, leptomeningitis, cerebral abscesses, spinal cord abscesses, or basilar empyema.[1] The most common bacterial considerations for these conditions are *Listeria monocytogenes*, *Escherichia coli*, *Trueperella pyogenes*, and *Proteus mirabilis*.[1] In adult goats and sheep, the most common cause of suppurative central nervous system disease is listerial meningoencephalitis or encephalitis as a result of *Listeria monocytogenes* infection.[1]

Ruminants with Listeriosis often present for depression, high fever, incoordination, blindness, anorexia, salivation, drooping of the ear or eyelid, redness of the ocular conjunctiva, circling, and/or facial paralysis.[2,3] Onset can be quick and result in death within 24-48 hours, therefore prevention is the best form of management against Listeriosis.[2,3,7] *Listeria* is of great zoonotic concern in humans with infection possible from shedding in the environment, as well as the milk and meat products of carrier or sick goats.[2,5,6] Infection with *Listeria monocytogenes* occurs in neuropathologically similar ways in humans and ruminants, allowing for greater research in pathogenesis and treatment of the disease.[4,5]

## History and Presentation

Duchess, an approximately 3 to 4 year old mixed breed doe, presented to the MSU-CVM Food Animal Service on March 29th, 2021 for lethargy and coughing,. Duchess was bought from a sale barn on February 8th, 2021 and was treated two weeks later at MSU for anemia of chronic disease with parasitic infection from Coccidia and *Haemonchus*. She was treated with a variety of anti-parasitic medications and a blood transfusion. During her March 16th recheck, she was found apparently healthy. She lived with 4 other goats, and her diet consisted of  Purina goat grain, and

an assortment of bermuda grass hay, alfalfa, timothy, and freshly picked grass, as they were currently not on pasture due to ongoing repairs. Duchess had a laceration on the left side of her nose from a previous suspected dog bite that has mostly healed. Her owner mentioned that occasionally some hay gets stuck in that opening after eating, however she had otherwise been doing well since her last visit prior to now.

On presentation, Duchess was dull but responsive. She had a slightly elevated temperature of 103.5 F, a slightly decreased heart rate of 52 beats per minute, and a normal respiratory rate of 24 breaths per minute. She had a body condition score of 1/5 with prominent hip and pin bones, and easily palpable, lightly muscular ribs and spinal structures. She had two intact horns and an orange USDA ear tag in the right ear. Her FAMACHA score was 2 out of 5 when looking at her right eye. Her left eye appeared to have some purulent discharge and redness. Otherwise, both eyes had a normal menace and palpebral reflex, , and the eyes were in the correct position. Her oral mucous membranes appeared pink and moist with a normal capillary refill time of less than two seconds, however she had a prominent skin tent and sunken globes that may be attributed to her body condition. Alopecia was appreciated along her dorsal spinal processes, and there was a patch of alopecia just distal to the thoracic spine on the right side. A cough could be induced by palpating her trachea. Additionally, Duchess' heart sounds auscultated within normal limits, however lung sounds were harsh in the cranio-ventral aspects on both sides. No crackles or wheezes were appreciated, however an intermittent whistling or grunting sound on expiration was appreciated. nd She had a mostly healed laceration on the left side of her nose that remained open with some granulation tissue around the edges. Duchess also has a scarred bit of muzzle on the upper right side of her lip. She had decreased rumen contractions and borborygmi, indicating that she may not be eating very well. During examination, she urinated with some straining and inconsistent

streams. She also defecated in clumped fecal piles. She also stood with some valgus in her hindlimbs. Her ears and nose appeared clean, symmetrical, and free of discharge, and other facial muscles appear symmetric as well. Her teeth seem to indicate an age of 4 at the time. All other parameters were within normal limits at the time.

**Diagnostic Approach and Case Overview**

On the day of Duchess' presentation, March 29th, a number of procedures were performed. A PCV of 29% and total protein of 8.8 g/dl were obtained using in house diagnostics, indicating she was regenerating her red blood cells since her previous anemia, and likely not experiencing a high parasite re-infestation. Additionally, a urine specific gravity of 1.020 and pH of 7 (normal) were obtained from Duchess after she urinated. Ultrasound of Duchess' lung revealed very mild comet-tail signs, which could indicate lung disease. A CBC and Chemistry were also submitted but results were not obtained until the next day. Over that night, Duchess did not eat much other than grass, or drink a notable amount of water. However, Duchess urinated several times, and passed several clumped fecal piles. Her respiratory rate was monitored closely throughout the night, due to her presumptive pneumonia, and she was checked frequently to ensure she had adequate hay and water.

On the morning of March 30th, Duchess appeared alert and responsive, but occasionally held her head in an abnormal position, suggesting some neurologic abnormality. Additionally, she seemed to be having some difficulty standing in her cage, but this was presumed to be due to the slippery paper cage matt, so straw and shavings were added to improve footing. In further attempts to determine her neurologic status, she was walked around the clinic and her gait appeared normal. During physical examination, her temperature was noted at 104.1 F. Lung sounds remained harsh,

particularly at the cranio-ventral aspect of both lungs. Rumen sounds appeared strong and normal, however, some pus was noted in her left eye, left nose, and the sinus opening above her left nostril.

Duchess's entry bloodwork was reviewed, and the vast majority of parameters were within normal limits. The few exceptions to this on CBC were a high fibrinogen of 900 mg/dl (reference range 100-400) indicating severe inflammation, mildly elevated neutrophils at 8823.6/ul (reference range 700-7600), and mildly decreased lymphocytes at 1231.2 (reference range 2500-12000). On the chemistry panel, AST was elevated at 1244 U/L (reference range: 58-196) which could indicate hepatocellular or skeletal muscle injury. This was difficult to interpret as her GGT, another liver enzyme, and her CK, another skeletal muscle enzyme, were not greatly elevated. Additionally, albumin was low at 2.2 g/dl (reference range: 3.8-4.5).

At 10am, Duchess was brought to radiology for 3 view thoracic radiographs with plans for a trans-tracheal wash and broad spectrum antibiotics if she remained stable. On Duchess' radiographs, a patchy, unstructured interstitial coalescing to alveolar pulmonary pattern consistent with aspiration pneumonia was seen in the cranial and middle right lung lobes, and in the cranial and caudal subsegments of the left cranial lung lobe. However, Duchess' history did not fit with aspiration as the most likely cause of her pneumonia. Additionally, a structure on the cranial subsegment of the left cranial lung lobe was thought to resemble a lung abscess, but was not confirmed and mostly speculation. Immediately after she was removed from the radiology table and placed down with good footing, Duchess appeared to trip over herself and thrash about in an effort to right herself. After being helped to stand, a physical was performed. Her temperature was 104.5 F indicating a fever but heart rate and respiratory rate were normal. Her glucose was measured after tremors were noted, and found to be very low at 37 g/dL (normal 70 - 90). Karo syrup was rubbed on her gums, she was given a dextrose bolus intravenously, and a catheter was

placed in her left jugular vein. She was given Banamine for her fever at 1.1 mg/kg intravenously and was started on Lactated Ringers Solution with 5% dextrose. Her glucose was rechecked at noon and found to be at 63 g/dl. Given her pneumonia diagnosis, she was placed on Nuflor (florfenicol) at 40 mg/kg SC every 4 days, and procaine penicillin G at 44,000 IU/kg SC every 24 hours. This combination of antibiotics should have been effective against any bacterial causes of pneumonia.

Around 2pm, after continuous monitoring since 10 am, Duchess was noted to be sitting sternally and still with her head tilted and neck outstretched for a prolonged period of time. However, when stimulated she would eat green grass normally and behave in a normal manner. She was given thiamine for possible polioencephalomalacia at 10 mg/kg intravenously, then subcutaneously every 6-8 hours for the remainder of her hospitalization. A full neurologic examination was conducted and no abnormalities were identified, other than gait abnormalities that seemed likely due to chronic musculoskeletal problems (tendon or ligament injuries or arthritis) in her hind legs. As her blood glucose had increased and she was eating, her intravenous dextrose infusion was discontinued.

Duchess had another physical exam at 4pm that was within normal limits, and a plan was made for the night, however at 6pm she was seen laying oddly with her head at an abnormal angle, though she immediately perked up when touched. Another physical exam was performed that was within normal limits, and she walked around normally. Once left to herself again a few minutes after her physical, she turned into a corner and began head pressing and star gazing. Overnight, she was fed grass, hay, grain, and water. She ate well, especially the grass. She defecated and urinated appropriately. She was monitored continuously through the night.

On March 31st, around 6:30 am, Duchess was seen stargazing, having a mostly left sided head tilt, nystagmus that changed directions (but most commonly went left), and a right sided ear droop. She remained sternal however, and was alert, responsive, and eating. The remainder of her physical exam was within normal limits. Her blood glucose was measured at 53 g/dL, and she was given 3 mL bolus of 50% dextrose IV then intravenous fluids with 5% dextrose at 1.5x her maintenance fluid needs were started. In spite of her central nervous system signs, she remained sternal, ruminating, and apparently comfortable. A chemistry panel was taken again and a bile aid test was submitted to assess her liver function. The serum chemistry revealed no important changes from the day before. At noon, because of the continued nystagmus, there was consideration that this may be seizure activity. She was given diazepam, and immediately became laterally recumbent and sedate. No improvement was seen in the nystagmus, confirming it is unlikely to be a seizure response. A CSF tap was performed, and within the syringe, despite sterile technique, clumps were visible in the fluid. Analysis revealed suppurative pleocytosis with a cell count of 63% neutrophils, 9% lymphocytes, and 28% foamy large mononuclear cells with no evidence of microorganisms and a CSF protein of 710.0 mg/dl. A neurologic consult was requested as the CSF tap was being analyzed, and their assessment aligned with the likely bacterial meningoencephalitis (brain inflammation) due to the bacteria *Listeria*, or possibly other bacteria. The antibiotics Duchess was receiving for pneumonia were confirmed appropriate for all likely causes of meningoencephalitis, including *Listeria*. Daily treatment continued with a steroid (dexamethasone) to suppress the inflammation in her brain, and she was given a bolus of hypertonic saline to decrease cerebral edema. After these treatments Duchess temporarily improved, although by April 1 she was no longer able to stand without assistance. Between April 1 - 2 she deteriorated, showing little response to stimulation, and she was no longer able to stand even with assistance. She was given

a second bolus of hypertonic saline, and amino acids were added to her dextrose-containing fluids for nutritional support. Pantoprazole therapy was begun to prevent abomasal ulcers.

**Pathophysiology**

*L. monocytogenes* is a facultative, intracellular, gram positive rod that can be found in soil, water, moist environments, food sources, feces, decaying vegetation and animals, and raw materials.[3,5,6] In sheep or goats, it is most often a result of environmental or fecal contamination, or the feeding of moldy or spoiled hay or silage.[2,3] Infection most commonly occurs in ruminants age 1-3 years old, but can affect animals of any age.[3,7] The majority of listeriosis cases in ruminants appear to occur during cooler months such as November to May, with February and March being peak times.[2,7] Listerial encephalitis pathogenesis is controversial.[7] There are indications that *L. monocytogenes* may enter through oral mucous membranes, potentially through pre-formed lesions or oral lesions from changing teeth, and migrate centripetally within cranial nerves to the brain and brainstem.[7] In tissue culture models of infection, there appear to be 5 stages with the first stage being the internalization of *L. monocytogenes* within the host cell, and the second being *Listeria*'s escape from the host's vacuole.[7] After escaping, multiplication of *Listeria* within the host cell's cytoplasm and movement through the cytoplasm by virtue of Listerially directed polymerization of host actin filaments occurs, followed by movement of *Listeria* to the host cell's surface and ejection of Listerial cells in pseudopod-like structures.[7] Finally, phagocytosis of these pseudopod-like Listerial structures by neighboring cells, followed by escape of the *Listeria* from the resulting double-membrane vacuole occurs, allowing the cycle to repeat.[7] Clinical diagnosis of listeriosis in ruminants is generally difficult due to a variety of inflammatory and infectious diseases that cause clinical signs similar to those of listerial encephalitis and septicemia.[7] Some important differential diagnoses for Listeriosis should include rabies, viral, bacterial, and fungal

causes of CNS infections, polioencephalomalacia, lead poisoning and other intoxications.[7] In general, definitive diagnosis of listeriosis should be achievable by bacterial culture of the CSF or blood, histopathology, and occasionally serology.[7] In most cases, definitive diagnosis of listeriosis is too difficult and expensive to isolate in live animals, and often requires post-mortem microbial cultures, pathologic examination, and/or histopathological examination.[7]

**Treatment and Management Options**

Listeriosis progresses rapidly, with death ensuing in anywhere from 24 hours to 2 weeks after the onset of clinical signs.[2,3,7] This makes rapid diagnosis and treatment paramount with high doses of antibiotics such as Oxytetracycline and Penicillin G.[2,3,7] Recommended treatment requires high doses such as 10mg/kg/day of Oxytetracycline for at least 5 days, or Penicillin G at 44,000U/kg/day for 1-2 weeks in order to be effective.[7] In addition to antibiotic therapy, supportive therapy such as fluid and electrolyte replacement for animals having difficulty eating and drinking may also be necessary.[3,7] Acidosis caused by excessive salivation may require intravenous replacement of bicarbonate ions.[7]

Treatment of Listeriosis in ruminants often proves expensive, difficult, and unsuccessful, so the best method of control is prevention and prophylaxis.[3,7] Keeping silage fresh and at a pH lower than 5.0-5.5 can minimize listerial growth, as can effective compacting and sealing of bale/ bunk silage to prevent air or mold pockets.[2,3,7] Silage control may be particularly important at peak infection times, as this is when the likelihood of feeding poor quality and older silage is more common.[7] Since *Listeria* is environmental, keeping fecal contamination from birds or other animals at a minimum can assist in reducing the environmental risk.[3,7] As goats and sheep often are less prone to sileage exposure, natural immunity to *Listeria* is likely the main source of protection for most animals exposed to L. monocytogenes.[7]

**Case Outcome and Necropsy Findings**

In spite of her treatments, Duchess continued to deteriorate, and on April 3 she was not responding to stimulation. Given her failure to respond to intensive care including broad spectrum antimicrobials, anti-inflammatory therapy, treatment with thiamine to prevent polioencephalomalacia, and nutritional support, euthanasia was recommended. She was euthanized the morning of April 3 and submitted for necropsy.

Gross necropsy provided further information about Duchess's nasal defect, with the nasal septum deviating to the right, and the left nares opening approximately twice the diameter of the right. Just caudal to the left nares on the dorsal aspect of the rostral left nasal cavity, there was an irregularly round, 1-2 cm, epithelial defect covered by a thin mat of purulent debris and fibrin. The defect communicated with the nasal cavity.

Dorsal to the esophagus and down the left side of the fascial planes was a locally extensive, 30 cm, dark red, gelatinous structure (hematoma). The thoracic cavity contained approximately 100 mLs of serosanguinous fluid. The distal half of the trachea contained a moderate amount of white foam that extended into the mainstem bronchi. The caudodorsal lung fields had few rib impressions and exuded a small amount of watery foam on cut surface. The interlobular septae were mildly expanded by edema in the cranial lung fields. The dorsal half of the lungs had an irregular, medium red to purple mottled pattern and floated when placed in formalin. The brain appeared symmetrical with appropriate gyri and sulci depths. The spinal cord was diffusely smooth, white, and shiny. No masses or debris were appreciated in the calvarium or spinal canal.

Histopathology of the brain revealed multifocal, mild hemorrhage and scant fibrin with increased populations of neutrophils, lymphocytes, and plasma cells. Perivascular edema was seen as uniform expansion of Virchow Robin's spaces throughout the cerebrum. There was multifocal,

mixed inflammatory perivascular cuffing of mostly neutrophils with lymphocytes and plasma cells, most commonly near the cerebellum and brainstem, and mild rarefaction of the white matter. The cervical to sacral spinal cord had marked and extensive, multifocal accumulations of degenerate neutrophils, large foamy macrophages, with fewer lymphocytes, plasma cells, and scant fibrin amid amorphous necrotic cellular debris. A few macrophages contained clusters of small, linear, negatively staining, partially refractile material that were suspected organisms. The cranial cervical cord was the most severely affected. There were large perivascular cuffs of degenerate neutrophils around the majority of vessels. There was diffuse and marked spongiosis of the white matter with dilated myelin sheaths, spheroid formation, and scattered digestion chambers. Inflammation frequently extended into the nerve rootlets. There were scattered hypereosinophilic, shrunken, angular neuronal cell bodies (neuronal necrosis). With Giemsa staining, a few small clusters of large, rod-shaped organisms were occasionally seen in macrophages. Aerobic culture of the brain revealed a light growth of gram positive and negative enteric and environmental organisms, but no *Listeria*. Additionally, a PCR of the spinal cord at Cornell University revealed a negative result for *Listeria*.

In one section of lungs on histopathology, the parenchyma was markedly hypercellular. The bronchi and bronchioles were filled by variable amounts of marked numbers of degenerate neutrophils, lightly eosinophilic to amphophilic fluid (protein and mucous), amorphous to stippled cellular debris, fewer foamy macrophages, and scant hemorrhage. The alveoli contained marked amounts of proteinaceous fluid, scant hemorrhage, and large numbers of foamy alveolar histiocytes. There were several random multifocal nodular aggregates of degenerate neutrophils, necrotic cellular debris, fibrin, and few macrophages (microabscesses). The interlobular septae were moderately expanded by edema, fibrin, degenerate neutrophils, and scant hemorrhage. In

other sections of lung, the alveolar interstitium contained markedly increased numbers of mature neutrophils within capillaries. Most alveolar spaces contained proteinaceous fluid with mildly increased populations of foamy histiocytes. Aerobic culture of the lung revealed Pseudomonas aeruginosa and Trueperella pyogenes.

Histopathology of the liver revealed hepatic sinusoids that were mildly congested and contained increased numbers of mature neutrophils and hemosiderophages. The portal regions had mildly increased numbers of biliary profiles, low numbers of lymphocytes and plasma cells, and the lymphatics were ectatic. There were several random multifocal nodular aggregates of degenerate neutrophils, necrotic cellular debris, fibrin, and few macrophages (microabscesses). Histopathology of the spleen showed that the splenic white pulp was mildly decreased. Lymphoid follicles frequently contained increased numbers of histiocytes. There was occasional lymphocytolysis. The red pulp was markedly hypercellular, the majority of cells being mature neutrophils. There was a low amount of dark brown granular pigment (hemosiderin). Aerobic culture of the liver and spleen revealed Pseudomonas aeruginosa. No anaerobes were isolated.

Histopathologic abnormalities of the kidneys, urinary bladder, abomasum, jejunum, mesenteric lymph nodes, cecum and colon were also visualized, but less significantly pertained to the outcome of this case. Other tests submitted were negative, but included GMS, Gram Stain, Acid Fast, and PAS special stains. Histologically normal tissues included the adrenal glands, rumen, reticulum, and omasum.

**Conclusion**

Although the organism was unable to be isolated during the CSF tap and necropsy, *Listeria monocytogenes* is still the top differential for Duchess's suppurative pleocytosis based on the localization and type of inflammation observed within the brain and cranial spinal cord. The

presence of a mononuclear predominant inflammation within the brainstem is typical of *Listeria*, as is the microabscessation that was occasionally appreciated in this case. The microabscesses in the liver and suppurative splenitis in this case were supportive of septicemia. Duchess's pneumonia was characteristic with aspiration pneumonia. This may be what she presented with prior to her central nervous system signs, as supported by radiographs, or it may be that Duchess underwent some degree of dysphagia as the nervous centers that control swallowing are located in the brainstem, or some combination thereof. However, it is possible that her pneumonia, abnormal nasal opening, and immune compromise from her previous parasite anemia contributed to her system's compromise to listeriosis. It's possible that concurrent treatment with penicillin G and Nuflor contributed to difficulties in isolating the organism, or that other organisms such as those mentioned previously were contributors instead. In the future, vaccination may be a solution for immune compromised populations or individuals to reduce significant health problems and economic losses caused by listeriosis outbreaks.[7] Unfortunately, a licensed vaccine is not yet available in the USA or UK, but some European countries have a live, attenuated vaccine and claim it is effective in sheep and goats.[7] Since *L. monocytogenes* is an intracellular pathogen, a live vaccine would be necessary to induce protective cell-mediated immunity.[7]

**References:**


1. Konradt G., Bassuino D.M., Prates K.S., Bianchi M.V., Snel G.G.M., Sonne L., Driemeier D. & Pavarini S.P. 2017. Suppurative infectious diseases of the central nervous system in domestic ruminants. Pesquisa Veterinária Brasileira 37(8):820-828. Setor de Patologia Veterinária, Departamento de Patologia Clínica Veterinária, Faculdade de Veterinária, Universidade Federal do Rio Grande do Sul, Av. Bento Gonçalves 9090, Prédio 42505, Porto Alegre, RS 91540-000, Brazil.
2. Luginbuhl, J. M. (2020, September 17). Listeriosis in your herd. NC State Extension. Retrieved November 8, 2021, from https://content.ces.ncsu.edu/listeriosis-in-your-herd#:~:text=Listeriosis%20is%20a%20common%20clinical%20problem%20in%20intensively,on%20plants%2C%20and%20in%20feed%20bunks%20and%20feed.
3. Metzger, M. (2018, November 28). Listeriosis in sheep and goats. Michigan State University Extension. Retrieved November 8, 2021, from https://www.canr.msu.edu/news/listeriosis-in-sheep-and-goats.
4. Precht C, Vermathen P, Henke D, et al. Correlative Magnetic Resonance Imaging and Histopathology in Small Ruminant Listeria Rhombencephalitis. Front Neurol. 2020;11:518697. Published 2020 Dec 14. doi:10.3389/fneur.2020.518697
5. Rogalla D, Bomar PA. Listeria Monocytogenes. [Updated 2021 Jul 10]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK534838/
6. U.S. Food and Drug Administration. (2019, March 29). Listeria (listeriosis). Listeria (Listeriosis). Retrieved November 8, 2021, from https://www.fda.gov/food/foodborne-pathogens/listeria-listeriosis.

7. Wiedmann, M. (2008). Listeria monocytogenes: Transmission and disease in ruminants. VIN ACVIM. Retrieved November 5, 2021, from https://www.vin.com/apputil/content/defaultadv1.aspx?pId=11262&catId=32572&id=3865527.