Cerebrospinal Nematodiasis in 20 Camelids

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Background: Information about the clinical and clinicopathologic aspects of cerebrospinal nematodiasis (CN) in camelids is limited.

Hypothesis: Clinical and therapeutic variables will be identified as factors predictive of survival.

Animals: Client-owned camelids suspected of having CN admitted to Purdue University between 1995 and 2015.

Methods: A retrospective study was performed. A diagnosis of CN was based on cerebrospinal fluid (CSF) eosinophilic pleocytosis or postmortem findings.

Results: Eleven alpacas and 9 llamas met the inclusion criteria. Seventy-five percent of the camelids were male (27% castrated and 73% intact). Common clinical abnormalities included proprioceptive deficits (100% of animals), recumbency (55%), tachypnea (55%), and ataxia (40%). Among the 85% of treated animals, 100% received PO fenbendazole, and 88% received a nonsteroidal anti-inflammatory drug. The survival rate to discharge was 45%. Plasma fibrinogen concentration, creatine kinase activity, and serum creatinine concentration were significantly higher in nonsurvivors. Blood eosinophil count, platelet count, and total CO_2 were significantly lower in nonsurvivors. Factors associated with survival were species, sex, absence of treatment with corticosteroids, and clinical improvement. There was no association between recumbency at admission and survival. A plasma fibrinogen concentration above >266 mg/dL was an excellent diagnostic test to predict survival in the presence of neurological signs or CSF eosinophilia.

Conclusions: Although prognosis for CN in camelids is guarded, presence of recumbency at admission is not predictive of nonsurvival. Male camelids and llamas appear more likely to die from CN. Corticosteroid treatment is contraindicated in animals diagnosed with CN.

Key words: Camelid; Eosinophil; Meningeal; Myelopathy; Neurological; Parasite.

Cerebrospinal nematodiasis (CN) is a neurologic disease of camelids (alpacas and llamas) caused by aberrant migration of the nematode *Parelaphostrongylus tenuis*, also known as the "meningeal worm."[1–4] The definitive and intermediate hosts of *P. tenuis* are the white-tailed deer (*Odocoileus virginianus*) and molluscs, respectively. Camelids become infected by ingesting infected molluscs. The third-stage larvae of *P. tenuis* migrate from the gastrointestinal tract to the spinal cord within 45–55 days.[5] Once in the spinal cord, the larvae mature and ascend, causing destructive tracts within the spinal cord. Migration of larvae occurs most frequently in the white matter of the spinal cord, but occasionally affects spinal cord gray matter and the brain.[6–8]

The geographical distribution of the disease relies on the presence of both hosts in the same location. Although the disease is mainly found in eastern North

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Abbreviations:

CBC	complete blood count
CN	cerebrospinal nematodiasis
CNS	central nervous system
CSF	cerebrospinal fluid
DEC	diethylcarbamazine
DMSO	dimethyl sulfoxide
FBZ	fenbendazole
IVM	ivermectin
NSAID	nonsteroidal anti-inflammatory drug
SBA	serum biochemical analysis

America,[9,10] it has been reported in areas of central North America as well.[3,11–13]

Clinical signs of CN typically reflect spinal cord involvement and include a wide-based hind limb stance, ataxia that often is worse in the hind limbs than in the forelimbs, and recumbency in later stages.[4,14] Most camelids with CN have normal mentation and appetite. In atypical cases of parasite migration within brain tissue, abnormal mentation, and cranial nerve dysfunction may be observed. Cervical scoliosis also has been reported in camelids with CN.[6] The onset of clinical signs may be gradual, with animals presenting ataxic or exhibiting a wide-based stance, or affected animals may be found acutely recumbent. Although there is no definitive antemortem test for CN, the majority of affected camelids have eosinophilic pleocytosis of cerebrospinal fluid (CSF).[9] Although the presence of eosinophilic pleocytosis in camelids presenting with neurologic signs does not definitively diagnose CN, the paucity of other diseases that induce CSF eosinophil production allow CSF analysis to presumptively diagnose CN in most cases. In a retrospective study, only 8% of camelids presenting with neurologic signs and

CSF eosinophilic pleocytosis were not diagnosed with CN (1 was diagnosed with *Toxoplasma gondii* and a conclusive diagnosis was not made for the other camelid).[9] A CBC and serum biochemical analysis (SBA) often are reported to be unremarkable, but the majority of available reports are from experimental infection with *P. tenuis*, describe a single case, or are anecdotal.[4,5] Definitive diagnosis of CN requires observation of nematodes within the CNS at postmortem examination, but histologic findings of migratory tracts are consistent with infection.

Currently, a standard treatment recommendation for animals with CN is lacking. Rather, a combination of medical treatments often is administered, and although most treatment programs include anthelmintics and anti-inflammatory drugs, recommendations vary among clinicians. Medications reported to be administered to affected camelids include fenbendazole (FBZ), ivermectin (IVM), diethylcarbamazine (DEC), nonsteroidal anti-inflammatory drugs (NSAIDs) such as flunixin meglumine ors meloxicam, corticosteroids such as dexamethasone, dimethyl sulfoxide (DMSO), vitamin E, and thiamine.[6,14] Although it generally is accepted that nonrecumbent animals with CN have a better prognosis for survival if they are treated as compared to recumbent animals, this is currently unproven.

Limited information about the clinical and clinicopathological aspects of CN is available, including factors that influence survival. Therefore, the objectives of this retrospective study were to describe the signalment, history, clinical signs, clinicopathologic results, CSF cytology, treatment, and outcome in camelids diagnosed with CN, and to identify variables associated with survival.

Materials and Methods

Data Collection

Medical records from camelids presented to Purdue University Veterinary Teaching Hospital over a 20-year period (June 1995–June 2015) were reviewed. Inclusion criteria included complete medical records, abnormal neurologic examination at the time of presentation, and either CSF eosinophilic pleocytosis or postmortem findings consistent with CN. Data collected included signalment, history, clinical signs, laboratory findings, CSF analysis results, treatments, duration of hospitalization, and outcome. When available, necropsy results were recorded. Survival was defined as discharge from the hospital.

Data Analysis

Animals were grouped by outcome (discharged alive or not) and compared. Statistical analysis was performed using the commercially available software, PRISM.[a] Normality was assessed by a Shapiro-Wilk test. Normally distributed data were reported as mean (±SD) and compared using an unpaired *t*-test. Nonparametric data were reported as median and range (bracketed) and were compared using a Mann-Whitney *U*-test. A receiver operating characteristic (ROC) curve was plotted to analyze the prognostic value of a given variable if a significant difference was found between survivors and nonsurvivors. Categorical data were compared using a Chi-square or a Fisher's exact test depending on the

numbers expected, and odd ratios were calculated when relevant. For all comparisons, a *P*-value <.05 was considered significant.

Results

Signalment and History

Twenty animals met the inclusion criteria. Species included 11 alpacas (55%) and 9 llamas (45%). Alpaca species was highly associated with survival ($P < .01$) and alpacas were 21 [1.8–251.4] times more likely to survive than were llamas.

Camelid ages ranged from 8 months to 16 years with a median of 4.5 years. Five (25%) were female and 15 (75%) were male. Among the males, 4 were castrated (27%). There was no significant overrepresentation by sex and the percentage of alpacas and llamas that were male was similar at 8 cases (73%) and 7 cases (78%), respectively. Female sex was highly associated with survival ($P < .01$) and females were 28 [1.3–620.4] times more likely to survive than were males. The month of presentation ranged from January to December with a peak in winter months (January, February, and March; 8 cases, 40%).

Before presentation, animals had clinical signs from 1 to 120 days, with a median of 2 days. There was no association between duration of clinical signs and outcome. Common historical complaints included recumbency (11 cases, 55%), ataxia (8 cases, 40%) and decreased mentation (4 cases, 20%). There was no association between historical complaint and outcome. Twelve animals (60%) had a history of treatment before presentation. The most common treatments administered before presentation were NSAIDs (7 cases, 58%), fenbendazole (4 cases, 33%), ivermectin (4 cases, 33%) and antibiotics (3 cases, 25%). There was no association between history of treatment and outcome.

Clinical Findings

The most common clinical signs on presentation were proprioception deficits (20 cases, 100%), recumbency (11 cases, 55%), tachypnea (respiratory rate > 30 breaths/min; 11 cases, 55%), ataxia (8 cases, 40%), cranial nerve deficits (5 cases, 25%), and cervical scoliosis (4 cases, 20%). Among the animals presented with proprioceptive deficits, 12 camelids (60%) had deficits in all 4 limbs and 8 (40%) had deficits in hind limbs only. Among the ataxic camelids, ataxia was noted in all 4 limbs in 3 animals (38%) and in the hind limbs only in 5 animals (62%). Among the camelids with cranial nerve deficits, the most common nerves affected were cranial nerves II (2 cases, 40%), VII (2 cases, 40%), and VIII (4 cases, 80%). Neither there was difference between alpacas and llamas nor association between clinical signs on presentation and outcome.

A CBC, plasma fibrinogen concentration and SBA were available in 15 cases (75%). The most common CBC abnormalities at admission were presence of band neutrophils (4 cases, 27%, 430/µL [0.12–1.26]), lymphopenia (lymphocyte count <1000/µL; 4 cases, 27%,

600/μL [310–700]), and decreased red blood cell count (red blood count $<11.3 \times 10^6/\mu$L; 4 cases, 27%, $10.4 \times 10^6/\mu$L [9.5–11.2]). There were no differences in CBC variables between species. The variables significantly different between survivors and nonsurvivors are presented in Table 1. Plasma fibrinogen concentration was significantly higher in llamas than in alpacas (422 mg/dL [268–535] versus 255 mg/dL [193–427], $P = .03$). In our study, the ROC curve showed that a plasma fibrinogen concentration >266 mg/dL (the algorithm's suggestion of optimal cutoff) was an excellent diagnostic test to predict survival in the presence of neurological signs or CSF eosinophilia with an area under the ROC curve of 0.92, yielding to a sensitivity of 100% (95% CI: 63–100) and a specificity of 83% (95% CI: 36–100; Fig 1). Using a critical value of 321 mg/dL decreased the sensitivity to 63% (95% CI: 24–91) without changing the specificity.

The most common SBA abnormalities at admission were increased aspartate aminotransferase (AST) activity (AST > 298 IU/L; 10 cases, 67%, 513 IU/L [343–2201]), decreased albumin (albumin <3 g/dL; 9 cases, 60%, 2.7 $\pm$ 0.2 g/dL), increased gamma-glutamyl transferase (GGT) activity (GGT > 46 IU/L; 9 cases, 60%, 55 $\pm$ 7 IU/L), hyperglycemia (glucose >151 mg/dL; 9 cases, 60%, 245 $\pm$ 76 mg/dL), and increased creatine kinase (CK) activity (CK > 750 IU/L; 7 cases, 47%, 1101 IU/L [802–17 865]). There were no differences in SBA variables between species. The variables significantly different between survivors and nonsurvivors at admission are presented in Table 1.

Diagnostic Tests

In all cases, lumbosacral CSF analysis was performed at admission. The most common CSF findings were eosinophilic pleocytosis (>17% eosinophils; 19 cases, 95%, 62 $\pm$ 25%), increased protein concentration (protein concentration >45 mg/dL; 18 cases, 90%, 79 mg/dL [48–1153]), increased white blood cell count (>3/μL; 18 cases, 90%, 21/μL [9–560]) and increased red blood cell count (>3/μL; 18 cases, 90%, 122/μL [4–5650]). The

Table 1. Complete blood count and serum biochemical profile data from camelids with clinical signs of cerebrospinal nematodiasis. Camelids were characterized as survivors or nonsurvivors. Data are presented as mean $\pm$ SD or median [range].[38] Only clinicopathologic variables that were significantly different ($P < .05$) are presented.

	Survivors	Nonsurvivors	P-value
Fibrinogen	253 $\pm$ 81 mg/dL	396 $\pm$ 112 mg/dL	.02
Eosinophils	920/μL [140–4540]	280/μL [0–810]	.03
Platelets	632.7 $\pm$ 70.5 $\times 10^3/\mu$L	321.0 $\pm$ 29.7 $\times 10^3/\mu$L	.01
Creatine kinase	240 [67–802] IU/L	2203 [98–17 865] IU/L	.02
Creatinine	1.3 md/dL [1.1–1.9]	2.2 mg/dL [1.3–3.5]	.02
Total CO$_2$	30 mmol/L [28.5–36]	26.5 mmol/L [26–31]	.02
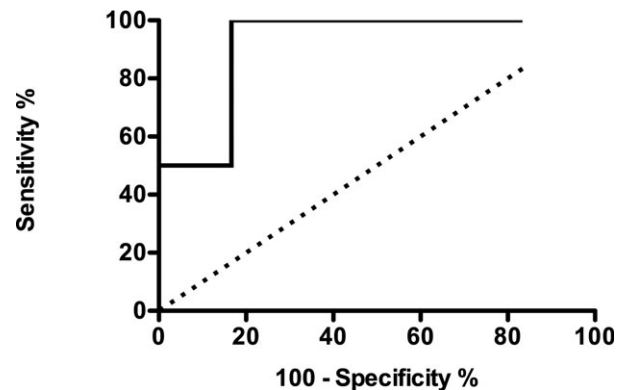
Fig 1. Receiver operating characteristic (ROC) curve for plasma fibrinogen concentration to predict survival in camelids suspected to have cerebrospinal nematodiasis. ROC analysis was performed based on 14 camelids (6 survivors and 8 nonsurvivors). Area under the curve (AUC) for plasma fibrinogen concentration is 0.92 with $P < .01$.

mean percentage of CSF eosinophils was 58 $\pm$ 28%. White blood cell count in the CSF was significantly higher in alpacas than in llamas (143 cells/μL [1–559] versus 10 [2–195]; $P = .03$). There was no association between CSF findings and outcome.

Treatment

Treatment was administered to 17 animals (85%). The most common treatments were fenbendazole (50 mg/kg PO for 5 days; 17 cases, 100%), an NSAID (flunixin meglumine at 0.5–1.1 mg/kg IV or IM, q 24 hour or a 12 hour, or meloxicam at 0.5 mg/kg PO q 24 hour; 15 cases, 88%), a corticosteroid (dexamethasone, 0.05–0.1 mg/kg IV or IM; 6 cases, 35%) and DMSO (IV; 5 cases, 29%). Other treatments included vitamin E, ivermectin, antibiotics, and thiamine (4 cases each, 24%). One camelid was placed in a sling and 1 camelid was floated in a flotation tank (6% each), both of which failed to survive. Administration of a corticosteroid was highly associated with failure to survive ($P < .01$) and animals that received a corticosteroid were 49 [2–1208] times less likely to survive. Treatment with DMSO was not associated with increased survival ($P = 1$).

Clinical improvement assessed by the attending clinician during hospitalization was highly associated with survival ($P < .01$) but 2 animals that showed clinical improvement failed to survive whereas 1 animal that did not show clinical improvement survived. Overall, animals that showed signs of improvement during hospitalization were 36 [2.7–476.6] times more likely to survive.

Outcome

Nine camelids (45%) survived to discharge: 1 animal (11%) was discharged with no neurological signs, 7 (78%) were discharged with ataxia but not requiring assistance to stand, and 1 (11%) was discharged with ataxia and required assistance to stand. The median

duration of hospitalization was 5 days [0–17]. There was no association between hospitalization duration and outcome.

Eleven camelids (55%) did not survive to discharge, 7 of which had postmortem examinations performed. All postmortem examinations were consistent with larval migrans. In some cases, cylindrical nematode larvae were identified within spinal cord or cerebral malacic linear tracts, whereas others had hemorrhage or hemosiderosis within the CNS. Three of the 4 animals with cervical scoliosis were examined postmortem; gross lesions were not detected in the cervical spinal cord in these animals, but white matter degeneration was observed microscopically in all 3 of them.

Discussion

The presence of recumbency at admission did not influence the likelihood of survival. A review of neurologic diseases in camelids states that recumbent camelids diagnosed with CN typically have a poorer prognosis, but our findings were inconsistent with this observation.[14] Although a larger sample size might have identified a higher mortality rate in recumbent animals, our results suggest that the decision to treat should not be based on the presence or absence of recumbency. The best predictors of a positive outcome were lower plasma fibrinogen concentration, absence of corticosteroid treatment, and clinical improvement during hospitalization. Although CN has a guarded prognosis, alpacas, and females are more likely to survive than llamas and males.

Acquired cervical scoliosis has been described as an unusual manifestation of P. tenuis infection in camelids, but was present on admission in 20% of camelids in our study.[6,14] Cervical scoliosis has been described in a llama that was experimentally infected with P. tenuis,[15] and in an alpaca diagnosed with P. tenuis on postmortem examination.[6] In both cases, lateral curvature of the cervical spinal column was observed on gross examination, and microscopic examination disclosed degenerative changes in the white matter of the cervical spinal cord, including Wallerian degeneration with inflammatory cell infiltrates and fibrosis.[6,15] These findings are consistent with necropsy results from the 3 camelids with scoliosis that did not survive in this study. Dorsal gray column myelitis in the cervical spinal cord was described in 6 horses with acquired cervical scoliosis, 1 of which was diagnosed with aberrant parasite migration based on postmortem examination.[16] The proposed mechanism of cervical scoliosis is lateral deviation of the spinal column due to weakened cervical muscles on the convex (affected) side.[6]

Cranial nerve deficits were found in 25% of our sample population. The most common deficits involved cranial nerves II, VII, and VIII. In a previous study, only 8% of the population presented with cranial nerve deficits, and the affected nerve(s) was not identified.[9] Eighty percent of the camelids in our present study that presented with cranial nerve deficits failed to survive. Postmortem lesions, however, were not identified in cranial nerve nuclei.

Plasma fibrinogen concentration was found to be useful in predicting survival in camelids diagnosed with CN. Although increased plasma fibrinogen concentration is nonspecific and can occur with various inflammatory diseases, a concentration > 266 mg/dL was found to be highly sensitive and specific in predicting nonsurvival in animals clinically diagnosed with CN. Although quite low, the critical concentration (provided by the algorithm) only shows that, in our study, all survivors had plasma fibrinogen concentrations <266 mg/dL, not that all animals with a plasma fibrinogen concentration >266 mg/dL failed to survive. Thus, plasma fibrinogen concentration should be measured in animals suspected of having CN and interpreted carefully. Interestingly, llamas presented with higher plasma fibrinogen concentrations than did alpacas. The reason for this difference could be the lower survival rate of llamas compared to alpacas. Unfortunately, because of the low number of surviving llamas, no adjustment could be made to identify the confounding effect.

A critical herd management question is whether to recommend routine prophylactic treatment with IVM to decrease the infection rate of P. tenuis. Without knowing how many animals received the treatment and did not develop the disease, we can only state that 4 animals presenting with CN in our study were routinely treated with IVM (and had been treated within 1 month of presentation); 2 of these animals survived and 2 died. These limited data raise the question of whether routine administration of IVM should be recommended, considering the increased anthelmintic resistance of gastrointestinal parasites.[17,18] A case–control study would be required to address this question.

Camelids in our study that were treated with a corticosteroid were less likely to survive. The use of corticosteroids to treat neurologic diseases is controversial. In human medicine, several studies have failed to show a beneficial or a deleterious effect of corticosteroids in patients with infectious or traumatic meningitis, or both,[19,20] suggesting the presence of confounding factors. For example, the use of corticosteroids is recommended for treatment of Haemophilus influenza meningitis in children, but evidence for beneficial or deleterious effects in adults for tuberculous meningitis is lacking.[19] It is possible that, in our study, corticosteroids were administered to animals that were clinically deteriorating, because corticosteroids often are administered as a last resort. Of the 6 animals that received corticosteroids in the hospital, 4 presented with a clinical sign associated with the brain (decreased mentation or cranial nerve dysfunction), and 4 presented with recumbency. These signs might have prompted the attending clinician to administer corticosteroids. Alternatively, corticosteroids might have had a deleterious metabolic effect on the presumably stressed animals, leading to nonsurvival. Therefore, our study is supportive but not conclusive that adjunctive corticosteroid treatment is deleterious in camelids with CN, and a larger sample size is required to draw definitive conclusions regarding corticosteroid administration in sick camelids.

Intact males were more commonly affected in this study and were more likely to die from CN than were females. Sexually intact, mature males of many mammalian species generally are more susceptible to infection with parasites, particularly nematodes, and carry higher parasite burdens compared to females.[21,22] Testosterone has been implicated as a cause for this phenomenon. One study found that parasite load with the nematode *Nippostrongylus brasiliensis* in rats was higher in intact males compared to females, a difference that disappeared after castration.[23] Similar results have been reported in rodents experimentally infected with several different parasites.[24–27] There is evidence that testosterone directly affects parasite growth and development,[24,28,29] and that testosterone indirectly affects parasite establishment in the host by influencing the immune system.[30,31] In general, testosterone has been shown to decrease components of the humoral and adaptive immune responses, and up-regulate a Th2 immune response, all of which might contribute to susceptibility to parasite infection.[32–34] In contrast, estrogen is associated with enhancement of a Th1 immune response, which contributes to resistance to parasite infection.[35–37]

Despite a similar incidence of CN between alpacas and llamas, the mortality rate was significantly higher in llamas. This result remained unchanged despite statistical adjustment for body weight and sex, suggesting a true species difference. Experimental intragastric infection of 6 adult llamas with only 5 third-stage *P. tenuis* larvae resulted in fatal infection in 4 llamas, suggesting that llamas are highly susceptible to infection.[5] In another study investigating *Eimeria macusaniensis* infection in llamas and alpacas, llamas were more likely to die or be found dead than alpacas.[38] These studies suggest that llamas might be more susceptible to deleterious effects of parasites but studies directly comparing llama and alpaca susceptibility to *P. tenuis* infection are lacking. Another possible explanation for the poorer outcome in llamas compared to alpacas could be related to shifts in demographics and monetary valuation of camelids over the 20-year study period. The increasing popularity of alpacas over the study time period may have influenced demographics and case representation, and might have led to decreased monetary valuation of llamas. The effects of changing animal demographics on the study population were not evaluated because of the small sample size and retrospective nature of the study.

In conclusion, no specific clinical finding was associated with survival. Although the prognosis is guarded, presentation of a recumbent animal should not preclude treatment. In addition, plasma fibrinogen concentration should be measured in animals suspected of having CN.

Footnote

References

1. Baum KH. Neurologic diseases of llamas. Vet Clin North Am Food Anim Pract 1994;10:383–390.

2. Baumgartner W, Zajac A, Hull BL, et al. Parelaphostrongylosis in llamas. J Am Vet Med Assoc 1985;187:1243–1245.

3. Brown TT, Jordan HE, Demorest CN. Cerebrospinal parelaphostronglylosis in llamas. J Wildl Dis 1978;14:441–444.

4. Krogdahl DW, Thilsted JP, Olsen SK. Ataxia and hypermetria caused by *Parelaphostrongylus tenuis* infection in llamas. J Am Vet Med Assoc 1987;190:191–193.

5. Rickard LG, Smith BB, Gentz EJ, et al. Experimentally-induced meningeal worm (*Parelaphostrongylus tenuis*) infection in the llama (*Lama-Glama*) - clinical-evaluation and implications for parasite translocation. J Zoo Wildlife Med 1994;25:390–402.

6. Johnson AL, Lamm CG, Divers TJ. Acquired cervical scoliosis attributed to *Parelaphostrongylus tenuis* infection in an alpaca. J Am Vet Med Assoc 2006;229:562–565.

7. Mitchell KJ, Peters-Kennedy J, Stokol T, et al. Diagnosis of *Parelaphostrongylus spp.* infection as a cause of meningomyelitis in calves. J Vet Diagn Invest 2011;23:1097–1103.

8. Tanabe M, Kelly R, de Lahunta A, et al. Verminous encephalitis in a horse produced by nematodes in the family protostrongylidae. Vet Pathol 2007;44:119–122.

9. Pinn TL, Bender HS, Stokol T, et al. Cerebrospinal fluid eosinophilia is a sensitive and specific test for the diagnosis of *Parelaphostrongylus tenuis* in camelids in the northeastern United States. J Vet Diagn Invest 2013;25:54–60.

10. Purdy SR, Gagliardo LF, Lefman S, et al. Analysis of heavy-chain antibody responses and resistance to *Parelaphostrongylus tenuis* in experimentally infected alpacas. Clin Vaccine Immunol 2012;19:1019–1026.

11. Dobey CL, Grunenwald C, Newman SJ, et al. Retrospective study of central nervous system lesions and association with Parelaphostrongylus species by histology and specific nested polymerase chain reaction in domestic camelids and wild ungulates. J Vet Diagn Invest 2014;26:748–754.

12. Wasel SM, Samuel WM, Crichton V. Distribution and ecology of meningeal worm, *Parelaphostrongylus tenuis* (Nematoda), in northcentral North America. J Wildl Dis 2003;39:338–346.

13. Comer JA, Davidson WR, Prestwood AK, et al. An update on the distribution of *Parelaphostrongylus tenuis* in the southeastern United States. J Wildl Dis 1991;27:348–354.

14. Whitehead CE, Bedenice D. Neurologic diseases in llamas and alpacas. Vet Clin North Am Food Anim Pract 2009;25:385–405.

15. Foreyt WJ, Rickard LG, Dowling S, et al. Experimental infections of 2 llamas with the meningeal worm (*Parelaphostrongylus tenuis*). J Zoo Wildlife Med 1991;22:339–344.

16. Van Biervliet J, de Lahunta A, Ennulat D, et al. Acquired cervical scoliosis in six horses associated with dorsal grey column chronic myelitis. Equine Vet J 2004;36:86–92.

17. Jabbar A, Campbell AJ, Charles JA, et al. First report of anthelmintic resistance in *Haemonchus contortus* in alpacas in Australia. Parasit Vectors 2013;6:243.

18. Gillespie RA, Williamson LH, Terrill TH, et al. Efficacy of anthelmintics on South American camelid (llama and alpaca) farms in Georgia. Vet Parasitol 2010;172:168–171.

19. Coyle PK. Glucocorticoids in central nervous system bacterial infection. Arch Neurol 1999;56:796–801.

20. Hirohata S, Kikuchi H, Sawada T, et al. Retrospective analysis of long-term outcome of chronic progressive neurological manifestations in Behcet's disease. J Neurol Sci 2015;349:143–148.

21. Zuk M, McKean KA. Sex differences in parasite infections: patterns and processes. Int J Parasitol 1996;26:1009–1023.

22. Klein SL. Hormonal and immunological mechanisms mediating sex differences in parasite infection. Parasite Immunol 2004;26:247–264.

23. Tiuria R, Horii Y, Tateyama S, et al. The Indian soft-furred rat, *Millardia meltada*, a new host for *Nippostrongylus brasiliensis*, showing androgen-dependent sex difference in intestinal mucosal defence. Int J Parasitol 1994;24:1055–1057.

24. Harder A, Wunderlich F, Marinovski P. Effects of testosterone on *Heterakis spumosa* infections in mice. Parasitology 1992;105(Pt 2):335–342.

25. Beck JW. Effect of Gonadectomy and gonadal hormones on singly established *Hymenolepis diminuta* in rats. Exp Parasitol 1952;1:109–117.

26. Solomon GB. Development of *Nippostrongylus brasiliensis* in gonadectomized and hormone-treated hamsters. Exp Parasitol 1966;18:374–396.

27. Mock BA, Nacy CA. Hormonal modulation of sex differences in resistance to *Leishmania major* systemic infections. Infect Immun 1988;56:3316–3319.

28. Drutz DJ, Huppert M, Sun SH, et al. Human sex hormones stimulate the growth and maturation of *Coccidioides immitis*. Infect Immun 1981;32:897–907.

29. Elmofty MM, Smyth JD. Endocrine control of encystation in *Opalina ranarum* parasitic in *Rana temporaria*. Exp Parasitol 1964;15:185–199.

30. Daniels CW, Belosevic M. Serum antibody responses by male and female C57Bl/6 mice infected with *Giardia muris*. Clin Exp Immunol 1994;97:424–429.

31. Eidinger D, Garrett TJ. Studies of the regulatory effects of the sex hormones on antibody formation and stem cell differentiation. J Exp Med 1972;136:1098–1116.

32. Grossman CJ. Interactions between the gonadal steroids and the immune system. Science 1985;227:257–261.

33. Grossman C. Possible underlying mechanisms of sexual dimorphism in the immune response, fact and hypothesis. J Steroid Biochem 1989;34:241–251.

34. Lynch NR, Yarzabal L, Verde O, et al. Delayed-type hypersensitivity and immunoglobulin E in American cutaneous leishmaniasis. Infect Immun 1982;38:877–881.

35. Alexander J. Sex differences and cross-immunity in DBA/2 mice infected with *L. mexicana* and *L. major*. Parasitology 1988;96 (Pt 2):297–302.

36. Satoskar A, Al-Quassi HH, Alexander J. Sex-determined resistance against *Leishmania mexicana* is associated with the preferential induction of a Th1-like response and IFN-gamma production by female but not male DBA/2 mice. Immunol Cell Biol 1998;76:159–166.

37. Satoskar A, Alexander J. Sex-determined susceptibility and differential IFN-gamma and TNF-alpha mRNA expression in DBA/2 mice infected with *Leishmania mexicana*. Immunology 1995;84:1–4.

38. Cebra CK, Valentine BA, Schlipf JW, et al. *Eimeria macusaniensis* infection in 15 llamas and 34 alpacas. J Am Vet Med Assoc 2007;230:94–100.