
Balazs Toth, DVM, MS; Monica Aleman, MVZ, PhD, DACVM; Nora Nogradi, DVM, DACVIM; John E. Madigan, DVM, MS, DACVM

Objective—To describe clinical and clinicopathologic findings and outcome of horses with meningitis and meningoencephalomyelitis.

Design—Retrospective case series.

Animals—28 horses.

Procedures—Medical records of horses admitted to the hospital during a 25-year period were reviewed. Horses with a definitive diagnosis of meningitis or meningoencephalomyelitis were included in this study. Information extracted from the medical records included signalment, history, reason for admission, clinical signs, results of clinicopathologic testing and diagnostic procedures, treatment, outcome, and necropsy findings.

Results—22 horses had confirmed infectious disease (19 bacterial, 2 parasitic, and 1 fungal), 4 had suspected infectious disease on the basis of CSF cytologic examination findings, and 2 had noninfectious meningitis or meningoencephalomyelitis. Trauma of the head and vertebral column with disruption of the blood-brain barrier and local ascending or hematogenous spread were the most common routes of infection. Common neurologic signs included abnormal mental status, cranial nerve deficits, vestibular dysfunction, ataxia, tetraparesis, and apparent neck pain. Common hematologic abnormalities included leukocytosis, neutrophilia, lymphopenia, and hyperfibrinogenemia. Cytologic examination of CSF samples revealed moderate to marked suppurative inflammation. Mortality rate was 96.4%. Microbial culture of CSF yielded bacterial growth in 15 of 23 horses (before death [2 horses], after death [11], and both [2]).

Conclusions and Clinical Relevance—Results suggested that meningitis and meningoencephalomyelitis are uncommon disorders in horses. Infectious disease was more common than noninfectious disease. Local trauma, ascending infection, or hematogenous spread of infection were the most common causes of meningitis or meningoencephalomyelitis. Neurologic deficits, neutrophilia, lymphopenia, hyperfibrinogenemia, and CSF with neutrophilic pleocytosis were common findings in affected horses. (J Am Vet Med Assoc 2012;240:580–587)

Meningitis, defined as inflammation of the meninges, and meningoencephalomyelitis, defined as inflammation of the meninges, brain, and spinal cord, may be caused by infectious and noninfectious processes. Meningitis in horses is typically caused by infectious agents. Microbial invasion of the CNS most commonly occurs directly via traumatic injury or an ascending infection, hematogenously, or via iatrogenic routes. Ascending infections can originate from the ocular structures, oral cavity, nasal passages, and sinuses and osteomyelitis of cranial bones or vertebrae. Hematogenous spread could originate from colonization via the mucous membranes or from distant septic foci that reached access to the systemic circulation. Meningeal inflammation is exacerbated by bacterial cell wall components and characterized by production of prostaglandins, leukotrienes, cytokines, and attraction of leukocytes. Meningeal inflammation may lead to increased BBB permeability, vasculitis, CNS edema, and secondary inflammation of tissues adjacent to the meninges. Proliferating bacteria in the subarachnoid space may penetrate through the pores of the arachnoid villi, reaching the venous sinuses and entering the systemic circulation, resulting in bacteremia. Studies in people have shown that both congenital and acquired immunodeficiencies play an important role in the etiology of meningitis. Common variable immunodeficiency has been recently implicated in the development of meningitis in adult horses. Bacterial meningitis and meningoencephalomyelitis are uncommon conditions of mature horses. Bacterial meningitis or meningoencephalomyelitis can spread rapidly, causing irreversible neural tissue damage, and is usually considered to be a highly fatal disease in many species. Horses are particularly prone to deteriorate because of their size as nursing care is challenging and can be hazardous if neurologic deficits progress to recumbency. The prognosis has been reported to be poor to grave in horses with infectious meningitis, despite treatment.
Survival rates of 60% and 0% were documented in a case series of 5 and 7 horses, respectively, with bacterial meningitis. However, there are a few clinical reports of successful outcome in horses with bacterial or fungal meningitis.

Presently, there are no comprehensive studies in a large population of horses with meningitis or meningoencephalomyelitis. The low number of reported instances of these diseases in horses has not provided information on the most common physical, neurologic, and clinicopathologic alterations and pathogens causing meningitis or meningoencephalomyelitis in horses. Further, these diseases appear to be rare disorders in horses, resulting in nonspecific clinical signs that may be easily missed or misinterpreted, delaying the recognition and treatment of disease. Therefore, the purpose of the study reported here was to describe the history, clinical signs, clinicopathologic and postmortem findings, causative agents, treatment, and outcome in a large population of horses with meningitis and meningoencephalomyelitis (infectious and noninfectious).

Materials and Methods

Horses with a definitive diagnosis of meningitis or meningoencephalomyelitis based on findings on cytologic examination of CSF or postmortem macroscopic and histologic findings were included in the study. The electronic medical database of the William R. Pritchard Veterinary Medical Teaching Hospital was searched from the years 1985 to 2010 by use of the words meningitis, meningoencephalitis, and meningoencephalomyelitis under the clinical, laboratory, and pathological diagnosis fields. Medical records were reviewed, and data extracted included signalment, history, reason for admission, clinical signs, clinicopathologic testing, diagnostic procedures, treatment, outcome, and necropsy findings. Descriptive statistical analysis of data was performed with a commercially available statistical software program.

Results

Horses—Twenty-eight horses met the inclusion criteria. Twenty-two of 28 horses had confirmed infectious meningitis or meningoencephalomyelitis. Of the 22 horses with infection, 19 horses had bacterial infections (15 had bacteria isolated from a CSF sample or tissue specimen, 3 had bacteria identified on cytologic examination of a CSF sample, and 1 had bacteria detected in a CSF sample by use of a PCR assay), 1 horse had fungus identified on cytologic examination of a CSF sample, and 2 horses had parasites identified on histologic examination of tissue specimens. Four of 28 horses had suspected bacterial meningitis because of findings on cytologic examination of CSF samples of neutrophilic pleocytosis with degenerate neutrophils. Two horses had noninfectious meningitis: one horse had noninfectious meningitis related to myelography, and the other had chronic granulomatous meningitis of undetermined cause.

Signalment and history—Breed distribution for 28 horses was as follows: 9 (32.1%) Thoroughbreds, 7 (25.0%) Quarter Horses, 6 (21.4%) Arabsians, 2 (7.1%) Paint Horses, 2 (7.1%) mixed, 1 (3.6%) Morgan, and 1 (3.6%) American Miniature Pinto. Twenty-two horses were > 1 year of age (median, 5 years; range 1 to 21 years), 4 foals were weanlings (4 to 7 months old), and 2 were neonatal foals (2 and 20 days old). Twelve (42.9%) horses were sexually intact males; 10 (35.7%) were females, and 6 (21.4%) were geldings.

Nine of 28 (32.1%) horses had a previous history of head or neck trauma (5 days to 2 weeks before hospital admission). One horse with a history of head trauma also had a draining nonhealing wound in the ventral aspect of the mandible for 1.5 months. Eight of 28 (28.6%) horses had a long-standing (1-week to 2-month) neurologic problem of unknown etiology. The remaining horses had acute colic episodes (2 [7.1%] horses), chronic nasal discharge (2 [7.1%]; duration of 2 months in one horse and unknown duration in the other horse), and chronic weight loss for several weeks (2 [7.1%]), and 1 (3.6%) horse each had the following: a 1-month history of Streptococcus equi subsp. equi infection of the upper respiratory tract, Corynebacterium pseudotuberculosis infection in the nasal cavity and nasomaxillary sinuses, and pyogranulomatous celulitis of the prepuce. One horse that received an IM injection in the neck developed stiffness 4 to 5 days later and was admitted to the hospital 2 weeks following the initial signs.

Both neonatal foals had septicemia, and 1 was a premature foal with failure of passive transfer. The other foal was originally seen at 2 days of age for failure of passive transfer, discharged from the hospital, and readmitted for lethargy and neurologic signs at 20 days of age. The foal developed septic thrombophlebitis at the previous catheter site. Both foals developed septic polyarthritis, thrombosis at multiple sites, and multiorgan failure.

Physical examination—At the time of hospital admission, 9 of 26 (34.6%) horses had tachycardia and 7 (26.9%) had tachypnea (Table 1); neonatal foals were excluded from these values because of physiologically higher resting heart and respiratory rates, compared with those of older horses. Four of 28 (14.3%) horses had fever, and 1 (3.6%) had hypothermia. One of these horses was a neonatal foal with a rectal temperature of 39.2°C (102.6°F).

Neurologic examination—Mentation was normal in 8 of 28 (28.3%) horses. Obtundation and stupor were seen in 18 (64.3%) and 2 (7.1%) of the horses, respectively. Two (7.1%) horses had seizures and 2 were apparently blind (ie, running into objects and lack of a menace response) at the time of hospital admission. Nineteen of 28 (67.9%) horses were ambulatory, and 9 (32.1%) were recumbent. Symmetric ataxia and tetraparesis were seen in 17 of 28 (60.7%) horses, with a mean grade of ataxia of 3 of 5, according to a published grading scale. Other gait abnormalities included hypermetria in 4 of 28 (14.3%) horses. Extensor rigidity of the thoracic limbs was found in 1 (3.6%) horse, and 1 (3.6%) horse was reluctant to move. Cranial nerve deficits were found in 20 of 28 (71.4%) horses. Head tilt, nystagmus, and strabismus were observed.
Cerebrospinal fluid samples were collected from a horse with meningoencephalomyelitis and IgA measurements had been performed on a blood sample from this horse. Total lymphocyte count, including T- and B- cell populations, lymphocyte stimulation testing, and immunoelectrophoresis for IgG, IgM, and IgA measurements, had been performed on a blood sample from a horse with meningoencephalomyelitis. Blood samples were also collected from 3 horses before death and for 13 horses after death, with cultures and biochemical analyses performed. Microbiological culture of CSF from 23 horses yielded bacterial growth before death and for 13 horses after death, with results of microbiological culture of CSF from 23 horses, bacteria were observed in CSF of 8 horses and fungi were observed in CSF of 1 horse. On the basis of cytologic examination of CSF (1/19), two horses had CSF with a normal macroscopic appearance and 19 (82.6%) had CSF with an abnormal macroscopic appearance. Abnormalities included hypoalbuminemia (8/20 [40%] horses) and hyperglobulinemia (2/20 [10%]).

**CSF analysis**—Cerebrospinal fluid samples were collected from 23 horses. Bacteria were observed in CSF of 8 horses and fungi were observed in CSF of 1 horse. Microbiological culture of CSF from 23 horses yielded bacterial growth for 4 horses before death and for 13 horses after death. The reference range for WBC count (cells/µL) was 4/25 (16%) horses, including a weanling colt. Neutrophilia (15/24 [62.5%]), neutropenia (3/24 [12.5%]), lymphopenia (13/24 [54.2%]), and hyperfibrinogenemia (12/24 [50%]). Total lymphocyte count, including T- and B- cell populations, lymphocyte stimulation testing, and immunoelectrophoresis for IgG, IgM, and IgA measurements, had been performed on a blood sample from a horse with meningoencephalomyelitis caused by a Halicephalobus gingivalis infection; findings in this affected horse were comparable to those of an unaffected (control) horse. Serum biochemical abnormalities included hypoalbuminemia (8/20 [40%] horses) and hyperglobulinemia (2/20 [10%]).

**Hematologic and serum biochemical findings**—Hematologic abnormalities (Table 1) included hemocytocentrifugation (4/25 [16%] horses), anemia (4/25 [16%]), leukocytosis (12/25 [48%]), leukopenia (2/25 [8%]), neutrophilia (15/24 [62.5%]), neutropenia (3/24 [12.5%]), lymphopenia (13/24 [54.2%]), and hyperfibrinogenemia (12/24 [50%]). Total lymphocyte count, including T- and B- cell populations, lymphocyte stimulation testing, and immunoelectrophoresis for IgG, IgM, and IgA measurements, had been performed on a blood sample from a horse with meningoencephalomyelitis caused by a Halicephalobus gingivalis infection; findings in this affected horse were comparable to those of an unaffected (control) horse. Serum biochemical abnormalities included hypoalbuminemia (8/20 [40%] horses) and hyperglobulinemia (2/20 [10%]).

**Physical and clinicopathologic findings in 28 horses with meningitis or meningoencephalomyelitis.**

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. of horses</th>
<th>Mean ± SD</th>
<th>Median (range)</th>
<th>Reference range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart rate (beats/min)*</td>
<td>26</td>
<td>56.9 ± 17</td>
<td>60 (32–96)</td>
<td>28–40</td>
</tr>
<tr>
<td>Respiratory rate (breaths/min)*</td>
<td>26</td>
<td>24.8 ± 10.8</td>
<td>20 (16–48)</td>
<td>8–16</td>
</tr>
<tr>
<td>Rectal temperature (°C)*</td>
<td>26</td>
<td>38.2 ± 0.8</td>
<td>37.9 (33.3–41.1)</td>
<td>37.5–38.2</td>
</tr>
<tr>
<td>Hematologic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCV (%)</td>
<td>25</td>
<td>37.1 ± 9.14</td>
<td>35 (25.9–69)</td>
<td>30–46</td>
</tr>
<tr>
<td>WBC count (cells/µL)</td>
<td>25</td>
<td>14,118 ± 7,842</td>
<td>11,600 (2,000–33,200)</td>
<td>5,000–11,600</td>
</tr>
<tr>
<td>Neutrophil count (cells/µL)</td>
<td>24</td>
<td>11,014 ± 7,328</td>
<td>8,170 (900–25,900)</td>
<td>2,600–6,800</td>
</tr>
<tr>
<td>Lymphocyte count (cells/µL)</td>
<td>24</td>
<td>1,705 ± 1,205</td>
<td>1,500 (171–5,000)</td>
<td>1,600–5,800</td>
</tr>
<tr>
<td>Fibrinogen (mg/dL)</td>
<td>24</td>
<td>541.7 ± 244.8</td>
<td>660 (200–1,100)</td>
<td>100–400</td>
</tr>
<tr>
<td>Serum biochemical</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>20</td>
<td>2.9 ± 0.6</td>
<td>2.9 (2.1–4.1)</td>
<td>2.7–4.2</td>
</tr>
<tr>
<td>Globulin (g/dL)</td>
<td>20</td>
<td>3.9 ± 1.1</td>
<td>3.8 (2.4–6.2)</td>
<td>1.6–5.0</td>
</tr>
<tr>
<td>CSF cytologic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total nucleated cell count (cells/µL)</td>
<td>23</td>
<td>20,991 ± 1,224</td>
<td>1,224 (0–240,000)</td>
<td>≤ 5</td>
</tr>
<tr>
<td>RBC count (cells/µL)</td>
<td>23</td>
<td>27,959 ± 65,380</td>
<td>280 (0–245,000)</td>
<td>0</td>
</tr>
<tr>
<td>Total protein (mg/dL)</td>
<td>23</td>
<td>691 ± 1,177</td>
<td>282 (45–3,900)</td>
<td>≤ 7.0</td>
</tr>
<tr>
<td>Neutrophils (%)</td>
<td>23</td>
<td>74.1 ± 30.2</td>
<td>87 (0–98)</td>
<td>0</td>
</tr>
<tr>
<td>Small mononuclear cells (%)</td>
<td>23</td>
<td>14.8 ± 22.5</td>
<td>7 (0–83)</td>
<td>50–70</td>
</tr>
<tr>
<td>Large mononuclear cells (%)</td>
<td>23</td>
<td>5.9 ± 6.9</td>
<td>3 (0–24)</td>
<td>10–30</td>
</tr>
<tr>
<td>Eosinophils (%)</td>
<td>23</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Organisms†</td>
<td>23</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>CSF biochemical</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Creatine kinase (U/L)</td>
<td>9</td>
<td>26.2 ± 38.4</td>
<td>5 (0–102)</td>
<td>0–8</td>
</tr>
<tr>
<td>Glucose (mg/dL)</td>
<td>6</td>
<td>41.1 ± 14.6</td>
<td>30 (11–82)</td>
<td>40–70</td>
</tr>
<tr>
<td>pH</td>
<td>1</td>
<td>7.296</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>l-lactate (mmol/L)</td>
<td>1</td>
<td>13</td>
<td>NA</td>
<td>≤ 2</td>
</tr>
<tr>
<td>l-lactate (µmol/L)</td>
<td>1</td>
<td>300</td>
<td>NA</td>
<td>0</td>
</tr>
<tr>
<td>CSF bacterial culture</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before death‡</td>
<td>23</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>After death‡</td>
<td>23</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

*Data from 2 neonatal foals were excluded from these values because of physiologically higher resting heart rate, respiratory rate, and rectal temperature, compared with older horses. †On cytologic examination of CSF from 23 horses, bacteria were observed in CSF of 8 horses and fungi were observed in CSF of 1 horse. ‡Microbiological culture of CSF from 23 horses yielded bacterial growth for 4 horses before death and for 13 horses after death. NA = Not applicable.
to marked suppurative inflammation as indicated by neutrophilic pleocytosis in 20 of 22 (91%) horses; 13 of these 20 (69%) horses had degenerate neutrophils on cytologic examination of CSF. Intracellular and extracellular bacteria were seen in 8 of 22 (36.4%) CSF samples. Encapsulated yeasts compatible with Crypto-
coccus neoformans were observed in a CSF sample from 1 horse. Biochemical analysis of CSF was performed in a limited number of horses. Electrolyte and lactate concentrations and pH were measured in a CSF sample from 1 horse and supported local lactic acidosis. Cerebrospinal fluid glucose concentration in this horse was 11 mg/dL, and extracellular cocci and coccobacilli were evident on CSF cytologic examination.

Antemortem microbial culture of CSF yielded the following organisms in 4 of 23 (17.4%) horses: Escherichia coli (1 horse; organism susceptible to multiple antimicrobials), Capnocytophaga canimorsus (1 horse; antimicrobial susceptibility report not available), C pseudotuberculosis (1 horse; organism susceptible to multiple antimicrobials), and Fusobacterium sp and Bacteroides sp (1 horse; antimicrobial susceptibility results not available). Antemortem PCR assay of a CSF sample from a weanling with recent S equi subsp equi infection identified DNA of this organism.

Diagnostic imaging—Radiographic images of the skull (15 horses), cervical vertebral column (2), and thorax (1) were available for review. Skull radiographs revealed abnormalities in 12 horses. Fracture of the cranium was found in 8 horses (cribriform plate [3 horses], basisphenoid bone [1], sphenopalatine bone [1], multiple fractures of the cranium [2], and tooth root abscess of second premolar and mandibular fistula with severe osteomyelitis [1]). Pneumocephalus was evident in 1 horse with multiple fractures of the cranial vault. Radiographic alterations consistent with sinusitis were observed for 4 horses (ventral and dorsal conchal, frontal, and maxillary sinuses), and blood within multiple sinuses was observed for 1 horse with multiple fractures. Two of the horses with severe frontal sinusitis had pathological fractures of the cribriform plate. Two of the horses with maxillary sinusitis also had tooth abscesses. Cervical vertebral column radiographs revealed atlanto-occipital subluxation in 2 horses, and thoracic radiographs revealed pleuropneumonia in 1 horse.

Computed tomographic images of the skull were available for 3 horses. Computed tomography revealed cerebellar coning at the foramen magnum (1 horse), fracture of the cribriform plate and pneumocephalus (1), and right-sided otitis media and interna with remodeling and suspected osteomyelitis of the temporal bone (1). Magnetic resonance imaging was performed immediately after euthanasia in 1 horse. Sagittal and transverse T1-, T2-, proton density-, and fluid-attenuated inversion recovery–weighted images were obtained and revealed submeningeal hyperintensity in the cerebrum, brainstem, and cerebellum on T2-weighted and fluid-attenuated inversion recovery sequences. On sagittal images, there was coning of the caudal aspect of the cerebellum with protrusion of the cerebellum through the foramen magnum. These findings were compatible with a diagnosis of cerebellar herniation. Severe meningeal and submeningeal edema was compatible with meningitis.

Management and outcome—Treatment was initiated in 17 of 28 (60.7%) horses. Nine horses were hospitalized for > 24 hours (median, 6 days; range, 3 to 15 days). The remaining horses were hospitalized for < 24 hours when either the horses died or were euthanized because of severity of disease. Medical management consisted of IV administration of polyionic fluids, broad-spectrum antimicrobials, anti-inflammatory drugs (most horses received NSAIDs, and 5 horses received a single dose of dexamethasone), sedatives, gastrointestinal tract protectants, and nursing care. A variety of antimicrobials at high doses were administered and included ampicillin, potassium penicillin, aminoglycosides, trimethoprim sulamethoxazole, third-generation cephalosporins, chloramphenicol, rifampin, and metronidazole. The mortality rate was 96.4% (27/28 horses). Seven horses died, and 20 were euthanized. The survivor horse had meningitis caused by C pseudotuberculosis infection and was treated long term with chloramphenicol.

Postmortem findings—Examination of the CNS was performed in 24 horses and revealed moderate to severe, diffuse, suppurative meningitis or meningoencephalomyelitis in 22 horses. Of the 2 horses that had normal findings on antemortem cytologic examination of CSF without bacterial growth, one had evidence of chronic multifocal inflammation of the meninges of undetermined cause and the other had diffuse subacute moderate meningitis that was suspected to be associated with a myelogram performed 2 days prior to euthanasia. Two horses with meningoencephalomyelitis had H gingivalis infection with migration and leukoencephalomalacia, and another had a displaced fracture at T6 with extradural compressive myelopathy and diskospondylitis at T6-T7. Osteomyelitis of fractured bones was observed in 3 horses. One horse with meningitis also had pituitary abscessation.

Postmortem microbial culture of CSF was performed for 23 horses, of which 13 (56.5%) CSF samples yielded bacterial growth. In these 13 horses, the following organisms were isolated from CSF: Streptococcus equi subsp zooepidemicus (3 horses), E coli (2), mixed bacterial growth (2; ie, Pasteurella caballii, E coli, Pepto-streplococcus sp, Fusobacterium sp, Actinomyces sp, Fu-sobacterium sp, and Bacteroides sp), C neoformans (1), S equi subsp equi (1), Actinobacillus sp (1), Proteus sp (1), Klebsiella sp (1), and C pseudotuberculosis (1). Two of the 13 horses also had the same bacteria isolated on CSF samples obtained before death. The horse with an antemortem isolation of C canimorsus from CSF did not have a necropsy performed. Disseminated hematogenous infection was evident upon necropsy in 8 horses (5 adults, 1 weanling, and 2 neonatal foals). The adult horses had pleuropneumonia, interstitial pneumonia, pericardial effusion, osteomyelitis, disseminated intravascular coagulation, and a tooth root abscess. The weanling had previous upper airway S equi subsp equi infection.

Discussion

Diagnoses of meningitis and meningoencephalomyelitis were made for 28 equine patients from our institution during a 25-year period. Previous literature

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has described single or a few sporadic cases, with the largest number of horses with meningitis of 5 and 7 horses in 2 studies. These studies have provided useful information about clinical and clinicopathologic variables, pathogens, and outcome. However, the most common physical, neurologic, and clinicopathologic alterations as well as pathogens causing meningitis or meningoencephalomyelitis cannot be definitively concluded from reports on individual horses. Although meningitis and meningoencephalomyelitis in horses have been almost exclusively associated with infection, it is also important to consider noninfectious causes because they do occur but are seldom reported. Clinical signs of disease are nonspecific and could result in delayed recognition and treatment. From the present study and other studies, altered mental status, cranial nerve deficits, and gait abnormalities were identified as the most common neurologic signs. Signs of vestibular dysfunction have been sporadically reported. Findings of the present study highlight vestibular dysfunction as a common abnormality in affected horses. Repeated CSF collection in a few horses from the present study also revealed the lack of cytologic abnormalities on first analysis. However, this finding did not rule out meningitis or meningoencephalomyelitis, and a second CSF sample may be necessary. The evaluation of biochemical variables in CSF such as glucose concentration in comparison to serum glucose concentration and in conjunction with CSF pH and lactate (l- and d-lactate) concentration has not been reported for affected horses. Alterations in these variables strongly supported infection in horses with suspected bacterial meningitis and could be used as an adjunctive diagnostic modality. Microbial culture of CSF has been reported to have a low yield, which is supported by results of the present study. We believe that this is not a justification for not pursuing microbial culture. Furthermore, postmortem bacterial isolation from affected horses with a confirmed diagnosis had a higher yield. Additionally, 5 pathogens not previously described were isolated from a few horses of the present study, 3 of which were isolated from CSF samples obtained before death. Lastly, horses with meningitis or meningoencephalomyelitis of unknown etiology must be evaluated for transient or long-standing immunodeficiencies.

Meningitis is an uncommon neurologic disorder in horses as evidenced by a few isolated case studies and a retrospective study of 450 horses with neurologic disease over a 12-year period in which 2 horses had fungal meningitis and 3 horses had bacterial meningitis. The overall prevalence of disease for the study period at our hospital was 0.04% (28/70,000) and 0.2% (28/14,000) for horses with neurologic disease. Nearly 40 years ago, bacterial meningitis was reported in 8% to 10% of neonatal foals with septicemia. At our hospital, the overall prevalence of disease in neonatal foals was 0.2% (2/1,000) and 0.5% (2/400) in foals with septicemia. Early recognition, treatment, and referral of neonatal foals with septicemia as well as better intensive care and monitoring units, trained personnel, and availability of newer-generation broad-spectrum antimicrobials may have contributed to the lower prevalence.

In the present study, both the patients’ age and sex distribution were different from the hospital population during the same period, largely attributed to the high number of young Thoroughbred colts in training or racing, which shifted the median age and sex distribution. Because of their temperament, young male horses may be more predisposed to sustain head trauma with disruption of the BBB as documented in 11 horses from the present study. Human studies have shown that the incidence of posttraumatic meningitis after moderate to severe head injury is 1.4%, whereas after a compound skull fracture, it could be as high as 2% to 11%. Concurrent infections in the head, such as sinusitis, tooth root abscess, osteomyelitis, and otitis media and interna were seen in 7 horses in the present study. Similarly, ascending infectious processes adjacent to the CNS have been reported in adult horses prior to the development of meningitis. Dissemination from hematogenous spread was found upon histologic and microbiological evaluation in 8 horses, which has been reported for adult horses and septicemic foals. Another possible route of infection is through the vascularization of the pituitary gland because of the lack of a blood-brain barrier (BBB) and meningitis. One of the horses from the present study had a pituitary abscess. Hematogenous meningoencephalomyelitis caused by H gingivalis, a free-living saprophyte nematode, enters via wounds in the skin and mucous membranes; spreads locally to adjacent tissues, including bones; and disseminates to distant sites, such as the kidneys and CNS in horses, as observed in 2 horses in the present study.

Vital signs at admission were within reference range in most of the horses of the present study. However, many clinical records were not detailed enough to determine recent NSAID, analgesic, or sedative administration that could have altered these findings. A wide variety of signs have been described in horses with meningitis, including lethargy, fever, weakness, signs of neck pain, and those associated with other concurrent diseases. Similar to reports in other species with meningitis or meningoencephalomyelitis, abnormal mental status (71.4%) was a common neurologic alteration in these horses. Cranial nerve deficits were a frequent finding in affected horses (71.4%), similar to a canine study in which deficits were reported to be present in 56% of affected dogs. Vestibular dysfunction was also a common abnormality (46.4%) in the present study. Common gait abnormalities included ataxia and tetraparesis. Other signs reported for horses with meningitis or meningoencephalomyelitis, such as disorientation, head pressing, aggressive behavior, seizures, reluctance to move, and compulsive circling, were also inconsistently found in our population of horses. People and dogs with meningitis have severe neck pain, which is considered one of the most characteristic and early signs of meningitis. Signs of neck pain may be more difficult to assess and interpret in horses, especially in recumbent animals. In the present study, apparent neck pain was noted in a third of affected horses.

The most important hematologic findings were leukocytosis, neutrophilia, lymphopenia, and hypalbuminemia. Neutrophilia and hyperfibrinogenemia are the most commonly reported clinicopathologic abnormalities in horses with infectious meningitis. Combined variable immunodeficiency is an acquired
disorder of adult horses manifested as recurrent fevers and bacterial infections. In a study of 14 horses with CVID, 6 horses had meningitis, 1 of which had 3 episodes of infectious meningitis. The disease is characterized by persistent severe B-cell lymphopenia as determined by the B-cell markers CD19, CD21, and IgM and hypogammaglobulinemia or agammaglobulinemia (IgG and IgM). In addition, serum IgA concentrations have been reported to decline over time, as shown by serial immunologic testing. Ten horses from the present study had a history of chronic infection at other sites prior to the development of meningitis. None of the horses with lymphopenia (lymphocyte counts, 171 to 1,500 cells/µL) had hypogammaglobulinemia (globulins, 2.4 to 5 g/dL). Immunologic testing to investigate which population of lymphocytes and immunoglobulins isotypes were depleted in these horses was not performed, except for in 1 mare with meningoencephalomyelitis caused by H. gingivalis infection for which these variables were comparable to those of a clinically normal horse. Horses with CVID can have a lymphocyte count and total globulin concentration within reference range and yet, on lymphocyte immunophenotyping, be identified with B-cell lymphopenia and immunoglobulin hypogammaglobulinemia. Therefore, if CVID (or other immune deficiency) is suspected, appropriate testing should be performed (immunoglobulin isotype testing performed for IgG, IgG[T], IgA, IgM, and immunophenotyping for lymphocyte subsets). All immunodeficiencies cannot be ruled out on the basis of a total lymphocyte count or total immunoglobulin concentration alone. In the present study, hypoalbuminemia was not severe, and there were no clinical manifestations, such as edema.

Both in human and veterinary medicine, CSF analysis is considered to be the gold standard for the ante-mortem diagnosis of meningitis. Most of the horses of the present report had abnormal CSF upon macroscopic evaluation. Xanthochromia was the most common macroscopic abnormality that reflected BBB leakage or damage. Bloody discoloration can be due to blood contamination, intrathecal hemorrhage, hemorrhagic infarct, or diapedesis also consistent with BBB disruption. The high protein concentration in the CSF in the horses of the present study could be attributed to protein leakage from the disruption of the BBB and local production as the result of inflammation. Neutrophilic pleocytosis and the high percentage of degenerate neutrophils in the CSF samples supported an infectious process. It is important to emphasize that neutrophilic pleocytosis in the absence of degeneration and bacteria does not rule out bacterial meningitis, as shown in 2 horses of the present study in which CSF analysis at different times did not reveal neutrophilic degeneration in the first CSF sample but did show an increased neutrophil count with degeneration (2/2) and organisms in the second CSF sample (1/2). Furthermore, results of a study indicated that 1 horse with CVID and presumed bacterial meningitis had an initial lymphocytic pleocytosis that became neutrophilic in a subsequently tested CSF sample. Infectious organisms were observed in almost half of the CSF samples: bacterial organisms in 8 horses and fungal in 1 horse. Similar to other studies on horses, marked increases in CSF protein concentration and profound neutrophilic pleocytosis were seen in the horse with cryptococcal organisms. One horse with H. gingivalis and bacterial meningoencephalomyelitis had a high CSF protein concentration with severe neutrophilic pleocytosis. A second horse with an H. gingivalis infection had CSF cytologic findings within reference range on initial evaluation when no neurologic signs were present. A CSF sample was not available when this horse developed neurologic signs. Creatine kinase concentration in CSF was high in half of the horses in which creatine kinase was measured and could suggest CNS trauma. Glucose concentration in CSF < 50% of serum glucose concentration is a common finding in people with bacterial meningitis. In the present study, glucose concentration in CSF was low in 4 of 6 horses and was < 50% of serum glucose concentration in 3 horses. Increased lactate concentration in body fluids could be an indication of increased anaerobic metabolism (if lactate is evaluated) or the presence of fermenting bacteria (if lactate is evaluated) such as Klebsiella, E. coli, Lactobacillus, and Eubacterium, among others. In the present study, high concentrations of 1-lactate and β-lactate in CSF from 1 horse supported infection.

Despite limitations to identify many skull abnormalities with radiography, this modality was helpful in the present study to recognize fracture of cranial bones, pneumocephalus, alterations supportive of osteomyelitis, and sinusitis. Computed tomography was useful to identify penetrating trauma to the cribriform plate in 1 horse and otitis media and interna with local spread into the CNS in another horse in which skull radiographs failed to reveal these abnormalities. However, intracranial lesions may also be missed on computed tomographic evaluation. Magnetic resonance imaging is considered an excellent diagnostic modality for meningitis and meningoencephalomyelitis in humans and small animals because the disease causes characteristic imaging changes. The cost, availability, and anesthetic risk in neurologically compromised horses frequently limit its use.

In the present study, 19 horses were confirmed to have bacterial meningitis or meningoencephalomyelitis with 4 additional suspect horses on the basis of neutrophilic pleocytosis with degenerate neutrophils on cytologic examination of CSF. Antemortem bacterial isolation from CSF has been documented to be of low yield in various species, including horses. In the present study, antemortem microbial culture yielded bacterial organisms in 4 of 19 horses with confirmed bacterial infections, suggesting a low sensitivity. Polymerase chain reaction analysis of a CSF sample proved to be useful for the diagnosis of streptococcal meningoencephalomyelitis in 1 coli for which microbial culture revealed no growth. Cryptococcal organisms may be visualized on cytologic evaluation of CSF samples, as in 1 horse from the present study. Postmortem microbial culture of CSF and CNS tissues had a higher yield for the isolation of organisms than the antemortem microbial culture of CSF (68.4% vs 21%, respectively). The following organisms have been reported to cause suppurative meningitis, meningoencephalomyelitis, or
intracranial abscessation in adult horses: *S equi* subsp *equi*, *S equi* subsp *zoopneumonicus*, *Streptococcus suis*, *Actinomyces* sp., *C pseudoibericus*, *E coli*, *Listeria monocytogenes*, *Sphingobacterium multivorum*, *Staphylococcus aureus*, coagulate negative *Staphylococcus* sp, *Actinobacillus equuli*, *Pasteurella caballi*, and *Klebsiella pneumoniae*.

Pathogens causing respiratory disease such as *S equi* subsp *equi* and *S equi* subsp *zoopneumonicus* have been the most commonly reported organisms causing bacterial meningitis in horses. Four of the horses in the present study were infected with streptococcal species. Instances of bacterial meningitis due to *S equi* subsp *zoopneumonicus* and *S equi* subsp *equi* in adults and children who have had close contact with horses have been rarely reported. In the present study, 5 bacterial species not previously reported were identified and included *Proteus* sp, *Pestrostreptococcus* sp, *C canimorsus*, *Fusobacterium* sp, and *Bacteroides* sp. Bacterial meningitis caused by a single organism was more common than meningitis caused by multiple organisms (11 vs 4 horses, respectively). Parasitic meningoencephalomyelitis in horses has been documented to be caused by *H gingivalis* and *Trypanosoma evansi*.

In the present study, *H gingivalis* was identified on histologic evaluation in 2 horses. In foals, *L monocytogenes*, *Salmonella agona*, *S equi* subsp *equi*, *S equi* subsp *zoopneumonicus*, *S aureus*, *E coli*, and *K pneumoniae* have been reported to cause supportive meningitis. Pathogens causing bacterial meningitis in neonatal foals are usually those causing bacteremia and septicemia, as in the case of 1 neonatal foal (*E coli*) in the present study.

Medical management was limited in this study because of the apparent advanced stage and severity of disease, safety concerns, and cost, which resulted in death or euthanasia in <24 hours after admission for most affected horses. Bactericidal and fungicidal drugs are preferred for the treatment of infectious meningitis. However, the limited success of treatment of a few horses, including the 1 horse from this study with bacterial meningitis treated with chloramphenicol and 1 reported horse with cryptococcal meningitis treated with fluconazole, suggests that bacteriostatic and fungistatic drugs may also be effective. Antimicrobials that readily penetrate the BBB include imipenem, trimethoprime and sulfonamides, fluorinated quinolones, metronidazole, chloramphenicol, rifampin, and macrolides. States of inflammation may facilitate drug penetration for penicillins, selected cephalosporins (*cefotaxime, ceftriaxone, and cefazidime*), and vancomycin. Favorable and unfavorable outcomes have been reported for affected horses treated with various antimicrobials.

Local factors within infected meninges such as pH and inflammatory proteins may alter penetration, availability, and activity of antimicrobials. Specific dosing regimens and duration of treatment for horses with bacterial and fungal meningitis are unknown, but long-term maximal doses if tolerated are indicated. Duration of treatment in horses with successful outcome has ranged from 3 weeks to a few months. The sole survivor in the present study was referred as soon as mild neurologic deficits were noted. Early recognition and referral may have played an important role in the favorable outcome in this horse. The clinical signs of a few horses from the present study worsened after the initiation of treatment with an antimicrobial. This may have been the result of the killing of organisms and local production and release of inflammatory cytokines. Therefore, the use of NSAIDs is indicated prior to and during the early stages of antimicrobial treatment. A recent study about the use of dexamethasone in the acute stages of bacterial meningitis in adult people found no reduction of neurologic disabilities or death.

**References**


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