Ophthalmic lesions in neonatal foals evaluated for nonophthalmic disease at referral hospitals

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Objective—To determine types and frequency of ophthalmic lesions detected in neonatal foals evaluated for nonophthalmic disease at 3 veterinary referral hospitals and to investigate associations between systemic and ophthalmic diseases in these foals.

Design—Prospective cross-sectional study.

Animals—70 foals < 30 days old.

Procedures—Complete ophthalmic examinations were performed. Signalment, clinical signs, mentation during ophthalmic examination, results of clinicopathologic tests, and diagnosis of systemic disease were recorded. Descriptive data analysis including a χ² test for associations was performed.

Results—Most foals (39/70 [55.7%]) with systemic disease had ≥ 1 ophthalmic lesion detected. Of the 39 foals with ophthalmic disease, 24 (61.5%) had potentially vision-threatening lesions. Clinically important abnormalities included conjunctival hyperemia or episcleral injection (30/70 [42.9%]), uveitis (18/70 [25.7%]), ulcerative keratitis (13/70 [18.6%]), nonulcerative keratitis (10/70 [14.3%]), entropion (9/70 [11.4%]), retinal hemorrhage (8/70 [11.4%]), and cataract (6/70 [8.6%]). Foals with sepsis were significantly more likely to have uveitis than those without sepsis. Foals with sepsis and uveitis were also significantly less likely to survive to discharge than were foals that had sepsis without uveitis. Acquired ophthalmic disease (detected in 37/70 [52.9%] foals) was significantly more common than congenital ophthalmic disease (detected in 9/70 [12.9%]).

Conclusions and Clinical Relevance—Ophthalmic lesions were detected in 55.7% of neonatal foals with systemic disease. Acquired ophthalmic disease was more commonly detected than congenital ophthalmic disease. Foals with sepsis were more likely to have uveitis than were foals without sepsis. A complete ophthalmic examination is indicated in neonatal foals evaluated for systemic disease. (J Am Vet Med Assoc 2011;239:486–492)

Equine neonates are commonly evaluated by veterinarians for clinical signs of systemic disease. Although systemic diseases of foals have been described, the ocular manifestations of disease have received little attention in the peer-reviewed literature, with the exceptions of adenoviral conjunctivitis and Rhodococcus equi uveitis.1–3 It has been stated in veterinary textbooks4–6 that foals affected with sepsis may develop uveitis. In fact, some sepsis grading schemes include the presence or absence of uveitis as part of the grading criteria4; however, the authors are aware of only 1 published study5 in the peer-reviewed literature that described the proportion of neonatal foals with uveitis as an ocular manifestation of systemic disease.

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Abbreviations

| FPT | Failure of passive transfer |
| IOP | Intraocular pressure |
| NMS | Neonatal maladjustment syndrome |
| OD | Right eye (oculus dexter) |
| OS | Left eye (oculus sinister) |
| PLR | Pupillary light reflex |
| STT | Schirmer tear test |

Most studies6–13 on equine neonatal ophthalmology focus on congenital disease, with limited information regarding the prevalence or clinical descriptions of acquired disease. Normal ocular anatomy and neuro-ophthalmic examination findings in neonatal foals have been described.14–16 The normal appearance and atrophy of the hyaloid artery system and associated tunica vasculosa lentis remnants17 and the presence of conjunctival and retinal hemorrhages in normal, healthy foals18,19 have also been reported.

Some investigators have examined ophthalmic findings in systemically ill neonatal foals.20,21 One study20 focused on corneal sensitivity and revealed that systemically compromised neonates had decreased corneal sensation compared with that of adult horses and healthy
neonates. All foals in that study, regardless of systemic disease status, had lower STT values than did adult horses. The authors speculated that decreased corneal sensitivity and relatively low volumes of tear production may contribute to increased frequency of ulcerative keratitis in neonatal foals. In 1 clinical report, 20% of ill foals in a referral hospital were affected with ulcerative keratitis.

Investigators of a study that focused on uveitis as an ocular manifestation of sepsis found that foals with sepsis and bacteremia were more likely to have a diagnosis of uveitis than were nonbacteremic foals with sepsis, nonseptic foals, or clinically normal foals. In that study, foals with sepsis, bacteremia, and uveitis were less likely to survive to discharge than were foals without uveitis.

The purpose of the study reported here was to describe the types and frequency of ophthalmic lesions in neonatal foals evaluated for nonophthalmic disease at 3 veterinary referral hospitals. We also sought to determine associations between ophthalmic and systemic disease in these foals. The null hypotheses were that foals with systemic disease would have a low frequency of ophthalmic disease and that no association would be detected between ophthalmic disease and systemic disease.

Materials and Methods

Study protocol—All foals ≤ 30 days of age with systemic, nonophthalmic diseases evaluated at the Equine Medicine and Surgery Service at the Veterinary Teaching Hospital of the University of Illinois Urbana-Champaign between January 1, 2008, and July 30, 2009; the William R. Pritchard Veterinary Medical Teaching Hospital of the University of California-Davis between January 1, 2009, and July 30, 2009; or the Veterinary Teaching Hospital of Michigan State University between January 1, 2009, and July 30, 2009, were eligible for inclusion in the study. Foals ≥ 31 days of age or foals that were primarily evaluated for ophthalmic disease were excluded from the study.

Owner and agent consent for ophthalmic examination as part of the initial assessment and stabilization was obtained for all foals. Because the examination protocol was within the standards of normal clinical practice and assessment, institutional animal care and use committee approval was not required. Complete ophthalmic evaluation was performed within 12 hours after admission to one of the study hospitals; this included examination with diffuse illumination and slit-lamp biomicroscopy before and after mydriasis was induced via topical application of 1% tropicamide solution. Indirect funduscopy with a 2.2-diopter or 13-diopter lens, STT, fluorescein staining of applanation tonometry, and rebound tonometry were also performed. During tonometry, each foal’s head was positioned or at above the level of the heart to prevent any entropion or entropion during hospitalization.

Results—Seventy foals (39 females [55.7%] and 31 males [44.3%]) were included in the study. The foals were of 18 breeds, including American Miniature Horse (n = 2), Appaloosa (3), Arabian (4), Belgian (3), Clydesdale...
(4), Dutch Warmblood (2), Fresian (1), Irish Cob (1), mixed breed (1), Morgan (2), American Paint Horse (5), Percheron (1), Pony of the Americas (1), Quarter Horse (12), Saddlebred (2), Standardbred (16), Rocky Mountain Horse (1), and Thoroughbred (9). Forty-nine of these 70 (70.0%) foals were admitted to the University of Illinois Urbana-Champaign, 12 (17.1%) were admitted to the University of California-Davis, and 9 (12.9%) were admitted to Michigan State University. Median age was 1.5 days (interquartile range, 1.0 to 3.0 days; minimum to maximum value range, 1 to 21 days), with 91.4% (64/70) of foals enrolled in the study at < 7 days of age.

Foals with > 1 systemic disease diagnosis were entered into multiple systemic disease categories. Twenty of 70 (28.6%) foals had FPT, 18 (25.7%) had sepsis, 17 (24.3%) had NMS, 16 (22.9%) had diarrhea, 16 (22.9%) had other gastrointestinal or urogenital disease, and 8 (11.4%) had musculoskeletal disease.

Thirty-nine of 70 (55.7%; 95% CI, 44.1% to 67.3%) foals had a diagnosis of ≥ 1 ophthalmic lesion. Most of these foals (24/39 [61.5%]; 95% CI, 50.2% to 72.8%) had ≥ 1 lesion that was considered potentially vision threatening if not treated appropriately (ie, entropion, ulcerative keratitis, or uveitis). The most common nonpathological ophthalmic diagnoses included prominent lenticular Y-sutures in 5 of 70 (7.1%) foals (95% CI, 0.5% to 12.0%) and remnants of the tunica vasculosa lentis–hyaloid artery system in 38 of 70 (54.3%) foals (95% CI, 42.6% to 66.1%; Figure 1). The most commonly detected pathological ophthalmic lesion was conjunctival hyperemia or episcleral injection (30/70 [42.9%] foals; 95% CI, 35.4% to 58.8%), followed by uveitis (18/70 [25.7%]; 95% CI, 15.3% to 35.9%) and ulcerative keratitis (13/70 [18.6%]; 95% CI, 9.3% to 27.7%). Other lesions included nonulcerative keratitis (10/70 [14.3%]; 95% CI, 6.1% to 22.5%), entropion (8/70 [11.4%]; 95% CI, 4.0% to 18.4%), retinal hemorrhage (8/70 [11.4%]; 95% CI, 4.0% to 18.4%), palpebral abrasion or edema (6/70 [8.6%]; 95% CI, 3.2% to 17.3%), cataract (6/70 [8.6%]; 95% CI, 1.0% to 12.6%), conjunctival icterus (2/70 [2.9%]; 95% CI, 0.35% to 10.0%), and vitritis (1/70 [1.4%]; 95% CI, 0.04% to 7.0%).

Tonometry with an applanation tonometer was performed in all 70 foals, and tonometry with a rebound tonometer was performed in 21 of 70 (30.0%) foals because not all participating institutions had access to a rebound tonometer. The mean IOP of all foals was estimated by means of applanation tonometry (OS, 13.3 ± 5.4 mm Hg [minimum to maximum value range, 10 to 22 mm Hg]; OD, 12.9 ± 4.9 mm Hg [minimum to maximum value range, 5 to 21 mm Hg]) and rebound tonometry (OS, 14.5 ± 3.9 mm Hg [minimum to maximum value range, 7 to 22 mm Hg]; OD, 14.7 ± 3.3 mm Hg [minimum to maximum value range, 10 to 22 mm Hg]). Bland-Altman plots revealed moderate agreement between the 2 devices (n = 21 foals) for left and right eyes (Figure 2). Foals with uveitis had significantly (P = 0.01) lower IOP (mean, 12.9 ± 4.5 mm Hg [minimum to maximum value range, 6 to 19 mm Hg]) than did foals without uveitis (mean, 17.6 ± 4.5 mm Hg [minimum to maximum value range, 12 to 25 mm Hg]) as measured with the applanation tonometer.

Median STT value for the left eye was 19 mm/min (10% to 90% value range, 10 to 35 mm/min; minimum to maximum value range, 6 to 35 mm/min). Median STT for the right eye was also 19 mm/min (10% to 90% value range, 12 to 35 mm/min; minimum to maximum value range, 10 to 35 mm/min).

A χ² test for homogeneity indicated that acquired ophthalmic disease (37/70 [52.8%]; 95% CI, 34.1% to 57.4%) was significantly (P < 0.001) more common...
than congenital ophthalmic disease (9/70 [12.9%]; 95% CI, 6.1% to 23.0%) among foals with systemic disease. Several foals (7/70 [10%]; 95% CI, 3.0% to 17.0%) in the present study had both acquired and congenital ophthalmic diseases. The only congenital lesions detected were cataract (6/70 [8.6%]; 95% CI, 3.2% to 17.7%) and anatomic or primary entropion (4/70 [5.7%]; 95% CI, 1.6% to 14.0%). In the remaining 4 foals with entropion (4/70 [5.7%]; 95% CI, 1.6% to 14.0%), the condition was spastic (secondary to ulcerative keratitis and blepharospasm).

Ophthalmic lesions were assessed among foals grouped according to systemic disease category. Clinically important lesions included entropion, ulcerative keratitis, uveitis, and retinal hemorrhage (Table 1; Figure 3). Lesions were detected most frequently among foals with sepsis (14/18 [77.8%]; 95% CI, 52.4% to 93.6%) and least frequently among foals with musculoskeletal disease (3/8 [37.5%]; 95% CI, 8.5% to 75.5%). Uveitis was detected most frequently in foals with sepsis, followed by those with diarrhea and NMS, whereas ulcerative keratitis was detected most frequently in foals with NMS. Retinal hemorrhages were not detected in foals with musculoskeletal disease and were observed infrequently in all other groups. Uveitis was significantly ($P = 0.003$) more common in foals with sepsis (9/18 [50%]; 95% CI, 29% to 77%) than in those without sepsis (9/52 [17.3%]; 95% CI, 8.2% to 30.3%).

A poor outcome (ie, not surviving to discharge) was significantly ($P = 0.02$) more likely for foals with sepsis and uveitis (3/8 [37.5%] foals that died; 95% CI, 8.5% to 75.5%) than for foals with sepsis that did not have uveitis (1/8 [12.5%]; 95% CI, 3.2% to 52.7%). The overall survival rate (percentage of foals surviving to discharge) was 88.6% (62/70; 95% CI, 78.7% to 94.9%). The proportion of foals with a diagnosis of uveitis was not significantly ($P = 0.06$) greater among those with diarrhea (7/16 [43.8%]; 95% CI, 19.8% to 70.0%), compared with foals that did not have diarrhea or sepsis (9/54 [16.7%]; 95% CI, 8.0% to 29.3%). The power for this comparison was 0.51, suggesting the potential for a type II error. Because the regression models did not include any variables beyond these described data, the $\chi^2$ test results are reported.

Of 6 foals > 7 days old at the time of the study, 4 (66.7%) had a diagnosis of patent urachus, 2 (33.3%) had colic, and 1 (16.7%) had diarrhea. The foal with diarrhea also had uveitis, and 1 foal had incipient cortical

<table>
<thead>
<tr>
<th>Variable</th>
<th>Sepsis (n = 18)</th>
<th>NMS (n = 17)</th>
<th>Diarrhea (n = 16)</th>
<th>GIUG (n = 16)</th>
<th>Musculoskeletal (n = 8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ophthalmic lesion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Entropion</td>
<td>4 (20.0)</td>
<td>3 (16.7)</td>
<td>2 (11.8)</td>
<td>1 (6.3)</td>
<td>2 (12.5)</td>
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<tr>
<td>Ulcerative keratitis</td>
<td>4 (20.0)</td>
<td>3 (16.7)</td>
<td>6 (35.3)</td>
<td>1 (6.3)</td>
<td>3 (18.8)</td>
</tr>
<tr>
<td>Uveitis</td>
<td>3 (15.0)</td>
<td>9 (50.0)</td>
<td>5 (29.4)</td>
<td>7 (43.8)</td>
<td>1 (6.3)</td>
</tr>
<tr>
<td>Retinal hemorrhage</td>
<td>2 (10.0)</td>
<td>1 (5.5)</td>
<td>1 (5.9)</td>
<td>2 (12.5)</td>
<td>2 (25.0)</td>
</tr>
<tr>
<td>≥ 1 ophthalmic lesion</td>
<td>14 (70.0)</td>
<td>14 (77.8)</td>
<td>11 (64.7)</td>
<td>11 (68.8)</td>
<td>6 (37.5)</td>
</tr>
<tr>
<td>No ophthalmic abnormalities</td>
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<td>6 (35.3)</td>
<td>5 (31.3)</td>
<td>10 (62.5)</td>
<td>5 (62.5)</td>
</tr>
</tbody>
</table>

Clinically important ophthalmic abnormalities are shown. Foals were grouped according to systemic disease diagnosis; most foals had ≥ 1 diagnosis and were included in ≥ 1 category. GIUG = Gastrointestinal or urogenital disease (other than diarrhea).
EQUINE cataracts; however, the other 4 foals had no ophthalmic abnormalities detected. The small number of foals in this age group precluded statistical comparisons between foals < 7 days and > 7 days old.

Discussion

To the authors’ knowledge, no previous study has described the types and frequency of ophthalmic lesions in systemically compromised neonatal foals. Results of the study reported here indicate that the percentage of systemically ill neonatal foals that have ophthalmic disease is high (55.7%), and greater than half the ophthalmic lesions detected in this group of foals had the potential to be vision threatening if not treated appropriately.

Although conjunctival hyperemia and episcleral injection were the most commonly detected ophthalmic lesions of foals in the present study, the conjunctiva is a highly vascular and reactive tissue that can develop local vasodilation in response to ophthalmic and systemic diseases. Episcleral injection is the vasodilation of episcleral vessels in response to intraocular disease. Conjunctival hyperemia frequently accompanies episcleral injection. These ophthalmic abnormalities did not always appear to be associated with intraocular disease and were not considered to be specific for intraocular or systemic disease.

Uveitis is inflammation of the vascular uveal tissue with resultant breakdown of the blood-aqueous barrier and accumulation of inflammatory cells, mediators, and debris within the eye. In the present study, uveitis was detected more frequently in foals with sepsis than in systemically ill foals without sepsis. Similar to foals, calves are not infrequently affected with sepsis and bacteremia and can also develop anterior uveitis, panuveitis, and retinitis in association with sepsis. Sepsis results in alterations in microcirculation, vascular insult, and subsequent disruption of endothelial barriers. Recent studies have focused on these alterations in microcirculation and the resultant perfusion deficits that develop in septic shock. It is possible that alterations in ocular microcirculation create local endothelial hypoxia, which in turn causes endothelial dysfunction, loss of vascular integrity, and ultimately local tissue hypoxia, resulting in breakdown of the blood-aqueous barrier in the eye. Further investigation is necessary to elucidate the mechanisms of blood-aqueous barrier compromise in the presence of systemic disease.

Human neonates, similar to neonatal foals, may also be affected by sepsis; however, the ocular manifestations of sepsis vary between these species. Results of a survey of human pediatric patients hospitalized for systemic disease in a tertiary referral center revealed no cases of uveitis or septic endophthalmitis in patients with sepsis or other systemic infection. Ocular manifestations of sepsis are more common in neonatal and adult humans with fungal rather than bacterial sepsis, and endophthalmitis is the most common clinical finding in these patients. In adult humans, sepsis is also associated with conjunctival hemorrhages, retinitis, panuveitis, and endophthalmitis. This is markedly different from findings in neonatal foals with sepsis, in which fungemia and fungal endophthalmitis are uncommon, and only 1 case study of nonseptic endophthalmitis in a premature Thoroughbred foal has been reported. Rhodococcus equi has been reported as a cause of septic and nonseptic uveitis and endophthalmitis in horses.
however, this is generally seen in foals > 3 weeks of age \(^1\) and was not identified as an etiologic agent in any foals in the present study. Evidence of endophthalmitis was not detected in foals in the present study, and retinal lesions were uncommon, in contrast to findings reported in humans.\(^2\)-\(^3\),\(^3\),\(^6\),\(^7\)

One of the limitations of the study reported here was the relatively small population and the high proportion of foals that had multiple systemic and ophthalmic diagnoses, which made meaningful data analysis challenging. Although foals with diarrhea were not significantly more likely to have uveitis, compared with foals that did not have diarrhea, results of power analysis indicated that a type II error was likely. It is possible that a larger sample size would have yielded the statistical power required to reach significance. Conversely, many foals with diarrhea also had sepsis, and foals without sepsis that had diarrhea may have been less likely to have uveitis, preventing the difference between foals with diarrhea and uveitis and foals with diarrhea but without uveitis from reaching statistical significance. Although the only significant association that was detected between systemic and ocular disease was between sepsis and uveitis, results of the study reported here are clinically useful for equine practitioners. Although there was not a statistically significant relationship between ulcerative keratitis and NMS, the percentage of foals in this group with ulcerative keratitis was greater than that of other groups. The authors hypothesize that this may result from peripheral neuropathy or may be a function of altered mentation in this group of foals, resulting in recumbency and increasing the likelihood of sustaining environmental ocular trauma.

Several authors have indicated that the prevalence of congenital ophthalmic disease is greater than that of acquired disease in foals.\(^8\),\(^9\),\(^10\),\(^11\) In the present study, acquired ophthalmic disease was detected in a significantly greater percentage of systemically compromised neonatal foals than was congenital ophthalmic disease. In a previous survey of 144 healthy Thoroughbred, Standardbred, and Saddlebred foals at 1 breeding farm, the incidence of congenital ophthalmic lesions was described as low, although no definitive numbers were reported.\(^10\) A preliminary report involving mostly Thoroughbred foals in a farm environment also indicated that the prevalence of congenital ophthalmic lesions was low after cursory examination. No ocular manifestations of systemic disease were identified in the foal population of either study\(^12\),\(^13\),\(^14\),\(^15\), however, 5 foals in the first study\(^16\) were described as having punctate corneal opacities consistent with resolving ulcerative keratitis, which would be considered an acquired disease.

In the present study, uveitis was the most commonly detected clinically important ophthalmic disease, followed by ulcerative and nonulcerative keratitis. The presence of uveitis may be useful in sepsis scoring systems, and its progression or resolution may prove to be a clinically useful tool for monitoring the response of foals with sepsis to treatment.\(^1\) Foals with uveitis and sepsis were also significantly less likely to survive to discharge in the present study. This data may provide the clinician with additional tools for formulating a prognosis when treating foals with sepsis.

The percentage of foals with retinal hemorrhages (11.4%) in the present study was lower than that previously reported (16%) in healthy Thoroughbred foals in New Zealand\(^16\); however, the 95% confidence intervals for the 2 populations overlap, which suggests the prevalence may not be different between these groups. Retinal hemorrhages were previously thought to be associated with NMS, but more recent investigation indicated that this is more common in larger foals and foals born to dams experiencing dystocia, and is not associated with the development of NMS.\(^13\),\(^19\) Only 1 of 8 foals with retinal hemorrhages in the present study was reportedly born to a dam with dystocia; however, many foalings were unattended and thus dystocia may not have been reported by the owner.

The Bland-Altman analysis of tonometry data in this study revealed moderate agreement between the applanation and rebound tonometers. The level of agreement does not reflect accuracy of each device. Therefore, this data cannot be used to determine if one device is more accurate than another. Both applanation and rebound tonometry have previously been reported\(^20\),\(^21\) as accurate methods of estimating IOP in adult horses. Further controlled studies of the use of these instruments in healthy foals are warranted. Although rebound tonometry is easily performed in adult horses, the authors did find that use of the rebound tonometer was more technically challenging in recumbent foals because of the need to keep the device perpendicular to the ground.

The range of STT values varied widely among foals in the present study. Median STT values for the left and right eyes (19 mm/min for both) were higher than previously reported mean values for clinically normal (12.8 ± 2.4 mm/min) and systemically ill foals (14.2 ± 1.0 mm/min).\(^22\) Low numbers of foals with keratitis prevented meaningful statistical analysis of associations between keratitis and STT results, and additional clinical studies are warranted.

Results of the present study suggest that acquired ophthalmic disease is more common in systemically ill neonatal foals than previously reported. These findings underscore the importance of a complete ophthalmic examination in all foals undergoing veterinary evaluation for systemic illness.

References


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\(^{a}\) Finoff Transilluminator, Welch-Allyn, Skaneateles, NY.
\(^{b}\) Zeiss HSO 10 hand-held slit lamp, Zeiss, Dublin, Calif.
\(^{c}\) Tropicamide 1% USP, Alcon Laboratories Inc, Fort Worth, Tex.
\(^{d}\) PanRetinal 2.2D, Volk Optical Inc, Mentor, Ohio.
\(^{e}\) Volk 13D, Volk Optical Inc, Mentor, Ohio.
\(^{f}\) Merion VFS, Schering-Plough Animal Health, Union, NJ.
\(^{g}\) BioGlo Fluorescein Sodium Ophthalmic Strips USP, Ocularvision Inc, Solvang, Calif.
\(^{h}\) Tonopen-XL, Reichert Inc, Depew, NY.
\(^{i}\) Tonovet, Icare Finland Oy, Espoo, Finland.
\(^{j}\) Nikon D200, Nikon Inc, Melville, NY.
\(^{k}\) Nidek NM-100, Nidek Inc, Fremont, Calif.
\(^{l}\) MedCalc, version 10.1.8, MedCalc; Mariakerke, Belgium.
\(^{m}\) SPSS, version 17.0, SPSS Inc, Chicago, Ill.