

## Clinical Findings and Survival in 56 Sick Neonatal New World Camelids

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**Background:** Information pertaining to clinical presentation and outcome of neonatal New World camelids (NWC) is limited when compared to calves and foals.

**Hypothesis:** Values of variables at admission and subsequent treatment would predict survival in sick neonatal NWC.

**Animals:** Fifty-six client-owned sick neonatal NWC presented over a 10-year period to the Purdue University Veterinary Teaching Hospital.

**Methods:** A retrospective study was performed. Inclusion criteria were NWC less than 30 days of age with complete medical records that presented between 2000 and 2010.

**Results:** The median age at presentation was 1 day (range 1–20). The most common diagnoses were systemic inflammatory response syndrome (50%), congenital defects (41%), ophthalmic lesions (21%), sepsis (16%), and gastrointestinal diseases (16%). Sixty-six percent of NWC survived to discharge. Clinicopathologic findings on admission were variable and not specific for disorders. Factors associated with survival were absence of choanal atresia ( $P = .001$ , OR: 55.9 [2.5–1,232]), administration of llama plasma ( $P = .013$ , OR: 4.9 [1.4–17.7]), and antimicrobial treatment with trimethoprim-sulfamethoxazole (TMS) ( $P = .016$ , OR: 6.5 [1.3–32.2]).

**Conclusions and Clinical Importance:** The use of antibiotics, particularly TMS, and llama plasma are recommended in sick neonatal NWC. Results from this study could contribute toward defining a NWC-specific sepsis scoring system.

**Key words:** Atresia; Camelid; Congenital; Cria; Sepsis.

New World camelid (NWC) is an umbrella term that includes the domestic species llamas (*Lama glama*) and alpacas (*Vicugna pacos*). There are large numbers of NWC in North America; unfortunately, the demand for veterinary services for these animals usually exceeds the traditional education program at most North American veterinary schools, and funding to investigate diseases of NWC is relatively limited. As such, many practitioners extrapolate what is known in the more thoroughly studied large animal species when they treat neonatal NWC. This raises the possibilities of error when species differences exist. More research is necessary to match the needs of this industry.

In many large animal species, the neonatal period is critical as morbidity and mortality are high.<sup>1,2</sup> In foals and in calves, prematurity and dysmaturity are associated with a poor prognosis for life.<sup>1,3</sup> In NWC, however, neither prematurity nor dysmaturity have been associated with a poor prognosis for long-term survival.<sup>4</sup> It has been shown that, like foals and calves, neonatal NWC are at risk for developing sepsis.<sup>5</sup> The clinical features of neonatal sepsis in NWC are poorly specific and might differ from foals and calves.<sup>1,3,5,6</sup> These examples suggest that information pertaining to

### Abbreviations:

CBC	complete blood count
FTPI	failure of transfer of passive immunity
NWC	New World camelids
OR	odds ratio
SIRS	systemic inflammatory response syndrome
TMS	trimethoprim-sulfamethoxazole

foals or calves might not be applicable to NWC. Moreover, NWC differ in basic hemovascular and respiratory physiology, suggesting that different pathophysiologic mechanisms and clinical features might be encountered in these species. For example, NWC exhibit increased oxygen conductance of red blood cells compared to foals and calves, characterized by both an increased hemoglobin-oxygen affinity and an increased oxygen extraction from tissues. Because of this, NWC are able to maintain cardiac output and brain-blood flow in the face of hypoxemia.<sup>7–13</sup>

The objectives of this retrospective study were to describe the signalment, historic complaints, clinical signs, clinicopathologic variables, diagnostic tests, treatment, and outcome in sick neonatal NWC presented to a referral hospital.

## Materials and Methods

### Data Collection

Medical records of NWC presented to the Purdue University Veterinary Teaching Hospital from 2000 through 2010 were reviewed. Animals were included if they were less than 30 days of age at presentation and if a final diagnosis at either death or discharge was available.

Data collected from the records included signalment (species, sex and age), relevant history when available (including month of presentation), physical examination findings at admission, clinico-

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pathologic variables at admission, diagnostic tests, final diagnosis, treatments, and outcome.

### Data Analysis

Animals were grouped by outcome (discharged alive or not) and type of disease. Disease type was categorized by organ system affected (gastrointestinal, respiratory, neurologic, musculoskeletal, or ophthalmic) and the presence or absence of a diagnosis of systemic inflammatory response syndrome (SIRS), sepsis, and congenital defects. The diagnosis of SIRS was made based on the presence of 2 or more of the following conditions: temperature  $>39^{\circ}\text{C}$  or  $<37.2^{\circ}\text{C}$ , heart rate  $>120$  beats/min, respiratory rate  $>40$  breaths/min, WBC count  $>12,000/\mu\text{L}$  or  $<6,000/\mu\text{L}$ , or  $>10\%$  band neutrophils.<sup>14,15</sup> The diagnosis of sepsis was made if SIRS was present and if bacterial infection was confirmed with any microbial culture.<sup>15</sup>

Statistical analysis was performed using commercially available software.<sup>a</sup> Normality was assessed with a Shapiro-Wilk test. Normally distributed data were reported as mean and standard deviation and compared using an unpaired *t*-test. Nonparametric data were reported as median and range and compared using a Mann-Whitney *U*-test. Categorical data were compared using a Chi-square test or a Fisher's exact test depending on the number expected and odd ratios were calculated when relevant. For all comparisons, a *P*-value  $<.05$  was considered significant.

## Results

### Signalment/History

Fifty-six animals met the inclusion criteria. Neonatal NWC ranged from 0 to 20 days of age with a median age of 1 day. Seventeen (30% of cases) were males and 39 (70%) were females; however, there was no significant overrepresentation of females ( $P = .053$ ). Species included 23 llamas and 33 alpacas. The months of presentation ranged from January to December with a peak in May and June (21 cases, 38%). Common historic complaints included weakness/failure to thrive (18 cases, 32%), choanal atresia (9 cases, 16%), colic (6 cases, 11%), presence of neurologic signs (5 cases, 9%), and lameness (4 cases, 7%). Seven cases (13%) were suspected to be premature.

### Clinical Findings

The most common clinical signs upon presentation were tachypnea (respiratory rate  $>40$  breaths/min, 26 of 51 cases, 51%), tachycardia (heart rate  $>120$  beats/min, 27 of 54 cases, 50%), hypothermia (temperature  $<37.2^{\circ}\text{C}$ , 9 of 50 cases, 18%), and hyperthermia (temperature  $>39^{\circ}\text{C}$ , 5 of 50 cases, 10%). There was no association between clinical signs and final diagnosis or outcome. At admission, llamas had a higher respiratory rate than alpacas ( $49 \pm 3$  breaths/min and  $37 \pm 2$  breaths/min, respectively,  $P = .005$ ).

A complete blood count (CBC) and serum chemistry was available in 46 cases (82%). The most common CBC abnormalities at admission were neutrophilia (neutrophil count  $>7,000/\mu\text{L}$ , 24 cases, 52%), leukocytosis (WBC count  $>12,000/\mu\text{L}$ , 14 cases, 30%), leukopenia (WBC count  $<6,000/\mu\text{L}$ , 13 cases, 28%), and

neutropenia (neutrophil count  $<3,000/\mu\text{L}$ , 9 cases, 20%). None of these initial clinicopathologic values were associated with outcome.

Abnormalities on serum chemistry at admission included hyperchloremia (chloride  $>103$  mmol/mL, 40 cases, 87%), hypernatremia (sodium  $>144$  mmol/mL, 34 cases, 74%), hyperphosphatemia (phosphorus  $>5.7$  mg/dL, 30 cases, 65%), increased creatinine concentration (creatinine  $>1.8$  mg/dL, 26 cases, 57%), hypocalcemia (calcium  $<10.7$  mg/dL, 25 cases, 54%), hypoglobulinemia (globulin  $<2.2$  mg/dL, 22 cases, 48%), increased blood urea nitrogen (BUN  $>27$  mg/dL, 19 cases, 41%), hyperglycemia (glucose  $>124$  mg/dL, 16 cases, 35%), hypoproteinemia (total protein  $<4.5$  mg/dL, 14 cases, 30%), hypoalbuminemia (albumin  $<2.5$  mg/dL, 14 cases, 30%), hypoglycemia (glucose  $<73$  mg/dL, 14 cases, 30%), and decreased TCO<sub>2</sub> (TCO<sub>2</sub>  $<23$  mmol/mL, 11 cases, 24%). Among these variables, none were associated with survival. Blood glucose concentration at admission was significantly higher in females than in males ( $135 \pm 16$  and  $83 \pm 15$  mg/dL, respectively,  $P = .049$ ). With respect to gastrointestinal disease, hematocrit was significantly higher in animals not affected by gastrointestinal disease ( $35 \pm 3\%$  and  $30 \pm 5\%$ , respectively,  $P = .024$ ).

Based on the criteria used, 28 cases (50%) were diagnosed with SIRS on admission. Seventeen cases (61% of SIRS cases) were tachycardic, 18 cases (64%) were tachypneic, 10 cases (36%) had leukocytosis, 10 cases (36%) were leukopenic, 4 cases (14%) were hypothermic, 5 cases (18%) were hyperthermic, and 5 cases (18%) had  $>10\%$  band neutrophils. Overall, 16 cases (57%) had 2 positive criteria for SIRS, 8 cases (29%) had 3 positive criteria for SIRS and 4 cases (14%) had 4 positive criteria for SIRS. The absence of SIRS was not associated with survival and there was no association between the number of positive SIRS criteria and survival. Animals diagnosed with SIRS had significantly higher respiratory rates compared to those without SIRS (48 breaths/min [30–90] and 36 breaths/min [24–60], respectively,  $P = .002$ ), higher band neutrophils (1,300/ $\mu\text{L}$  [0–3,270] and 0/ $\mu\text{L}$  [0–560], respectively,  $P = .010$ ), and a lower albumin/globulin ratio ( $1.1 \pm 0.2$  and  $1.2 \pm 0.2$ , respectively,  $P = .037$ ). Among animals diagnosed with SIRS, survivors had a significantly higher monocyte count than nonsurvivors (640/ $\mu\text{L}$  [0–4,910] and 110/ $\mu\text{L}$  [0–1,760], respectively,  $P = .013$ ).

### Diagnostic Tests

In 11 cases (20%), an aerobic blood culture was performed, 6 (55%) of which yielded significant growth and were diagnosed with septicemia (blood culture positive in the presence of SIRS). Bacteria identified included *Staphylococcus epidermidis* (3 cases, 50% of positive blood cultures), alpha-hemolytic *Streptococcus* (3 cases, 50% of positive blood cultures), *Micrococcus* sp. (2 cases, 33% of positive blood cultures) and *Escherichia coli* and *Sphingomonas paucimobilis* (each

counting for 1 case, 17% of positive blood cultures). In 3 cases, multiple bacteria were recovered. Growth of bacteria or multiple types of bacteria in blood cultures was not negatively associated with survival as 5 cases (83% of animals with positive blood culture) survived to discharge.

In 9 of the 28 cases diagnosed with SIRS (32% of SIRS cases), a diagnosis of sepsis could be confirmed. In 6 cases (67% of septic cases), the infectious agent was recovered from the blood, and in 5 cases (56% of septic cases), the infectious agent was recovered at necropsy from lungs, spleen, kidneys or liver. In 3 cases (33% of septic cases), the infectious agent was recovered from multiple locations. There was no difference in the number of positive criteria for SIRS between septic and nonseptic animals. Among septic animals, the most common clinical and clinicopathologic data were hyperchloremia (8 cases, 88%), tachypnea (6 cases, 67%), tachycardia (5 cases, 56%), abnormal blood glucose concentration (6 cases, 67%), including 5 cases of hyperglycemia and 1 case of hypoglycemia, abnormal neutrophil count (7 cases, 78%), including 4 cases of neutropenia and 3 cases of neutrophilia, hypernatremia (9 cases, 67%), abnormal WBC count (6 cases, 67%), including 4 cases of leukopenia and 2 cases of leukocytosis, hypoglobulinemia (3 cases, 33%), decreased TCO<sub>2</sub> (3 cases, 33%), increased creatinine (2 cases, 22%) and decreased albumin (1 case, 11%). There was no significant association between confirmed sepsis and survival ( $P = .07$ ). Animals diagnosed with sepsis had a significantly higher respiratory rate than nonseptic cases ( $56 \pm 6$  breaths/min and  $42 \pm 2$  breaths/min, respectively,  $P = .011$ ), and also had significantly higher band neutrophils (0/ $\mu$ L [0–1,030] and 260/ $\mu$ L [0–3,270], respectively,  $P = .004$ ), higher blood glucose (170 mg/dL [36–297] and 88 mg/dL [22–296], respectively,  $P = .033$ ), and increased gamma-glutamyl-transferase activity (77 IU/L [32–246] and 36 IU/L [21–481], respectively,  $P = .047$ ). Among the animals diagnosed with sepsis, survivors had lower hemoglobin concentration than nonsurvivors ( $14.0 \pm 1.4$  g/dL and  $16.0 \pm 0.4$  g/dL, respectively,  $P = .043$ ) and higher total calcium ( $10.6 \pm 0.2$  mg/dL and  $9.8 \pm 0.2$  mg/dL, respectively,  $P = .047$ ).

In 3 cases (5%), a fecal culture was performed and 1 (33%) of these yielded positive results (*Escherichia coli*, which could have been insignificant). In 3 cases (5%), a fecal floatation or a direct fecal smear was performed and 2 (66%) of these yielded positive results (1 each of *Eimeria sp.* and *Cryptosporidium sp.*). There was no association between fecal culture or direct fecal smear results and outcome.

### Final Diagnosis

The most common final diagnosis was the presence of at least 1 congenital defect (23 cases, 41%). The most common congenital defects were choanal atresia (8 cases, 35% of congenital defects), ocular malformations (3 cases, 13%), bone deformation (4 cases, 17%),

vulvar malformation (3 cases, 13%), and cardiac malformations (2 cases, 9%). Ocular malformations included congenital cataracts in 1 case, congenital blindness in 1 case and microphthalmus in 1 case. Bone deformations included deformity of the appendicular skeleton in 3 cases and the skull in 1 case. Cardiac malformation included tetralogy of Fallot in 1 case, patent ductus arteriosus in 1 case and ventricular septal defect in 1 case. In 3 cases, more than 1 defect was noted. There was 1 case of hermaphroditism. Absence of choanal atresia was associated with survival ( $P = .001$ , OR: 55.9 [2.5–1,232]).

An ophthalmic lesion was found in 12 cases (21%). The most common lesion was ulcerative keratitis (8 cases, 67% of ophthalmic lesions). Other lesions included 1 case each of cataracts, conjunctivitis, chemosis, and microphthalmus (8% of ophthalmic lesions). In 1 case, 2 lesions were noted. None of the cases diagnosed with an ophthalmic lesion were initially presented with an ophthalmic complaint. There was no association between the presence of an ophthalmic lesion and survival.

A gastrointestinal lesion was diagnosed in 9 cases (16%). The most common diagnosis was meconium impaction (3 cases, 33% of gastrointestinal lesions), followed by peritonitis (2 cases, 22% of gastrointestinal lesions, 1 caused by rupture of a C3 ulcer and 1 from unknown origin) and diarrhea (3 cases, 33% of gastrointestinal lesions, 1 caused by cryptosporidiosis and 2 from unknown origins). There was 1 case of colic of unknown origin (11% of cases with gastrointestinal lesions). There was no association between the presence of a gastrointestinal lesion and survival.

A lesion of the appendicular skeleton was diagnosed in 6 cases (11%). The most common anomaly was the presence of an angular limb deformity (3 cases, 50% of skeletal lesions). In all cases, the angular limb deformity was reported in the front limbs. Other lesions included tendon laxity (1 case, 13% of skeletal lesions), congenital patella luxation (1 case, 13% of skeletal lesions), and incomplete ossification of carpal bones (1 case, 13% of skeletal lesions). There was no association between presence of a skeletal lesion and survival.

In addition to the 9 cases of choanal atresia, 5 animals were diagnosed with other respiratory disease (9%). All 5 of these cases were diagnosed with pneumonia including 1 caused by aspiration and 1 after a rib fracture associated with pneumothorax. There was no association between presence of a respiratory disease (other than choanal atresia) and survival. Animals with a respiratory disease other than choanal atresia that did not survive had significantly higher peripheral blood lymphocytes than animals that survived ( $1,900 \pm 200/\mu$ L and  $500 \pm 200/\mu$ L, respectively,  $P = .017$ ).

In 4 cases (7%), a neurologic lesion was found. In all cases, the lesion was localized to the central nervous system with 2 cases of presumptive hypoxic ischemic encephalopathy (50% of neurologic cases), 1 case of septic meningitis (25% of neurologic cases), and 1 case of central nervous system lesions of unknown



origin (25% of neurologic cases). There was no association between the presence of a neurologic lesion and survival.

### Treatment

Treatment was attempted in 44 cases (79%). Among those cases, 34 received an antimicrobial drug (77% of treated cases) in the hospital. Administration of at least 1 antimicrobial drug was associated with survival ( $P = .019$ , OR: 4.6 [1.4–15.1]). The most commonly used antimicrobial drugs were potassium penicillin G administered IV (25 cases, 74% of cases receiving antimicrobials), TMS administered PO (18 cases, 53% of cases receiving antimicrobials), amikacin administered IV (15 cases, 44% of cases receiving antimicrobials), sodium ceftiofur administered IV (8 cases, 24% of cases receiving antimicrobials), cefotaxime administered IV (5 cases, 15% of cases receiving antimicrobials), ampicillin administered IV (4 cases, 12% of cases receiving antimicrobials), and gentamicin administered IV (3 cases, 9% of cases receiving antimicrobials). Oral administration of TMS was associated with survival ( $P = .016$ , OR: 6.5 [1.3–32.2]). Antimicrobial drugs were given as a combination of 4 antimicrobials in 5 cases (15% of cases receiving antimicrobials), as a combination of 3 antimicrobials in 10 cases (29% of cases receiving antimicrobials), as a combination of 2 antimicrobials in 12 cases (35% of cases receiving antimicrobials), or as a single antimicrobial in 7 cases (21% of cases receiving antimicrobials). The most common combination was the association of potassium penicillin and amikacin, followed by TMS (9 cases, 26% of cases treated with antimicrobials).

In 22 cases (50% of treated cases), an anti-inflammatory drug was administered. In 14 cases (64%), ketoprofen was administered IV, in 9 cases (41%), flunixin meglumine was administered IV and in 1 case (5%), dexamethasone was administered IV. In 2 cases (9%), flunixin meglumine and ketoprofen were administered separately. There was no association between anti-inflammatory treatment and survival.

Intravenous administration of llama plasma was reported in 25 cases (57% of treated cases). There was a significant association between survival and llama plasma administration ( $P = .013$ , OR: 4.9 [1.4–17.7]).

In 15 cases (34% of treated cases), ophthalmic medications were administered. The most common treatment was atropine (10 cases, 67%) followed by bacitracin-neomycin-polymixin ointment (5 cases, 33%), ofloxacin (3 cases, 20%) and artificial tears (3 cases, 20%). There was no association between ophthalmic treatments and survival ( $P = 1.000$ , OR: 0.8 [0.2–4.1]).

Nine cases (20% of treated cases) received oral omeprazole either alone (8 cases; 18%) or in combination with cimetidine (1 case; 2%). Although all of those cases survived to discharge, there was no significant association between administration of gastroprotectant drugs and survival ( $P = .047$ , OR: 10.1 [0.5–188.5]).

All 7 animals with vulvar malformation underwent labial reconstruction. Among those animals, 5 cases (71%) survived to discharge and there was no association between surgery and survival ( $P = 1.000$ , OR: 1.2 [0.2–6.8]).

### Outcome

Thirty-seven animals (66%) survived to discharge and the median duration of hospitalization was 5 days (range: 1–31 days). Hospitalization time was significantly shorter for nonsurvivors ( $P < .01$ ) as 12 animals (63% of nonsurvivors) were euthanized or died within 24 hours of admission. No other statistically significant difference in epidemiologic data between survivors and nonsurvivors was detected.

### Discussion

The main finding of this study is that sick neonatal NWC treated with antimicrobial drugs and plasma have a better outcome than untreated sick neonatal NWC. Furthermore, the presence of choanal atresia is associated with a poor outcome.

Unlike what has been developed in foals, no scoring system has been established in NWC to predict the likelihood of sepsis.<sup>6</sup> Therefore, our definition of sepsis was based on the presence of microbial infection (confirmed by microbial culture) in the presence of SIRS. Multiple criteria for SIRS have been proposed in both adult horses and foals. To date, however, none have been developed after outcomes analysis. Rather, they are used to help clinicians consider various clinical and clinicopathologic findings as separate aspects of a common disease process. Animals that fit our definition of SIRS had significantly higher respiratory rates, more band neutrophils and lower albumin/globulin ratios than animals without SIRS. There was no difference in blood pH between groups. Acid-base disorders are negatively associated with survival in foals and in calves, and it is possible that a similar finding could have been seen in a larger sample.<sup>2,16,17</sup> In our study, we failed to find an association between SIRS and survival.

Although 50% of animals in our study were diagnosed with SIRS, only 16% were diagnosed with sepsis. Other causes of SIRS include trauma, hypothermia, burns, and acidemia. Thus, some animals could have developed SIRS secondary to these nonseptic processes. An additional explanation is that SIRS criteria used in this study might have allowed inclusion of some animals without systemic inflammation, as these criteria are nonspecific. Perhaps, a more rigorous definition of SIRS such as 3 or more (rather than 2 or more) of hyperthermia, hypothermia, tachycardia, tachypnea, leukocytosis, leukopenia, or >10% band neutrophilia should be used. Finally, diagnostic criteria for sepsis could have allowed exclusion of animals that did indeed have sepsis, given the insensitivity of microbial culture (especially blood culture).<sup>18</sup>

Among animals diagnosed with SIRS, survivors had a higher monocyte count. In human medicine, monocyte consumption is increased in patients with severe sepsis and platelet-monocyte aggregate formation is associated with mortality.<sup>19</sup> In our study, we did not observe a difference in platelet count between survivors and nonsurvivors, likely because of the low number of cases; however, in proinflammatory conditions, platelets are activated and release many proinflammatory cytokines that support the recruitment of leukocytes.<sup>20</sup> Therefore, similar mechanisms could explain the association between survival and monocyte count in our patients diagnosed with SIRS.

Bacterial sepsis is associated with poorer outcome in foals, calves, and neonatal NWC.<sup>1,3,5,21–24</sup> Similar to what has been developed for predicting sepsis in foals, a specific scoring system could be useful in predicting outcomes in neonatal NWC.<sup>6</sup> In our study, the criteria that seem to be the most consistent in confirmed septic patients were hyperchloremia, tachycardia, tachypnea, abnormal blood glucose concentration, abnormal neutrophil count, hypernatremia, and abnormal WBC count. Animals with confirmed sepsis had significantly higher respiratory rates, band neutrophils, blood glucose concentration, and gamma-glutamyl-transferase activity. As described above, higher respiratory rate and band neutrophils have been shown to be associated with disease severity and survival in other species.<sup>2,3,16</sup> In calves, increased gamma-glutamyl-transferase is associated with transfer of passive immunity and better outcome.<sup>25</sup> In our study, animals with confirmed sepsis had significantly increased gamma-glutamyl-transferase activity, suggesting that either colostrum was ingested but not protective against sepsis, or that colostrum was not the source of the enzyme activity. Despite the small sample size, there was a significant difference in hemoglobin concentration and total calcium between survivors and nonsurvivors among animals with confirmed sepsis. Similar results have been previously described in gram-negative infections in neonatal NWC.<sup>21</sup> Based on these observations, this work could serve as a starting point to test a neonatal NWC-specific sepsis scoring system that includes the criteria used in this study. Such a study would require a larger population.

In our study, 80% of the blood culture isolates were gram-positive, including *Staphylococcus sp.*, *Streptococcus sp.*, and *Micrococcus sp.* This differs from the findings of Dolente and coworkers, who found that the most commonly identified bacteria from neonatal NWC blood cultures were *E. coli*, *Enterococcus sp.*, *Listeria monocytogenes*, and *Citrobacter sp.*<sup>5</sup> In foals, it has been described that gram-negative organisms are more common and represent 69% of blood culture isolates, with *E. coli* being the most commonly identified.<sup>3,26</sup> Furthermore, recovery of multiple bacteria from blood cultures is associated with poor outcome.<sup>26</sup> This was not the case in our population. Possible explanations for the discrepancy are the low number of positive blood cultures in our sampled population with possible false negative results or potential con-

tamination of some samples causing false positive results. Although possible, the latter explanation seems unlikely as all the animals with positive blood culture had SIRS.

In foals, it has been described that septic neonates develop septic arthritis and umbilical infections.<sup>22,23</sup> This was not the case in our study as none of the animals diagnosed with sepsis developed septic arthritis or an umbilical infection. This suggests that the presence of long-term complications in severely ill NWC could be less than in foals. This, in turn, might justify aggressive initial treatment as our data suggest that if a neonatal NWC survives the primary disease, it is unlikely to develop further complications during hospitalization.

The high number of congenital defects in neonatal NWC has been observed in other studies.<sup>7,8,27–29</sup> The 2 main defects found in this study were, as previously reported, choanal atresia and vulvar deformity.<sup>27,30</sup> Although choanal atresia can be corrected, this study suggests that the presence of this defect is associated with a poor outcome. The poor prognosis of NWC with congenital defects could be associated with the purpose of the animals presented. The presence of congenital defects might limit the value of an animal as some defects, like choanal atresia, have been shown to have a genetic component.<sup>30</sup>

Similarly to what has been observed in foals, the number of ophthalmic lesions in animals presented for nonophthalmic reasons appears high with 21% of our cases exhibiting at least 1 ophthalmic lesion.<sup>31</sup> In another study, ocular manifestations of gram-negative sepsis were detected in up to 50% of septic crias.<sup>21</sup> Taken together, these studies suggest that ophthalmic examinations should be performed routinely in crias, even in the absence of ocular clinical signs. Traumatic lesions appear to be common and are perhaps because of globe anatomy. Consistent with previous reports, both leukogram and serum chemistry abnormalities in sick neonatal NWC were nonspecific and only a few were associated with survival in specific cases.<sup>5</sup>

A surprising finding in our study was the difference in blood glucose concentration between males and females. In neonatal pony foals, shortly after birth, fillies are more insulin-resistant than colts as they have higher plasma insulin concentrations in response to glucose.<sup>32</sup> In our study, plasma insulin concentration was not measured in any case; however, in the absence of other differences (eg, age at admission, severity of disease, or final diagnosis), the marked difference in blood glucose concentration between male and female NWC suggests that, similar to foals, there could be sex-related differences in the secretion or action of insulin, or in some other aspect of glucose metabolism, in early postnatal life.

The pathogens identified in neonatal NWC diarrhea are very diverse, including bacteria, protozoa, viruses, and parasites with no obvious age predisposition.<sup>33,34</sup> *Cryptosporidium sp.* appears to be a commonly identified pathogen of NWC diarrhea.<sup>34,35</sup> In our study, *Cryptosporidium sp.* was identified in 1 case, representing 50% of diarrhea cases. This is consistent with

other studies, in which *Cryptosporidium sp.* was identified between 10% and 100% in cases of diarrhea.<sup>34,35</sup> *Eimeria sp.* was also found in 50% of our diarrhea cases. *Eimeria macusaniensis* has also been described as a major gastrointestinal pathogen for NWC of all ages.<sup>36,37</sup> Furthermore, the presence of *Eimeria sp.* in the intestinal mucosa of neonatal NWC would facilitate the overgrowth of *Clostridium perfringens* with toxin production potentially leading to endotoxemia and death.<sup>38</sup> Although we failed to identify any association between diarrhea and survival, the zoonotic potential and the reported frequency of *Cryptosporidium sp.* as well as the possible severity of *Eimeria sp.*-associated diseases indicate that biosecurity measures should be taken in the management of hospitalized neonatal NWC and that careful attention should be paid to diarrheic patients.<sup>39</sup>

We found that animals that received oral TMS were 6 times as likely to survive. Therefore, although the majority of the bacterial isolates recovered in our study were gram-positive, broad spectrum antimicrobial coverage should be instituted empirically in sick neonatal NWC. It is possible that the positive association between administration of TMS and survival might be because it was initially administered to crias that were not judged to be as ill as those given intravenous antimicrobials, and not because of any property of the drug itself. Although the bioavailability of oral TMS was found to be less than 10% in adult alpacas, the functionally monogastric neonate likely achieves therapeutic plasma concentrations similar to what has been observed in horses and calves with oral bioavailability around 60%.<sup>40-42</sup>

Our results clearly show that early administration of llama plasma is associated with a better outcome, as animals that received plasma were almost 5 times more likely to survive than animals that did not. As previously described in NWC, neonates are born hypogammaglobulinemic and failure of transfer of passive immunity (FTPI) is a determinant factor in neonatal morbidity.<sup>43,44</sup> The use of total protein concentration does not accurately reflect the serum immunoglobulin concentration in neonatal NWC.<sup>5</sup> A diagnosis of FTPI can be made at 48 hours of age if serum immunoglobulin concentration is less than 9 mg/mL;<sup>43</sup> however, a large variation was observed in a study comparing protein electrophoresis, radial immunodiffusion, and immunoturbidimetric assays for measuring serum immunoglobulin in neonatal NWC.<sup>45</sup> It appears that the immunoglobulin measurement in NWC is largely dependent on the assay used and that there is, thus, no widely accepted definition of FTPI in NWC. Although a cut-off point of 10 mg/mL of serum immunoglobulin would seem appropriate, clinical expertise is required to limit over- and underdiagnosis of FTPI and prevent neonatal morbidity.<sup>44</sup> Unfortunately, in the absence of a rigorous definition and diagnostic tests for FTPI, we could not objectively assess the role of FTPI in survival in our study.

In summary, our results suggest that the use of TMS administered PO and llama plasma administered

IV in neonatal NWC could improve survival. This study could serve as a starting point to define a neonatal NWC-specific scoring system to diagnose sepsis. It should also be noted that congenital defects are common, and that ophthalmic lesions are not unusual.

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## Footnote

<sup>a</sup> Prism 5 for Mac OS X; GraphPad Software, Inc, La Jolla, CA

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