Physiologic effects of nasopharyngeal administration of supplemental oxygen at various flow rates in healthy neonatal foals

David M. Wong
Iowa State University, dwong@iastate.edu

Cody J. Alcott
Iowa State University, cjalcott@iastate.edu

Chong Wang
Iowa State University, chwang@iastate.edu

Bonnie L. Hay-Kraus
Iowa State University, bhkraus@iastate.edu

Follow this and additional works at: http://lib.dr.iastate.edu/vdpam_pubs

Part of the Large or Food Animal and Equine Medicine Commons, Statistical Methodology Commons, Veterinary Physiology Commons, and the Veterinary Preventive Medicine, Epidemiology, and Public Health Commons

The complete bibliographic information for this item can be found at http://lib.dr.iastate.edu/vdpam_pubs/77. For information on how to cite this item, please visit http://lib.dr.iastate.edu/howtocite.html.
Physiologic effects of nasopharyngeal administration of supplemental oxygen at various flow rates in healthy neonatal foals

Abstract
Objective—To evaluate the effects of various flow rates of oxygen administered via 1 or 2 nasal cannulae on the fraction of inspired oxygen concentration (\(F_{\text{io}}\)) and other arterial blood gas variables in healthy neonatal foals.

Animals—9 healthy neonatal (3- to 4-day-old) foals.

Procedures—In each foal, a nasal cannula was introduced into each naris and passed into the nasopharynx to the level of the medial canthus of each eye; oxygen was administered at 4 flow rates through either 1 or both cannulae (8 treatments/foal). Intratracheal \(F_{\text{io}}\), intratracheal end-tidal partial pressure of carbon dioxide, and arterial blood gas variables were measured before (baseline) and during unilateral and bilateral nasopharyngeal delivery of 50, 100, 150, and 200 mL of oxygen/kg/min.

Results—No adverse reactions were associated with administration of supplemental oxygen except at the highest flow rate, at which the foals became agitated. At individual flow rates, significant and dose-dependent increases in \(F_{\text{io}}\), \(P_{\text{ao}}\), and oxygen saturation of hemoglobin (\(S_{\text{ao}}\)) were detected, compared with baseline values. Comparison of unilateral and bilateral delivery of oxygen at similar cumulative flow rates revealed no differences in evaluated variables.

Conclusions and Clinical Relevance—Results indicated that administration of supplemental oxygen via nasal cannulae appeared to be a highly effective means of increasing \(F_{\text{io}}\), \(P_{\text{ao}}\), and \(S_{\text{ao}}\) in neonatal foals. These findings may provide guidance for implementation of oxygen treatment in hypoxemic neonatal foals.

Disciplines
Large or Food Animal and Equine Medicine | Statistical Methodology | Veterinary Physiology | Veterinary Preventive Medicine, Epidemiology, and Public Health

Comments
This article is from American Journal of Veterinary Research 71 (2010): 1081, doi: 10.2460/ajvr.71.9.1081. Posted with permission.

Authors
David M. Wong, Cody J. Alcott, Chong Wang, Bonnie L. Hay-Kraus, Benjamin R. Buchanan, and Charles W. Brockus
Physiologic effects of nasopharyngeal administration of supplemental oxygen at various flow rates in healthy neonatal foals

David M. Wong, DVM, MS; Cody J. Alcott, DVM; Chong Wang, PhD; Bonnie L. Hay-Kraus, DVM; Benjamin R. Buchanan, DVM; Charles W. Brockus, DVM, PhD

Objective—To evaluate the effects of various flow rates of oxygen administered via 1 or 2 nasal cannulae on the fraction of inspired oxygen concentration (FIO2) and other arterial blood gas variables in healthy neonatal foals.

Animals—9 healthy neonatal (3- to 4-day-old) foals.

Procedures—In each foal, a nasal cannula was introduced into each naris and passed into the nasopharynx to the level of the medial canthus of each eye; oxygen was administered at 4 flow rates through either 1 or both cannulae (8 treatments/foal). Intratracheal FIO2, intratracheal end-tidal partial pressure of carbon dioxide, and arterial blood gas variables were measured before (baseline) and during unilateral and bilateral nasopharyngeal delivery of 50, 100, 150, and 200 mL of oxygen/kg/min.

Results—No adverse reactions were associated with administration of supplemental oxygen except at the highest flow rate, at which the foals became agitated. At individual flow rates, significant and dose-dependent increases in FIO2, PaO2, and oxygen saturation of hemoglobin (SaO2) were detected, compared with baseline values. Comparison of unilateral and bilateral delivery of oxygen at similar cumulative flow rates revealed no differences in evaluated variables.

Conclusions and Clinical Relevance—Results indicated that administration of supplemental oxygen via nasal cannulae appeared to be a highly effective means of increasing FIO2, PaO2, and SaO2 in neonatal foals. These findings may provide guidance for implementation of oxygen treatment in hypoxic neonatal foals. (Am J Vet Med 2010;71:1081–1088)
alveolar oxygen tension, awareness of potential detrimental effects of prolonged exposure to supraphysiologic concentrations of inspired oxygen administered to foals should be considered. Relatively minor complications associated with supplemental oxygen administration include nasal irritation and rhinitis, airway drying, and stimulation of excessive airway secretions. However, hyperoxemia may result in the generation of reactive oxygen species that are injurious to the lungs and other organs through oxidative stress. For example, it is known that fatal ALI develops in mice that are experimentally exposed to 100% oxygen for 4 days. Furthermore, hyperoxic conditions result in DNA damage in lung tissue of mice, and hyperoxia has been associated with direct toxic effects in the lungs and the development of bronchopulmonary dysplasia in premature infants. In general, to decrease the likelihood of oxidative stress and damage, it is recommended to maintain the FiO₂ at ≤ 60% While the foal is being ventilated and supplemental oxygen is to be administered for a prolonged (> 24 hours) period. Thus, equine clinicians should attempt to maintain an FiO₂ < 60% when administering supplemental oxygen to foals; however, the relationship between flow rate and FiO₂ in neonatal foals is currently not known.

Knowledge of FiO₂ in foals that are being administered supplemental oxygen also would be useful in grading pulmonary disease severity in affected foals. Acute lung injury and ARDS are syndromes of noncardiogenic respiratory failure that have been widely recognized in people and less well described in foals. These syndromes are characterized by diffuse alveolar damage. In horses, diagnosis of these syndromes requires that at least 4 of 5 criteria are met: acute onset of tachypnea and labored breathing at rest; presence of risk factors such as inflammation, infection, sepsis, or trauma; evidence of pulmonary capillary leakage without increased pulmonary capillary pressure (eg, radiographic evidence of diffuse pulmonary infiltrates); evidence of diffuse pulmonary injury; and evidence of inefficient gas exchange (derived via determination of the PaO₂/FiO₂ ratio). With regard to gas exchange, ALI in horses is characterized by a PaO₂/FiO₂ ratio < 300 mm Hg (but > 200 mm Hg), whereas ARDS is characterized by a PaO₂/FiO₂ ratio < 200 mm Hg. However, the PaO₂/FiO₂ ratio has not been specifically investigated in healthy neonatal foals, to our knowledge. In addition, the FiO₂ must be assessed to determine whether a foal has ALI or ARDS. Although the FiO₂ in foals that are breathing room air or being ventilated mechanically may be known, the FiO₂ in foals that are receiving oxygen via intranasal administration has not been determined. The purpose of the study reported here was to evaluate the effects of different flow rates of oxygen administered via 1 or 2 nasal cannulae on the FiO₂ and other arterial blood gas variables in healthy neonatal foals. We sought to establish a dosage protocol for supplemental oxygen delivery via nasal cannulae in foals. We hypothesized that increasing oxygen flow rates would increase FiO₂ and PaO₂ in a dose-dependent manner.

**Materials and Methods**

**Foals**—For the investigation, 9 healthy neonatal foals from Iowa State University’s teaching herd were used. Each foal was considered healthy on the basis of physical examination findings, adequate passive transfer of maternal antibodies (plasma immunoglobulin concentration at 24 hours after birth, ≥ 800 mg/dL), and the absence of any disorders in the dam during pregnancy or parturition. The duration of gestation in all foals was considered normal. Breeds included Thoroughbreds (n = 5) and Quarter Horses and related breeds (4). There were 5 fillies and 4 colts. The foals’ ages ranged from 3 to 5 days (mean ± SD age, 3.9 ± 0.5 days), and weights ranged from 55 to 67 kg (mean weight, 60.4 ± 3.8 kg). The study protocol was approved by the Iowa State University Animal Care and Use Committee.

**Instrumentation**—On the day of the experimental procedure, each foal was weighed, a physical examination was performed, and rectal temperature, heart rate, and respiratory rate were recorded. The hair of the foal was shaved over the left dorsal metatarsal artery to allow for catheter placement. A local anesthetic cream was applied liberally in the region of the dorsal metatarsal artery at least 10 minutes prior to catheter placement. The foal was sedated with diazepam (0.16 mg/kg, IV) and placed in right lateral recumbency. Subsequently, 0.25 mL of 2% lidocaine was injected ID in the skin superficial to the dorsal metatarsal artery. A 20-gauge, 1.5-inch, over-the-needle intraarterial catheter was placed under aseptic conditions into the dorsal metatarsal artery, and a low-volume (0.9-mL) extension set was attached; the apparatus was secured with adhesive and protected with a bandage.

While the foal was still sedated, a polyethylene sampling line (outer diameter, 3 mm) was inserted through the left ventral metatus with the guidance of a preplaced nasotracheal tube (internal diameter, 8 mm); the sampling line was advanced into the trachea to a point just caudal to the thoracic inlet for measurement of PaO₂ and PETCO₂. Placement of the tracheal catheter was confirmed radiographically. Additionally, a nasal cannula (internal diameter, 4 mm) that was made of soft plastic tubing was inserted into each ventral meatus so that the tip of each cannula was positioned in the nasopharynx at the level of the medial canthus of the eye. Each cannula was secured in place with tape and sutures.

**Experimental protocol**—Baseline values of rectal temperature, heart rate, and respiratory rate were recorded at least 1 hour after administration of the sedative, while each foal was standing. Immediately after collection of those baseline data, a baseline arterial blood sample (2 mL) was collected anaerobically through the left ventral metatus with the guidance of a preplaced nasotracheal tube (internal diameter, 8 mm); the sampling line was advanced into the trachea to a point just caudal to the thoracic inlet for measurement of PaO₂ and PETCO₂. Placement of the tracheal catheter was confirmed radiographically. Additionally, a nasal cannula (internal diameter, 4 mm) that was made of soft plastic tubing was inserted into each ventral meatus so that the tip of each cannula was positioned in the nasopharynx at the level of the medial canthus of the eye. Each cannula was secured in place with tape and sutures.

**Materials and Methods**

Foals—For the investigation, 9 healthy neonatal foals from Iowa State University’s teaching herd were
humidifier and flow meter and then connected to a flow splitter and a high-pressure tank that contained medical-grade (100%) oxygen. The tracheal catheter was interfaced with an airway gas analyzer that measured \( F_{\text{io}2} \) and \( \text{PETCO}_2 \). The analyzer was calibrated prior to each procedure by use of gas supplied by the manufacturer. Each foal was observed for coughing, behavioral changes, or adverse effects during the approximately 3-hour experimental procedure period.

Each foal was manually restrained in a standing position in the stall with the mare present. Oxygen administration at the first predetermined rate was initiated, and a minimum of 5 minutes elapsed before measurements were made. A previous study in foals revealed that a 2-minute interval is adequate for equilibration. During the 5-minute equilibration period, the rate at which \( F_{\text{io}2} \) changed along with the fluctuations in \( F_{\text{io}2} \) was subjectively assessed until a stable reading was established. In 5 foals, oxygen was initially administered bilaterally (ie, through both nasal canulae) and 4 rates of oxygen administration were evaluated. The flow rate for each cannula was initially 50 mL of oxygen/kg/min, which was adjusted to 100, 150, and 200 mL of oxygen/kg/min in sequence (total dosages of 100, 200, 300, and 400 mL of oxygen/kg/min, respectively). Those total dosages of supplemental oxygen corresponded to 6, 12, 18, and 24 L/min, respectively, in a 60-kg foal. In those 5 foals, oxygen was subsequently administered in the same sequence of increasing flow rates through only 1 randomly selected (ie, left or right) cannula (total dosages of 50, 100, 150, and 200 mL of oxygen/kg/min). Those total dosages of supplemental oxygen corresponded to 3, 6, 9, and 12 L/min, respectively, in a 60-kg foal. In the other 4 foals, oxygen was initially administered bilaterally (ie, through both nasal canulae) and the same 4 rates of oxygen administration were evaluated. However, the flow rate for each cannula was initially 200 mL of oxygen/kg/min, which was adjusted to 150, 100, and 50 mL of oxygen/kg/min in sequence (total dosages of 400, 300, 200, and 100 mL of oxygen/kg/min, respectively). In those 4 foals, oxygen was subsequently administered in the same sequence of decreasing flow rates through only 1 randomly selected (ie, left or right) cannula (total dosages of 200, 150, 100, and 50 mL of oxygen/kg/min). On the day that a foal was to be used in an experimental procedure, it was allocated to receive one or the other of the dosage regimens on an alternating schedule (ie, evaluated foals 1, 3, 5, 7, and 9 received the increasing flow rate regimen and evaluated foals 2, 4, 6, and 8 received the decreasing flow rate regimen).

For all foals, a minimum of 5 minutes was allowed to elapse before measurements were made at each flow rate; data collection at each flow rate was completed within 10 minutes. If a foal became excited during handling, it was allowed to regain a quiet demeanor with minimal restraint prior to collection of data. At each flow rate, measurements included assessments of rectal temperature, heart rate, and respiratory rate and the \( F_{\text{io}2} \) and \( \text{PETCO}_2 \) values were obtained from a gas sample aspirated through the tracheal catheter; an arterial blood sample (2 mL) was collected and analyzed, as described. At the end of data collection at each oxygen flow rate, the foal was disconnected from all monitors and external devices and was allowed free access to the mare for at least 10 minutes. Prior to administration of oxygen at the various oxygen flow rates, the \( F_{\text{io}2} \) was evaluated to ensure that no residual effects from previous oxygen administration were present.

**Statistical analysis**—All data are reported as mean ± SD. A repeated-measures ANOVA was applied to each of the response variables (rectal temperature, heart rate, respiratory rate, \( F_{\text{io}2} \), pH, \( \text{PaO}_2 \), \( \text{Paco}_2 \), \( \text{PETCO}_2 \), blood bicarbonate concentration, \( \text{TCO}_2 \), \( \text{SaO}_2 \), and \( \text{PaO}_2/\text{FiO}_2 \) ratio) by use of computer software. For each response variable, an \( F \) test with Kenward and Roger adjustment to degrees of freedom was used to test for differences among the variable means of 9 data groups (baseline values and 8 treatment groups [bilateral administration of oxygen at rates of 50, 100, 150, or 200 mL/kg/min and unilateral administration of oxygen at rates of 50, 100, 150, and 200 mL/kg/min]) with significance set at a value of \( P < 0.05 \). When a significant \( F \) test was calculated, post hoc Tukey \( t \) tests were applied for pairwise comparisons between treatment means. To evaluate the effects of oxygen flow rate on 2 particular response variables, \( \text{FiO}_2 \) and \( \text{PaO}_2 \), a linear regression analysis with repeated measures was applied to each of the responses by use of computer software. The coefficient of determination also was calculated for the regression model for each response variable. In addition, the correlation coefficient between \( \text{PaCO}_2 \) and \( \text{PETCO}_2 \) was estimated and tested for significance. A value of \( P < 0.05 \) was considered significant.

**Results**

There were no complications associated with instrumentation or data collection in any foal. Most foals tolerated handling and restraint calmly, but some foals became excited; those foals were allowed to regain a quiet demeanor prior to collection of data. No adverse effects were observed during administration of oxygen at the lower flow rates (50, 100, and 150 mL/kg/min). However, foals developed signs of agitation during oxygen administration at the highest flow rate (200 mL/kg/min) exemplified by head tossing, rubbing of the muzzle, and hyperesthesia, regardless of whether oxygen was administered via 1 or both nasal canulae. There were no significant differences among foals with regard to rectal temperature, heart rate, or respiratory rate at any oxygen flow rate, compared with baseline values (Table 1). Likewise, comparisons of data obtained at the various oxygen flow rates revealed no significant difference in rectal temperature, heart rate, or respiratory rate, with the exception of a significant (\( P = 0.04 \)) difference in respiratory rate between unilateral administration of oxygen at a rate of 50 mL/kg/min and bilateral administration of oxygen at a rate of 100 mL/kg/min.

Data regarding \( \text{FiO}_2 \), pH, \( \text{PaO}_2 \), \( \text{Paco}_2 \), \( \text{PETCO}_2 \), blood bicarbonate concentration, \( \text{TCO}_2 \), \( \text{SaO}_2 \), and \( \text{PaO}_2/\text{FiO}_2 \) ratio were obtained for all foals at each oxygen flow rate (Table 2). The \( \text{FiO}_2 \) measurement fluctuated, depending on the foal’s activity and respiratory rate, but generally increased and reached a plateau within
30 to 60 seconds of the commencement of oxygen administration at each flow rate. Compared with baseline values, significant (P < 0.001) increases in FiO₂, PaO₂, and SaO₂ were detected at all oxygen flow rates. Other significant differences from baseline values included changes in pH during unilateral delivery of oxygen at a rate of 200 mL/kg/min (P = 0.04) and in PaCO₂ during unilateral delivery at rates of 100 and 200 mL/kg/min and during bilateral delivery at a rate of 100 mL/kg/min (P ≤ 0.04). Compared with baseline values, there were no significant differences in values of PetCO₂, blood bicarbonate concentration, and TCO₂ at any flow rate, regardless of delivery method.

Administration of supplemental oxygen increased FiO₂ and PaO₂ in a dose-dependent manner. However, at any given flow rate, measured variables were not affected by delivery method (ie, unilateral or bilateral administration). More specifically, values of the measured variables obtained during unilateral administration of 100 mL of oxygen/kg/min did not differ significantly from those obtained during bilateral administration of 50 mL of oxygen/kg/min; similarly, values of the measured variables obtained during unilateral administration of 200 mL of oxygen/kg/min did not differ significantly from those obtained during bilateral administration of 100 mL of oxygen/kg/min.

In addition, comparisons among individual oxygen flow rates delivered by either method revealed significant (P ≤ 0.02) differences in FiO₂, with the exception of 100 mL/kg/min administered bilaterally versus 150 mL/kg/min administered unilaterally, 150 mL/kg/min administered bilaterally versus 200 mL/kg/min administered unilaterally, and 150 mL/kg/min administered bilaterally versus 200 mL/kg/min administered unilaterally. Also, comparisons among individual oxygen flow rates delivered by either method revealed significant (P ≤ 0.03) differences in PaO₂, with the exception of 100 mL/kg/min administered bilaterally versus 150 mL/kg/min administered bilaterally 100 mL/kg/min administered bilaterally versus 150 mL/kg/min admin-

Table 1—Mean ± SD respiratory rate, heart rate, and rectal temperature in 9 healthy neonatal foals before (baseline) and during administration of supplemental oxygen at various flow rates via 1 or 2 nasal cannulae (unilateral and bilateral oxygen delivery, respectively).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>Unilateral (mL/kg/min)</th>
<th>Bilateral (mL/kg/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>50</td>
<td>100</td>
<td>150</td>
</tr>
<tr>
<td>Respiratory rate (breaths/min)</td>
<td>39</td>
<td>±10</td>
<td>47</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>94</td>
<td>±10</td>
<td>101</td>
</tr>
<tr>
<td>Temperature (°C)</td>
<td>38.4±0.4</td>
<td>38.7±0.3</td>
<td>38.6±0.3</td>
</tr>
</tbody>
</table>

*Within a row, mean values with different superscript letters differ significantly (adjusted P < 0.04).

Table 2—Mean ± SD arterial blood gas and tracheal gas variables in 9 healthy neonatal foals before (baseline) and during administration of supplemental oxygen at various flow rates via 1 or 2 nasal cannulae (unilateral and bilateral oxygen delivery, respectively).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>Unilateral (mL/kg/min)</th>
<th>Bilateral (mL/kg/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>50</td>
<td>100</td>
<td>150</td>
</tr>
<tr>
<td>FiO₂ (%)</td>
<td>18.0±3.4b</td>
<td>23.0±1.4</td>
<td>38.9±2.1</td>
</tr>
<tr>
<td>pH</td>
<td>7.43±0.02</td>
<td>7.41±0.02</td>
<td>7.41±0.01</td>
</tr>
<tr>
<td>PaO₂ (mm Hg)</td>
<td>92.5±8.2a</td>
<td>139.5±13.2</td>
<td>175.2±14.6</td>
</tr>
<tr>
<td>PaCO₂ (mm Hg)</td>
<td>47.7±2.8b</td>
<td>69.7±2.4</td>
<td>50.5±2.3</td>
</tr>
<tr>
<td>PvCO₂ (mm Hg)</td>
<td>53.9±3.3</td>
<td>52.6±4.9</td>
<td>52.7±7.8</td>
</tr>
<tr>
<td>Bicarbonate (mmol/L)</td>
<td>31.4±2.7</td>
<td>30.7±1.3</td>
<td>31.2±1.3</td>
</tr>
<tr>
<td>TCO₂ (mmol/L)</td>
<td>33.3±2.0</td>
<td>32.9±1.5</td>
<td>33.8±1.3</td>
</tr>
<tr>
<td>SaO₂ (%)</td>
<td>96.7±0.7b</td>
<td>98.5±0.3b</td>
<td>99.2±0.1b</td>
</tr>
<tr>
<td>PaO₂/FiO₂ ratio</td>
<td>514±39</td>
<td>594±73c</td>
<td>569±61</td>
</tr>
</tbody>
</table>

*Within a row, mean baseline value and and values at individual oxygen flow rates that have different superscript letters differ significantly (P < 0.05).  †† Within a row, FiO₂ or PaO₂ at individual oxygen flow rates that have different superscript letters differ significantly (P ≤ 0.02 and P ≤ 0.03, respectively). *Within a row, mean ratio values at individual oxygen flow rates that have different superscript letters differ significantly (P < 0.05).

Table 3—Linear regression analysis results for FiO₂ and PaO₂ in 9 healthy neonatal foals that were administered supplemental oxygen at various flow rates via 1 or 2 nasal cannulae (unilateral and bilateral oxygen delivery, respectively).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Delivery method</th>
<th>Derived equation</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FiO₂</td>
<td>Unilateral</td>
<td>FiO₂ = 17.33 + (0.1297 × oxygen flow/cannula)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>Bilateral</td>
<td>FiO₂ = 17.33 + (0.2665 × oxygen flow/cannula)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>PaO₂</td>
<td>Unilateral</td>
<td>PaO₂ = 91.93 + (0.8247 × oxygen flow/cannula)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>Bilateral</td>
<td>PaO₂ = 91.93 + (1.4513 × oxygen flow/cannula)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>
istered unilaterally, 150 mL/kg/min administered bilaterally versus 200 mL/kg/min administered unilaterally, and 150 mL/kg/min administered unilaterally versus 200 mL/kg/min administered unilaterally. With regard to the PaO₂/FIO₂ ratio, a significant difference between 200 mL of oxygen/kg/min administered bilaterally and 50 mL of oxygen/kg/min administered unilaterally \( (P = 0.03) \) and between 50 mL of oxygen/kg/min administered unilaterally and 150 mL of oxygen/kg/min administered unilaterally \( (P = 0.04) \) was detected. No significant differences in pHa, PaCO₂, PetCO₂, blood bicarbonate concentration, and TCO₂ were identified among individual oxygen flow rates.

Linear regression analysis yielded equations for FIO₂ and PaO₂ associated with unilateral or bilateral oxygen delivery (Table 3). The coefficient of determination was 0.9223 for the regression model of FIO₂ and 0.8632 for the regression model of PaO₂. In other words, the linear regression model could explain 92.23% and 86.32% of the variation in FIO₂ and PaO₂, respectively. There was a significant correlation \( (r = 0.497; P < 0.001) \) between PaCO₂ and PetCO₂.

### Discussion

Results of the study reported here indicated that PaO₂ and FIO₂ increased in a dose-dependent manner as the flow of supplemental oxygen into the nasopharynx of healthy neonatal foals increased. Intuitively, this was an expected response to oxygen administration. Nevertheless, these findings support the rationale for nasopharyngeal administration of supplemental oxygen in hypoxemic foals and provide a dosage guide for oxygen administration as well as expected changes in PaO₂ and FIO₂ in response to treatment with oxygen in healthy neonatal foals. Also, data obtained in the present study indicated that measured variables did not differ when oxygen was administered at a specific flow rate through 1 or 2 nasal cannulae; this suggests that oxygen administration via 1 nasal cannula can provide adequate changes in PaO₂ and FIO₂ within certain flow rate limits. If a maximum increase in FIO₂ in healthy neonatal foals is desired, nasopharyngeal administration of oxygen at a rate of 200 mL/kg/min simultaneously in each nares (400 mL/kg/min total) can increase the FIO₂ to approximately 75%.

Physiologically, nasopharyngeal administration of oxygen increases the FIO₂, thereby allowing higher concentrations of oxygen to reach the alveoli; consequently, this creates a higher concentration gradient of oxygen between the alveoli and arterial blood within the pulmonary vasculature. The increase in FIO₂ is a result of direct flow of supplemental oxygen into the trachea and the capacity of the nasopharynx to act as a reservoir for inspired air (ie, oxygen). During supplemental oxygen administration, the nasopharynx is progressively filled with higher concentrations of oxygen, particularly during the pause in air movement between expiration and inspiration. The fixed volume of air contained within the nasopharynx is gradually filled with supraphysiologic concentrations of oxygen, thereby increasing the FIO₂ upon inspiration. The pause between expiration and inspiration will vary with the respiratory rate; therefore, higher oxygen flow rates may be necessary to achieve anticipated FIO₂ values in animals with higher respiratory rates. This is supported by the fact that FIO₂ is inversely related to respiratory rate in infants receiving oxygen via intranasal administration. Other factors that affect the FIO₂ in infants and foals include cannula flow rate, the FIO₂ in the cannula gas flow, patency of cannula openings, placement of the nasal cannula, patient’s body weight, minute ventilation, and the relative duration of inspiration and expiration.

On the basis of the present study’s results, it is apparent that there is a rapid change in FIO₂ and PaO₂ in response to administration of supplemental oxygen in healthy neonatal foals. Increases in FIO₂ were observed within 30 to 60 seconds after commencement of oxygen administration, similar to findings in other species. In addition, based on the rapid decrease in FIO₂ once supplemental oxygen administration was discontinued, clearance of oxygen was rapid—a factor that should be considered when administering supplemental oxygen in a clinical setting. Another point of interest was the irritation or discomfort caused by unilateral or bilateral intranasal administration of oxygen at a flow rate of 200 mL/kg/min in the foals in the present study. However, the authors have administered supplemental oxygen at flow rates > 200 mL/kg/min to ill neonatal foals without observing adverse effects. It is likely that ill neonatal foals are lethargic and less responsive to the irritation caused by high rates of oxygen administration. Nonetheless, if nasal irritation or discomfort develops during unilateral administration of oxygen at a specific flow rate, distribution of the same total flow rate through 2 nasal cannulae may be a viable alternative delivery method. Despite the high flow rates of oxygen, no retardation of exhalation or trapping of carbon dioxide was evident in the foals of the present study. Although there was a significant increase in PaCO₂, during unilateral administration of oxygen at flow rates of 100 and 200 mL/kg/min and during bilateral administration at a flow rate of 200 mL/kg/min, compared with baseline values, the degree of hypercapnea was considered clinically unimportant in the healthy study foals. Moreover, no significant differences were detected between baseline PetCO₂ and PetCO₂ values at the individual oxygen flow rates. However, in infant studies, the administration of oxygen via nasal cannula generated positive end-expiratory pressure, depending on the size of the nasal cannula (with respect to infant size) and flow rate. Therefore, it is possible that positive end-expiratory pressure can be generated in neonatal foals receiving supplemental oxygen via nasal cannula, particularly in ill foals that have decreased or weakened respiratory effort as a result of exhaustion or weak contraction of respiratory muscles. This can potentially result in elevated airway pressure with both positive (increased functional residual capacity, alveolar recruitment, and improvement in ventilation-perfusion matching) and negative (retention of carbon dioxide and hypercapnia) consequences, especially at high oxygen flow rates.

The relationship and correlation between PaCO₂ and PetCO₂ has been examined in various studies in efforts to use PetCO₂ as a less invasive means of monitoring PaCO₂ in clinical cases such as emergency room.
admissions and during anesthesia; overall correlation between these 2 variables has been high in several studies in people. Likewise, a significant correlation between PaCO\textsubscript{2} and PETCO\textsubscript{2} was determined in the healthy neonatal foals used in the present study. However, the actual correlation between PETCO\textsubscript{2} and PaCO\textsubscript{2} was only moderate (r = 0.497). This can be partially explained by the fact that administration of supplemental oxygen had a significant effect on PaCO\textsubscript{2} but not on PETCO\textsubscript{2}. Therefore, oxygen administration accounted for part of the variation in PaCO\textsubscript{2} that was not correlated with PETCO\textsubscript{2}. Nevertheless, it is possible that PETCO\textsubscript{2} could be used to reflect and monitor changes in PaCO\textsubscript{2} in ill foals, although further studies are necessary. It should be noted that the gas sample used for measurement of PETCO\textsubscript{2} in the present study was aspirated from the intrathoracic portion of the trachea rather than from the nares or nasopharynx, which are more easily accessible locations and are more likely to be used for PETCO\textsubscript{2} measurement in ill foals. The possibility that the anatomic location at which PETCO\textsubscript{2} is measured may change PETCO\textsubscript{2} values slightly requires further investigation.

One important reason to attempt to estimate FIO\textsubscript{2} is the ability to use the Pao\textsubscript{2}:FIO\textsubscript{2} ratio to evaluate pulmonary gas exchange in hypoxemic patients and to assess respiratory tract disease severity. Acute lung injury is defined as a Pao\textsubscript{2}:FIO\textsubscript{2} ratio < 300 mm Hg (but > 200 mm Hg), whereas ARDS is defined as a Pao\textsubscript{2}:FIO\textsubscript{2} ratio < 200 mm Hg (along with other previously described criteria). Specific modifications to the definition of ALI and ARDS have been made to account for the documented changes in gas exchange efficiency that develop in neonatal foals (< 7 days old) as well as in infants. In the consensus definitions of ALI and ARDS in veterinary medicine, the threshold of equine neonatal ALI is defined as a Pao\textsubscript{2}:FIO\textsubscript{2} ratio of < 250 mm Hg, whereas equine neonatal ARDS is defined as a Pao\textsubscript{2}:FIO\textsubscript{2} ratio of < 160 mm Hg at 4 days after birth. The Pao\textsubscript{2}:FIO\textsubscript{2} ratio that was considered normal in that report was a value > 400 mm Hg. In the study reported here, the mean Pao\textsubscript{2}:FIO\textsubscript{2} ratio in healthy neonatal foals (mean age, 3.9 days) ranged from 501 to 594 mm Hg and was established in standing foals that were, at times, receiving intranasal administration of supplemental oxygen. The difference in the Pao\textsubscript{2}:FIO\textsubscript{2} ratio between the present and previous studies may be explained, in part, by the fact that the consensus definitions were based on arterial blood gas values from foals that were breathing room air in lateral recumbency, a position that is known to decrease Pao\textsubscript{2} values. Overall, only a few veterinary reports have documented the use of the Pao\textsubscript{2}:FIO\textsubscript{2} ratio in foals, and accordingly, the use of the Pao\textsubscript{2}:FIO\textsubscript{2} ratio in neonatal foals with pulmonary diseases is in its infancy. The information obtained from the study of this report confirmed that the mean Pao\textsubscript{2}:FIO\textsubscript{2} ratio in healthy neonatal foals that are breathing room air should be approximately 500 mm Hg (range, 477 to 594 mm Hg). Furthermore, this information can be used to estimate the FIO\textsubscript{2} in hypoxemic neonatal foals, which will facilitate the further investigation of the Pao\textsubscript{2}:FIO\textsubscript{2} ratio in clinical cases. Clearly, additional studies are necessary to assess Pao\textsubscript{2}:FIO\textsubscript{2} ratio values in foals with ALI or ARDS and evaluate the sensitivity and specificity of the extrapolated threshold ratios for diagnosis of ALI and ARDS in neonatal foals.

Another reason to be aware of the FIO\textsubscript{2} induced by administration of supplemental oxygen in neonatal foals is to avoid development of oxygen toxicosis as a result of high flow rates of oxygen. On the basis of the findings of the present study, it is unlikely that the recommended maximum FIO\textsubscript{2} (60%) during supplemental oxygen administration or mechanical ventilation would be exceeded, particularly with unilateral administration of the oxygen dosages investigated. However, in severely hypoxemic neonatal foals, bilateral nasal cannulae have been used to administer oxygen in combined flow rates of up to 30 L/min (eg, administration of 250 mL of oxygen/kg/min in each naris in a 60-kg foal). The maximum mean FIO\textsubscript{2} measured in the present study was approximately 75% when foals received oxygen intranasally at a rate of 200 mL/kg/min bilaterally. Maintenance of a unilateral oxygen flow rate of ≤ 200 mL/kg/min or a bilateral flow rate of ≤ 150 mL/kg/min should avoid excessively high FIO\textsubscript{2} concentrations in neonatal foals, if prolonged intranasal administration of oxygen is necessary. The guidelines set forth by the Society of Critical Care Medicine recommend that the lowest possible FIO\textsubscript{2} should be used at all times to achieve treatment goals and should not exceed 50% in patients with respiratory failure.

Although it is important to be cognizant of the FIO\textsubscript{2} to avoid development of oxygen toxicosis and to evaluate the efficacy of pulmonary gas exchange, the clinical endpoints of supplemental oxygen administration are improved PaO\textsubscript{2} and SaO\textsubscript{2}. The value of PaO\textsubscript{2} in foals receiving unilateral administration of oxygen intranasally at a flow rate of 200 mL/kg/min in the present study (mean PaO\textsubscript{2}, 269.7 mm Hg) was similar to the finding in slightly younger foals receiving unilateral administration of oxygen intranasally at a flow rate of 10 L/min in another study (mean PaO\textsubscript{2}, 268.5 mm Hg). At the flow rates used in the present study, the mean maximum PaO\textsubscript{2} values that could be achieved via unilateral and bilateral intranasal oxygen administration in healthy neonatal foals are approximately 270 and 375 mm Hg, respectively. However, this information is of limited clinical use in ill neonatal foals with compromised cardiopulmonary function (ie, diffusion impairment, ventilation-perfusion mismatch, or intrapulmonary or intracardiac right-to-left shunting of blood) that results in impaired alveolar gas exchange and hypoxemia. For example, in a 1 study, the mean PaO\textsubscript{2} value in response to administration of supplemental oxygen via facemask was significantly decreased in abnormal neonatal foals, compared with the value in similarly treated healthy neonatal foals (mean PaO\textsubscript{2}, 129.4 and 312.8 mm Hg, respectively). Therefore, adjustment of the flow rate of supplemental oxygen in ill foals with cardiopulmonary disease should be based on evaluation of the response to supplemental oxygen administration (eg, measurement of PaO\textsubscript{2} and SaO\textsubscript{2}). Physiologically, as PaO\textsubscript{2} increases, SaO\textsubscript{2} concomitantly increases. Not surprisingly, SaO\textsubscript{2} increased from baseline (as PaO\textsubscript{2} increased) during oxygen administration at all of the flow rates used in the present study. Recommended therapeutic goals of oxygen administration in neon-
tal foals include maintenance of \( P_{aO_2} \) at 80 to 110 mm Hg and \( SaO_2 > 90\% \).1,2,8

In the study reported here, other significant differences in measured variables were detected when findings at the individual oxygen flow rates were compared with baseline values or with one another. Compared with the baseline value, there was a significant decrease in pH during unilateral administration of oxygen at a rate of 200 mL/kg/min, but the difference between the 2 values (0.024) is not likely to have any clinical importance. Furthermore, the exact reason why respiratory rate during unilateral administration of 100 mL of oxygen/kg/min and during bilateral administration of 100 mL of oxygen/kg/min differed significantly is unknown. Although restraint of the foals could have resulted in excitement, no specific explanation could be provided for this observation.

One distinct limitation of the present study that should be highlighted was the varied temperaments of the foals. Most foals tolerated handling and restraint without resentment. However, some foals became very excited upon handling, which increased heart and respiratory rates and potentially altered the variables being measured. In particular, \( FIO_2 \) appeared to fluctuate the most, depending on the foal’s activity and respiratory rate. If a foal was excited, the investigators allowed the foal to regain a quiet demeanor with minimal restraint prior to collection of data. Nonetheless, the few highly anxious foals may have provided skewed results. Another limitation of the study was that the foals were all in good health, and the response to nasopharyngeal administration of supplemental oxygen may be different in ill neonatal foals with pulmonary disease. Evaluation of the response to nasopharyngeal administration of oxygen at different flow rates in ill neonatal foals, including those with pulmonary diseases, is warranted.

Results of the present study have indicated that nasopharyngeal administration of supplemental oxygen effectively increases \( FIO_2 \), \( P_{aO_2} \), and \( SaO_2 \) and allows clinicians to estimate \( FIO_2 \) in neonatal foals. Previously recommended oxygen flow rates in foals vary from 2 to 15 L/min, depending on the size, needs, and response of the foal.1,11,13 Information obtained from the present study has provided linear regression equations to estimate the \( FIO_2 \) (based on body weight) in neonatal foals in response to different oxygen flow rates and to predict the response (ie, \( P_{aO_2} \)) to a specific oxygen flow rate in healthy neonatal foals and subsequently compare this theoretical response with the response of an ill foal. It should be emphasized that the findings of the present study and the linear regression equations are estimates of \( FIO_2 \) and \( P_{aO_2} \) in response to nasopharyngeal administration of supplemental oxygen in healthy standing neonatal foals and should not be used as absolute therapeutic values or goals. Adequate response to oxygen administration is best evaluated by monitoring arterial blood gas variables such as \( P_{aO_2} \) and \( SaO_2 \) and the clinical response of the patient.

References

20. Locke RG, Wolfson MR, Shaffer TH, et al. Inadvertent adminis-


