Effect of gastric ulceration on physiologic responses to exercise in horses

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Objective—To develop a protocol to induce and maintain gastric ulceration in horses and to determine whether gastric ulceration affects physiologic indices of performance during high-speed treadmill exercise.

Animals—20 healthy Thoroughbreds.

Procedures—Each horse was acclimatized to treadmill exercise during a 2-week period. Subsequently, baseline data were collected (day 0) and each horse began an incrementally increasing exercise training program (days 1 through 56). Beginning on day 14, horses were administered omeprazole (4 mg/kg, PO, q 24 h until day 56) or no drug (10 horses/group) and underwent alternating 24-hour periods of feeding and feed withholding for 10 days to induce gastric ulceration. Extent of gastric ulceration was assessed weekly thereafter via gastroscopy. Physiologic indices of performance were measured at days 0 and 56. Gastric ulceration and exercise performance indices were compared within and between groups.

Results—In untreated horses, gastric ulcers were induced and maintained through day 56. Gastric ulcer formation was prevented in omeprazole-treated horses. There were significant interactions between time (pre- and posttraining data) and treatment (nonulcer and ulcer groups) for mass-specific maximal O$_2$ consumption (VO$_{2\text{max}}$/M$_b$) and mass-specific maximal CO$_2$ production (VCO$_{2\text{max}}$/M$_b$). Post hoc analysis revealed a difference between groups for VO$_{2\text{max}}$/M$_b$ at day 56. Within-group differences for VO$_{2\text{max}}$/M$_b$ and VCO$_{2\text{max}}$/M$_b$ were detected for omeprazole-treated horses, but not for the horses with ulcers.

Conclusions and Clinical Relevance—In horses, gastric ulcers were induced and maintained by use of alternating periods of feeding and feed withholding in association with treadmill exercise (simulated racetrack training). Gastric ulcers adversely affected physiologic indices of performance in horses. (Am J Vet Res 2009;70:787–795)

The availability of endoscopes of sufficient length to allow visual examination of the stomachs of adult horses has led to identification of gastric ulcers in many performance horses. 1-4 In 2 endoscopic surveys of the stomachs of Thoroughbreds in active training, the prevalence of gastric ulceration was estimated at 82% and 93%. 4,5 In horses, gastric ulceration has been linked with clinical signs related to the digestive system and to poor performance. 3,4,6 However, the evaluation of performance in horses with ulcers has been subjective and largely based on trainers’ expectations. 1 Studies performed at racetracks with privately owned horses are difficult to control because of variations in management that are almost impossible to standardize. Speed and distance over which a horse runs, characteristics of the track, and weights of riders are also difficult to standardize. Additionally, quantitative evaluation of physiologic variables related to performance requires sophisticated equipment, which cannot be used practically in the racetrack setting.

To evaluate the effects of gastric ulcers and anti-ulcer medication on athletic performance, a reproducible means for experimental induction of gastric ulceration that is similar to ulceration that develops in performance horses is required. Gastric ulceration has been experimentally induced by alternately providing and withholding feed from horses. 1 However, experimentally induced ulcers appear healed endoscopically in most horses within 7 days following the final period of feed withholding, 7 whereas spontaneous resolution of naturally occurring ulcers is uncommon in horses maintained in active training. Administration of NSAIDs induces ulcers in ponies experimentally, 8,9 although gastric ulceration in horses in race training has not

Abbreviations

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<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>HR$_{\text{max}}$</td>
<td>Maximum heart rate</td>
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<tr>
<td>VCO$_{2\text{max}}$/M$_b$</td>
<td>Mass-specific maximal CO$_2$ production</td>
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<tr>
<td>VO$_{2\text{max}}$/M$_b$</td>
<td>Mass-specific maximal O$_2$ consumption</td>
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been associated with the administration of NSAIDs.  

Spontaneous healing of ulcers following induction of ulceration via feed withholding or NSAID administration would preclude evaluation of the effects of gastric ulceration or treatments with antiulcer medication on performance. Gastric ulceration has also been induced and maintained in horses via simulated race training at the racetrack; however, the interval required for unfit horses to develop stable gastric ulceration after the start of the simulated race training was 21 days.

The objective of the study reported here was to develop a protocol to induce and maintain gastric ulceration in horses by mimicking a racetrack environment and maintaining precise control of exercise, feeding, and management to determine whether gastric ulceration affects physiologic indices of performance assessed during high-speed treadmill exercise. The hypothesis of the study was that gastric ulceration in horses will affect physiologic indices of performance during high-speed treadmill exercise.

**Materials and Methods**

**Horses and study design**—Twenty 2- to 4-year-old Thoroughbreds (10 males and 10 females) were used in the study. The horses were considered healthy on the basis of results of physical and lameness examinations, a CBC, and serum biochemical analyses; no evidence of gastric ulceration was detected via endoscopy in any horse. Horses were housed in individual stalls at the Veterinary Medical Teaching Hospital, University of California, Davis. All horses had free access to water and were fed 7 kg of grass hay and 8 kg of alfalfa daily (divided into 3 meals); an additional 5 kg of oats and 1 kg of sweet feed (corn, oats, barley, and molasses) were added to the diet once the horses began their exercise program. Horses were randomly allocated to 1 of 2 groups (10 horses/group) in which they would or would not receive treatment with omeprazole to prevent ulcer development during the gastric ulcer induction procedures. Horses had previously been broken to ride and had been engaged in light exercise prior to beginning the exercise program on the treadmill. All horses were acclimatized to the treadmill for approximately 14 days prior to the experiment. Baseline performance data were collected on day 0. From days 1 through 56 of the experiment, horses participated in an incrementally increasing exercise training program on a treadmill. From days 14 through 24, all horses underwent alternating 24-hour periods of feeding and feed withholding to induce gastric ulceration. Horses were examined endoscopically every 7 days from the start of the experiment (day 1). Horses were weighed daily by use of an electronic balance. All procedures were approved by the Institutional Animal Care Use Committee at the University of California, Davis.

**Exercise protocol**—During the acclimatization and experimental period, horses ran on the treadmill for 9 days of each week; on the days that they were not exercised, horses were either hand walked or turned out in round corrals (radius, 5 m). Horses were shod in aluminum shoes with polyurethane soles. To simulate the weight of a rider, a custom-made pad and surcingle that carried 50 kg of lead blocks were attached to each horse before it ran on the treadmill. At the end of each session, horses were removed from the treadmill, the surcingle and weights were removed, and the horses were cooled down by use of a water shower and hand walked for approximately 30 minutes. During the 14-day acclimatization period, horses were exercised for a total of 10 days. On the first 4 days, horses were walked at 2 m/s for 700 m and then trotted at 4 m/s for a further 1,400 m. Galloping was included in the remainder of the acclimatization period as follows: a 2-minute gallop at 7 m/s for 3 days, followed by a 3-minute gallop at 8 m/s for 3 additional days.

Following the initial performance evaluation at the end of the acclimatization period (day 0), horses entered a standardized treadmill exercise training program. Horses initially walked (2 m/s) for 4 minutes and trotted (4 m/s) for 3.5 minutes, after which they galloped for 3 minutes at a speed that elicited 80% of their HRmax (generally 10 to 11 m/s on a horizontal treadmill platform). The HRmax was determined for each horse while it ran at 10 m/s on an inclined treadmill platform (inclined to 0%, 3%, 6%, and 10% gradient). Heart rate was determined after steady state had been reached (2 to 3 minutes), and HRmax was identified as the heart rate that did not increase with increasing gradient. As training progressed, some horses required an increase in speed at the 10% gradient to attain HRmax. The HRmax was determined 8 days before day 0 and then once weekly. Heart rate was measured by use of a polar telemetered signal of a bipolar ECG measured with electrodes attached to the girth.

**Gastroendoscopy and ulcer induction**—Prior to endoscopic examination, food and water were withheld from each horse for 18 to 24 hours and 6 hours, respectively. Each horse was sedated with xylazine hydrochloride (0.5 mg/kg, IV); an endoscope (length, 3 m; diameter, 9.9 mm) was passed into the stomach. Following inflation of the stomach with air, the surface was cleared of feed material by use of a jet of water passed down the biopsy port. The stomach was systematically evaluated, and images of the squamous portion of the stomach were recorded on videotape.

Four regions of the squamous portion of the stomach (right side of the stomach, greater curvature, lesser curvature, and dorsal aspect of the fundus) were evaluated and graded by one of the authors (JEN), who was unaware of the group assignment of the horse. Severity of ulceration was graded on a scale of 0 to 5 as follows: 0 = normal mucosa; 1 = mucosal erosions (hyperemia with or without hyperkeratosis or superficial mucosal erosions); 2 = mild ulceration (multifocal or generalized areas of ulceration that appear to be superficial with or without hyperemia and mild to moderate hyperkeratosis); 3 = moderate ulceration (extensive superficial lesions or deeper focal lesions with or without proliferation along lesion margins and small amount of bleeding); 4 = severe ulceration (deep multifocal or generalized ulceration with or without moderate mucosal proliferation along lesion margins and active hemorrhage); and 5 = extensive severe ulceration (extensive areas of deep ulceration with or without extensive mucosal proliferation along lesion margins and active hemorrhage).
hemorrhage; Figure 1). A combined ulceration score was obtained by summing the grades assigned to each of the 4 examined stomach locations (maximum possible score, 20).

To induce ulcers, each horse underwent alternating 24-hour periods of feeding and feed withholding from days 14 through 24. All horses in both groups underwent the 10-day ulcer induction regimen. One group of horses was administered omeprazole (4 mg/kg, PO) once daily beginning on day 14 through to the end of the study (day 56) in an attempt to prevent development of ulceration. The drug treatments consisted of enteric-coated granules that were mixed with corn syrup for oral administration. The other group of horses was similarly treated but with corn syrup alone.

Performance evaluation—Physiologic indices of performance were evaluated by use of a previously described protocol with modifications. During the acclimatization period, each horse was trained to wear an open-flow mask over its nose and mouth; the mask was attached to the horse’s halter. Prior to the induction of gastric ulceration in all horses, a baseline pretraining evaluation of physiologic variables was conducted at day 0; a similar evaluation was conducted at the completion of the study (day 56). Prior to an evaluation, each horse was instrumented with 3 ECG electrodes affixed to shaved patches on the dorsal and ventral aspects of the thorax. The electrodes were then connected to an ECG amplifier. A 14-gauge jugular catheter was placed aseptically in each horse. A flow-through polyvinyl chloride gas collection mask, which was connected via 20-cm-diameter polyvinyl chloride tubing to a 5-horse power vacuum blower, was placed over the horse’s nose and mouth and affixed to the halter to collect expired gases for measurement of O₂ and CO₂ concentrations. Samples of expired gas were pumped with a diaphragm pump from the bias flow line and passed through an ionomer tube with a counter-current external flow of dry air that passed over CaSO₄ to remove all water vapor from the sample. The samples were then passed through a CO₂ analyzer and then through an O₂ analyzer. The bias flow through the mask was measured with an electronic mass flow meter that was connected in parallel with the bias line via a 5-cm-diameter polyvinyl chloride pipe; the flow was maintained at a rate (approx 8,000 L [ambient temperature and pressure]/min) that was sufficient to prevent rebreathing of expired gas. Additionally, static pressure in the tubing was measured by use of a differential pressure transducer, and temperature and relative humidity were measured by use of an electronic thermohygrometer. All transducer outputs were recorded on a computer by use of data acquisition hardware and software. Data were analyzed by use of playback and analysis software. Treadmill speed was continuously recorded by use of an optical tachometer; readings were obtained from the unpowered roller drum of the treadmill. Stride length was calculated by dividing the treadmill speed (calibrated daily) by the stride frequency, which was measured by timing strides on the treadmill for 13 seconds with a stopwatch as well as

Figure 1—Endoscopic views of gastric lesions in horses to illustrate the grading system used to characterize lesion severity in each of 4 regions of the stomach. A—Mucosal erosions (hyperemia with or without hyperkeratosis or superficial mucosal erosions; grade 1). B—Mild ulceration (multifocal or generalized areas of ulceration that appear to be superficial with or without hyperemia and mild to moderate hyperkeratosis; grade 2). C—Moderate ulceration (extensive superficial lesions or deeper focal lesions with or without proliferation along lesion margins and small amount of bleeding; grade 3). D—Severe ulceration (deep multifocal or generalized ulceration with or without moderate mucosal proliferation along lesion margins and active hemorrhage; grade 4). E—Extensive severe ulceration (extensive areas of deep ulceration with or without extensive mucosal proliferation along lesion margins and active hemorrhage; grade 5). Apparently normal mucosa was considered grade 0. A combined ulceration score was obtained from the sum of the grades at each of the 4 examined stomach locations (maximum possible score, 20).
by calculating the frequency of pressure fluctuations in the expired gas line via fast-Fourier transformation of the recorded pressure signal.

The horses performed a standardized exercise protocol that consisted of walking at 2 m/s for 4 minutes, trotting at 4 m/s for 3.5 minutes, and galloping on a horizontal surface for 90-second intervals at speeds of 11, 12, 13, 14, and 15 m/s. Horses were galloped until the point of fatigue, which was defined as the time point at which the horse was unable to maintain its position on the treadmill despite vigorous encouragement. Heart rate was determined by counting the number of QRS complexes on an ECG during a 15-second period. Blood samples (6 mL each) were collected from the jugular catheter at 30-second intervals once the treadmill speed was increased to 11 m/s. Collected blood samples were placed in fluoride-oxalate tubes, which were stored in crushed ice until after the run was completed. Each blood sample was centrifuged to harvest the plasma for determination of lactate concentration; the lactate accumulation rate was calculated as the change in plasma lactate concentration per unit time (mM/min). The measurements of O$_2$ and CO$_2$ concentrations in expired gas and heart rate were obtained during the final 30-second interval at each speed when each horse had reached steady state. The maximal specific O$_2$ uptake (ie, VO$_{2max}$/M$_b$, [mL of O$_2$ [standard temperature and pressure, dry]/[kg]s]) and maximal specific CO$_2$ production (VCO$_{2max}$/M$_b$, [mL of CO$_2$ [standard temperature and pressure, dry]/[kg]s]) were calculated as described by Pascot et al$^11$ with the N$_2$-dilution/CO$_2$-addition technique of Fedak et al$^13$ and by use of mass flow controllers to deliver measured flows of calibration gases.

**Statistical analysis**—Variables obtained from the performance evaluations (interval between beginning of treadmill exercise to fatigue, speed at which VO$_{2max}$ was elicited, stride length, VO$_{2max}$/M$_b$, VCO$_{2max}$/M$_b$, plasma lactate accumulation rate, and HR$_{peak}$) were compared by use of a 2-way repeated-measures ANOVA for the effects of time and group. When a significant group and time interaction was detected, a post hoc Student $t$ test (between groups) and paired $t$ test (within groups) were performed to identify the source of the interaction. Differences in ulcer severity were evaluated by use of the Friedman nonparametric repeated-measures test (between groups) and the Wilcoxon signed rank test (within groups). Body weights obtained before the 2 periods of feed withholding (third endoscopic examination) were used in the analyses: 7 horses were in the group that did not receive omeprazole during the study, and 6 horses were in the group that did receive omeprazole during the study. Although horses lost weight during the period of alternate feeding and feed withholding, their weights returned to values recorded prior to commencement of that feeding protocol within 14 days following reinstitution of the normal feeding routine.

**Ulcer severity**—All horses that did not receive omeprazole during and after the gastric ulcer induction phase developed gastric ulceration by the third or fourth period of feed withholding (third endoscopic examination). There was a significant ($P < 0.001$) change in the mean combined ulceration score following the 5 feed-withholding periods in the untreated horses. Induced ulcers were generally mild to moderate (grade 2 or 3 at ≥1 locations) and were located exclusively within the squamous portion of the stomach adjacent to the margo plicatus. The glandular mucosa around the margo plicatus was evaluated, but no attempt was made to evaluate the pyloric antrum or proximal portion of the duodenum in these horses. It is possible that some glandular lesions may have been present but not detected or that horses with apparently normal squamous mucosa and ulcers in the pyloric antrum were not identified. Ulcers remained visible in the untreated horses from day 21 to the end of the experiment (day 56); however, there was no notable progression of ulceration after day 21. Horses that received omeprazole during and after the gastric ulcer induction phase did not develop gastric ulceration despite the alternating periods of feeding and feed withholding (Figure 2). Although some horses developed hyperemia, hyperkeratosis, or mucosal ero-
sions, there was a significant (P = 0.001) difference in the severity of gastric lesions in this group, compared with findings in the untreated horses.

Performance evaluation—In both groups of horses, initial (day 0) and final (day 56) values of performance index variables were evaluated and compared (Table 1). The training program significantly increased time to fatigue (P = 0.024), stride length (P < 0.001), \( V_{\text{O}_2\text{max}}/M_b \) (P < 0.001), and \( V_{\text{CO}_2\text{max}}/M_b \) (P = 0.001) over time (days 0 through 56) and overall in the 13 horses. Significant interactions between time (pre- and post-training data) and treatment (horses with and without ulcers) were detected for \( V_{\text{O}_2\text{max}}/M_b \) (P = 0.005) and \( V_{\text{CO}_2\text{max}}/M_b \) (P = 0.036). Post hoc analysis revealed no differences in \( V_{\text{O}_2\text{max}}/M_b \) (P = 0.337) and \( V_{\text{CO}_2\text{max}}/M_b \) (P = 0.229) at baseline and no difference in \( V_{\text{O}_2\text{max}}/M_b \) at the end of the trial (P = 0.147) between groups. However, there was a significant (P = 0.031) difference in \( V_{\text{O}_2\text{max}}/M_b \) at the end of the trial between groups. There were significant within-group differences in \( V_{\text{O}_2\text{max}}/M_b \) (P = 0.005) and \( V_{\text{CO}_2\text{max}}/M_b \) (P = 0.016) for horses without ulcers but not for horses with ulcers (P = 0.097 and P = 0.051, respectively). Weights of the horses did not change significantly between days 0 and 56 in either group. Mean ± SD weight of horses without ulcers was 477 ± 57 kg at day 0 and 465 ± 71 kg at day 56; mean weight of the horses with ulcers was 516 ± 31 kg at day 0 and 512 ± 28 kg at day 56. Although the mean time to fatigue increased by 37% in the horses without ulcers and only by 18% in the horses with ulcers, these data were sufficiently variable among horses that the mean changes from baseline were not significantly (P = 0.306) different.

**Discussion**

As reported for a previous investigation,14 the protocol of alternate 24-hour periods of feeding and feed withholding induced gastric ulceration in the stratified squamous gastric mucosa of horses that did not receive treatment with a gastroprotective agent in the present study. To maintain the induced gastric ulcers in those horses, they were exercised on the treadmill with simulated racetrack training conditions (including diet, type and level of exercise, and weight carried [representative of a rider]). The successful induction and maintenance of ulcers by alternating periods of feeding and feed withholding combined with treadmill exercise suggested that this method may be valuable in establishing gastric ulceration in performance horses for evaluation under controlled conditions. Results of other investigations performed by our group (data not shown) indicated that treadmill exercise will induce gastric ulceration in horses without application of the feeding-feed withholding protocol. A previous study15 in Thoroughbred racehorses with no ulceration on arrival at the racetrack revealed that most of the horses developed gastric ulceration after 4 to 9 weeks of active training; however, in some horses, gastric ulceration developed only after 19 weeks of training. Therefore, for purposes of the present study, we decided to induce ulcers in horses by alternating periods of feeding and feed withholding in an attempt to achieve uniform ulcer formation and ulcer severity. In the present study, 2 groups of horses were evaluated—horses with ulcers and horses without ulcers. Alternatively, we could have included additional groups to provide more standardized control groups, such as horses that did not undergo alternate periods of feeding and feed withholding and that were or were not exercised on a treadmill with simulated racetrack training conditions. However, this was not feasible because of cost and logistic issues.

The severity of ulcers in horses of the present study was slightly lower than the severity that we have observed in horses at the racetrack with naturally occurring ulcers. The horses in our study had not been previously exposed to racetrack and were younger than the general popu-

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**Table 1—Mean ± SD physiologic indices of performance before (day 0) and 56 days after commence-
ment (day 1) of an incrementally increasing treadmill exercise program in 20 horses that underwent
alternating 24-hour periods of feeding and feed withholding beginning on day 14 for 10 days. At the
time that the feeding-feed withholding regimen was initiated, horses were administered omeprazole (4
mg/kg, PO, q 24 h until day 56) or no treatment. Horses that were not treated with omeprazole de-
veloped endoscopically detectable gastric ulcers that persisted for the duration of the study; horses that
were treated with omeprazole did not develop ulcers.**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Horses with ulcers</th>
<th>Horses without ulcers</th>
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<tr>
<td></td>
<td>Day 0</td>
<td>Day 56</td>
</tr>
<tr>
<td>Time to fatigue* (s)†</td>
<td>164.4 ± 66.8</td>
<td>193.4 ± 39.7</td>
</tr>
<tr>
<td>Speed (m/s)</td>
<td>14.3 ± 0.2</td>
<td>14.8 ± 0.2</td>
</tr>
<tr>
<td>Stride length (m)</td>
<td>7.01 ± 0.29</td>
<td>7.17 ± 0.25</td>
</tr>
<tr>
<td>HR-max (beats/min)</td>
<td>209 ± 10</td>
<td>216 ± 8</td>
</tr>
<tr>
<td>(V_{\text{O}_2\text{max}}/M_b ) (mL/[s•kg])</td>
<td>2.24 ± 0.25</td>
<td>2.39 ± 0.08</td>
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<tr>
<td>(V_{\text{CO}_2\text{max}}/M_b ) (mL/[s•kg])</td>
<td>2.81 ± 0.18</td>
<td>3.05 ± 0.15</td>
</tr>
<tr>
<td>Respiratory quotient</td>
<td>1.25 ± 0.09</td>
<td>1.26 ± 0.07</td>
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<tr>
<td>Plasma lactate accumulation rate (mM/min)</td>
<td>9.6 ± 2.9</td>
<td>9.6 ± 2.4</td>
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Because of musculoskeletal problems or inability to adapt to exercising on the treadmill, data were available for only 6 omeprazole-treated horses and 7 untreated horses. All volumes are standard temperature and pressure, dry values.

*Interval from beginning of treadmill exercise to fatigue, which was defined as the time point at which the horse was unable to maintain its position on the treadmill despite vigorous encouragement. †For this variable, there was an overall (all 13 horses included) significant (P < 0.001) difference between values at days 0 and 56. ‡For this variable at this time point, values differed significantly (P < 0.05) between groups. §For this variable, values at days 0 and 56 differed significantly (P < 0.05) within the group.
lation of horses at racetracks. Correlations of decreasing performance with increasing age in Thoroughbred racehorses\(^4\) and increasing severity of ulcers with increasing age in racing Standardbreds\(^5\) have been reported. Therefore, it is possible that age may be a factor contributing to the less severe ulcers observed in our study; alternatively, the simulated race training may have not been sufficiently vigorous or of sufficient duration.

The present study was designed to have 10 horses in each of the 2 groups; however, some horses had to be removed from the study, and this probably reduced the statistical power of the data analyses. On the basis of calculations involving fractional changes detected in the present study, the number of horses required in each group to have a power of 0.8 for \(\frac{V_{CO2,max}}{M\cdot h}\) and to detect a significant difference between groups was 17. Therefore, given the small group size and low power of the test, the nonsignificant differences must be interpreted with caution because of the possibility of having type II errors (failing to identify a difference when there actually is one).

Five of the 20 horses in the present study were removed because of musculoskeletal lesions (metacarpal stress fracture, rhabdomyolysis, desmitis of the suspensory ligament, superficial digital flexor tendinitis, and muscle strain) that were associated with training on the treadmill. The risk of lesion development among horses in racing and training has been reported,\(^6\) but a similar risk among horses that are exercised on treadmills to simulate race training has not been identified to our knowledge. An association between surface hardness and the occurrence of lameness in Thoroughbred racehorses has also been determined.\(^7\) Recently, artificial surfaces have been introduced at various racetracks in an attempt to reduce the incidence of racing injuries among horses. In addition, horseshoe characteristics have been reported to influence the type and anatomic sites of lesions that develop in Thoroughbred racehorses.\(^8-10\) In the present study, it was not possible to exercise the horses with the typical shoes used at the racetrack, and instead, aluminum shoes with polyurethane soles were used. Those shoes are heavier than aluminum shoes and are reported to have increased traction, factors that may have altered the gait of the horses in our study. Most likely, the cause for the high number of musculoskeletal lesions observed among the study horses was multifactorial. Possible factors include the hardness of the treadmill surface, the type of shoes used, and the training protocol. Even though we could have treated some of our horses and returned them to exercise on the treadmill, we decided to remove them from the study to prevent the introduction of possible confounding variables.

Reports\(^11,12\) on the prevalence of gastric ulceration in equids have focused on Thoroughbred racehorses. Further studies have identified a high prevalence of gastric ulcers in other groups of horses, including racing Standardbreds,\(^13,14\) show horses,\(^1\) and broodmares maintained on pasture.\(^15\) In our study, the exercise protocol was an attempt to simulate the training of racing Thoroughbreds; therefore, results from the study may not be relevant to horses performing other types of physical activities.

It is thought that squamous gastric ulcers develop in horses because of exposure of the unprotected squamous mucosa to hydrochloric acid and organic acids (volatile, fatty, and bile acids). Equine gastric ulcer syndrome is similar to human gastroesophageal reflux disease, in which gastric acid is refluxed into the esophagus and affects the squamous mucosa of the esophagus. In a recent study,\(^22\) it was observed that when horses are exercised on a treadmill, the gastric pH decreases rapidly (< 4), even at the beginning of the exercise. The researchers concluded that an increase in intra-abdominal pressure produces gastric compression that moves gastric contents into contact with the squamous mucosa of the stomach. In humans, upper gastrointestinal tract problems develop in as many as 58% of surveyed athletes and are related to the type and intensity of exercise.\(^23,24\) In addition, exercise contributes to gastroesophageal reflux disease in asymptomatic healthy volunteers, inducing reflux that is proportional to the intensity of exercise.\(^25,26\) Athletes and nonathletes develop more signs of upper gastrointestinal tract problems when their \(V_{O2,max}\) is exceeded during exercise, even though the absolute levels of exercise in each group were different.\(^27,28\)

In the present study, omeprazole was administered to 1 group of horses to prevent ulcer formation and maintenance caused by the application of the feeding-feed withholding protocol combined with treadmill exercise. Omeprazole is a proton-pump inhibitor that inhibits gastric acid production and is used to treat or prevent gastric ulcer formation. Omeprazole usually is administered as a paste that protects the drug from degradation as a result of the acidic pH of the stomach contents. Omeprazole decreases acid production in a dose-dependent manner. Results of previous studies\(^29,30\) have indicated that gastric ulcers can be treated or prevented in Thoroughbred racehorses via administration of the paste formulation at different doses. However, at the time that our study was performed, a preparation of omeprazole was not commercially available for use in horses. Therefore, drug treatments comprised enteric-coated capsules mixed with corn syrup for oral administration; the untreated horses were administered corn syrup alone. A previous study\(^31\) revealed that enteric-coated capsules of omeprazole (1 mg/kg, q 24 h) administered orally for 3 days to clinically normal horses will decrease gastric acid production. In another study\(^32\) to evaluate the use of enteric-coated capsules of omeprazole in horses, nasogastric administration of omeprazole at a single dose of 5 mg/kg inhibited 98% of acid secretion, whereas a single lower dose (1.5 mg/kg) inhibited only 57% of acid secretion. In the present study, oral administration of enteric-coated granules of omeprazole at a dose of 4 mg/kg was effective at preventing ulcer formation in the treated horses. The effect of administration of omeprazole paste on indices of performance in horses without gastric ulcers that were exercised on a treadmill has been previously evaluated.\(^33,34\) Oral omeprazole paste (administered orally at a dose of 4 mg/kg) resulted in no detectable changes in physiologic indices of performance (ie, \(V_{O2,max}, V_{CO2,max},\) stride length, plasma lactate accumulation rate, or \(HR_{max}\)).\(^33,34\)
The magnitudes of the plasma lactate accumulation rate measured during the performance evaluations in our study (8 to 10 mM/min) are consistent with findings in horses that are exercising at \( V_{\text{O}}_{2\text{max}} \). Heart rates in the range of 209 to 216 beats/min also indicated that horses of these ages were exercising at their maximal aerobic capacities. Additionally, horses exercised on the treadmill with respiratory quotients that exceeded 1.1, which also indicates that the exercise conditions were eliciting \( V_{\text{O}}_{2\text{max}} \) from the horses.

After 56 days of training, the horses’ time to fatigue, stride length, \( V_{\text{O}}_{2\text{max}}/M_{\text{b}} \), and \( \text{VE}/M_{\text{b}} \) were affected; these results indicated that increasing training load over time increased physiologic indices of performance. Significant interactions that were identified for \( V_{\text{O}}_{2\text{max}}/M_{\text{b}} \) and \( \text{VE}/M_{\text{b}} \) with regard to time and group suggested that the effect of 1 variable depended on the magnitude of the other variable. When the interaction was further analyzed, a difference was detected in \( V_{\text{O}}_{2\text{max}}/M_{\text{b}} \) at the end of the trial between the 2 groups: horses without ulcers had a greater increase in oxygen consumption over time than did the horses with ulcers. Horses without ulcers increased their aerobic capacities by a greater amount than did horses with ulcers.

Maximal oxygen consumption is a quantifiable and reproducible variable (coefficient of variation is approx 3% with the system used by our group) that indicates the limits of the cardiopulmonary system’s ability to transport oxygen from the air to the tissues at a given level of physical conditioning and oxygen availability; and that is frequently regarded as a primary correlate of flat racing performance. The magnitude of \( V_{\text{O}}_{2\text{max}} \) is determined by interactions between convective and diffusive \( O_{2} \) transport processes (including pulmonary ventilation and diffusion, cardiac output, and \( O_{2} \) capacitance of the blood) and the extraction of \( O_{2} \) (primarily by the working muscles). In horses, changes in \( V_{\text{O}}_{2\text{max}} \) depend on the type and intensity of training. The \( V_{\text{O}}_{2\text{max}} \) of Standardbred geldings increased 15% after 7 weeks of endurance training, by 20% after 9 weeks of high-intensity training, and by 29% when signs of overtraining were observed. The specific \( V_{\text{O}}_{2\text{max}} \) of Thoroughbred yearlings increased by 16% over a 6-month period of training; that increased aerobic capacity was subsequently maintained over an additional 4 months of training. The \( V_{\text{O}}_{2\text{max}}/M_{\text{b}} \) of horses without ulcers in our study increased approximately 35% after 8 weeks of undergoing an incrementally increasing exercise program on the treadmill; however, horses with ulcers did not have a significant increase in \( V_{\text{O}}_{2\text{max}}/M_{\text{b}} \). Because blood samples collected during the study were not assessed for \( O_{2} \) or hemoglobin concentrations, we cannot determine whether the changes in \( V_{\text{O}}_{2\text{max}} \) in the horses without ulcers were correlated with changes in cardiac output or \( O_{2} \) capacitance of the blood, as reported for another investigation in young Thoroughbreds. Furthermore, because of the lack of blood gas analyses or measurements of ventilation during our study, we cannot determine whether the smaller increase in stride length observed in the horses with ulcers, compared with the horses without ulcers, may have been associated with decreased tidal volume and alveolar ventilation that were possibly caused by increased abdominal pain. Although the causative mechanism cannot be determined, the results indicated enhanced aerobic capacity after training in horses without ulcers versus horses with ulcers.

Plasma lactate accumulate rate—an index of net anaerobic power—did not change significantly between the performance evaluations before and after the training interval, which indicated that the horses were exercising at approximately the same percentage of supramaximal intensity during both evaluations. Although the time to fatigue increased more in the horses without ulcers than it did in the horses with ulcers, the inherent variability in values of this variable rendered that difference nonsignificant. Stride length has been described as one of the strongest correlates of performance, particularly in Thoroughbreds. Similar to the results of the present study, novice human runners increased stride length after a 5-week treadmill training program. It is possible that pain from ulceration may have prevented horses with ulcers from increasing stride length as much as the horses without ulcers (2.3% vs 4.8%, respectively).

In the present study, the horses were randomly selected for inclusion in each group and all horses were managed with the same feeding and training protocols, with the exception of the administration of omeprazole for the prevention of gastric ulceration. The presence of gastric ulceration has been previously correlated with decreased performance in Thoroughbred racehorses. However, data in that study were subjective and were obtained by use of a questionnaire from either the horses’ trainers or veterinarians. A recent case report described 4 poorly performing horses in which gastric ulceration was the only abnormal finding. The report described improvement of performance after treatment of the ulceration. However, only 2 horses were endoscopically examined after treatment, treatment varied among horses, and management changes were recommended for 3 of them. Gastric ulceration in horses has been correlated with a poor coat, with becoming a selective eater, and with signs of abdominal discomfort. Additionally, another study revealed that horses with gastric ulceration had reduced hemoglobin concentrations and RBC counts, compared with horses with gastric ulceration. The mechanisms by which gastric ulcers may affect performance in horses have not been elucidated, but could include any of the aforementioned factors: decreased food intake, signs of abdominal pain or discomfort affecting tidal volume and alveolar ventilation, or low hemoglobin concentration or PCV. In the horses of the present study, there was no difference in horses’ weights between days 0 and 56. A CBC was performed for each study horse initially; all horses had values within reference limits, and there were no differences between groups (data not shown). However, CBCs were not performed at the end of the study, so it is not known whether the effect of ulceration on performance might have been related to changes in \( O_{2} \)-carrying capacity of the blood or to other factors such as pain. Nevertheless, gastric ulceration was not associated with an increase in \( V_{\text{O}}_{2\text{max}} \) after an incrementally increasing exercise program of 8 weeks’ duration, unlike horses without ulcers in which \( V_{\text{O}}_{2\text{max}} \) increased significantly.
On the basis of results of the present study, it appears that manipulation of diet and treadmill exercise can be used to induce and maintain gastric ulceration in horses, and the described method may have application in controlled studies of the effects of gastric ulcers on indices of exercise performance. In horses, gastric ulceration in the squamous mucosa has a detrimental effect on indices of performance, although the mechanisms causing this effect remain to be determined.

References