How to Diagnose and Manage Gastric Ulcers as a Medical Reason for Poor Performance

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Poor athletic performance in horses is often multifactorial, and a comprehensive examination is needed to determine the cause. A comprehensive examination should include endoscopic examination of the stomach to determine the presence of equine squamous gastric disease and/or equine glandular gastric disease, as they might be causing or contributing to the poor athletic performance. If gastric ulcers are present, then appropriate antiulcer treatment could improve stomach health and athletic performance. Author's address: Equine Health Studies Program, Veterinary Clinical Sciences, Louisiana State University School of Veterinary Medicine, Skip Bertman Drive, Baton Rouge, LA 70803; e-mail: fandrews@lsu.edu.

1. Introduction

Poor athletic performance in horses can be multifactorial, and it is difficult to determine the effects of one component on athletic performance.[1] Thus, a comprehensive clinical evaluation, at rest and during exercise, is needed to determine causes and prescribe effective interventions. The gastrointestinal (GI) tract has largely been overlooked as a cause of poor athletic performance in horses. Nearly 60% of human athletes complain of upper GI symptoms while exercising, which likely affects performance.[2] Several reports have implicated equine gastric ulcer syndrome (EGUS) as a cause of poor athletic performance in horses, but only one of these studies collected objective data.[1,3,4]

EGUS involves ulcerative lesions in the squamous mucosa (equine squamous gastric disease [ESGD]) and glandular mucosa (equine glandular gastric disease [EGGD]; Fig. 1). ESGD is similar to gastroesophageal reflux disease (GERD) in humans, for which stomach acids are refluxed onto the sensitive esophagus squamous mucosa. In horses, the esophageal tissue (squamous epithelium) is present in the proximal one-third of the stomach and is not protected by the lower esophageal sphincter and, therefore, is constantly exposed to gastric acids (hydrochloric, volatile fatty, and bile acids). The condition of GERD is common in human athletes, and a number of provocative physiological events, including increased gastric acid secretion, impaired gastric emptying, and increased internal gastric pressure, occur during exercise that exacerbate esophageal reflux.[6] In fact, published epidemiological data on GERD indicate that upper GI symptoms occur in 58% of surveyed athletes, and these symptoms are proportional to exercise intensity.[2] As exercise intensity increases and blood flow shifts away from the GI tract to working skeletal muscles, GI motor activity is modified and gastric emptying is delayed. Factors

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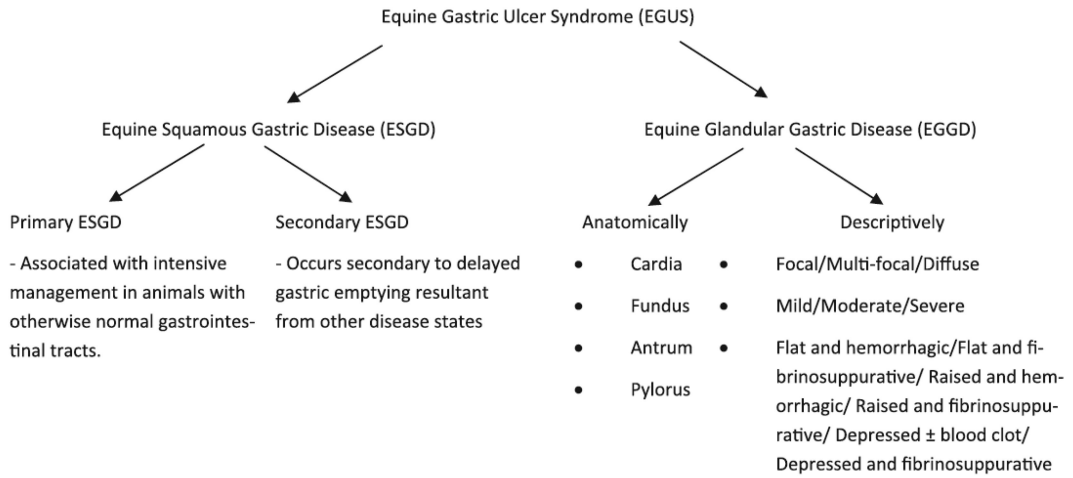

Fig. 1. Summary of the terminology of describing erosive and ulcerative diseases of the horse stomach (with permission).[5]

that could explain exercise-induced gastroesophageal reflux in humans include the following: body position, which delays esophageal clearance as subjects shift away from the upright position (e.g., sprinter); increased abdominal pressure generated by the Valsalva maneuver (i.e., weightlifters); or the bent-over racing position maintained by most cyclists.[6] All of these activities can increase the abdominal component of the vectorial force, pushing gastric contents up against the lower esophageal sphincter. This scenario might be similar in horses with ESGD during exercise. Previously, Lorenzo-Figueras and Merritt[7] showed that intragastric pressure in horses sharply increased at a trot and gallop, which was due to increased intra-abdominal pressure related to the exercise. Increased abdominal pressure led to increased gastric pressure, refluxing acid stomach contents as measured by a pH probe inserted in the stomach just distal to the lower esophageal sphincter. Reflux of acids on the squamous mucosa might explain the high prevalence of ESGD in racehorses. It is also consistent with the following observations:

- Squamous lesions regress or disappear when horses are taken out of training or are treated with acid-suppressing drugs.
- Lesions are most often found in the squamous mucosa near the margo plicatus on the lesser curvature, where acids are in constant contact with gastric mucosa.

This "how to" article discusses the specific approach for determining if EGUS is causing or contributing to poor athletic performance. The impact of EGGD on performance remains to be determined.

Comprehensive Approach

A comprehensive examination to determine poor athletic performance should include a general physical examination with a rebreathing examination, lameness examination, upper respiratory endoscopy examination at rest without sedation and during work (dynamic endoscopy), blood work (hematology and biochemical panel), and an endoscopic examination of the distal esophagus, stomach, and proximal duodenum.

Clinical Signs

Because the prevalence of EGUS is high in performance horses and clinical signs are often vague, signs of EGUS are often subclinical and missed by trainers and owners. Clinical signs of EGUS typically include poor body and coat condition, weight loss, behavioral changes, mild colic, discomfort after eating, and reluctance to train. However, in a previous study in 4 horses with gastric ulcers as a cause of poor athletic performance, clinical signs were absent and there was no evidence of abdominal pain, which makes it difficult to determine GI causes of poor performance.[1]

Endoscopic Examination of the Distal Esophagus, Stomach, and Proximal Duodenum

A thorough endoscopic examination of the distal esophagus, stomach, and proximal duodenum should be performed as part of a comprehensive athletic performance examination. The preparation, sedation, endoscopy procedure, and care postendoscopy are available online (https://www.youtube.com/watch?v=l_ZAxnxmE-0).

Briefly, gastroscopy can be performed in the standing and sedated horse or a horse under general anesthesia.[8] To perform standing gastroscopy in the horse, feed, but not water, should be withheld for at least 8–12 hours prior to the procedure. A muzzle should be placed on the horse during the feed-deprivation period to prevent ingestion of fecal material or residual feed in the stall. All bedding and feed material should be removed from the stall during the feed-deprivation period. Three people might be needed to perform a thorough standing endoscopic examination of the stomach; one person restrains the horse, one passes the endoscope, and one drives the endoscope. Xylazine (0.5 mg/kg bodyweight [bwt],

Table 1. EGUS Scoring System for ESGD[5,10]

Score	Explanation
0	The mucosa is intact and there is no appearance of hyperemia
1	The mucosa is intact, but there are areas of reddening
2	Small single or multifocal superficial lesions (<5)
3	Large single or multifocal lesions or extensive superficial lesions (≥5)
4	Extensive lesions with areas of apparent deep ulceration

IV) or detomidine (0.01–0.02 mg/kg bwt, IV), and/or butorphanol (0.02 mg/kg bwt, IV) can be administered prior to the procedure, and the horse is left undisturbed until sedation is observed. A twitch might be applied to the horse's muzzle on the opposite side from which the endoscope is to be passed. Endoscopy of the stomach should be performed using a 3 m or longer endoscope, as shorter endoscopes do not provide a complete view of the stomach and proximal duodenum. To improve visualization of the stomach and enable observation of the squamous mucosa (fundus ventriculi), margo plicatus, and glandular mucosa (corpus ventriculi), the stomach can be insufflated using the air-feed directly from the endoscope or an air compressor attached to the endoscope biopsy channel (until the rugae or stomach folds disappear). Mucosa should be rinsed of adherent feed material and mucus using tap water flushed through the endoscope biopsy channel using 60-ml syringes or fluid pump. Ulcers might be seen under adherent feed material and mucus and might be obscured by debris. When horses are difficult to handle, are under general anesthesia for abdominal surgery, or when a complete examination of the stomach is not possible standing, endoscopy can be performed under general anesthesia. To perform endoscopy under general anesthesia, it is best to place the horse in right lateral recumbency so that the stomach is up. The horse can be rolled up on its back and then to the left side so that all of the stomach can be viewed. Orienting oneself to the anatomy can be more challenging than in the standing horse. Care must be taken not to overinsufflate the stomach, as this could result in air escaping into the small and large intestine, resulting in bloating and abdominal pain during recovery. Residual air should be removed from the stomach after the procedure to prevent colic or other complications.[9] Ulcerations, hyperkeratosis, and hyperemia should be recorded, and a scoring system can be used to keep track of severity. Several scoring systems are available for use and include the one recommended by the EGUS Council and European College of Equine Internal Medicine (Table 1)[10,11] that evaluates the size of ulcers. Another scoring system evaluating lesion number and severity can also be used for both squamous and glandular regions of the stomach (Table 2).[5] In addition, EGGD can be described using another system (Table 3).[11] The advantage of recording ulcer scores is to assess improvement or worsening on follow-up examinations. The presence of gastric ulcers on endoscopic examination does not confirm cause and effect, as ulcers could be secondary to other causes of poor performance.

Measuring Gastric Juice pH

Upon endoscope entry into the stomach and before insufflation or flushing with tap water, one can aspirate gastric fluid from the biopsy channel and measure pH within 2 hours by using a benchtop pH meter, pH paper, or a urine dipstick, with pH disk. Measuring gastric juice pH, especially in horses treated with antiulcer medications, is important to determine if treatment with acid-suppressing drugs is effective. A pH of ≥4.0 is desirable, and it has been shown that a pH <4.0 can damage the squamous stomach mucosa.[12]

Other Diagnostic Testing

Hematology

There are no clinicopathologic parameters that are pathognomonic for EGUS as a cause of poor athletic performance. However, hematology, at the

Table 2. Number and Severity Scoring System for Squamous and EGGD[5]

Parameter	Descriptions
Lesion Number Score	
0	No lesions
1	1–2 localized lesions
2	3–5 localized lesions
3	6–10 localized lesions
4	>10 lesions or diffuse (very large) lesions
Lesion Severity Score	
0	No lesions
1	Appears superficial (only mucosa missing)
2	Deeper structures involved (>depth than number 1)
3	Multiple lesions and variable severity, (1, 2, and/or 4)
4	Deeper structures involved (>depth than number 1) and has active appearance (hyperaemic and/or darkened)
5	Same as number 4 plus hemorrhage or blood clot

Table 3. Descriptive Scoring for EGGD[11]

Severity	Distribution	Appearance	Location
Mild	Focal	Flat and hemorrhagic	Cardia
Moderate	Multifocal	Flat and fibrinosuppurative	Fundus
Severe	Diffuse	Raised and hemorrhagic	Antrum
		Raised and fibrinosuppurative	Pylorus
		Depressed ± blood clot	
		Depressed and fibrinosuppurative	
		Other (describe)	

minimum, should be performed in horses presenting for poor athletic performance. In one report, 3 of 4 horses presenting for poor performance due to EGUS had hemoglobin concentrations below the reference range.[1] In another study, horses with EGUS had significantly lower red blood cell counts and hemoglobin concentrations than horses without EGUS.[13] Unfortunately, these values were not outside reference ranges. In addition, previous epidemiological studies have failed to find an association between hematological parameters and poor athletic performance in populations of racehorses.[3]

Fecal Occult Blood Testing

It is probably worth mentioning the use of fecal occult blood to determine horses with EGUS. A guaiac-based fecal occult blood test was used in one study and showed high specificity, low sensitivity, and high false-negative results for determining the location of ulceration (stomach or colon).[14] Also, in a recent study, there was a high number of false-negative tests, and no significant correlation was found between results of a new fecal blood test and gastric ulcer scores in horses undergoing stall confinement and bolus feeding.[15]

2. Treatment

The gold standard for the treatment of horses with EGUS is omeprazole.[a] However, other pharmacologic agents have been used for the treatment and prevention of EGUS with variable success (Table 4).In the study by Franklin et al.,[1] all horses presenting with poor performance due to EGUS had severe ESGD and mild-to-moderate EGGD. All horses were treated with omeprazole paste (4 mg/kg bwt, orally daily) and one horse received sucralfate (20 mg/kg bwt, orally twice daily), and all returned to racing after treatment. Two of the 4 horses in that study had follow-up gastroscopy and the squamous ulcers healed, whereas the glandular mucosa still had hyperemia in 1 horse and was healed in the other horse. Improvement in athletic performance was documented by an increase in mean Raceform rating and increased earnings after treatment.[1] It should be noted that omeprazole has no performance-enhancing properties by itself, as confirmed by a previous study.[17] A recent study in human runners addressed the effect of GERD and treatment with antisecretory agents on poor performance.[18] In that study, runners with frequent GERD had a significantly decreased time to exhaustion compared to runners without reflux. However, prophylactic rabeprazole (omeprazole-like proton-pump inhibitor) administration did not improve performance in the runners with GERD. Therefore, treatment in these human athletes did not result in a significant effect on performance. The authors speculated that decreased performance in human athletes with GERD might be caused by esophageal pain and not stomach pain. In contrast, because the squamous mucosa is located in the stomach, stomach pain (due to acid reflux and resultant ESGD) might be the cause of poor

Table 4. Commonly Used Therapeutic Agents and Doses for Treatment and Prevention of EGUS[16]

Drug	Dose[a]	Dosing Interval (h)	Route of Administration
Ranitidine	6.6	q 6–8	PO
Ranitidine	1.5	q 6	IV, IM
Omeprazole	4 (treatment)	q 24	PO
Omeprazole	1–2 (prevention)	q 24	PO
Omeprazole	0.5–1.0	q 24	IV
Esomeprazole	1.0	q 24	IV
Esomeprazole	1.0–2.0	q 24	PO
Pantoprazole	1.0–1.5	q 24	IV or PO
Sucralfate	12–20	q 8	PO
Al- or Mg hydroxide	0.5 mL/kg	q 4-6	PO
Misoprostol, prostaglandin analogues	1–5 μg	q 8-12	PO

[a]Units are (mg/kg) unless otherwise indicated.

performance in horses. Recent investigations have shown a reduced efficacy in omeprazole-treated horses with EGGD, when compared with ESGD.[19] Only 36% of EGGD cases healed when treated with omeprazole (4 mg/kg, orally every 24 hours) compared with a 78% healing rate in horses with diagnosed ESGD.[20] The reason for this finding is not known but is likely a reflection of the different pathogenesis causing EGGD, and therefore, EGGD is considered a related but distinct disease from ESGD. Because of the poor response of EGGD to omeprazole administration, sucralfate has been recommended for treatment. It should be noted that sucralfate, as a monotherapy, was shown to be ineffective in improving foals with ESGD lesions[21] but has efficacy in treatment of EGGD.[11] Sucralfate binds to stomach ulcers and promotes healing. Sucralfate is an aluminum complex sulfated polysaccharide (a-D-glucopyranoside, β-D-fructofuranosyl-, octakis- [hydrogen sulfate]), in combination with octasulfate and aluminum hydroxide. Its mechanism of action involves adherence to ulcerated mucosa, forming a proteinaceous bandage, and stimulating prostaglandin E1 synthesis and mucus secretion. Sucralfate also inactivates pepsin and adsorbs bile acids. Omeprazole plus sucralfate (12 mg/kg bwt, orally, q6h-q12h) led to healing in 63% of horses with EGGD grade $\geq$2 and improvement of at least 1 grade in 83% of horses with EGGD grade $\geq$2.[19,22]

The synthetic prostaglandin E2 analogue misoprostol has been recommended for use in treating EGUS.[11] Misoprostol is a methylester analogue of prostaglandin, and it showed a time-dependent increase in the basal gastric pH in horses. Misoprostol enhances mucosal protection by stimulating mucus and bicarbonate production and might aid in the treatment and prevention of EGGD.[23] A recent report showed that misoprostol significantly inhibited inflammatory mediators (tumor necrosis factor alpha, interleukin-1β, and interleukin-6, and superoxide) produced *ex vivo* from equine leukocytes exposed to lipopolysaccharide.[24] This study showed that misoprostol has anti-inflammatory effects that might be effective for treating EGGD because lesions in the glandular mucosa are frequently inflammatory. In more recent studies, misoprostol (5 μg/kg bwt, orally every 12 hours) was found to be superior to combined omeprazole (4 mg/kg, orally every 24 hours) and sucralfate (12 mg/kg, orally every 12 hours) therapy in horses with EGGD.[19,25,26] Misoprostol might cause diarrhea and/or colic signs and should not be used in pregnant mares because it might induce parturition and termination of the pregnancy.

3. Antibiotic Treatment of Chronic ESGD and EGGD

Helicobacter pylori and other *Helicobacter* spp. have not been shown to cause ESGD or EGGD, although *Helicobacter* DNA has been isolated from the stomach and feces of horses.[27] Instead, other resident, acid-tolerant bacteria (*Escherichia coli*, *Lactobacillus* spp., and *Streptococcus* spp.) are suspected to contribute to the worsening of squamous ulcers.[28] In that study, bacteria were isolated from the gastric contents of horses with spontaneous ESGD that were fed a high-concentrate diet. It was found that trimethoprim sulfadimidine (15 mg/kg bwt, orally, once daily) decreased EGSD ulcer numbers and severity compared to untreated control horses. These data suggest that resident stomach bacteria are important for the maintenance and progression of EGSD. However, once-daily administration of trimethoprim-sulfadimidine did not improve healing of EGGD in horses receiving omeprazole.[29] The author has used trimethoprim sulfadiazine (15–20 mg/kg bwt, orally, twice daily) for treatment of nonresponsive ESGD. Recently, doxycycline (10 mg/kg bwt, orally twice daily) has been used to some success to treat nonresponsive EGGD. Tetracycline compounds have antibiotic, anti-inflammatory, and antioxidant tissue-protective properties.[30] Frequently, EGGD lesions are inflammatory in nature, and recently, it was shown that EGGD lesions might be colonized by resident bacteria.[31] Antibiotics should be used responsibly and only when acid-suppressive therapy alone is not effective.

4. Prevention

Prevention of ulcer recurrence is important, as in one study squamous ulcers recurred within 8 days after discontinuing omeprazole treatment in horses engaged in light and heavy training regimes.[32] The use of low-dose omeprazole (1 mg/kg bwt, orally, q24h) has been shown to prevent recurrence of ESGD.[33] In a recent meta-analysis study, omeprazole prophylaxis in active training horses significantly reduced gastric ulceration compared with no prophylaxis (sham), with the absolute effect of 566 fewer ulcers per 1000 horses treated.[34]

5. Management

Management changes may be more cost effective but difficult, especially in Thoroughbred racehorses housed in stalls. To reduce gastric acidity, horses can be provided access to pasture grazing, fed *ad libitum* forage, and provided smaller and more frequent concentrate feedings. Serum gastrin concentrations are high in horses fed high-concentrate (grain) diets. Large bolus grain feeding can increase soluble carbohydrates in the stomach, which are fermented by resident stomach bacteria (*Lactobacillus* spp.), resulting in the production of volatile fatty acids, which in the presence of low stomach pH ($\leq$4), have been shown to cause acid damage to the squamous muscosa.[12] A previous study, using an *in vitro* model, showed that feeding grain at greater than 0.5 kg/100 kg bwt every 5 hours resulted in volatile fatty acid concentrations above the threshold (20 mmol), which led to acid damage, as indicated by changes in

squamous tissue bioelectrical properties.[35] Thus, smaller grain feedings every 5 to 6 hours may help in the prevention of EGUS. Regarding EGGD, when management factors associated with EGGD were evaluated, dietary factors were not included in the final multivariable models, suggesting that dietary factors may be less important for the control of EGGD than for the control of ESGD.[19] However, decreased pasture turnout or increased grain concentrate frequency were retained in the univariate model and might be associated with EGGD.[36,37] Therefore, increasing pasture turnout and decreasing grain concentrates might be useful management strategies for preventing EGGD.[19] In the previous study, horses with EGUS as a cause of poor performance were managed with increased pasture grazing and showed improvement in EGGD.[1] Another dietary strategy, feeding alfalfa hay, has been shown to decrease gastric ulcers in horses. A previous study showed that horses fed an alfalfa hay/grain diet had significantly higher stomach pH (for 5 hours after feeding) and fewer, less severe gastric ulcers than horses fed brome grass hay.[38] In a more recent study, horses fed alfalfa hay and exercised showed decreased gastric ulcer scores compared to horses fed a coastal hay diet.[39] Thus, feeding alfalfa, because of its superior buffering capacity (high calcium and protein concentrations), may protect the squamous mucosa from acid damage. There are no studies on the effect of alfalfa hay on EGGD. Intense exercise, racing, and race training have been shown to contribute to worsening of ESGD; thus, taking the horse out of training, reducing exercise intensity, and incorporating pasture turnout might improve ESGD.[40] However, there are no studies showing that exercise intensity or exercise restriction has any effect on EGGD. In summary, gastric ulceration, part of EGUS, is common in racehorses throughout the world and has been linked to poor athletic performance. It should be emphasized that EGUS could be the sole cause of poor athletic performance, but it also could contribute to or be secondary to other causes of poor performance. Omeprazole is the treatment of choice; however, complementary pharmaceutical agents such as sucralfate and misoprostol might improve healing in horses with EGGD. Because ulcers will likely return after cessation of treatment, prophylaxis with a low dose of omeprazole (1–2 mg/kg bwt, orally daily) is beneficial for long-term prevention of recurrence. Management, such as increasing pasture turnout and decreasing dietary concentrate feeding, is suggested, but more research is needed to determine which management strategies are effective and which ones are of the greatest benefit for maintaining a high level of athletic performance.

Acknowledgments

Declaration of Ethics

The Author has adhered to the Principles of Veterinary Medical Ethics of the AVMA.

Conflict of Interest

The Author has no conflicts of interest.

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[a]Gastrogard paste, Boehringer-Ingelheim Animal Health, Duluth, GA 30096.