Today horses with gastric ulcers are diagnosed with ESGD or EGGD

Gastric Ulcers, Two Diseases

STUDY FINDS DIFFERENT APPROACHES BETTER SUITED FOR EACH DISEASE

By **AMANDA DUCKWORTH**

IN SOME WAYS gastric ulcers are one of the simpler issues horses face. There is a standard way to diagnose them (gastroscopy), and there is a single approved medication that treats the issue (GastroGard).

However, as studies continue and understanding grows, researchers remind everyone that things are rarely straightforward. For instance, there are different diseases that have been put under the umbrella of equine gastric ulcer syndrome. Over the years researchers have come to understand that equine squamous gastric disease is a separate entity from equine glandular gastric disease.

Last November, Dr. Ben Sykes, an associate professor of equine internal medicine at Massey University, discussed equine gastric ulcer syndrome while participating in the Grayson Vet Chats series presented by the Grayson-Jockey Club Research Foundation.

"We've probably gotten a little complacent over time of saying, 'Well we've identified this problem. We found the solution. We've solved the problem. We cannot worry about that one anymore and move on to the next problem,' because there is always another problem to solve," Sykes said.

His discussion focused on what has been learned over the last five years about EGUS. One of the key takeaways is the fact equine squamous gastric disease and equine glandular gastric disease should not be approached the same way.

"About five years ago we had a very clear shift in the terminology we use for the disease, and this is still filtering through somewhat," Sykes said. "Equine gastric ulcer syndrome has been in use since 1999 when we first started talking about this as a disease syndrome in the horse in a meaningful way. As we started getting bigger scopes and started looking at the stomach more thoroughly, we recognized there's more to it than we originally thought.

"As a diagnosis in an individual horse, there's really no such thing as EGUS. We sort of talk about it as this overarching term, but when we actually talk about the specific diagnosis in a specific horse, we are going to have something more specific than that."

Today, horses will be diagnosed with ESGD or EGGD. However, this can make interpreting studies done before 2015 difficult because they predate the clarification of the terminology. However, most earlier studies relate to squamous mucosa, as that was the focus then because of what could be seen with the shorter scopes in use at the time.

"What we know about one we cannot apply to the other," Sykes said. "We need to broaden the conversation beyond what was traditionally recognized for the last 10 or 15 years. Squamous disease is primarily a disease of domestication and intensive management. Yet we see glandular disease, also a disease of domestication, but we see it with relatively high

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prevalence in our traditionally low-risk groups."

Sykes said those groups include riding horses, particularly warmbloods, but to some degree off-track Thoroughbreds as well.

"Glandular disease is not a disease of diet. We can reduce the carbohydrates and increase the roughage, which is a very important management strategy for squamous disease, but it is not going to change or make a difference with glandular disease," Sykes said. "We need to do things like make sure we've got rest days, reduce behavioral stress—these sorts of factors—to reduce the risk of glandular disease."

Because so much of the previous research done on EGUS was really about ESGD, EGGD requires some catching-up. Sykes published the study "Management factors and clinical implications of glandular and squamous gastric disease in horses" in the January 2019 edition of the *Journal of Veterinary Internal Medicine*.

For the study, 109 Thoroughbred racehorses from eight training yards across two countries—the United Kingdom and Aus-

Equine glandular gastric disease is not a disease of diet

tralia—were used to determine management factors associated with EGGD, identify clinical signs in affected horses, and compare these to ESGD. Researchers used gastroscopic examination combined with a questionnaire regarding management, feeding, exercise, and health of the horses for the study.

A risk factor for EGGD according to the study was the horse's training.

"Management factors and clinical signs were different for EGGD versus ESGD," the study found. "Exercising five (or more) days per week was associated with a 10.4-times increased risk of EGGD. Horses racing below expectation were 3.7-times more likely to have EGGD.

"The findings of our study further support the notion that EGGD should be considered as a distinct disease entity to ESGD. Exercising four (or fewer) days per week could reduce the risk of EGGD. Horses with EGGD are more likely to perform below expectation and, as such, EGGD might be performance limiting in some affected individuals. Although further work is needed to substantiate this finding, stress appears to play a role in the pathogenesis of EGGD, and management strategies aimed at stress minimization could reduce the risk of EGGD in some individuals."

These findings were referenced in "Equine glandular gastric disease: prevalence, impact and management strategies" published in July 2019 by *Veterinary Medicine: Research and Reports* (Auckland). The review sought to explain why EGGD will require more research and study.

"There remains limited understanding of the pathophysiology of equine glandular gastric disease," explained the review. "Factors that have been proposed to contribute to spontaneous EGGD include breakdown of mucosal defense, bacterial colonization, stress, and inflammation. The glandular mucosa is constantly exposed to hydrochloric acid, and unlike the squamous epithelium, has a number of protective factors to prevent mucosal damage. Therefore, it has been proposed that breakdown of protective factors, rather than exposure to hydrochloric acid alone, may be a key factor in development of EGGD.

"EGGD remains a poorly understood disorder of the equine stomach. Present data suggest that management for prevention of EGGD should be directed at decreasing exercise and stress, and potentially limiting grain intake and increasing pasture turnout. Treatment recommendations include omeprazole with or without sucralfate or misoprostol. Further research into pathophysiology may allow for development of additional targeted, effective treatments."

> **"WHAT'S THE RISK ASSOCIATED WITH ITS USE, PARTICULARLY GIVEN ITS HIGH PREVALENCE OF USE IN SOME OF OUR HIGH-PERFORMANCE HORSES?"**
>
> — DR. BEN SYKES ON SIDE EFFECTS OF GASTROGARD, WHICH HE BELIEVES WILL BE THE NEXT BIG QUESTION

In addition to understanding the causes of EGGD, an ongoing area of research focuses on how to diagnose it. In May 2021, *Equine Veterinary Journal* published "Inter-observer variability of two grading systems for equine glandular gastric disease."

This cross-sectional study was done because currently no validated scoring system exists for EGGD. It sought to determine if two previously described grading systems for EGGD had inter-observer reliability—meaning different observers gave consistent estimates of the same issue. Additionally, the study explored whether agreement between observers improved depending on their experience with gastroscopy, specialist training, or familiarity with the descriptive system.

In all, 82 veterinarians responded to an electronic questionnaire containing 20 images of glandular lesions. Of those 82 veterinarians, 49 of them were diplomates (a title reserved for someone who is board certified in a veterinary specialty area). Participants were asked to score lesions using descriptive terminology and a 0-2 verbal rating scale. Researchers then used Krippendorff's alpha reliability estimate to determine agreement in these ratings. Additionally, a mixed-effects model was used to determine which descriptive categories were associated with lesions being described as severe.

"There was no agreement when all four descriptive variables were combined," researchers found. "Agreement was fair to moderate for severity, distribution, appearance, and shape. Agreement for the VRS was similar to that for severity. Agreement was better among diplomates across all categories. Lesion appearance and shape, but not distribution, were associated with both a decision to treat; and lesions being described as severe. A VRS score 2/2 was associated with a lesion being described as severe.

"Overall, agreement for the descriptive system was poor. Better delineation of descriptive category boundaries and characteristics should be determined. Agreement was similar when comparing the severity category and the VRS. Extrapolation to a VRS based on lesion severity may therefore be possible."

While the findings show room for improvement in these areas, what is well known is that gastric ulcers can occur at any age and can happen with any breed. Furthermore, they are believed to affect up to 90% of racehorses. In 1999 GastroGard was given Food and Drug Administration approval, and it remains

the only federally approved omeprazole treatment for horses.

While less reliable, unregulated compounded medicines exist at a cheaper price point. The American Association of Equine Practitioners reminds owners that approved medication is a much safer and more effective course of action.

In addition to researching ways to lower the risk of ESGD or EGGD occurring in the first place, there also is work being done to improve understanding of the long-term effects of the go-to treatment for gastric ulcers—omeprazole.

The *Journal of Equine Veterinary Science* published "Omeprazole Reduces Calcium Digestibility in Thoroughbred Horses" in March 2020 while the *Journal of Veterinary Internal Medicine* published "Effect of oral administration of omeprazole on the microbiota of the gastric glandular mucosa and feces of healthy horses" in November 2020.

For the calcium study, Thoroughbreds were used to evaluate the digestibility of diets containing different calcium sources with or without omeprazole over four 21-day periods.

"Proton pump inhibitors such as omeprazole reduce nutrient digestibility in humans," explained researchers. "This study determined the effect of omeprazole on the digestibility of diets containing limestone or marine-derived calcium and to assess changes in blood parameters associated with gastric acid production and calcium status in horses."

For the study, each 21-day period had a 15-day diet adaptation phase followed by a six-day collection phase, consisting of a five-day fecal collection period and a final day for gastroscopy and blood sampling. The horses who were given omeprazole received GastroGard once every day for the last 14 days of the research period.

"Omeprazole and calcium source did not affect digestibility of phosphorus, magnesium, potassium, sodium, iron, copper, zinc, or manganese but did affect calcium digestibility," the study found. "Omeprazole reduced apparent calcium digestibility from 52% to 41.4% in limestone and from 55.1% to 46.5% in BMC, equaling a 20.3% and 15.6% decrease in calcium digestibility in the limestone and BMC, respectively. Mineral source had a significant effect on calcium digestibility with BMC at 50.8% and limestone at 46.7%."

The other study was conducted because researchers are aware omeprazole administration is associated with changes in gastric and fecal microbiota and increased incidence of *Clostridioides difficile enterocolitis* in humans and dogs. They wanted to see whether this would carry through to adult horses.

For the prospective controlled study, eight healthy horses were used, and transendoscopic gastric glandular biopsies, gastric fluid, and fecal samples were obtained from each horse twice at a seven-day interval before the administration of omeprazole. Then, samples were taken after a seven-day administration of omeprazole.

"Omeprazole did not induce significant major changes in composition of fecal or gastric glandular microbiota; however, after administration, certain microbial genera became more predominant in the gastric glandular mucosa," researchers found. "Oral administration of omeprazole could have fewer effects in gastrointestinal microbiota in the horse compared to other species."

Because domesticated horses are likely to have ulcers, and GastroGard is the only approved treatment, it is important to continue to research what other effects the medication has. While reducing the frequency of ulcers is an ongoing goal, realistically the need for medication is not going anywhere, so it is important to understand it as best as possible.

Sykes discussed this as well in his presentation, stating: "I think in the next five years, the next biggest question that we need to answer in the omeprazole world is, 'What's the risk associated with its use, particularly given its high prevalence of use in some of our high-performance populations?'

"When we start talking about the potentials of side effects, it is always important to come back and say, these are drugs with clear benefits in many horses and in many of our populations. What we need to do is balance that up against the potential for risk and we need to understand more about risk before we can say that in a meaningful way." BH

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A study found that horses that exercise five or more times a week are more susceptible to equine glandular gastric disease