Rethinking equine gastric ulcer syndrome: Part 1 – Terminology, clinical signs and diagnosis

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Summary
Equine gastric ulcer syndrome (EGUS) is a common condition in the horse. A series of recent articles highlighting differences in healing of squamous and glandular ulceration have reinvigorated interest in the condition. The purpose of this series of articles is to review the current thinking on EGUS with particular emphasis on the differences between diseases of the squamous and glandular mucosae. This article, the first will review the terminology, clinical signs and diagnosis of EGUS in the horse.

Introduction
Gastric ulceration is the most common disease condition of the equine stomach with a high prevalence of both squamous and glandular disease reported in various populations (Luthersson et al. 2009a; Tamzali et al. 2011; Habershon-Butcher et al. 2012). Significant confusion exists surrounding the terminology used to describe disease in various regions of the stomach. A flow-on effect of this is that factors such as pathophysiology and risk factors from one specific region of the stomach, in particular the squamous mucosa, which is the best studied, are often inappropriately extrapolated to other regions of the stomach, namely the glandular body and pyloric antrum. The objectives of this series of articles are to: 1) clarify the distinction between diseases in different regions of the stomach; and 2) carry this distinction through into separate reviews of disease of the squamous and glandular mucosa.

Terminology
The term equine gastric ulcer syndrome (EGUS) was first adopted by the EGUS Council in 1999 to describe gastric ulceration in the horse (Andrews et al. 1999). However, numerous disease entities exist under the umbrella of the term EGUS, and recently an attempt has been made to clarify the terminology to recognise this distinction (Merritt 2009). The development of a clear distinction between diseases of different anatomical regions is essential in furthering an understanding of gastric ulceration in the horse and in the clinical treatment of affected horses. Reported differences between the squamous and glandular mucosae include differences in risk factors (Habershon-Butcher et al. 2012) and in the response to treatment with omeprazole (Sykes et al. 2014a,b,c). Further, the prevalence of squamous and glandular disease within a population differ (Murray et al. 2001; Begg and O’Sullivan 2003; Luthersson et al. 2009a; Tamzali et al. 2011; Habershon-Butcher et al. 2012) and the presence of squamous and glandular ulceration within an individual are unrelated [Murray et al. 2001; Begg and O’Sullivan 2003; Luthersson et al. 2009a]. As such, the direct extrapolation of findings from the squamous mucosa to the glandular mucosa is inappropriate and instead, disease of the squamous mucosa should be considered as a distinct entity to disease of the glandular mucosa. It is likely that disease of the glandular body differs from that of the pyloric antrum, although at present little work has been done to distinguish the two.

Further complicating the terminology of EGUS is that true ulceration of the glandular mucosa is rare with the majority of lesions more appropriately graded as erosions based on histological examination (Hepburn 2012). Similar to the term EGUS in horses, the term peptic ulcer disease is used in man to describe a wide variety of diseases under a single umbrella term (Malfertheiner et al. 2009). It is recognised in human medicine that many of the lesions described clinically as ulceration are in fact erosions by the true histopathological definition, but the term peptic ulcer disease is maintained for its ease of use (Malfertheiner et al. 2009). Consensus surrounding the terminology used to describe ulcerative and erosive disease in the stomach of the horse is needed. However, for the purpose of this series of articles a distinction is made between disease of the squamous mucosa and disease of the glandular mucosa. Accordingly, the term equine squamous gastric ulcer syndrome (ESGUS) will be used to discuss diseases of the squamous mucosa, while the term equine glandular gastric ulcer syndrome (EGGUS) will be used to discuss diseases of the glandular mucosa as proposed recently (Sykes et al. 2014a).

Anatomy of the stomach
The equine stomach consists of a single large compartment that can be divided into 3 regions approximately equal in size. The dorsal third of the stomach is covered with a stratified squamous epithelium and is otherwise referred to as the nonglandular region of the stomach. Entry to the stomach via the cardia is within the squamous mucosa. The remaining two-thirds of the stomach is covered with glandular mucosa which can be further divided into the glandular fundus (body), which occupies the mid third of the stomach, and the pyloric antrum, which occupies the most distal third (Hepburn 2011). The delineation between the squamous and glandular regions of the stomach is termed the margo plicatus.

Clinical signs
Clinical signs of EGS are wide and varied, but include recurrent colic, poor appetite, weight loss, hair coat changes, poor performance, behavioural changes and pain on
tightening of the girth (Murray et al. 1989; Murray 2009; Hepburn 2012). Attempts to correlate clinical signs with ulcer severity at a population level have been largely unrewarding, but this should not lead to the conclusion that EGUS is clinically insignificant at the individual horse level when clinical signs are present. Similarly, many horses with gastroscopic evidence of EGUS display no apparent clinical signs and this is commonly used as a reason to dismiss the clinical significance of EGUS. However, the authors have observed that many supposedly “asymptomatic” horses change behaviour, or have an improvement in their appetite and/or performance, in response to treatment, suggesting that subclinical disease may be common.

Considering this, the authors believe that EGUS should be considered as a differential diagnosis in any horse demonstrating vague clinical signs potentially referable to gastrointestinal discomfort. Importantly, the prevalence of ESGUS, and thus risk of associated clinical signs, increases with increasing intensity of exercise and management, while, in contrast, the prevalence of EGGUS, and thus risk of associated clinical signs, appear largely independent of use (Luthersson et al. 2009b). As such, EGGUS should be considered as a differential diagnosis in any case demonstrating compatible clinical signs, regardless of usage type. In such cases, it is equally important that other differential diagnoses be considered and the response to treatment followed. Lastly, although the link between colic and EGUS is controversial, the authors believe that EGUS should be considered as a differential diagnosis in all cases of idiopathic colic, especially in recurrent cases.

**Diagnosis**

A variety of methods including gastroscopy, the response to therapeutic trials, faecal occult blood and sucrose permeability testing are used, or have been proposed, as means of diagnosing gastric ulceration in the horse and thus warrant discussion.

**Gastroscopy**

In the authors’ opinion gastroscopy remains the only accurate way to diagnose EGUS ante mortem. In addition to confirming the presence or absence of EGUS, it allows further distinction into whether the squamous mucosa, glandular mucosa or both are affected as well as allowing determination of the severity of the lesion. It is important to distinguish whether the squamous mucosa, glandular mucosa or both are affected as this has implications with regards to the agents used for treatment and the expected duration of treatment required. Furthermore, this allows exclusion of other diseases that may mimic the clinical signs of EGUS, such as gastric impaction (Vainio et al. 2011).

Historically, gastroscopy has been the domain of referral centres but the advent of smaller, portable units, and their increased affordability, has increased the availability to ambulatory veterinarians and those in smaller facilities. A range of scope sizes is available. The authors both use and recommend a scope with an insertion length of at least 3 m and an outer diameter of approximately 12.8 mm. Although used in the past, and often cited in the older literature, gastrosopes <3 m long are insufficient in length to allow examination of the entire stomach in larger breed horses. In particular, observation of the pyloric antrum is often not possible when using shorter gastrosopes, which, given that the majority of glandular disease occurs in this region (Begg and O’Sullivan 2003; Luthersson et al. 2009a; Tamzali et al. 2011), is essential. Similarly, while gastrosopes with a narrower outer diameter may have some advantages, namely the ability to examine smaller patients, the authors have found the gastrosopes <12.8 mm in diameter are too flexible, making entry into the pylorus difficult, if not impossible, in many animals. Consequently a complete examination of the stomach is often not accomplished. In the authors’ experience, although the diameter of 12.8 mm may preclude the examination of some smaller pony breeds, the vast majority of horses and many larger pony breeds can readily be examined with a gastroscope of that size.

Case preparation is important. The presence of even a small amount of residual food can impair visibility and make entry into the pyloric antrum difficult. In the authors’ experience the duration of fasting is dependent on the horse’s use and its diet. For sport and pleasure horses eating a standard, hay based diet, a minimum of 16 h of fasting is required to ensure complete emptying of the stomach. In contrast, the duration of fasting for Thoroughbred racehorses on high grain/low roughage diets appears much shorter with as little as 6–8 h required for complete gastric emptying (Sykes et al. 2014b). In practice, the owner/trainer is instructed to feed the horse its normal grain meal but only a small amount of hay (typically a single flake/biscuit) the evening before and to remove any remaining feed first thing in the morning upon arriving at the stables. The owner/trainer is then instructed to train the horse as per normal (if desired) and the gastroscopy examination is performed later that morning with the horse fed its morning feed after awakening from sedation. The authors have found that this approach significantly improves owner/trainer compliance and willingness to examine horses as, in effect, the horse does not skip a meal and the impact on its training is minimal. Removal of water one hour prior to examination is advantageous but not mandatory. Given the rapidity with which the horse empties fluid from its stomach, longer durations of water deprivation are unlikely to offer any advantage.

The technique of gastroscopic examination is relatively straightforward, although some patience and practice is required to achieve a complete examination of the stomach consistently. The authors use a 19 mm outer diameter × 80 cm long lightweight vinyl tube purchased from a local hardware store to protect the gastroscope and prevent retroflexion in the pharynx. Additionally, the use of such a tube appears to improve patient compliance with less agitation observed during passage of the gastroscope. Following appropriate sedation, the tube is preplaced and secured to the halter, extending from the rostral nares to approximately 15 cm into the oesophagus. The (well lubricated) gastroscope is then passed through the tube to a length of approximately 2 m until the stomach is entered. A variety of options can be used for insufflation but the authors prefer a 15 l pressure sprayer purchased from the local hardware store. The sprayer is presurised prior to sedation of the horse and a second sprayer is kept as a spare in the event of rupture. Once the stomach is entered the hose of the sprayer is attached to the biopsy channel of the scope and the air is injected into the stomach. Good insufflation of the stomach is essential for a thorough examination, and the authors have not observed any deleterious effects of ‘excessive’
insufflation. Once the stomach is insufflated, the gastroscope is partially withdrawn until it is sitting just inside the stomach at the cardia.

At this point, care should be taken to ensure that the image is correctly oriented with the squamous mucosa visible on the upper left of the screen, the glandular body on the lower right of the screen and the greater curvature of the margo plicatus dividing the 2 (Fig 1). The squamous fundus can be observed by flexing the scope up and to the left. The gastroscope is then inserted further. During insertion, the margo plicatus should be maintained in the centre of the screen, as this facilitates positioning of the gastroscope for entry into the pyloric antrum. As the gastroscope is inserted, the lesser curvature of the margo plicatus becomes visible with the opening to the pyloric antrum immediately ventral (Fig 2). The gastroscope is then advanced in one smooth motion whilst aiming towards the pyloric antrum (initially down and to the left, and then slightly up and to the left once the level of the lesser curvature has been passed). Commonly, the gastroscope will temporarily drop beneath the level of the gastric fluid, but it typically comes out within the pyloric antrum if inserted further (Figs 3 and 4). If the pyloric antrum is not visible with the gastroscope fully inserted, then further insufflation will often result in further stretching of the stomach and the gastroscope rising above the gastric fluid.

Once the pyloric antrum has been observed, the duodenum can be examined, if desired. Whether this is performed in every horse depends mostly on the operator’s preference as duodenal disease is rare in mature horses. To enter the duodenum the gastroscope is pushed further into the stomach with the pylorus kept in the centre of the screen. As
the level of the pylorus is reached the gastroscope is turned sharply to the left, pushing it into the duodenum. As soon as the duodenum is entered it is, somewhat counter intuitively, necessary to withdraw the gastroscope slightly to allow inspection of the duodenum. Once the examination of the stomach (± duodenum) has been completed the scope is then simply withdrawn. Removal of the air from the stomach by suction at the completion of the procedure is a matter of operator preference, although anecdotally it seems to be more important in foals than mature horses as they appear to be at increased risk of colic when the air is not removed. A complete examination of the stomach is important and the presence/absence of squamous ulceration cannot be used as a predictor for the presence/absence of glandular ulceration (Murray et al. 2001; Begg and O’Sullivan 2003; Luthersson et al. 2009a). Observation of the squamous mucosa is relatively easy, whereas passage through to the pyloric antrum is more technically demanding. However, observation of the pyloric antrum is critical, as the majority of glandular ulceration occurs in this region (Murray et al. 2001; Luthersson et al. 2009a; Habershon-Butcher et al. 2012; Sykes et al. 2014a,b,c). Observation of the most ventral portion of the fundus is typically not possible due to the presence of fluid. The fluid can be suctioned out via the biopsy channel of the gastroscope; however, this is usually not necessary as ulceration in this region is rare (Luthersson et al. 2009a; Hepburn 2012). The squamous and glandular mucosa should be scored separately. A variety of scoring systems have been described but, for simplicity, the authors prefer the system first described by the EGUS Council (Andrews et al. 1999), shown in Table 1 for the squamous mucosa. Currently, the authors use a similar scoring system for the glandular mucosa (Table 1) but it is recognised that the grading of lesions in the glandular mucosa along a linear scale of severity may not be appropriate.

The correlation between clinical signs and lesion grade is inconsistent, with some horses demonstrating clinical improvement with the treatment of mild lesions, whilst others appearing unchanged despite gastroscopic resolution of severe lesions. The authors believe that care should be taken in over interpreting mild changes such as hyperaemia of the glandular mucosa and the presence of thickened rugal folds with the authors only assigning clinical significance to lesions of the glandular mucosa that appear to have disruption to mucosal integrity. Although not commonly performed by the authors, biopsy may be useful in such cases to assess the integrity of the mucosa. Similarly, the authors believe that caution should be exercised in over interpreting mild grade 2 lesions of the squamous mucosa as many are inconsequential findings. Where the results of gastroscopy are equivocal, other differential diagnoses should be considered and/or a therapeutic trial considered.

**Therapeutic trials**

The use of a therapeutic trial is logical when gastroscopy is not readily available and a positive response to treatment increases the index of suspicion of EGUS. Likewise, a positive response to treatment supports the clinical significance of mild lesions if the results of gastroscopy are equivocal. Importantly, in animals where gastroscopy has not been performed, a positive response to a therapeutic trial does not differentiate between ESGUS and EGGUS and, as such, in the authors’ opinion, a positive response to treatment should be viewed as a clear indication for gastroscopy in order to obtain a definitive diagnosis and to determine the affected region. Where funds are limited, treatment with omeprazole for 28 days may be initiated; however, gastroscopy is recommended prior to the discontinuation of therapy as the expected healing rate of EGGUS in this time is substantially lower than that of ESGUS (Sykes et al. 2014a,b,c). A negative response to trial therapy with omeprazole reduces the likelihood of EGUS, but does not completely discount it, as some animals are slow to respond clinically and clinical signs may not completely resolve until healing has occurred, especially with EGGUS. As such, in light of a negative response to omeprazole, other more likely differential diagnoses should be discounted first, but gastroscopy remains indicated if no specific diagnosis is made.

**Faecal occult blood and sucrose permeability testing**

Testing for faecal occult blood is appealing due to its ease of use, simplicity and low cost. Recently the diagnostic accuracy of a commercial faecal blood test against gastroscopy has been tested in a population of Thoroughbred racehorses with the test performing poorly (Sykes et al. 2014d). A very high prevalence of faecal acidosis has previously been reported in this population (Sykes et al. 2013), and whether this affects test performance is not known. However, until further validated in the peer reviewed literature, the authors do not recommend the use of faecal occult blood testing as a diagnostic test for EGUS.

Similarly, use of the sucrose permeability test is appealing for its ease of use and it has been proposed as a screening test for EGUS (O’Conner et al. 2004; Hewetson et al. 2006). Recently a method of reliably measuring serum sucrose has been validated and pilot data on the use of the test in clinical patients are encouraging (Hewetson et al. 2014). However, at

| Grade 0 | The epithelium is intact and there is no appearance of hyperkeratosis (yellowing of the mucosa) |
| Grade 1 | The mucosa is intact but there are areas of hyperkeratosis |
| Grade 2 | Small, single, or multifocal (<5) superficial lesions |
| Grade 3 | Large single deep, or multiple (≥5) focal superficial lesions |
| Grade 4 | Extensive lesions with areas of apparent deep ulceration |

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the time of writing, further validation of the test is required in a population of clinical cases before use of the test can be recommended.

Summary

Disease of the squamous mucosa (ESGUS) and disease of the glandular mucosa (EGGUS) are distinct disease entities and should be viewed as such. Importantly, knowledge of one (i.e. ESGUS) cannot be directly extrapolated to the other (i.e. EGGUS). Instead, information such as prevalence, risk factors, treatment and prevention need to be specifically collected on each syndrome.

Despite the appeal of alternative means of diagnosis they remain largely unvalidated and gastroscopy remains the diagnostic test of choice, not just for its ability to confirm the presence or absence of disease but for its ability to distinguish ESGUS from EGGUS and assess the severity of disease. A thorough examination of the stomach is relatively easy to perform with the correct equipment, case preparation and operator expertise.

Authors’ declaration of interests

The authors do not have any conflicts of interest, financial or otherwise, that could reasonably be expected to influence the content of this article.

References


