Equine gastric ulcer syndrome in adult horses: A review

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Abstract
In recent years, gastric ulceration has been recognised as a common, possibly performance-limiting disease of adult horses. Here, we aim to provide the reader with a useful review of recent literature covering all aspects of equine gastric ulcer syndrome (EGUS) in adult horses. The anatomy and physiology of the stomach, with particular reference to secretion of acid and mucosal protective mechanisms, are reviewed, as are the differing theories relating to the aetio-pathogenesis of gastric ulceration. We also explore the possible influence of various management factors on development of the disease.

The prevalence of the disease in racehorses has been reported to be as high as 100%. In general, horses that are in active training for racing tend to have a prevalence of around 90%, whereas pleasure horses in full work have a reported prevalence of approximately 60%. Emerging diagnostic tests which could obviate the need for gastroscopy are introduced and current recommendations for treatment are summarised, focussing on proton pump inhibitors, in particular omeprazole, administered orally. The oral administration of omeprazole has been shown to be effective in both treating horses with gastric ulceration and at preventing re-occurrence whilst the horses are in training, provided that daily dosing is maintained.

KEY WORDS: Horse, equine, EGUS, gastric ulcer, diagnosis, treatment, review

Introduction
Gastric ulceration is a problem frequently seen in both foals and adult horses, especially sick foals and adult horses in active training. Due to its complicated and multifactorial nature, the term equine gastric ulcer syndrome (EGUS) has been used to describe this disease. There are two main subsets of the disease: the primarily glandular disease seen in neonates and foals; and the predominantly squamous form of the disease seen in adult horses. The terms gastric ulceration and EGUS are used interchangeably in this review to indicate the primarily squamous mucosal form of gastric ulceration seen in adult horses.

Due to the lack of any pathognomonic clinical signs, definitive diagnosis of EGUS currently relies on oesophagogastroscopy. Different scoring systems for grading the endoscopic appearance of gastric ulcers have been reported, based upon anatomical location (Murray et al 1989, 1996; Murray and Eichorn 1996), and number and severity of lesions (Murray et al 1989, 1996; Murray and Eichorn 1996; MacAllister et al 1997). Until recently, there has been no standard scoring system for gastric ulceration in the horse (Anonymous 1999), and no reports to date have demonstrated a definite relationship between ulcer score and severity of clinical signs (MacAllister et al 1997; Dionne et al 2003).

Clinical signs of EGUS in adults are non-specific and include lack of appetite, weight loss/poor body condition, mild or recurrent colic, and loose faeces. Foals tend to show a separate, more specific set of clinical signs, including less time spent suckling, poor body condition, diarrhoea, bruxism, ptyalism and intermittent colic (Murray 1999a). The remainder of this review focuses on the subset of EGUS seen in adult horses, rather than the clinical disorder seen in foals.

EGUS affects between 58 and 100% of adult horses in training (Orsini and Pipers 1997; Vatistas et al 1999a; Dionne et al 2003; Ferrucci et al 2003; Bell et al 2007a). In adult horses, 75–80% of ulcers are found in the squamous portion of the stomach (Anonymous 1999), especially along the margo plicatus, although ulcers may also be found in the glandular and pyloric regions. Most racehorses will develop gastric ulceration at some time in their careers, although not all horses with ulceration will show clinical signs of disease (Murray 1994a).

Currently, treatment for EGUS centres on pharmacological suppression of gastric acid secretion. Treatment must be continual whilst horses are in training, to prevent recurrence. Despite the high incidence, the aetiology of gastric ulcers in adult horses remains unknown, partly due to the lack of a suitable model with which to study the disease and partly due to the difficulties encountered in performing research on animals owned by clients (Vatistas et al 1999b).

BID Twice a day
ECL Enterochromaffin-like
EGF Epidermal growth factor(s)
EGUC Equine Gastric Ulcer Council
EGUS Equine gastric ulcer syndrome
H2 Histamine-type 2
HCl Hydrochloric acid
I/V Intravenous(lly)
MMC Migrating myoelectrical complex
NSAID Non-steroidal anti-inflammatory drug
PO Per os
SW Slow wave
TID Three times daily
VFA Volatile fatty acid

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Anatomy

The equine stomach is divided into two distinct anatomical regions, the non-glandular or squamous region, and the glandular region. These two regions are separated by the margo plicatus. The proximal third of the stomach is covered by non-glandular stratified squamous epithelium, and is considered to be an extension of the oesophagus. No glandular structures are evident histologically and there is no evidence for active transport within the squamous mucosa (Merritt 1999). The majority of ulcers associated with EGUS are found in this region of the stomach. The distal two-thirds of the stomach are covered by a glandular mucosa which secretes mucus, hydrochloric acid (HCl) and pepsinogen (Buchanan and Andrews 2003).

Squamous mucosa

In horses, the squamous epithelium extends from the oesophagus to cover the fundic portion of the stomach (Sisson and Grossman 1975). This stratified squamous gastric mucosa consists of four major histological layers: stratum corneum, stratum transitionale, stratum spinosum and stratum germinativum (Figure 1). The outermost layer is the stratum corneum, a cornified layer that is several cells deep. Next is the stratum transitionale, which is directly underneath the stratum corneum and contains cells with round nuclei (Argenzio 1999). Deep to the stratum transitionale is the stratum spinosum, with cells of a spiky appearance. The innermost layer is the stratum basale or stratum germinativum, comprising cuboidal cells and large nuclei positioned centrally. This final layer is two to four cells thick (Argenzio 1999). Epithelial thickness of the squamous mucosa is greatest at the margo plicatus in comparison to 15–25 mm proximal to it (Murray et al 2001b). The aforementioned arrangement of epithelial cells is present in full-term foals. However, the gastric mucosa becomes thicker with both increasing age and gestation. No glandular structures are evident histologically and there is no evidence for active transport of substances such as bicarbonate or HCl within this mucosa (Merritt 1999).

Glandular mucosa

The glandular portion of the stomach contains mucus-secreting cells and gastric glands, which provide secretions in response to different stimuli. These gastric glands contain six main cell types: parietal cells, zymogen cells, chief cells, D-cells, mast cells and enterochromaffin-like (ECL) cells (Murray 1991a). The glandular mucosa is divided into three distinct regions: the cardiac, fundic and pyloric glandular regions. The cardiac glandular region is located in a thin strip immediately adjacent to the margo plicatus. In the horse, little is known about the function of this region, as well as in other species. The fundic glandular region is located along the body of the stomach, including both the lesser and greater curvatures, to the junction of the cardiac glandular region (Anonymous 1999). This former region contains the typical gastric glands (Figure 2), which are made up of parietal cells (which secrete HCl), zymogen (chief) cells (which secrete pepsinogen), and ECL cells (which secrete histamine).

Histamine acts as an agonist at histamine-type 2 (H2) receptors on the parietal cells and stimulates acid secretion. The gastric glands also contain cells capable of secreting mucus and sodium bicarbonate, which aid in the mucosal defence against acidity. The pyloric glands, which line the portion of the glandular mucosa connecting with the pylorus, contain G-cells which secrete gastrin, D-cells which produce somatostatin, and numerous serotonin-producing ECL cells (Merritt 1999).

Physiology

Gastric motility

Gastric motility is initiated by the vagus nerve, which travels along the oesophagus, through the diaphragm and into the stomach, where it divides into several branches and inserts deep in the wall of the stomach. There are two main types of motor events that effect gastric emptying in the horse, peristaltic contractions that progress from the body of the stomach to the pylorus and result in a round bolus of ingesta moving towards the duodenum, and...
administration of acetaminophen (Doherty et al 1998). The study meal followed by scintigraphic imaging (Ringger et al 1996), and beads (Argenzio et al 1974), administration of a radio-labelled rate of gastric emptying. These studies have employed plastic Marker studies have been performed on the horse to identify the dency of the MMC in the horse is approximately 2 hours (Merritt 1999). In the equine stomach, three phases of the MMC are best achieved through myoelectrical recording of the peristaltic cycle, called the migrating myoelectrical complex (MMC) (Merritt 1999). In the equine stomach, three phases of the MMC are seen: Phase I, which has no action potential activity; Phase II, which has intermittent action potential activity and occurs when ingesta is propelled along the gastrointestinal tract; and Phase III, which has continuous intense action potential activity. The periodicity of the MMC in the horse is approximately 2 hours (Merritt 1999).

Assessment of the action potential activity within the stomach is best achieved through myoelectrical recording of the peristaltic cycle, called the migrating myoelectrical complex (MMC) (Merritt 1999). In the equine stomach, three phases of the MMC are seen: Phase I, which has no action potential activity; Phase II, which has intermittent action potential activity and occurs when ingesta is propelled along the gastrointestinal tract; and Phase III, which has continuous intense action potential activity. The periodicity of the MMC in the horse is approximately 2 hours (Merritt 1999).

Marker studies have been performed on the horse to identify the rate of gastric emptying. These studies have employed plastic beads (Argenzio et al 1974), administration of a radio-labelled meal followed by scintigraphic imaging (Ringger et al 1996), and administration of acetaminophen (Doherty et al 1998). The study utilising plastic beads illustrated that solid contents have a longer transit time through the stomach than liquids; 75% of plastic beads remained in the stomach after 1.5 hours compared with 25% of the liquid marker (Argenzio et al 1974). Recently, the use of the 13C-octanoic breath test has been reported. This test uses a 13C-octanoic-labelled meal that leaves the stomach without being metabolised. This then proceeds to the small intestine where it is rapidly absorbed and undergoes oxidation in the liver, leading to production of 13CO2, which is then exhaled. The ratio of the labelled CO2 is compared to normal CO2, and the rate of gastric emptying can then be calculated (Sutton et al 2003). Studies of gastric motility using this technique illustrated that the mean time to gastric half-emptying (time that half the contents are emptied from the stomach) in control horses fed a test meal was 2.58 hours, and the mean lag time until the maximal gastric emptying rate was achieved was 1.24 hours (Sutton et al 2002). The development of this method of evaluating gastric emptying is important because if the analytical equipment required to perform the test becomes more readily available at commercial laboratories it will offer the advantages of being simple, quantitative and non-invasive, making it more readily applicable to both clinical and research settings.

pH
Gastric acid output is the amount of HCl secreted by the stomach per unit of time. Gastric acidity is determined by the pH of the gastric contents, which is a mixture of salivary, gastric, duodenal, biliary and pancreatic secretions. The distinction between acid output and gastric acidity is important, as the administration of therapeutics that decrease acid secretion alone may not affect gastric pH until the acid output is greatly reduced (Moore and Scarlata 1965). Hydrochloric acid is secreted by parietal cells in the gastric glandular mucosa and is responsible for cleaving pep-sinogen into pepsin (Murray 1997). Pepsin is then responsible for the enzymatic breakdown of protein. The mean pH of gastric juices has been reported to be 2.72 ± 1.86 (Murray and Grodinsky 1989), 3.2 ± 2.0 (Nadeau et al 2000), and 3.1 (Murray and Schusser 1993) in non-fasted animals. Episodes of nearly neutral pH were a feature of the cycle of acidity in these animals (Baker et al 1993); these episodes may reflect duodenogastric reflux which may have both a buffering and dilutional effect on the gastric contents (Merritt 1999). The gastric pH of adult horses and foals has been shown to have a dorsoventral gradient, and the pH of the saccus caecus is greatest in adult horses and foals and the lowest pH is found in the more ventral fluid contents (pH 2.72 in adults and 1.85 in foals; Murray and Grodinsky 1989). Feeding has a buffering effect on gastric pH, and the mean intra-gastric pH increases by one to two units (Murray and Schusser 1993) mainly through the buffering effects of increased production of saliva. Saliva plays an important role in buffering gastric pH and it is thought that low-forage diets may decrease its production, thus decreasing the buffering provided by saliva and causing an increase in gastric pH. Such an increase in pH may predispose animals on such diets to gastric ulceration.

Gastric acid secretion
The horse is a continuous and variable secretor of gastric acid (Murray 1997). This means that acid secretion occurs even without the presence of feed material in the stomach. In fasted horses, gastric acid output is continuously variable, and non-parietal se-cretions such as bile acids and pancreatic juices are voluminous (Merritt 1999). Gastric acidity was greater in fasted horses compared to those fed hay (Murray 1994b).

Figure 2. Equine gastric gland.
Glandular mucosal defence

Gastric glandular epithelium has a number of mechanisms to prevent injury by HCl. These include epidermal growth factors (EGF), bicarbonate buffering, mucosal blood flow, secretion of mucus, cellular repair, and prostaglandins (Miller 1983). Of these, mucosal blood flow is considered to be the most important as it provides the mucus with the oxygen and nutrients necessary to produce the mucus-bicarbonate layer and allow rapid turnover of epithelial cells (Wallace 2001). EGF are found in salivary secretions and promote DNA synthesis and proliferation of gastric mucosal cells (Jeffrey et al 2001). Prostaglandin E2 has numerous protective functions, including promoting mucosal blood supply, maintaining intercellular tight junctions, stimulating secretion of bicarbonate and mucus, and suppression of the secretion of HCl (Miller 1983). Secretion of bicarbonate by gastric mucosal cells is triggered in response to increased concentration of acid, mechanical irritation and production of endogenous prostaglandin. Adherence of bicarbonate to the mucosa creates neutral pH at the mucosal surface, despite the acidic pH of the luminal surface (Murray 1999b). Mucus secreted by specialised neck cells is viscous and hydrophobic; it adheres to the mucosa and helps it to resist damage caused by contact with acid and pepsin (Anonymous 1999).

Squamous mucosal defence

Traditionally, it has been thought that there is no surface barrier to HCl in the equine gastric squamous mucosa and that the protection of this mucosa is dependent upon limited exposure to gastric secretions (Murray 1999b). Two recent investigations have raised the possibility of a surface barrier in the squamous mucosa (Ethem et al 2000; Bullimore et al 2001). One study of normal cadaver stomachs was able to demonstrate the presence of mucins, but no role has been determined for the mucus in horses and its physical properties have not been elucidated. It is important that this mucus be demonstrated in the live horse, rather than just in cadaver stomachs, and its physical properties determined, before any conclusions are drawn about its role in squamous mucosal protection (Bullimore et al 2001).

An additional study proposed the presence of an osmiophilic phospholipid material (surfactant) on the squamous mucosa. This material was demonstrated using electron microscopy and provides evidence for an additional protective mechanism via a physical barrier to acid (Ethem et al 2000). Again, this study was performed using post-mortem samples, and did not provide evidence of a functional barrier. It is possible that this osmiophilic layer provides an effective barrier which may be readily disrupted by substances such as bile acids (Geor 2000), to which the mucosa may be exposed through duodenal reflux.

Another potential protective mechanism within the squamous mucosa is EGF. EGF have physiological effects on the gastrointestinal tract such as inhibition of gastric acid secretion, and mucosal regeneration and protection. They have been shown to have a role in the healing of gastric ulcers in laboratory animals (Jeffrey et al 2001). Within the squamous mucosa, there are receptors for EGF, which are more concentrated in regions of high cell turnover. There is evidence that these EGF receptors can be induced in areas of injury to the mucosa (Jeffrey et al 2001). It is still not fully known what the role of these potential protective mechanisms is.

Healing of gastric ulcers

Healing of gastric ulcers commences immediately following mucosal injury. The rate of gastric healing is affected both by the size and depth of the lesions, although depth is the more important determinant. Superficial lesions in the squamous mucosa may take as little as 7 days to heal, whilst in deeper lesions the removal of tissue debris and wound contraction means that healing may take as long as 3 months (Murray et al 1997). One study using H2-receptor antagonists to promote healing found regional differences in healing times, and lesions in the saccus cæcum and around the cardia healed more rapidly than those at the margo plicatus. Lesions located at the lesser curvature along the margo plicatus took the longest time to heal (Furr and Murray 1989).

Spontaneous healing of gastric ulcers in horses that are actively being worked is rare. A study by Murray et al (1996) showed slight improvement in the severity of lesions in only 6/35 horses after 2–3 months, and none healed completely. Lesions in that study tended to worsen as the horses continued in training. In another study, gastric ulceration healed without treatment in one horse maintained in training, after 58 days, out of a control group of 25 horses (Andrews et al 1999a). Spontaneous healing was reported in only 3/34 control horses after 28 days in a study on the efficacy of omeprazole paste, although not all horses in that study were in active training (MacAllister et al 1999).

Actiopathogenesis

Horses continuously secrete gastric acid and exposure to acid is currently thought to be the major cause of EGUS. The development of gastric ulceration can be viewed as an imbalance between aggressive and protective factors on the mucosa (Andrews and Nadeau 1999). Ulcers occurring within the squamous mucosa are similar to gastro-oesophageal reflux disease in humans (Murray et al 2001a). The squamous mucosa near the margo plicatus is constantly exposed to acid and is the most common region for ulceration to occur (Murray 1999b), particularly at the lesser curvature of the stomach along the margo plicatus, in exercising horses (Murray 1999b; Merritt 2003). Continued exposure of the squamous mucosa to HCl results in loss of the superficial epithelial layers. The severity of the lesions is apparently related to the duration of exposure to HCl (Furr et al 1992).

Risk factors

Risk factors for EGUS include stress (McClure et al 1999), transport (Ferrucci et al 2003; McClure et al 2005c), high-energy feed (Murray and Eichorn 1996), confinement in stalls (Orsini and Pipers 1997), intermittent feeding, and intense exercise and racing (Buchanan and Andrews 2003; McClure et al 2005c). The horse has evolved as a grazing animal and it is postulated that the constant flow of saliva and feed material into the stomach during grazing acts as a buffer which protects against excess gastric acidity. When horses are put into training they are stabled for prolonged periods and often have no access to grazing. Even when provided with feed ad libitum they may spend less time actually eating when stabled, which may decrease this important salivary buffering mechanism (Buchanan and Andrews 2003). Recent work by us into a population of horses that were turned out to pasture daily showed that the prevalence of gastric ulceration was similar to that reported elsewhere (Bell et al 2007). In that study, horses in training that were kept in paddocks and not stabled at all, all had evidence of gastric ulceration, emphasising the importance of training/racing as a risk factor for the development of EGUS.

The type of diet and amount of roughage fed may play a role in the induction of gastric ulceration. Feeding hay alone increases
post-prandial gastrin, although feeding pellets, grain or ‘sweet feed’ results in a larger increase in post-prandial concentrations of gastrin in serum, which indicates that diet may significantly affect gastric acid secretion (Smyth et al 1989). Hay and grain contain variable concentrations of fermentable carbohydrates, which may be converted by bacteria to volatile fatty acids (VFAs). At low pH, these VFAs may become non-ionised and penetrate the squamous mucosa of the stomach. These VFAs can cause local acidification, uncoupling of sodium transport, cellular swelling, inflammation, and ulcers (Nadeau et al 2003a). Indeed, diets that are high in carbohydrates may lead to increased production of short-chain fatty acids, which, at a low pH, may result in an increased incidence and severity of gastric ulceration (Nadeau et al 1998).

Concentrations of VFAs in the stomach are highest 2–6 hours after feeding, and decrease rapidly as food moves out of the stomach. These effects may be offset by the buffering capacity of a high-protein diet. Thus, when feeding a high-carbohydrate diet it is important to also include a significant component of protein (Nadeau et al 2000). The prevalence of ulcers has been shown to be lower in horses fed a diet of alfalfa (Medicago sativa) hay compared with those fed grass hay, despite higher concentrations of VFAs in alfalfa hay. This was thought to be related to the high protein and calcium content of the alfalfa hay, which provides buffering for up to 6 hours after ingestion (Nadeau et al 1998).

As little as 48 hours of feed deprivation has been shown to induce gastric ulceration (Murray and Eichorn 1996). After feed was reintroduced such ulcers healed spontaneously in 2–5 weeks (Mur- ray et al 2001b). As fasting results in a decrease in pH and because exercise has been postulated to contribute to ulceration of the squamous mucosa (Orsini 2000), either due to decreased gastric motility or increased intra-gastric pressure. The latter may be the result of action of the abdominal muscles or increased respiratory effort, and leads to a disruption of the normally-occurring dorso-ventral pH gradient (Lorenzo-Figuera and Merritt 2002). Horses in race training have been shown to have a higher prevalence of gastric ulcers than those not in work (Murray et al 1989, 1996; Orsini and Pipers 1997; Dionne et al 2003). The use of simulated race training, i.e. working between 1.6–3.4 km six times per week on a track, resulted in 100% of horses developing ulcers within 2 weeks of entering training; all horses in that study were stabled (Vatistas et al 1999b).

Concurrent monitoring of gastric pH, intra-gastric and intra-abdominal pressure revealed a decrease in the gastric pH, and an increase in the intra-gastric and intra-abdominal pressures during exercise (trotting and faster). This was followed by a rapid return of all parameters to near-resting values once exercise ceased. It was suggested that the increase in intra-abdominal pressure during exercise causes compression of the stomach, which in turn leads to exposure of the squamous portion of the stomach to acid (Lorenzo et al 2001).

Stress has been postulated as a cause of gastric ulceration, especially in adult racehorses (Lloyd 1993). However, serum cortisol levels of racehorses in active training were reported to actually decline over the course of one study, most likely because the horses became acclimatised to their environs (Vatistas et al 1999b). Conversely, post-prandial concentrations of gastrin in serum in Arabian horses were shown to be increased after 6 weeks of training on a treadmill (Furr et al 1994), and Orsini and Pipers (1997) showed that horses in training for the longest period had the highest prevalence and severity of ulceration, although this study only involved small numbers of horses (33 in total).

Several different acids have been implicated in damaging the equine gastric squamous mucosa. Hydrochloric acid has a corrosive effect on squamous mucosa in vitro (Widenhouse et al 2002), and in combination with VFAs causes inhibition of cellular transport of sodium, cellular swelling, and eventual ulceration (Nadeau et al 2003b).

Pepsinogen, which is cleaved to pepsin at pH <4, is thought to play a role by acting in a synergistic fashion with HCl to cause damage to the mucosa. Bile acids have a major role in mucosal damage as they increase permeability of the mucosal cell to hydrogen ions. A combination of bile salts and acid affect electrolyte transport, and cause more mucosal damage than either substance alone. However, this occurs only at pH <4 (Berschneider et al 1999).

Although administration of non-steroidal anti-inflammatory drugs (NSAIDs) has been shown to cause gastric ulcers in the glandular mucosa of some horses, their role is controversial and they should probably not be viewed as a major cause of EUGS, which occurs primarily in the squamous mucosa (Orsini 2000). Some studies have failed to show any association between administration of NSAIDs and glandular gastric ulceration (Vatistas et al 1999b). Indeed, a study of the toxic effects of phenylbutazone, flunixin meglumine, and ketoprofen showed only horses that had pre-existing gastric glandular ulceration were affected, and an increase in number and severity of lesions was observed in those horses whilst animals in the control group that had glandular lesions actually healed (MacAllister et al 1993).

Helicobacter spp have been shown to be an important cause of gastric ulcers in humans, but as they are primarily associated with glandular ulceration are less likely to be important in EUGS (Murray 1999b). There are no reports to date documenting the presence of Helicobacter spp in horses. One group noted a difference between gender and the prevalence of gastric ulceration in Standardbred horses (Rabuffo et al 2002).
The relative risk for gastric ulceration increased with age in geldings but decreased for stallions and brood mares. It should be noted that none of the 2-year-old horses in that study were geldings, and indeed almost all the young horses were either intact males or females. Often, mares and stallions are retired for breeding rather than continuing their racing career, so may have shorter racing careers compared with geldings. Such factors may have influenced the findings in that study (Rabuffo et al 2002).

In one study, repeated administration of an hypertonic oral electrolyte solution caused an increase in the severity and number of lesions in the squamous mucosa of seven treated horses compared to controls (Holbrook et al 2005). However, the ulcers in the control group increased in severity, and were less severe than the ulcers in the treatment group at the start of the study (prior to treatment). It is possible that the increase in severity seen after administration of the oral paste was caused by the change in housing (small yards), withholding of feed for a total of 40 hours over 3 days, and the change in diet on the day between examinations, rather than the paste itself.

**Location of ulcers**

The majority of squamous ulcers are located along the margo plicatus (Furr and Murray 1989; MacAllister et al 1997; Sandin et al 2000). They are also commonly found in the saccus cæcius, the squamous mucosa along the lesser curvature, greater curvature and the cardia. A higher number and greater severity of ulcers seen at the lesser curvature along the margo plicatus has been reported (Murray and Eichorn 1996), although other authors reported no such site-dependent variation in severity (MacAllister et al 1997). Recent data from New Zealand show a higher prevalence of ulceration at the greater and lesser curvatures than at the saccus cæcius, and that ulcers were more severe at the lesser curvature than at the other two sites (Bell et al 2007a). Glandular and duodenal ulcers were less common in mature horses than ulceration of the squamous mucosa (Andrews and Nadeau 1999).

**Clinical signs**

Gastric ulcers can cause a wide range of clinical signs (Sandin et al 2000), or horses may be asymptomatic. Signs may include poor appetite (Dionne et al 2003), failure to thrive, dullness of coat (Murray 1991a), decrease in performance (Murray 1992; Collier and Stoneham 1997), loss of condition (Murray et al 1989), bruising and stereotypic behavior (Nicol et al 2002). Unfortunately, these clinical signs are non-specific, and horses presenting with clinical signs suggestive of EGUS may have no gastroscopic evidence of gastric ulceration. In one study, 80/87 (92%) horses with suggestive clinical signs did have gastric ulcers, whereas only 52/100 of those without clinical signs were affected (Murray et al 1989).

Gastric ulceration was found in 92/111 (83%) horses with recurrent colic. Gastric ulceration was deemed to be the sole cause of colic in 31 (28%) of these horses after first excluding other causes of recurrent colic, diagnosing ulceration gastroscopically, and then demonstrating a response to treatment with anti-ulcer medications (Murray 1992). It has also been suggested that the presence of severe ulceration may be associated with the presence of more severe symptoms (Murray et al 1999). However, none of the reports cited determined whether the severity of clinical signs correlated with the severity, number or location of gastric ulcers (Vatistas et al 1999a). Equally, in terms of poor performance, there has been no link made between the severity of gastric ulceration and subsequent poor performance.

**Diagnosis**

Gastroscopy is currently the only method for definitive ante-mortem diagnosis of EGUS. The procedure requires the use of a 3-m endoscope to allow visualisation of the pylorus. Horses must be fasted for a minimum of 6 hours. Once visualised, lesions should be scored, but no one scoring system has been universally accepted for the grading of gastric ulcers in horses (MacAllister et al 1997). To some extent this limits comparison and contrast between studies (Collier and Stoneham 1997).

Lesions are generally classified both according to location and severity. Measuring the size of lesions objectively, whilst ideal, is impractical due to the irregular appearance of these ulcers in the equine stomach (MacAllister et al 1997). Scoring systems range from 0–3 (MacAllister et al 1999; Murray et al 1999; Vatistas et al 1999b; Rabuffo et al 2002; Begg and O’Sullivan 2003), 0–4 (Furr and Murray 1989; Murray 1989, 1992; Murray et al 1989, 1990; Murray and Eichorn 1996; MacAllister et al 1997; Anonymous 1999; Vatistas et al 1999a; Johnson et al 2001), 0–5 (MacAllister et al 1997; Vatistas et al 1999c, Andrews et al 2002), 0–6 (McClore et al 1999; Nieto et al 2001), and 0–10 (Murray et al 1996; Venner et al 1999). Often, the scoring systems used have varied with the differing aims of the studies, e.g. prevalence studies vs treatment trials, and one group of authors used three different grading systems in three different studies (Vatistas et al 1999abc). Recently, the Equine Gastric Ulcer Council (EGUC) suggested a uniform scoring system which grades lesions on a 5-point scale, with 0 being normal and Grade 4 extensive deep lesions (Anonymous 1999).

One study which compared results of evaluation of ulcers between five experienced operators showed a good correlation between numbers of glandular ulcers but poor agreement when analysing squamous lesions (Andrews et al 2002). Additionally, when the results from endoscopic evaluation were compared with histopathology it was apparent that endoscopy alone did not accurately assess the depth or severity of squamous gastric ulceration and underestimated the number of gastric glandular lesions. A recent study (Bell et al 2007b) reported good agreement between operators using the EGUC system, who found it more repeatable, and faster and easier to use than the Number/Severity system validated by MacAllister et al (1997).

There are no haematological or biochemical markers currently available to diagnose EGUS (Vatistas et al 1999a). Faecal occult blood may be useful in diagnosing ulceration in neonatal foals, although in adults and older foals the colonic microflora digests the free haemoglobin (Murray 1991b). Evaluating sucrose concentrations in urine (O’Connor et al 2004) and blood (Hewetson et al 2006) after administration via nasogastric intubation has been reported. This technique relies on the fact that sucrose is rapidly hydrolysed as it crosses the brush border of the small intestinal epithelium. This occurs even in the face of significant mucosal damage in the small intestine (Meddings et al 1993). If the gastric mucosa is compromised, sucrose may be absorbed systemically and excreted in the urine, and increased gastric permeability to
sucrose is a reliable indicator of gastric ulceration in other species. The total amount of sucrose detected in urine over a specific time has been used in dogs, rabbits and people to indicate severity of ulceration. The concentration of sucrose in urine has also been shown to be a useful tool to diagnose gastric ulcers in adult horses, however urinary concentration by the animal may affect the outcome of the test (O’Connor et al. 2004). The use of sucrose concentrations in serum rather than urine to diagnose gastric ulceration has the advantage that it is less invasive and quicker to perform, and the amount of sucrose absorbed may be correlated with the severity of gastric ulceration seen on gastroscopy (Hewetson et al. 2006).

In the absence of gastroscopy, the clinician may elect to treat animals empirically, and use response to treatment as a means of indirectly diagnosing EGUS. This method has an obvious disadvantage because of the high cost of treatment.

Prevalence

The first study into the prevalence of EGUS was by Hammond et al (1986), on horses in Hong Kong undergoing post-mortem examination, and revealed that 109/165 (66%) racehorses in training had evidence of gastric ulceration. The horses in training not only had a higher prevalence of gastric ulceration but they also had more severe lesions than horses that were not in training for racing. More recent research has shown the prevalence in Thoroughbred racehorses to be as high as 100% (Murray et al 1996). It appears that most young racehorses have normal stomachs but once they begin training up to 90% develop EGUS. This occurs after as little as 3 months in work (Murray 1994a). Race training has been shown to increase both the prevalence and severity of gastric ulceration; 174/202 (86%) horses in training for at least 2 months showed gastric ulcers and 68 (39%) of these horses showed overt clinical signs (Vatistas et al 1999a).

Murray et al (1989) reported EGUS was evident in 52/100 clinically-normal yearlings and mature horses, in 67/113 (59%) horses not in training, and in 66/74 (89%) horses in training. Similar numbers have been reported for Standardbred racehorses, 195/224 (87%) of horses in training being affected (Rabuffo et al 2002). A recent study of Standardbred racehorses in Canada showed an overall prevalence of 121/275 (44%) horses, and 88/139 (63.3%) horses in training affected. There was also a significant difference between trotters and pacers, as trotters had a higher prevalence of gastric ulceration, leading those authors to speculate about the possibility that gait may play a role in the incidence of EGUS (Dionne et al 2003).

Begg and O’Sullivan (2003) reported 297/345 (86%) Thoroughbred racehorses in Australia had gastric ulceration, but the majority of horses in that study were exhibiting clinical signs consistent with EGUS and were examined on that basis which probably added significant bias to those results. Murray (1992) showed that 100% of horses in training with clinical signs consistent with EGUS had gastric ulceration.

The prevalence of ulceration in animals in work but not in active race training appears to be lower; 29/50 (58%) show horses had endoscopic evidence of ulceration (McCune et al 1999), and 23/62 (37%) horses used for riding lessons or showing/pleasure riding had lesions (Murray et al 1989). One small study of competitive mixed-breed horses showed that only 4/23 (17%) had superficial ulcers prior to starting competitive work. However, after three consecutive days of travel and competition 13 (56%) horses had ulceration, 36% of which had superficial lesions and 54% had deeper lesions (Hartmann and Frankeny 2003). In a preliminary study into the prevalence of gastric ulcers in endurance horses, ulcers were found in 23/37 (67%) immediately after competition (Nieto et al 2004). The size of the sample was small and the average severity of the ulcers was low, although eight horses had glandular mucosal ulcers that were actively bleeding. It was suggested that the ulcers observed in those horses were acute, i.e. had formed during the competition itself, and not the result of long-term management or training factors (Higgins 2004).

Treatment

The goals of treatment of gastric ulcers in horses are to eliminate clinical signs, promote healing of ulcers, and prevent both recurrence and complications (MacAllister 1999). Currently, treatment of gastric ulceration in horses focusses on suppression of acid secretion using H2-receptor antagonists and proton pump inhibitors. Other drug therapies include synthetic prostaglandins, antacids and mucosal protectants. Due to the high prevalence of gastric ulcers and the cost of anti-ulcer medications, some equine clinicians question the need to treat asymptomatic horses (Nieto et al 2001). In addition to pharmacological therapy, dietary and environmental modification alone may help healing (Buchanan and Andrews 2003). Merely taking horses out of work and turning them out to pasture has been suggested as the best dietary management treatment for EGUS (Murray 1994a).

The treatment options outlined in this review focus on the two most common groups of drugs used for the treatment and prophylaxis of ulcers, the H2-receptor antagonists and the proton pump inhibitors. Buchanan and Andrews (2003) provide a detailed review of other treatment options of EGUS in the horse.

H2-receptor antagonists

These compounds act by blocking the interaction of histamine with H2 receptors on the parietal cell and thus decrease the basal secretion of HCl. They also act to partially inhibit both feed- and pentagastrin-stimulated secretion of acid, and were developed by manipulating the chemical structure of histamine to form compounds that compete with histamine for H2 receptors (Sangiah et al 1988). They are selective for H2 receptors and have minimal effects on H1 receptors, which are found on glia, neurons and vessels and act to mobilise Ca2+ in receptive cells (Bloom 1996). They also appear to have minimal physiological effects on H2 receptors in other tissue (MacAllister 1999). Toxicity due to H2-receptor antagonists has not been reported in the horse (Furr and Murray 1989), but in humans is associated with inhibition of hepatic cytochrome P450 enzymes, causing alterations in drug metabolism and gastrointestinal absorption (Zimmerman and Schenker 1985).

There appears to be significant inter-horse variation in the response to H2-receptor antagonists, particularly at lower dosages, most likely because of the relatively poor oral bioavailability of these drugs in horses (Duran 1999). Thus, H2-receptor antagonist therapy should be undertaken at the high end of the dosing scale (Murray 2004). H2-receptor antagonists are not beneficial in preventing ulcers when glucocorticoids or NSAIDs are used.
concurrently (Duran 1999). Examples of H₂-receptor antagonists available for use in horses include ranitidine, cimetidine, nizatidine and famotidine. These drugs vary in potency; cimetidine is the least potent, ranitidine and nizatidine are of a similar potency and famotidine is the most potent. In horses, ranitidine is considered three to four times more potent than cimetidine (Sangiah et al 1988) and famotidine is considered to be approximately two to three times as potent as ranitidine (Murray 2004).

Ranitidine
Administration of ranitidine at 4.4 mg/kg and 6.6 mg/kg has been shown to raise the gastric pH of adult horses to above 6 in 4/5 and 5/5 horses, respectively (Murray and Grodinsky 1992). The half-life after oral administration was lower compared to intravenous (I/V) dosing (84.75 minutes vs 170.45 minutes), which was the opposite to what is seen in humans (Holland et al 1997). The dosing regimens for ranitidine have largely been empirical in nature and often extrapolated from human studies, despite the fact that it appears that ranitidine has a lower oral bioavailability in both adult horses and foals compared to humans (Holland et al. 1997).

Studies of the efficacy of H₂-receptor antagonists in the treatment of gastric ulcers in horses have elicited conflicting results. In one study, treatment with ranitidine (6.6 mg/kg per os (PO) three times daily; TID) was shown to be effective in healing gastric ulcers in adult horses, and 18/29 horses showed total resolution of the ulceration after 2–3 weeks of therapy (Furr and Murray 1989). Treatment with ranitidine at 6.6 mg/kg PO TID was able to prevent induction of ulcers in adult horses in a feed-deprivation model (Murray and Eichorn 1996). In contrast, another study showed more effective healing of flunixin-induced ulcers in control animals than in those receiving ranitidine therapy. This study used young (<12-month-old) ponies rather than adult large-breed horses, the gastric ulcers were induced by high-dose NSAID therapy, and the dose rate of ranitidine used was 30% lower than that currently recommended (MacAllister and Sangiah 1993). It is possible that these factors may have contributed to the failure of ranitidine therapy in that study. In yet another study, there was no difference in endoscopic ulcer scores between horses being treated with H₂ antagonists and those receiving no medications (Orsini et al 2003), although the specific dose regimens for the H₂ antagonists were not reported. A recent report showed that treatment of horses in race training with ranitidine administered orally did not result in a significant improvement in the mean severity of ulcers after 28 days of treatment (Lester et al 2005).

Other H₂-receptor antagonists
A number of different dosages of cimetidine have been reported ranging from 2.2 mg/kg to 20 mg/kg (Sangiah et al 1988; Furr and Murray 1989; Smyth et al 1990; Nieto et al 2001). Therapeutic levels of cimetidine in plasma are reported to be 1 μg/ml (Smyth et al 1990; Nieto et al 2001). To achieve these levels in horses requires dosages of 11 mg/kg I/V or 48 mg/kg PO per day. The bioavailability of cimetidine administered orally appears to be lower than that of humans, which is likely due to the differences in the gastrointestinal tract between the species (Smyth et al 1990). Mean oral bioavailability of cimetidine in the horse has been reported to be 14% (Sams et al 1997). The half-life of cimetidine is from 1–2.2 hours (Smyth et al 1990; Sams et al 1997), and it is excreted in the urine of horses both as the parent drug and the sulphoxide.

Studies into the efficacy of cimetidine in treating gastric ulceration in horses have yielded variable results. Horses treated at 20 mg/kg PO TID did not have a significant improvement in their mean ulcer scores from baseline after 30 days of treatment. Those horses that were initially treated with omeprazole for 30 days and then cimetidine for 30 days actually showed an increase in their mean ulcer scores at the end of the trial when compared to after the initial 30 days treatment with omeprazole (Nieto et al 2001). There is very little scientific evidence to indicate that cimetidine is effective in the treatment of EGIS (Buchanan and Andrews 2003), although there are anecdotal reports of its successful use (Murray 2004).

Famotidine is a potent H₂-receptor antagonist that has a half-life of 2 hours and a bioavailability after oral administration of 13% (Duran 1999). Recommended dosages are 0.3 mg/kg I/V twice a day (BID) or 2.8 mg/kg PO BID. Mild famotidine toxicity, manifested as medically-treated colic, has been reported in one horse given three times the recommended parenteral dose (Duran 1999).

Proton pump inhibitors
The proton pump inhibitors are substituted benzimidazoles that are rapidly transferred from the bloodstream to the acid secretory canaliculi of the parietal cells (Murray 2004). These drugs block gastric acid secretion through irreversible inhibition of hydrogen-potassium adenosine triphosphatase (H⁺/K⁺ ATPase, proton pump). This enzyme is the final step in the acid secretory pathway. Proton pump inhibitors bind irreversibly to the catalytic portion of the pump and prevent the activity of the enzyme until new enzyme is generated. A consequence of this irreversible binding is that the anti-secretory effects are prolonged, allowing for more convenient once-daily dosing (Vatistas et al 1999c).

Examples of proton pump inhibitors are omeprazole and lansoprazole. Omeprazole is metabolised in the liver and is excreted in the urine and bile. A recent study has shown that omeprazole alone, in comparison to buffers, sucralfate and H₂-receptor antagonists, lowered the risk of racehorses in training having moderate or severe gastric ulceration compared with no medication (Orsini et al 2003).

Omeprazole is available in a paste formulation (both enteric- and non-enteric-coated) for use in horses, and studies into its safety and efficacy have been completed in foals, yearlings and adult horses (Murray et al 1999; Plue et al 1999). An investigation into the duration of the anti-secretory effects of enteric-coated omeprazole administered orally (1.4 mg/kg/day) showed that there was no significant increase in basal or pentagastrin-stimulated pH for 7 hours after the first dose. However, after five doses there was a 70% decrease in both basal and pentagastrin-stimulated gastric acid secretion (Jenkins et al 1992).

Omeprazole (0.5 mg/kg) given I/V as a single dose increased the basal gastric pH significantly in adult horses from 2 hours after administration. This single dose also decreased basal gastric free-acid contents from 2 hours after administration, though these returned to basal levels by 8 hours (Sangiah et al 1989). Gastric acid secretion was significantly decreased 27 hours after the last of five I/V doses of omeprazole (Jenkins et al 1992).

A study into once-daily dosing compared to BID with oral omeprazole in Thoroughbred horses with spontaneous gastric ulcers showed no significant difference in either healing times or reduction of the severity of gastric ulceration (Vatistas et al 1999d). After oral administration of omeprazole (1.5 mg/kg/day) for
5 days, the basal and pentagastrin-stimulated acid secretion was decreased by 58% and stayed stable, i.e. below baseline, for the following 19 days (Haven et al 1999). Another study showed that this same dose of omeprazole healed all ulcers in affected horses within 10–21 days. The control group also had 3/8 horses with gastric ulcers heal within a month (Murray et al 1997).

Administration of oral omeprazole at 5 mg/kg decreased both basal and pentagastrin-stimulated acid secretion by 98%. There was no significant difference between the acid secretory responses at 4 mg/kg and 5 mg/kg (Daurio et al 1999). The maximal response to oral omeprazole occurred between 3–5 days after initiation of therapy compared with parenteral administration, where an elevation of gastric pH was observed within 2–3 hours (Sangiah et al 1989).

Thus, horses with acute signs of gastric ulceration may benefit from either concurrent parenteral administration of omeprazole or use of an H2-receptor antagonist early in the course of therapy (MacAllister 1999). However, in clinically-normal neonatal foals, there was a rapid response in gastric pH after oral administration of omeprazole at 4 mg/kg. Those foals showed an increase in gastric pH within 2 hours of administration of the drug. It appears that oral omeprazole may have a higher bioavailability in neonates. It should be noted that this drug has not been shown to be effective in sick neonates (Sanchez et al 2004).

The overall efficacy of oral omeprazole in decreasing gastric pH, at least in normal cannulated horses, varied between products, i.e. commercial paste formulation vs compounded formulations, possibly due to a differing pH in the vehicle in which these were formulated (Merritt et al 2003). Suspensions of omeprazole have been shown to be ineffective when compared to paste formulation (Nieto et al 2002). This is either due to variability in the concentration of active omeprazole, or decreased absorption of active omeprazole because of degradation (protonation) caused by the suspension agent or inadequate protection from the low pH of the gastric contents.

A multi-centre study into the treatment of spontaneously-occurring gastric ulcers in Thoroughbred racehorses with oral omeprazole at 4 mg/kg/day showed complete healing in 58/75 (77%) after 28 days, and significant improvement in ulcer scores in 69/75 (92%). Eighteen of 20 (90%) horses that were taken off the treatment after 28 days developed ulcers again by Day 58, whereas only 6/38 (16%) horses maintained on either 2 mg/kg or 4 mg/kg oral omeprazole had recurrence of the ulcers at that time (Andrews et al 1999b). Thus, after an initial treatment course of omeprazole for gastric ulceration, a lower daily dose may prevent recurrence in most horses in training (Doucet et al 2003). This has been supported by recent work in which 31/38 horses that were dosed with oral omeprazole at 1 mg/kg PO remained ulcer-free compared with 4/39 of the horses that were sham-dosed (McCulter et al 2005a). A similar study by the same authors showed that the same dose was successful in preventing re-occurrence of gastric ulceration in horses that had been treated for EGUS with oral omeprazole at 4 mg/kg PO for 28 days (McCulter et al 2005b).

In another study of racing Thoroughbreds with clinical signs of gastric ulcers (weight loss, poor haircoat and decreased appetite), Johnson et al (2001) reported an improvement in 375/403 (94%) and complete healing in 262/403 (65%) horses after 28 days of oral omeprazole therapy at 4 mg/kg/day (Johnson et al 2001).

MacAllister et al (1999) reported similar results, improvement in 105/106 (99%) and healing in 92/106 (86%), using the same drug protocol. The latter study involved a variety of types of horses in a variety of different field conditions.

**Antacids**

Antacids are basic compounds that neutralise the acid within the stomach. Most antacids are a mixture of aluminium hydroxide and magnesium hydroxide (MacAllister 1999). Due to their short-lived effect on the pH in the equine stomach they are not widely used. One study reported that 250 ml of a commercial antacid solution was required to raise the gastric pH to 4 for a period of 2 hours (Clark et al 1996). Another study reported the need for similarly large volumes of antacid and documented a variable response in pH (Murray and Grodinsky 1989). These studies indicate that in the clinical setting, the use of antacids for the prophylaxis/treatment of ulcers is likely to be impractical due to the large volume of drug and frequent dosing needed (Dowling 1995). However, these compounds may have a role in alleviating acute clinical signs in affected horses (MacAllister 1999).

**Sucralfate**

Sucralfate is an hydroxyl aluminium salt of sucrose octasulphate. At a pH <4 it forms a sticky viscous gel which adheres to both epithelial cells and to the base of ulcer craters, with a greater affinity for ulcerated regions. The gel is difficult to wash out once adhered and sticks to the ulcer crater for as long as 6 hours. Other effects of sucralfate include inhibition of pepsin and absorption of bile acids, increase in the thickness of the layer of mucus and prevention of degradation of mucus (MacAllister 1999). Sucralfate may interfere with the absorption of other drugs, e.g. flutroquinoxolones and H2-receptor antagonists. Concurrent administration of sucralfate and H2-receptor antagonists may reduce the absorption of the latter by 10% (Murray 2004).

Studies on the use of sucralfate to treat gastric ulcers in horses have yielded variable results. Treatment with 4 g sucralfate in foals experimentally intoxicated with phenylbutazone partially protected them, however all foals still developed gastric ulceration (Geor et al 1989). Sucralfate (22 mg/kg PO four times a day) did not result in increased healing of ulcers compared with foals receiving corn oil alone (Borne and MacAllister 1993). Those foals were between 6–7 months old and all had subclinical gastric ulceration. This study did not include a negative control group, which may be important given recent work which has shown that corn oil itself may be a useful treatment for EGUS (Cargile et al 2004).

Treatment with sucralfate decreased the odds of horses in active training having moderate or severe gastric ulceration, when compared to treatment with H2-receptor antagonists, however this was not significant when compared with horses receiving no treatment (Orsini et al 2003). Unfortunately, no details of the duration of therapy or doses of sucralfate used were reported in the latter study.

**Duration of treatment**

It is difficult to predict how long a gastric ulcer will take to heal. Generally, the period of treatment required, regardless of agent, is between 14–28 days but can depend on the severity of the gastric ulcers present. In general, large, severe ulcers and squamous ulcers take longer to heal than glandular ulcers or more superficial smaller squamous ulcers. Importantly, it should be noted that treatment requirements vary between individuals (Murray 1994a) and thus treatment should be tailored for each horse. In patients...
where clinical signs have resolved and risk factors for recurrence are absent, any remaining ulcers will likely heal spontaneously (MacAllister 1999).

**Treatment summary**

Current research indicates treatment of horses using omeprazole administered orally is the most effective treatment for EGUS (Haven et al 1999; Johnson et al 2001; Orsini et al 2003; McClure et al 2005ab). Other drugs such as H2-receptor antagonists, sucralfate, synthetic prostaglandins, corn oil and antacids have been variably reported as successful, but treatment regimens have largely been based on anecdotal evidence and extrapolation from human studies.

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**Conclusion**

EGUS is a condition that affects a large proportion of racing horses. Due to different grading systems used by various authors, it is difficult to compare efficacy of treatments between studies. The scoring system recently proposed by the EGUC has yet to be properly validated, and establishment of a standard scoring system is important as it allows for a more standardised approach to diagnosis and treatment of the disease. The effect of EGUS on racing performance is unknown, and the significance of low numbers of small, localised lesions is questionable. Excess acidity in the stomach is the primary cause of this condition, though it is likely that other factors such as exercise and dietary change contribute to the development of the excess acidity. Until more is understood about this disease, its pathogenesis, and its significance, treatment will continue to be symptomatic.

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**References**


Berschneider HM, Bilsokager AT, Roberts MC. Role of duodenal reflux in non-glandular gastric ulcer disease of the mature horse. *Equine Veterinary Journal* (Supplement 29), 24–9, 1999


Borne AT, MacAllister CG. Effect of sucralfate on healing of subclinical gastric ulcers in foals. *Journal of the American Veterinary Medical Association* 202, 1465–8, 1993


Cargile JL, Burrow JA, Kim I, Cohen ND, Merritt AM. Effect of dietary corn oil supplementation on equine gastric fluid acid, sodium, and prostaglandin E2 content before and during pentagastrin infusion. *Journal of Veterinary Internal Medicine* 18, 545–9, 2004


Duran SH. Farnadotin. *Compendium on Continuing Education for the Practicing Veterinarian* 21, 424–5, 1999


Geor RJ. Gastric surface active phospholipid – a role in protection of the squamous epithelial mucosa? *Equine Veterinary Journal* 32, 458–9, 2000


Haven ML, Dave K, Burrow JA, Merritt AM, Harris D, Zhang D, Hickey GJ. Comparison of the antisecretory effects of omeprazole when administered intravenously, as acid-stable granules and as an oral paste in horses. *Equine Veterinary Journal* (Supplement 29), 54–8, 1999


Lester GD, Smith RL, Robertson ID. Effects of treatment with omeprazole or ranitidine on gastric squamous ulceration in racing Thoroughbreds. *Journal of the American Veterinary Medical Association* 227, 1636–9, 2005

Lloyd KC. Ontogeny of gastric function is the ‘stress syndrome’. *Equine Veterinary Journal* 25, 179, 1993


Merritt AM. Gastric ulcer development in horses in a simulated show or training environment. *Journal of the American Veterinary Medical Association* 227, 775–7, 2005


Merritt AM, Campbell-Thompson ML, Lowrey S. Effect of xylazine treatment on equine proximal gastrointestinal tract myoelectrical activity. *American Journal of Veterinary Research* 50, 945–9, 1989


Murray MJ. The pathogenesis and prevalence of gastric ulceration in foals and horses. *Veterinary Medicine* 86, 815–9, 1991


Murray MJ. Gastric ulcers in adult horses. *Compendium on Continuing Education for the Practicing Veterinarian* 16, 792–4, 1994


Orsini J. Gastric ulceration in the mature horse: A review. *Equine Veterinary Education* 12, 24–7, 2000


Rabuffo TS, Orsini JA, Sullivan E, Engiles J, Norman T, Bostom R. Associations between age or sex and prevalence of gastric ulceration in Standardbred racehorses in training. *Journal of the American Veterinary Medical Association* 221, 1156–9, 2002


Smyth GB, Young DW, Hammond LS. Effects of diet and feeding on postprandial serum gastrin and insulin concentration in adult horses. *Equine Veterinary Journal* (Supplement 7), 56–9, 1989


Vatistas NJ, Nieto JE, Snyder JR, Thompson D. Clinical trial to determine the effect of omeprazole given once or twice daily on gastric ulceration. *Equine Veterinary Journal* (Supplement 29), 87–90, 1999 d


Widenhouse TV, Lester GD, Merritt AM. Effect of hydrochloric acid, pepsin, or taurocholate on bioelectric properties of gastric squamous mucosa in horses. *American Journal of Veterinary Research* 63, 744–9, 2002


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