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Equine Gastric Ulcer Syndrome
in New Zealand racehorses

A thesis presented
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Equine Gastric Ulcer Syndrome in New Zealand Racehorses

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Abstract

Aims

To establish the prevalence of gastric ulcers in New Zealand racehorses.

Methods

A prevalence study was conducted during 2003 and 2004 in New Zealand. One hundred and seventy one horses from 24 trainers across New Zealand were examined with gastroscopy as part of the study. Images of the examination were recorded and reviewed. The stomachs were assigned an ordinal score based on the severity of the gastric ulceration present.

Results

There were 171 horses in the study: 133 Thoroughbreds and 38 Standardbreds. One hundred and fifty one (88.3%) of these had evidence of EGUS. There was no significant difference in the prevalence of ulceration between the two breeds ($p=0.51$) or between horses of differing ages ($p=0.56$). There were 141 horses kept at pasture for at least four hours per day, of these 125 (89%) had EGUS. Thirteen horses were kept at pasture full time and all of these had EGUS. Seventeen horses were stabled full time and 16 (94.1%) of these had EGUS. There was no significant difference between the different housing groups and the prevalence or severity of EGUS ($p=0.33$ and 0.13 respectively), and there was no significant difference in the severity of gastric ulceration ($p=0.12$) between the horses grazed on different pasture qualities. There was no significant difference in the prevalence ($p=0.26$) or severity ($p=0.49$) of gastric ulceration based on the duration of training.

Conclusions

The prevalence of EGUS in New Zealand racehorses is similar to that reported elsewhere for horses in active race training. The type of turnout that these horses receive does not appear to be protective for EGUS.

Clinical relevance

Pasture turnout alone may not be protective against EGUS in racehorses that are in active training. Gastric ulceration is a common problem in New Zealand racehorses and may be a cause of decreased performance in these animals.

Key words

Horse, equine, gastric ulceration, pasture, prevalence

Abbreviations

EGUC Equine Gastric Ulcer Council

EGUS Equine Gastric Ulcer Syndrome

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Chapter 1

Introduction

Introduction

Gastric ulceration is a common problem of racehorses, particularly those in active training. The exact aetiology of Equine Gastric Ulcer Syndrome (EGUS) is currently unknown although exposure of the squamous mucosa to excess gastric acid is thought to be the most likely cause. Management practices associated with race training (such as stabling and feeding intermittently) and/or the physiological stress of training itself, are currently thought to predispose these horses to gastric ulceration.

The overall objective of this study was to establish the prevalence of EGUS in New Zealand racehorses, using randomly selected horses in active race training from throughout New Zealand. We also aimed to validate a scoring system for EGUS and to investigate whether there was any site predilection for gastric ulcers in the study population. We hypothesised that racehorses in New Zealand may have a lower prevalence of gastric ulceration, because most New Zealand racehorses spend at least part of the day at pasture and grazing has anecdotally been considered protective against EGUS.

This thesis is presented as a literature review in Chapter 2, three chapters describing the experimental work (Chapters 3, 4 and 5) and a conclusion (Chapter 6). References cited are listed at the end of each chapter.

Chapter 3 presents results of the prevalence study, conducted during 2003 and 2004, which gastroscopically examined racehorses in active race training from across New Zealand. It analyses various risk factors for EGUS and compares the prevalence according to these variables.

Chapter 4 presents results of a study to validate a scoring system for EGUS in horses. A random selection of horses from the prevalence study were graded using two different scoring systems. The Equine Gastric Ulcer Council (EGUC) system, which has recently been proposed as standard, was compared to the Number Severity system (which has already been validated in the literature). The scores from three independent examiners were analysed and compared for agreement between grades assigned to each horse.

Chapter 5 presents results of a study comparing the location and severity of EGUS lesions within the stomach of horses within the prevalence study. Each of these 3 chapters will be submitted for publication to a peer reviewed journal.

Chapter 2

Literature 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. A gastrointestinal ulcer is a disruption of the mucosa and the underlying layers of the gastric wall (E.G.U.C. 1999). Less severe lesions that do not result in a breach of the mucosa are referred to as erosions and may be precursors for ulcers.

Due to the lack of any pathognomonic clinical signs, definitive diagnosis of EGUS currently relies on oesophagogastroscopy. There are a number of different scoring systems for grading the endoscopic appearance of gastric ulcers that score based upon either anatomic location (Murray and Eichorn 1996; Murray, Grodinsky, Anderson *et al.* 1989; Murray, Schusser, Pipers *et al.* 1996), or number and severity (Macallister, Andrews, Deegan *et al.* 1997; Murray and Eichorn 1996; Murray *et al.* 1989; Murray *et al.* 1996). Until recently there has been no standard scoring system for gastric ulceration in the horse (E.G.U.C. 1999) and no reports to date have illustrated a definite relationship between ulcer score and severity of clinical signs (Dionne, Vrins, Doucet *et al.* 2003; Macallister *et al.* 1997).

Clinical signs of gastric ulceration 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: intermittent nursing, poor body condition, diarrhoea, bruxism, ptyalism and intermittent colic (Murray 1999a). The remainder of this review focuses on gastric ulceration in adult horses, rather than the clinical disorder seen in foals.

EGUS affects between 58 and 100% of adult horses in training (Dionne *et al.* 2003; Ferrucci, Zucca, Di Fabio *et al.* 2003; Orsini and Pipers 1997; Vatistas, Snyder, Carlson *et al.* 1999). In adult horses 75-80% of ulcers are found in the squamous portion of the stomach (E.G.U.C. 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 (Murray 1994b).

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

Anatomy

The equine stomach is divided into two distinct anatomic 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 consists of non-glandular stratified squamous epithelium, and is considered to be an extension of the oesophagus. 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 glandular mucosa which secretes mucus, acid and pepsinogen (Buchanan and Andrews 2003).

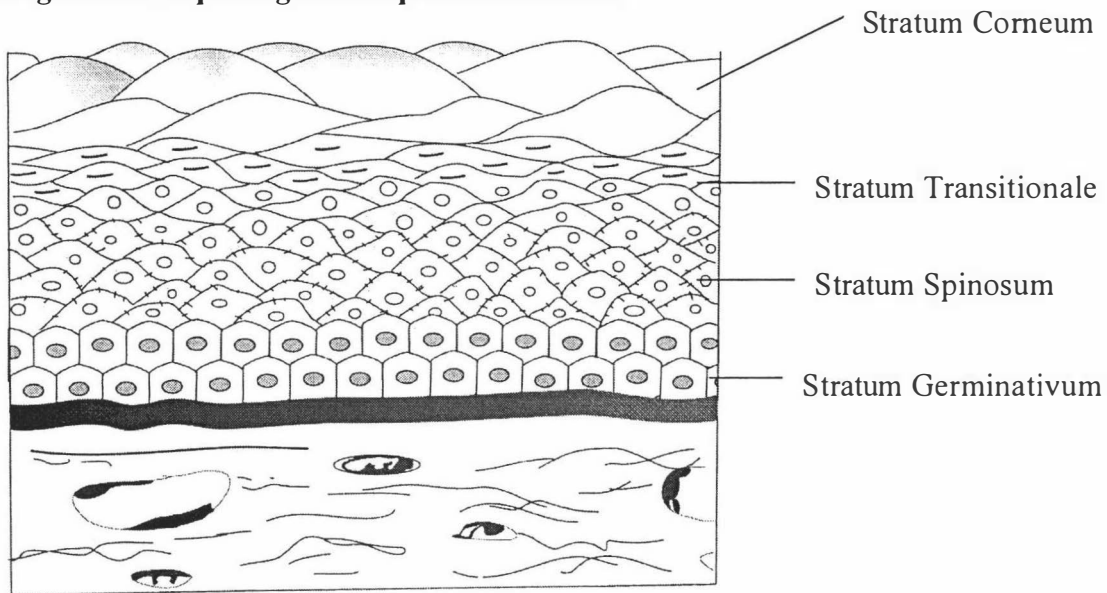
Squamous mucosa

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 transionale, stratum spinosum and stratum germinativum (Figure 2.1). 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, with cuboidal cells and large centrally positioned nuclei. This final layer is 2-4 cells thick (Argenzio 1999). Epithelial thickness of the squamous mucosa is greatest at the margo plicatus in comparison to 15-25mm proximal to it (Murray, Nout and Ward 2001). The aforementioned arrangement of epithelial cells is present in full term foals. However, the gastric mucosa becomes thicker with both increasing age and gestation.

The gastric mucosa in 300-day old equine foetuses consists of a single layer of polyhedral cells superficially, which becomes covered by a keratinised layer 1-2 cells thick by 335 days. These layers increase in thickness until they reach 10-12 cell layers underneath 4-5 layers of surface keratin in term foals, and further increases in thickness occur after parturition (Murray and Mahaffey 1993). This hyperplasia of the squamous mucosa is due to exposure to an acid environment and may also be caused by local and milk-derived growth factors. The gastric squamous mucosa reaches full thickness at around two weeks of age (Murray and Mahaffey 1993). No glandular structures are evident histologically and there is no evidence for active transport of

substances such as bicarbonate or hydrochloric acid within this mucosa (Merritt 1999).

Figure 2.1: Equine gastric squamous mucosa

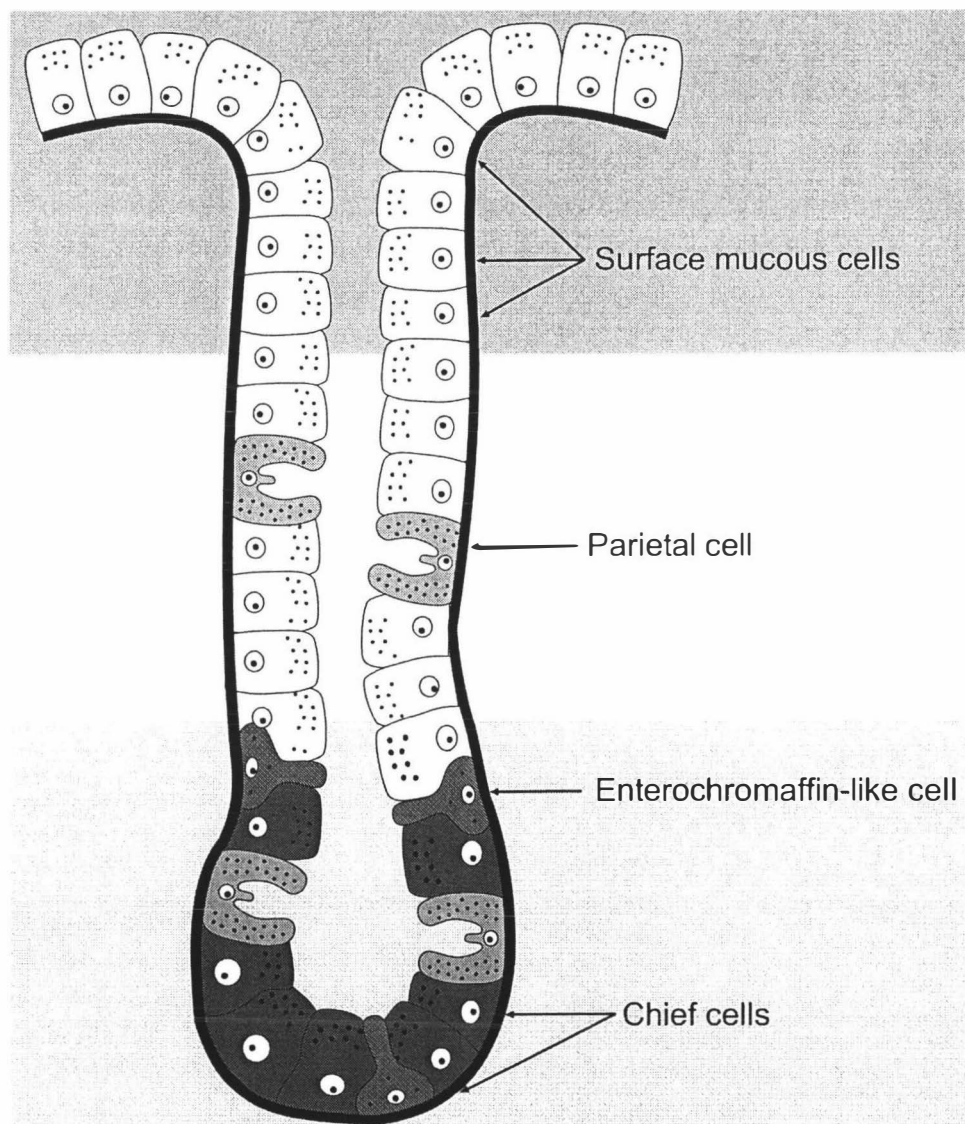


Glandular mucosa

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 1991b). The glandular mucosa is divided into three distinct regions: the cardiac, fundic and pyloric glandular regions. The cardiac gland 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 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 gland region (E.G.U.C. 1999). This former region contains the typical gastric glands (Figure 2.2), which are made up of parietal cells (which secrete hydrochloric acid), zymogen (chief) cells (which secrete pepsinogen), and ECL cells (which secrete histamine).

Histamine acts as an agonist at histamine-type 2 (H_2) 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).

Figure 2.2: Equine Gastric Gland.



Physiology

Gastric motility

Gastric motility is initiated by the vagus nerve. The vagus nerve 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 to the pylorus and result in a round bolus of ingesta moving towards the duodenum, and increased tone of the proximal half of the stomach which causes emptying of fluid contents (Merritt 2003).

Gastric motility has been measured by a number of different methods *in vivo*. These include measurement of myoelectrical impulses via electrodes sutured to the mucosa, mechanical activity via strain gauges sutured to the mucosa, intra-luminal pressure measurements, scintigraphic and radiologic imaging of a labelled meal, time of appearance of an inert marker into the blood (Merritt 1999) and analysing the appearance of ^{13}C -octanoic acid in the breath (Sutton, Bahr, Preston *et al.* 2003). Myoelectrical activity measurements can be used to assess gastric motility, and reflect a summation of the extra-cellular potential changes within the region being measured. Action potentials indicate muscle activity, and in the stomach are based around the periodic fluctuation in membrane potential, the slow wave (SW) frequency. In the stomach this frequency is approximately 3 times per minute (Merritt, Campbell-Thompson and Lowrey 1989). The action potential can only occur if the membrane potential fluctuation exceeds threshold, limiting the number of action potentials to the SW frequency.

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 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 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, Lowe, Pickard *et al.* 1974), administration of a radio-labelled meal followed by scintigraphic imaging (Ringger, Lester, Neuwirth *et al.* 1996) and administration of acetaminophen (Doherty, Andrews, Provenza *et al.* 1998). The study utilising plastic beads illustrated that solid contents have a longer transit time through the stomach than liquids, with 75% of plastic beads remaining in the stomach after 1.5 hours and only 25% of the liquid marker remaining (Argenzio *et al.* 1974). Recently the use of the ^{13}C -octanoic breath test has been reported. This test uses a ^{13}C -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 $^{13}\text{CO}_2$, which is then exhaled. The ratio of the labelled CO_2 is compared to normal CO_2 , 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, Preston, Christley *et al.*

2002). The development of this method of evaluating gastric emptying is important as 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 hydrochloric acid (HCl) secreted within the stomach. Gastric acidity is determined by the pH of the gastric contents, which is a mix of salivary, gastric, duodenal, biliary and pancreatic secretions. This distinction 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 the cleaving of pepsinogen into pepsin (Murray 1997). Pepsin is then responsible for the enzymatic breakdown of protein. The low pH subsequent to HCl secretion is also important in the inhibition of microbial growth (Smyth, Young and Hammond 1989). Gastric pH of adult horses has been measured via a variety of methods, including gastric cannulation (Campbell-Thompson and Merritt 1987a), sampling via nasogastric tube, post mortem measurements (Hammond 1990) and indwelling electrodes (Baker and Gerring 1993b). Results from studies in non-fasted horses with indwelling gastric catheters show a variable pH both within and between individuals. Mean pH of gastric juices has been reported to be 2.72 +/- 1.86 (Murray and Grodinsky 1989), 3.2 +/- 2.0 (Nadeau, Andrews, Mathew *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, Gerring and Fox 1993); these episodes may reflect duodenogastric reflux which may have both a buffering

and dilutional effect on the gastric contents (Merritt 1999). In dogs the duodenal phase III MMC activity in combination with antral relaxation is thought to be responsible for significant reflux of duodenal contents (Defilippi, Mamani and Gomez 1987) and in horses this may also be the case (Merritt 1999). Gastric pH of adult horses and foals has been shown to have a dorsal to ventral gradient, with the pH of the squamous fundus being greatest in adult horses and foals and the lowest pH is found in the fluid contents (pH 2.72 in adults and 1.85 in foals) (Murray and Grodinsky 1989). Feeding has a buffering effect on gastric pH with the mean intragastric pH increasing by 1-2 units (Murray and Schusser 1993) mainly through the buffering effects of increased saliva production. Saliva plays an important role in buffering gastric pH and it is thought that low forage diets may decrease saliva production, thus causing a decrease in gastric pH, and may predispose animals on low forage diets to gastric ulceration.

Gastric acid secretion

The horse is a continuous variable secretor of gastric acid (Murray 1997). This means that acid secretion occurs even without the presence of feed material in the stomach. Equine basal acid secretion on a per kg basis is similar to that of the pig and the rat, although maximal acid secretion is closer to that of the human or monkey (Campbell-Thompson and Merritt 1990). Although the maximal secretion is similar to humans, the basal secretion (i.e. unstimulated) is greater (Buchanan and Andrews 2003). In contrast to other species there does not appear to be a circadian pattern to basal gastric secretion in the horse (Murray and Schusser 1993) and they have low acid secretion and volume in relation to the total secretory volume. Gastrointestinal secretion, absorption and motility are regulated by neurohormonal responses to feeding and the presence of digestive by-products within the digestive tract. Histamine has a paracrine

effect on gastric acid secretion and is released from mast cells and ECF cells in the gastric gland and binds to type 2 histamine receptors on the parietal cell membrane. A further stimulus of gastric acid secretion is vagally mediated, through the release of acetylcholine which occurs after either the ingestion of food, the thought of food, or sham feeding (Murray 1992a). The only hormonal stimulus of gastric acid secretion is pentagastrin, which is produced in the G cells in the pyloric mucosa. Gastrin also has trophic effects on mucosal growth via proliferation of oxyntic cells (Furr, Taylor and Kronfeld 1994). In dogs and rats gastrin is thought to exert at least some, if not all of its secretory effects through H₂ receptors in the parietal cells (Merritt 2003). There is evidence that this is also the case in horses (Merritt 1999) although the response of gastric secretion to histamine is much lower in horses than in other species (Merritt 2003). A study using horses with an indwelling gastric cannula illustrated that the mean maximal pentagastrin-stimulated acid production in horses is lower than that expected when compared to other monogastrics (60mmol/L compared to 90-100mmol/L) (Campbell-Thompson and Merritt 1990). Additionally, as the acid concentration rises within the gastric contents, the sodium concentration remains stable rather than decreasing, which indicates that gastrin stimulates both parietal and non-parietal secretions (Merritt 1999). These non-parietal components have been shown to decrease after experimentally induced proximal duodenal obstruction and subsequent pentagastrin administration (Kitchen, Burrow, Heartless *et al.* 2000). This provides strong evidence that duodenal contents readily reflux into the stomach and that this reflux may provide a further buffer against excess acidity. Histamine administration, in contrast, evokes only a parietal response (Campbell-Thompson and Merritt 1987b; Kitchen, Merritt and Burrow 1998).

Inhibition of gastric acid secretion is mainly through the effects of somatostatin. Somatostatin is released from D cells in the gastric glands when there is a decrease in gastric pH. Somatostatin has inhibitory effects on both the parietal and G cells within the stomach (Murray 1992a).

There have been few studies into the effect of feeding on gastric physiology in the horse and these have mainly used indwelling gastric cannulae (Merritt 2003). In fasted horses, gastric acid output is continuously variable, non parietal secretions are voluminous (Baker and Gerring 1993b) and gastric acidity is up to 60 times greater in fasted horses than in those fed hay (Murray 1994a). Diets high in calcium inhibit gastric acid secretion immediately following digestion but may result in rebound hypersecretion. This was illustrated in horses fed a diet of lucerne hay (which is high in calcium), when 12 hours after feeding the pH dropped markedly (Nadeau *et al.* 2000). Although it has been shown that serum gastrin increases in response to feeding in the horse, this response was greater in horses fed grain rather than hay (Smyth *et al.* 1989). Horses fed diets with higher soluble energy (grain or processed pellets) had greater and prolonged secretion of gastrin (Smyth *et al.* 1989).

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, mucus secretion, cellular repair and prostaglandins (Miller 1983). Of these, mucosal blood flow is considered to be the most important as it provides the mucosa with the oxygen and nutrients necessary to produce the mucus-bicarbonate layer and allow rapid turnover of epithelial cells (Wallace 2001). Epidermal growth factors are found in salivary secretions and promote DNA synthesis and proliferation of gastric

mucosal cells (Jeffrey, Murray and Eichorn 2001). Prostaglandin E₂ has numerous protective functions, including: working to promote mucosal blood supply, maintaining intercellular tight junctions, stimulating bicarbonate and mucus secretion, and suppression of HCl secretion (Miller 1983). Bicarbonate secretion by gastric mucosal cells is triggered in response to increased acid concentration, mechanical irritation and endogenous prostaglandin. Bicarbonate adherence 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 (E.G.U.C. 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. One study of normal cadaver stomachs was able to demonstrate the presence of mucins in the equine squamous mucosa. This was illustrated by using AM1, which is a mixture of eight monoclonal antibodies to the human mucin gene (Bullimore, Corfield, Hicks *et al.* 2001). It was shown that AM1 cross-reacts with the material from the glandular portion of the equine stomach, the squamous portion of the equine stomach and in scrapings taken from histological sections of the squamous mucosa of the equine stomach. However, 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 with electron microscopy and provides evidence for an additional protection mechanism via a physical barrier to acid (Ethell, Hodgson and Hills 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), which the mucosa may be exposed to through duodenal reflux.

Another potential protective mechanism within the squamous mucosa is EGF. 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 known what the role of these potential protective mechanisms are, and recent publications have not attached significance to them (Merritt 2003).

Healing of gastric ulcers

Healing of gastric ulcers commences immediately following mucosal injury. The initial response of the gastric squamous epithelium to this insult is epithelial proliferation, accompanied by vascular proliferation and inflammatory cell infiltration in the lamina propria. These changes in the lamina propria are considered to be requirements for healing. There is a more intense inflammatory reaction in ulcers compared to erosions, with the healing of ulcers involving more wound contraction and fibroplasia (Murray, Eichorn and Jeffrey 2001). In the initial stages of healing,

reddening of the epithelium in both glandular and squamous mucosa is observed. The length of epithelial projections and the extent to which the capillaries from the lamina propria extend into the epithelium is greater in regions adjacent to ulcers/erosions (Murray, Eichorn *et al.* 2001).

The rate of gastric healing is affected both by the size and depth of the lesions, although depth is the most 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 mean that healing may take as long as 3 months (Murray, Haven, Eichorn *et al.* 1997). One study using H₂ receptor antagonists to promote healing found regional differences in healing times, with lesions in the squamous fundus and around the cardia healing more rapidly than those at the margo plicatus. Lesions located at the lesser curvature took the longest 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 lesion severity in only 6/35 horses after 2-3 months, with none being healed. Lesions in this study tended to worsen as the horses continued in training. Andrews *et al.* (1999) had 1 horse with spontaneous gastric ulcers maintained in training that showed spontaneous healing after 58 days, out of a control group of 25 horses (Andrews, Doherty, Blackford *et al.* 1999). Spontaneous healing was also reported in only 3/34 control horses after 28 days in a study on the efficacy of omeprazole paste although not all horses within this study were in active training (MacAllister, Sifferman, McClure *et al.* 1999).

Some studies into ulcer healing have used nonsteroidal anti-inflammatory drug (NSAID) administration to induce ulceration (Collier and Stoneham 1997; Geor,

Petrie, Papich *et al.* 1989; Macallister and Sangiah 1993; Macallister, Sangiah and Mauromoustakos 1992). The use of this model to evaluate ulcer healing may be flawed as ulcers caused by NSAID administration are usually found in the glandular rather than the squamous mucosa and therefore the model may not be representative of naturally occurring EGUS (Murray 1992b).

Aetiopathogenesis

Horses are continuous gastric acid secretors and acid exposure 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 (GERD) in humans (Murray, Eichorn *et al.* 2001). 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 in exercising horses at the lesser curvature of the stomach along the margo plicatus (Merritt 2003; Murray 1999b). Continued exposure of the squamous mucosa to HCl results in loss of the superficial epithelial layers. The degree of epithelial loss is what classifies these lesions as either erosions or ulcers. The severity of the lesions is apparently related to the time of exposure to HCl (Furr, Murray and Ferguson 1992).

Induction of ulcers

Risk factors for EGUS include: stress (McClure, Glickman and Glickman 1999), transport (Ferrucci, Zucca, Di Fabio *et al.* 2003; McClure, Carithers, Gross *et al.* 2005), high energy feed (Murray and Eichorn 1996), stall confinement (Orsini and Pipers 1997), intermittent feeding, intense exercise and racing (Buchanan and Andrews 2003; McClure, Carithers *et al.* 2005). The horse is a grazing animal and it

is postulated that the constant flow of saliva and feed material into the stomach acts as a buffer 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 *ad libitum* feed they may spend less time actually eating when stabled, which may decrease this important salivary buffering mechanism (Buchanan and Andrews 2003). The type of diet and amount of roughage may play a role in the induction of gastric ulceration.

Feeding hay alone does change post-prandial gastrin, although feeding pellets, grain or sweet feed results in a larger increase in post-prandial serum gastrin 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 (VFA). At low pH these VFAs may become non-ionised and penetrate the squamous mucosa of the stomach. These VFAs can cause acidification, uncoupling of sodium transport, cellular swelling, inflammation and ulcers (Nadeau, Andrews, Patton *et al.* 2003a). Indeed, diets that are high in carbohydrates may lead to increased short-chain fatty acid production, which at a low pH may result in increased incidence and severity of gastric ulceration (Nadeau, Andrews, Mathew *et al.* 1998). This effect is most pronounced in the presence of valeric acid, a long carbon chain VFA which is highly lipophilic (Nadeau, Andrews, Patton *et al.* 2003b). Gastric VFA concentrations 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 protein component (Nadeau *et al.* 2000). The incidence of ulcers has been shown to be lower in horses fed a diet of lucerne hay compared with those horses fed grass hay, despite higher

concentrations of VFAs in the lucerne hay. This was thought to be caused by the high protein and calcium content of the lucerne hay which provides buffering for up to 6 hours after ingestion (Nadeau *et al.* 1998). It is possible that horses in that study found the pasture hay less palatable, thereby spending less time actually eating, but the average weight gain for horses while they were being fed the pasture hay diet was higher than when they were on the lucerne hay.

As little as 48 hours of feed deprivation has been shown to induce gastric ulceration (Murray and Eichorn 1996). Such ulcers healed spontaneously 2-5 weeks after feed was re-introduced (Murray, Nout *et al.* 2001). As fasting results in a decrease in pH and because horses which receive H₂ receptor antagonists show improvement in the gastric lesions induced by fasting it should be considered that excess acidity is the cause of the squamous ulceration in these horses (Murray and Eichorn 1996).

In another study, stall confinement for seven days with *ad libitum* access to hay resulted in gastric ulceration in 10/11 horses (Murray and Eichorn 1996). It has been suggested that despite constant access to roughage, stall confinement itself may lead to a decrease in time spent eating compared to horses on pasture, either through a modification in behaviour patterns or due to the fact that the majority of their energy requirements are met by concentrated feeds (Murray 1994a).

A recent study assessed the development of gastric ulceration in horses in a simulated show/training environment. All horses were initially normal upon gastroscopy and had been kept at pasture. One group of horses was kept in their normal environment (controls) and the others were transported for four hours and kept in a separate facility indoors. These horses were lunged for 30 minutes per day and fed twice daily with grain and alfalfa hay. Gastric lesion scores for group 2 (experimental horses)

increased significantly whereas the control horses did not. This illustrated that horses in 'recreational use' can readily develop gastric ulceration in the course of their training and competition (McClure, Carithers *et al.* 2005).

Horses in race training have been shown to have a higher prevalence of gastric ulcers than those not in work (Dionne *et al.* 2003; Murray *et al.* 1989; Murray *et al.* 1996; Orsini and Pipers 1997). In a study of two-year-old horses it was demonstrated that those entering training had almost no gastric ulceration, but after just 2-3 months of training the prevalence had increased to 90% (Murray 1994b), and in an examination of a group of Thoroughbred racehorses the severity of their gastric ulcers increased as the intensity of training increased (Murray *et al.* 1996). The use of simulated race training (working between 1.6-3.4 km six times per week on a track) resulted in 100% of horses developing ulcers within two weeks of entering training. All horses in this study were stabled (Vatistas, Sifferman, Holste *et al.* 1999).

Exercise has been postulated to contribute to ulceration of the squamous mucosa (Orsini 2000) either due to decreased gastric motility or decreased gastric volume. The latter may be the result of the action of the abdominal muscles or increased respiratory effort, and leads to a disruption of the normally occurring proximo-distal pH gradient (Lorenzo-Figueras and Merritt 2002).

Concurrent gastric pH, intragastric and intra-abdominal pressure monitoring revealed a decrease in the gastric pH, and an increase in the intragastric 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, Burrow and Merritt 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, Sifferman, Holste *et al.* 1999).

Conversely, post-prandial serum gastrin levels 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 low 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, Lester and Merritt 2002) and in combination with VFAs causes inhibition of cellular sodium transport, 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 the mucosal cell permeability 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, Blikslager and Roberts 1999).

Although administration of 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 EGUS which occurs primarily in the squamous mucosa (Orsini 2000). Conversely some studies have failed to show any association between NSAID administration and glandular gastric ulceration (Vatistas, Sifferman, Holste *et al.* 1999). 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, with an increase in number and severity of lesions observed in these horses whilst those in the control group that had glandular lesions actually healed (Macallister, Morgan, Borne *et al.* 1993).

Helicobacter spp have been shown to be an important cause of gastric ulcers in humans and other species, but as they are primarily associated with glandular ulceration are less likely to be important in EGUS. No reports to date have reported the presence of *Helicobacter spp* in horses (Merritt 2003).

One group noted a difference between sex and prevalence of gastric ulceration in Standardbred horses. The relative risk for gastric ulceration increased with age in geldings but decreased for stallions and broodmares. It should be noted that none of the two year-old horses in this study were geldings, and indeed almost all the young horses were either intact males or mares. Often mares and stallions are retired for breeding rather than continuing their racing career, so may have shorter careers when compared to geldings. Such factors may have influenced the findings in this study (Rabuffo, Orsini, Sullivan *et al.* 2002).

Repeated administration of a 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 in one study (Holbrook, Simmons, Payton *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 three 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, Skidell, Haggstrom *et al.* 2000). They are also commonly found in the squamous fundus, the squamous mucosa along the lesser curvature, greater curvature and the cardia. An increase in both number and severity at the lesser curvature along the margo plicatus has been reported (Murray and Eichorn 1996), although other authors report no such site dependent variation in severity (Macallister *et al.* 1997). Glandular and duodenal ulcers are 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 1991b), decrease in performance (Murray 1992b) (Collier and Stoneham 1997; Murray 1992b), loose faeces (Ferrucci, Zucca, Croci *et al.* 2003), bruxism and stereotypic behaviour (Nicol, Davidson, Harris *et al.* 2002).

Unfortunately these clinical signs are non-specific, and horses presenting with clinical signs highly suggestive of EGUS may have no gastroscopic evidence of gastric ulceration. In one study 92% of horses with suggestive clinical signs did have gastric ulcers, whereas only 52% of those without clinical signs were affected (Murray *et al.* 1989).

Gastric ulceration was found in 92/111 horses with recurrent colic. Gastric ulceration was deemed to be the sole cause of colic in 31 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 1992b). In addition to an association between the presence of clinical signs and the presence of ulceration, it has also been suggested that the presence of severe ulceration may be associated with the presence of more severe symptoms (Murray, Eichorn, Holste *et al.* 1999).

However, none of the reports determine whether the severity of clinical signs correlates with the severity, number or location of gastric ulcers (Vatistas, Snyder, Carlson *et al.* 1999). Equally, in terms of poor performance there has been no link 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 3m endoscope to allow visualisation of the pylorus. Horses must be fasted for a minimum of 6 hours. Once visualised, lesions should be scored. At present there is no universally accepted scoring system for the grading of gastric ulcers in horses (Macallister *et al.* 1997). To some extent this

prevents comparison and contrast between studies (Collier and Stoneham 1997). Lesions are generally classified both according to location and severity. Measuring lesion size 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 (Begg and O'Sullivan 2003; MacAllister *et al.* 1999; Murray *et al.* 1999; Rabuffo *et al.* 2002; Vatistas, Sifferman, Holste *et al.* 1999), 0-4 (E.G.U.C. 1999; Furr and Murray 1989; Johnson, Vatistas, Castro *et al.* 2001; Macallister *et al.* 1997; Murray 1989, 1992b; Murray and Eichorn 1996; Murray *et al.* 1989; Murray, Murray, Sweeney *et al.* 1990; Vatistas, Snyder, Carlson *et al.* 1999), 0-5 (Andrews, Reinemeyer, McCracken *et al.* 2002; Macallister *et al.* 1997; Vatistas, Snyder, Nieto *et al.* 1999), 0-6 (Table 2.1) (McClure *et al.* 1999; Nieto, Spier, van Hoogmoed *et al.* 2001) and 0-10 (Table 2.2) (Murray *et al.* 1996; Venner, Lauffs and Deegen 1999).

Grade 0 is normal in all these scales though it may also include hyperkeratosis or hyperaemia in some reports. Grade 1 is assigned either to horses with hyperkeratosis or hyperaemia or small superficial ulcers. The remaining grades are generally based both on the number and severity of the lesions with the highest score in each system usually denoting multiple deep lesions that appear “active”. Often the scoring systems used have varied with the differing aims of the studies (e.g. prevalence studies versus treatment trials), with one group of authors using three different grading systems in three different studies (Vatistas, Sifferman, Holste *et al.* 1999; Vatistas, Snyder, Carlson *et al.* 1999; Vatistas, Snyder, Nieto *et al.* 1999). Recently the Equine Gastric Ulcer Council suggested a uniform scoring system which grades lesions on a 5 point grading scale (Table 2.3), with 0 being normal and grade 4 extensive deep lesions.

Table 2.1: Comparison of scoring systems used by differing authors to grade severity of EGUS in horses (systems using grades 0-6)

Author	0	1	2	3	4	5	6
Andrews et al 1999	Intact mucosa	Single small or multi-focal lesion	Large single or large multi-focal lesion	Extensive (often coalescing) ulcers with areas of apparent deep ulceration	-	-	-
Andrews et al 2002 Practitioner simplified	Intact mucosa	Single small or multi-focal lesion	Large single or large multi-focal lesion	Extensive (often coalescing) ulcers with areas of apparent deep ulceration			
Andrews et al 2002 Ulcer number score	No lesions	1-2 localised lesions	3-5 localised lesions	6-10 lesions	>10 or diffuse lesions		
Ulcer severity score	No lesions	Appears superficial	Deeper structure Involved	Multiple lesions and variable severity	Same as 2 but with active appearance	Same as 4 plus active haemorrhage	
Johnson et al 2001	As per EGUC						
Macallister et al 1999	All gastric mucosa appears intact	Small single or small multi-focal lesion	Large single or large multi-focal lesion	Extensive (often coalescing) lesions with apparent deep ulceration	-	-	-
Macallister et al 1997 Lesion number	No lesions	1-2 localised lesions	3-5 localised lesions	6-10 lesions	>10 lesions	-	
Lesion severity	No lesions	Appears superficial	Deeper structures involved	Multiple lesions and variable severity	Same as 2 and active appearance (hyperaemic etc)	Same as 4 plus active haemorrhage or adherent blood clot	
McClure et al 1999	Normal mucosa	Non-erosive changes	Mucosal erosions	Mild ulceration	Moderate ulceration	Severe ulceration	Extensive severe ulceration

Author	0	1	2	3	4	5	6
Furr and Murray 1989	No lesions	1-2 localised lesions with no haemorrhage	3-5 localised lesions with no haemorrhage or 1-5 localised lesions with haemorrhage	5-10 lesions with no haemorrhage or 3-5 lesions with haemorrhage	> 10 lesions with no haemorrhage or >5 lesions with haemorrhage or a large area of diffuse loss of surface epithelium	-	-
Murray et al 1989	No lesions	1-2 localised lesions	3-5 localised lesions with no haemorrhage	5-10 lesions with no haemorrhage or 1-5 lesions with haemorrhage	>5 lesions with haemorrhage or >10 lesions with no haemorrhage or large areas of diffuse loss of epithelium	-	-
Murray 1989	Normal	1-2 localised lesions	3-5 localised lesions or 1 diffuse lesion	1-5 localised lesions with haemorrhage or multiple diffuse lesions with moderate loss of surface epithelium	>5 localised lesions or multiple diffuse lesions with extensive epithelial loss or haemorrhage	-	-
Murray and Eichorn 1996	Normal	Generalised reddening/hyperkeratosis	Small single or multi-focal lesions	Large single or multi-focal lesions	Extensive lesions with areas of apparent deep ulceration	-	-
Murray et al 1990	No lesions	1-2 localised lesions	3-5 localised lesions	1-5 localised lesions with visible haemorrhage or multiple diffuse lesions	>5 lesions or multiple diffuse lesions with haemorrhage	-	-
Murray 1992	No lesions	1-2 localised lesions	3-5 localised lesions with no haemorrhage	5-10 lesions with no haemorrhage or 1-5 lesions with haemorrhage	>5 lesions with haemorrhage or >10 lesions with no haemorrhage or large areas of diffuse loss of epithelium	-	-

Author	0	1	2	3	4	5	6
Murray et al 1999	Intact mucosa	Small single or small multi-focal lesion	Large single or large multi-focal lesion	Extensive lesions with areas of apparent deep ulceration	-	-	-
Nieto et al 2001	Normal mucosa	Non erosive mucosal changes	Mucosal erosions	Mild ulceration	Moderate ulceration	Severe ulceration	Extensive severe ulceration
Rabuffo 2002	Normal mucosa	Small single lesions or small multi-focal lesions	Large single lesion or large multi-focal lesions	Extensive lesions with apparent areas of deep ulceration	-	-	-
Vatistas et al 1999a	Normal mucosa	Mucosal erosions, hyperaemia or hyperkeratosis	Mild ulceration	Moderate ulceration	Severe ulceration	Extensive severe ulceration	-
Vatistas et al 1999b	Intact mucosa	Small single or small multi-focal lesions	Large single or large multi-focal lesions	Extensive and coalescing ulcers	-	-	-
Vatistas et al 1999c	No lesions	1 or 2 localised lesions	3-5 localised lesions	5-10 localised lesions	>10 lesions or large diffuse loss of epithelium	-	-
Vatistas et al 1999d	Normal mucosa	Mucosal erosions, hyperaemia or hyperkeratosis	Mild ulceration	Moderate ulceration	Severe ulceration	Extensive severe ulceration	-

Table 2.2: Comparison of scoring systems used by differing authors to grade severity of EGUS in horses (systems using grades 0-10)

Author	0	1	2	3	4	5	6	7	8	9	10
Venner et al 1999											
Glandular mucosa	Normal	Focal hyperaemia	Multi-focal hyperaemia or 1 small lesion	Up to 3 small lesions	>3 small lesions	1-2 moderate sized lesions	1-2 large lesions	1-2 large lesions +/- smaller lesions	1-2 large deep lesions +/- smaller lesions	3-4 large deep lesions	>5 large deep appearing lesions
Squamous mucosa	Normal	Mild hyperkeratosis/hyperaemia	Moderate hyperkeratosis, hyperaemia 1-2 small erosions	Multi-focal small erosions with hyperaemia	1-4 small ulcers minimal thickening at margins	Deeper ulceration mild thickening at margin + bleeding	Multi-focal ulceration mild-moderate margin thickening	More extensive deep ulceration	Focal large ulcers with more surrounding changes	Extensive deep ulceration with bleeding larger area than 8	Most severe extensive deepest appearing ulceration
Murray et al 1996											
Glandular mucosa	Normal	Focal hyperaemia	Multi-focal hyperaemia or 1 small lesion	Up to 3 small lesions	>3 small lesions	1-2 moderate sized lesions	1-2 large lesions	1-2 large lesions +/- smaller lesions	1-2 large deep lesions +/- smaller lesions	3-4 large deep lesions	>5 large deep appearing lesions
Squamous mucosa	Normal	Mild hyperkeratosis/hyperaemia	Moderate hyperkeratosis, hyperaemia 1-2 small erosions	Multi-focal small erosions with hyperaemia	1-4 small ulcers minimal thickening at margins	Deeper ulceration mild thickening at margin + bleeding	Multi-focal ulceration mild-moderate margin thickening	More extensive deep ulceration	Focal large ulcers with more surrounding changes	Extensive deep ulceration with bleeding larger area than 8	Most severe extensive deepest appearing ulceration

Table 2.3: Equine Gastric Ulcer Council (E.G.U.C.) grading system for scoring gastric ulceration in horses (E.G.U.C. 1999)

Grade 0	Intact epithelium
Grade 1	Intact mucosa, evidence of hyperkeratosis or hyperaemia
Grade 2	Small, single, or multi-focal lesions
Grade 3	Large, single or multi-focal lesions or extensive superficial lesions
Grade 4	Extensive lesions with areas of apparent deep ulceration

Table 2.4: Number Severity scoring system for grading gastic ulceration in horses (Macallister *et al.* 1997)

Grade	Gastric Ulcer Number Score Description
0	No lesions
1	1-2 localised lesions
2	3-5 localised lesions
3	6-10 lesions
4	> 10 lesions
Grade	Gastric Ulcer Severity Score Description
0	Normal
1	Appears superficial
2	Deeper structures involved
3	Multiple lesions and variable severity
4	Same as grade 2 though with an active appearance
5	Same as 4 though with active haemorrhage or blood clot adherent

One study which compared results of ulcer evaluation between five experienced operators showed a good correlation between glandular ulcer numbers but poor agreement when analysing squamous lesions (Andrews *et al.* 2002). This is of interest considering that squamous lesions are the most commonly encountered lesions in horses affected by EGUS. When the Number Severity (N/S) score (Table 2.4), and Practitioner Simplified scores were compared with results of examination at necropsy/histopathology, it was found that endoscopy using the N/S scoring system may lead to misclassification, whereas the Practitioner Simplified (which estimates ulcer size) was more accurate for assessing ulcer severity (Andrews *et al.* 2002).

Prior to the widespread availability of endoscopes, pathologists defined gastric ulcers as mucosal lesions deep enough to penetrate the muscularis mucosa. Lesions of insufficient depth to penetrate this layer were defined as erosions (Macallister *et al.* 1992). A recent study showed that many lesions that appear to be ulcers on gastroscopy actually have intact epithelial layers. This error appears to occur due to the propensity for the margins around the lesions to become proliferative during healing, making them appear deeper than they are in reality (Murray, Eichorn *et al.* 2001).

There are no haematological or biochemical markers currently available to diagnose EGUS (Vatistas, Snyder, Carlson *et al.* 1999). Faecal occult blood may be useful in diagnosing ulceration in foals, although in adults and older foals the colonic microflora digests the free haemoglobin (Murray 1991a). Evaluating urine sucrose after administration via nasogastric intubation has been reported (O'Connor, Steiner, Roussel *et al.* 2004). 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. However if there is compromise of the gastric mucosa sucrose may be absorbed systemically and excreted in the urine. 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. Horses in the study were administered 454g of sucrose via a nasogastric tube after they ingested a 1kg meal. Baseline, 2 and 4 hour blood and urine samples were collected. The sucrose concentration was analysed and then each horse underwent gastroscopy to document the presence or absence of gastric ulceration. Urine sucrose concentration was shown to be a useful tool to diagnose gastric ulcers. However the effects of concentration of urine by the animal may affect the outcome of the test (O'Connor *et al.* 2004).

In the absence of gastroscopy the clinician may elect to treat animals empirically, and use response to treatment as a guide to the presence or absence of gastric ulceration. This method has an obvious disadvantage because of the high cost of treatment.

Prevalence

The first study into the prevalence of EGUS was work done by Hammond et al (1986) on horses in Hong Kong undergoing post mortem examination. This survey revealed that 66% of 165 racehorses in training had evidence of gastric ulceration at post-mortem examination. The horses in training not only had a higher prevalence of gastric ulceration but they also had more severe lesions than those that were not in race training (Hammond, Mason and Watkins 1986). However, 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 three

months in work (Murray 1994b). Race training has been shown to increase both the prevalence and severity of gastric ulceration, with 86% of 202 horses in training for at least two months shown to have gastric ulcers and 39% of these horses showing overt clinical signs (Vatistas, Snyder, Carlson *et al.* 1999).

Murray *et al.* (1989) also reported that 52% of 100 clinically normal yearlings and mature horses had EGUS, with 37% of those not in training and 76% of those in training affected. Similar numbers have been reported for Standardbred racehorses, with 87% of horses in training affected (Rabuffo *et al.* 2002). A recent study of Standardbred racehorses in Canada showed an overall prevalence of 44% (121/275 horses), but with only 63.3% of horses in training affected. There was also a significant difference between trotters and pacers with trotters having a higher prevalence of gastric ulceration, leading these authors to speculate about the possibility that gait may play a role in the incidence of EGUS (Dionne *et al.* 2003).

It was reported that 86% of 345 Thoroughbred racehorses in Australia had gastric ulceration. However, it should be noted that the majority of horses in this study were exhibiting clinical signs consistent with gastric ulceration and were examined on that basis (Begg and O'Sullivan 2003). This added a significant bias into the results, as Murray (1992) showed that 100% of horses in training with clinical signs consistent with gastric ulceration had EGUS (Murray 1992b).

The prevalence of ulceration in animals in work but not in active race training appears to be lower, with 29/50 (58%) show horses having endoscopic evidence of ulceration (McClure *et al.* 1999) and 23/62 horses (37%) 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 horses (17%) had superficial

ulcers prior to starting competitive work. However after three consecutive days of travel and competition 13 horses (56%) had ulceration (36% having superficial lesions and 54% had deeper lesions) (Hartmann and Frankeny 2003). In a preliminary study into the prevalence of gastric ulcers in endurance horses, gastric ulcers were found in 23/37 horses (67%) immediately after competition (Nieto, Snyder, Beldomenico *et al.* 2004). The sample size was small and the average severity of the ulcers was low, although 8 horses had actively bleeding glandular mucosal ulcers. It was suggested that the ulcers observed in these 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 ulcer healing, and prevent both recurrence and complications (MacAllister 1999). Currently treatment of gastric ulceration in horses focuses 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 pharmacologic therapy, dietary and environmental modification alone may help ulcer 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 1992c).

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 acid secretion (Sangiah, McAllister and Amouzadeh 1988). They were developed by manipulating the chemical structure of histamine to form compounds that compete with histamine for binding at the H₂ receptors (Sangiah *et al.* 1988). They are selective for H₂ receptors and have minimal effects on H₁ receptors. They also appear to have minimal physiological effects on H₂ receptors in other tissue (MacAllister 1999). Toxicity with H₂ receptor antagonists has not been reported in the horse (Furr and Murray 1989) but in humans is associated with inhibition of hepatic cytochrome P-450 enzymes, causing alterations in drug metabolism and gastrointestinal absorption (Zimmerman and Schenker 1985). 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 with cimetidine being the least potent, ranitidine and nizatidine being of a similar potency and famotidine being the most potent. In horses, ranitidine is considered 3-4 times more potent than cimetidine (Sangiah *et al.* 1988) and famotidine is considered to be approximately 2-3 times as potent as ranitidine (Murray 1992c).

Ranitidine

Three different patterns of response to treatment with ranitidine and famotidine have been observed in the horse: a complete response in which the pH of the gastric contents rises to >7 for 4-10 hours, an intermediate response where there is a biphasic increase in pH and finally a poor response to therapy (Murray 1997). 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 bio-availability of these drugs in horses (Duran, Ravis and Smyth 1993). Thus H₂ receptor antagonist therapy should be undertaken at the high end of the dosing scale (Murray 1992c). Early studies using male horses with gastric cannulae showed a decrease in acid production for up to four hours after ranitidine administration (0.5mg/kg intravenously [IV]) but no change in pH (Campbell-Thompson and Merritt 1987a). Another study showed a significant increase in 24 hour gastric pH with ranitidine therapy (6.6mg/kg per os thrice daily [PO TID]) (Murray and Schusser 1993). A single dose of 1mg/kg of ranitidine IV in fasted ponies resulted in a rise in gastric pH for 11 hours post-administration (Baker and Gerring 1993a). Ranitidine (2.2mg/kg) administered orally to unfed young horses increased the gastric pH from basal levels of 2.16 to 4.39 for six hours post-administration. In the same study intra-muscular (IM) administration of ranitidine (1.4 mg/kg) raised the gastric pH from 2.27 to 4.36 over an eight hour period (Sangiah *et al.* 1988). This study measured the pH via samples aspirated from an endoscope-guided nasogastric catheter, meaning that there was contamination with saliva and bile, which itself could increase the pH significantly, and this method did not allow constant measurement of the gastric pH. Administration of ranitidine at 4.4mg/kg and 6.6mg/kg has been shown to raise the gastric pH of adult horses to above 6 in 4/5 and 5/5 horses respectively. The pH in this study was measured by an indwelling nasogastric tube (Murray and Grodinsky 1992). 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 bio-availability in both adult horses and foals compared to humans (Holland, Ruoff, Brumbaugh *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 (6.6mg/kg PO TID) was shown to be effective in healing gastric ulcers in adult horses, with 18/29 horses showing total resolution of the ulceration after 2-3 weeks of therapy (Furr and Murray 1989). Treatment with ranitidine at 6.6mg/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 this 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, Haddock, Stine *et al.* 2003), though the specific dose regimens for the H₂ antagonists were not reported. This raises the possibility that the majority of treated horses were receiving sub-therapeutic dosing regimens, making the treatment ineffective. It is also apparent that horses in training respond more poorly to treatment with H₂ receptor antagonists than those out of training, a significant factor when comparing the results of different studies (Murray 1992c).

Other H₂ receptor antagonists

A number of different dosages of cimetidine have been reported ranging from 2.2mg/kg to 20mg/kg (Furr and Murray 1989; Nieto *et al.* 2001; Sangiah *et al.* 1988; Smyth, Duran, Ravis *et al.* 1990). Therapeutic plasma levels of cimetidine are

reported to be 1µg/ml (Nieto *et al.* 2001; Smyth *et al.* 1990). To achieve these levels in horses requires dosages of 11mg/kg IV or 48mg/kg PO per day. The bio-availability of orally administered cimetidine 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 bio-availability of cimetidine has been reported to range from 14% (Sams, Gerken, Dyke *et al.* 1997) to 30% (Duran *et al.* 1993). The half life of cimetidine is from 1-2.2 hours (Sams *et al.* 1997; Smyth *et al.* 1990) and it is excreted in the urine of horses both as the parent drug and the sulfoxide.

Studies into the efficacy of cimetidine in treating gastric ulceration in horses have yielded variable results. Cimetidine at 18mg/kg PO TID did not decrease the healing time for gastric ulcers induced by electrocautery (Macallister, Lowrey, Stebbins *et al.* 1994). Horses treated with cimetidine at 20mg/kg PO TID did not have a significant improvement in their mean ulcer scores from baseline after 30 days of treatment, and 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 compared to treatment with omeprazole alone (Nieto *et al.* 2001). There is very little scientific evidence to indicate that cimetidine is effective in the treatment of EGUS (Buchanan and Andrews 2003), although there are anecdotal reports of its successful use (Murray 2004).

Famotidine is a potent H₂ receptor antagonist that is considered to be 2-3 times as potent as ranitidine (Duran *et al.* 1993). Famotidine has a half life of 2 hours and a bioavailability after oral administration of 13% (Duran 1999). Recommended dosages are 0.3mg/kg IV BID or 2.8mg/kg PO BID. Mild famotidine toxicity (medically

treated colic) has been reported in horses given three times the recommended parenteral dose (Duran *et al.* 1993).

WY-45, 727 is an H₂ receptor antagonist that structurally incorporates several features of the ranitidine molecule in combination with a thienoisothiazole moiety on a side chain. It has been shown to be between 3-10 times more potent than ranitidine in healing gastric ulcers in animal models and was shown to effectively heal both spontaneous and NSAID-induced gastric ulceration in ponies (Macallister *et al.* 1992).

BMY-25368 is a potent H₂ receptor antagonist that has been shown to decrease hydrogen ion concentration and increase mean gastric pH in horses. It was investigated using 5 yearling mares that had gastric cannulae surgically implanted prior to the trial. The total gastric juices were collected and analysed after administration of this drug (Orsini, Dreyfuss, Vecchione *et al.* 1991). Neither of these products are currently commercially available.

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). 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, Snyder, Nieto *et al.* 1999).

Examples of proton pump inhibitors are omeprazole and lansoprazole. Omeprazole is metabolised in the liver and is excreted in the urine and bile. Long term administration of high doses of omeprazole causes hyperplasia of ECF cells and gastric carcinoid tumours in rats (Buchanan and Andrews 2003). Studies using gastric-cannulated horses have shown that the total volume of gastric secretions does not decrease after treatment with omeprazole, suggesting that omeprazole does not decrease secretion from non parietal cells (Sandin, Andrews, Nadeau *et al.* 1999).

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 to no medication (Orsini *et al.* 2003).

Omeprazole is available in a paste formulation 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, Wall, Daurio *et al.* 1999). An investigation into the duration of the anti-secretory effects of orally administered enteric-coated omeprazole (1.4mg/kg) 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 pH (Jenkins, Blackford, Andrews *et al.* 1992).

Intravenous omeprazole (0.5mg/kg) given 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, MacAllister and Amouzadeh 1989).

A study into once daily dosing (SID) compared to twice daily dosing (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, Nieto, Snyder *et al.* 1999). After once daily oral administration of omeprazole (1.5mg/kg) for 5 days the basal and pentagastrin-stimulated acid secretion was decreased by 58% and stayed stable (below baseline) for the following 19 days (Haven, Dave, Burrow *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 heal within a month (Murray *et al.* 1997).

Administration of oral omeprazole at 5mg/kg decreased both basal and pentagastrin-stimulated acid secretion by 98%. There was no significant difference between the acid secretory responses at 4mg/kg and 5mg/kg omeprazole (Daurio, Holste, Andrews *et al.* 1999). The maximal response to oral omeprazole occurs between 3-5 days after initiation of therapy compared to parenteral administration where an elevation of gastric pH is 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 is a rapid response in gastric pH after oral administration of omeprazole at 4mg/kg. These foals showed an increase in gastric pH within 2 hours of drug administration. This may indicate that foals more rapidly absorb omeprazole or oral omeprazole may have a higher bio-availability in neonates. It should be noted that this drug has not been shown to be effective in sick neonates (Sanchez, Murray and Merritt 2004).

Omeprazole (at either 2mg/kg PO SID or 4mg/kg PO SID) in adults has been shown to be more efficacious than cimetidine (20mg/kg PO QID) (Nieto *et al.* 2001). The efficacy of oral omeprazole in decreasing gastric pH, at least in normal cannulated horses, has been shown to be variable between products (commercial paste formulation versus compounded formulations) possibly due to a differing pH in the vehicle in which they are formulated (Merritt, Sanchez, Burrow *et al.* 2003).

Suspensions of omeprazole have been shown to be ineffective when compared to paste formulation (Nieto, Spier, Pipers *et al.* 2002), 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 (4mg/kg once daily [SID]) showed complete healing in 77% (58 horses) after 28 days and significant improvement in ulcer scores in 92% (69 horses). Eighteen out of 20 horses that were taken off the treatment after 28 days developed ulcers again by day 58, whereas only 6/38 horses maintained on either 2mg/kg or 4mg/kg oral omeprazole had recurrence of the ulcers at day 58 (Andrews, Sifferman, Bernard *et al.* 1999). Thus after an initial treatment course of omeprazole to treat ulceration, a lower daily dose may prevent the recurrence of ulceration in most horses in training (Doucet, Vrins, Dionne *et al.* 2003). This has been supported by recent work in which 31/38 horses that were dosed with oral omeprazole at 1mg/kg PO remained ulcer free compared with 4/39 of the horses that were sham dosed (McClure, White, Sifferman, Bernard, Doucet *et al.* 2005). A similar study by the same authors showed that the same dose (1mg/kg PO)

was successful in preventing re-occurrence of gastric ulceration in horses that had been treated for EGUS with oral omeprazole at 4mg/kg PO for 28 days (McClure, White, Sifferman, Bernard, Hughes *et al.* 2005).

In another study of racing Thoroughbreds with clinical signs of gastric ulcers (weight loss, poor hair-coat and decreased appetite), the authors reported an improvement in gastric ulcers in 94% and complete healing in 65% of horses after 28 days of oral omeprazole therapy (4mg/kg SID) (Johnson *et al.* 2001). MacAllister *et al.* (1999) reported similar results, improvement in 99% and healing in 86% of cases compared to controls after 28 days of omeprazole (4mg/kg PO SID). The latter study involved a variety of types of horses in a variety of different field conditions (MacAllister *et al.* 1999).

Omeprazole has also been administered to horses via intramuscular injection. In one study a dose rate of 0.25mg/kg was shown to reduce the stimulated secretion of gastric acid by 64% and the basal secretion by 49% following a single dose. It is possible that there may be a cumulative effect with repeated treatments (Sandin *et al.* 1999).

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 250ml of a commercial antacid solution was required to raise the gastric pH to 4 for a period of 2 hours (Clark, Merritt, Burrow *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 ulcer prophylaxis/treatment 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 a 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 six hours. Other effects of sucralfate include inhibition of pepsin and absorption of bile acids, increase in the thickness of the mucus layer and prevention of mucus degradation (MacAllister 1999). Sucralfate may interfere with the absorption of other drugs (e.g. fluoroquinolones 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 grams of sucralfate in foals experimentally intoxicated with phenylbutazone partially protected them, however all foals still developed gastric ulceration (Geor *et al.* 1989). Sucralfate (22mg/kg PO QID) did not result in increased healing of ulcers compared with foals receiving corn oil alone (Borne and MacAllister 1993). These foals were between 6-7 months old and all had sub-clinical gastric ulceration. This study did not include a negative control group, which may be important given the recent work of Cargile *et al.* which has shown that corn oil itself may be a useful treatment for EGUS (Cargile, Burrow, Kim *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 to those 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.

Bismuth compounds

These compounds act primarily as cytoprotectants by enhancing the secretion of mucus and bicarbonate, inhibiting the activity of pepsin activity and accumulating in ulcer craters to form a protective barrier (Brunton 1996). One study using oral doses of either 10.5g or 26.25g of bismuth subsalicylate failed to show an increase in gastric pH (Clark *et al.* 1996). There has been little other clinical work done in horses with this substance.

Synthetic prostaglandins

Prostaglandins inhibit the secretion of gastric acid, stimulate the secretion of bicarbonate and mucus, and provide protection for the gastric mucosa (Miller 1983). Misoprostol is a synthetic prostaglandin (PGE₁) that has potential beneficial effects with respect to the treatment of gastric ulceration. To date there is only one report of the investigation of misoprostol in horses, which showed a significant elevation in gastric pH over an eight hour period after administration (Sangiah *et al.* 1989). A synthetic PGE₂ was shown to limit gastric ulceration in horses with phenylbutazone toxicity (Collins and Tyler 1985). The use of corn oil (as a source of the arachidonic acid precursor linoleic acid) to increase endogenous prostaglandin production was investigated using healthy adult horses with gastric cannulae. The effects of 45 ml of corn oil orally on the basal and pentagastrin-stimulated gastric acid content, sodium

content and PGE₂ was studied. This revealed a significant decrease in gastric acid content and an increased PGE₂ content after corn oil administration. This indicates that corn oil supplementation may be a cost-effective treatment for gastric ulceration in horses (Cargile *et al.* 2004).

Pectin-lecithin complex

Pectin-lecithin complex is a mucosal protective agent commercially available as Pronutrin[®]. In this formulation the hydrophilic, gel-forming carbohydrate polymer (pectin) and the amphiphilic, surfactant phospholipids (lecithin) are bound in the form of a complex (Apolectol[®]). Pectin has been postulated to stabilise mucus, increase the buffering capacity of the stomach and prolong the post-prandial elevation of gastric pH (Venner *et al.* 1999). Lecithin is thought to be helpful in stabilising the protective barrier of the mucin layer on the gastric mucosa through the formation of a highly hydrophobic layer on the mucosal cells. A study involving 12 treated and 12 control horses showed a significant improvement in the severity of gastric ulceration in all horses in the treated group after 10 days of treatment, whereas none of the horses in the control group showed improvement (Venner *et al.* 1999). It should be noted in this study however that all horses in the treated group were displaying clinical signs of ulceration and had more severe ulceration scores than those of the controls. In addition all 12 control horses returned home whereas 4/12 treated horses remained hospitalised during the course of the treatment. None of the treated horses exhibited total healing of the gastric ulceration. Another study reported that 9/10 horses showed significant improvement after 30 days of treatment, with 3 horses showing complete ulcer healing. In this study all the horses were housed in boxes and kept in full race training, and there were no controls (Ferrucci, Zucca, Croci *et al.* 2003).

Motility modifiers

The use of prokinetic agents may be of use in patients with EGUS when there is ileus and significant gastroduodenal reflux. Bethanechol and erythromycin have both been shown to increase solid phase gastric emptying in normal healthy horses (Murray 2004). Erythromycin is a macrolide antibiotic that exerts its prokinetic effects by activating the motilin receptors. In adult horses antimicrobial doses of erythromycin have induced severe diarrhoea, however the dosages for the prokinetic effect are much smaller (approximately 1/50th). Dose rates for prokinetic effects are 0.1-1.0mg/kg IV (Ringger *et al.* 1996). Bethanechol is a synthetic muscarinic cholinergic agent that is not degraded by acetylcholinesterases. The only reported side effect of treatment with bethanechol is increased salivation. The recommended treatment regimen is dosing 0.025-0.030mg/kg subcutaneously every 2-3 hours, followed by oral maintenance at 0.3-0.45mg/kg 3-4 times per day.

Antibiotics

Although *Helicobacter spp* have not been cultured from the horse, anecdotal evidence suggests that some horses may benefit from treatment with antimicrobials in addition to acid suppressive therapy. In humans treatment with omeprazole or ranitidine is combined with clarithromycin and amoxicillin, or metronidazole. A suggested treatment for horses is omeprazole 4mg/kg PO SID, metronidazole 15mg/kg every six hours, and bismuth subsalicylate 3.8mg/kg every six hours (Buchanan and Andrews 2003).

Other agents

Agents such as furosemide, fenbendazole, octreotide and various nutraceuticals have been recommended for the treatment of gastric ulceration in horses. Furosemide use had a strong correlation with a decrease in ulcer severity in Thoroughbred racehorses

in one study, although other investigators have not shown the same effect. Its effects on ulcer healing were postulated to occur through modification of mucosal blood flow (Vatistas, Snyder, Carlson *et al.* 1994). Fenbendazole has been suggested as possible treatment of EGUS due to its chemical similarity to omeprazole. However it has not proved to be clinically useful at a dose of 6g PO once daily for five days (Buchanan and Andrews 2003).

Octreotide is a synthetic somatostatin analogue that acts as an inhibitor of gastric acid, gastrin and pepsin secretion. It has been shown to increase the pH of gastric fluid for eight hours after administration in healthy ponies (Sojka, Weiss, Samuels *et al.* 1992). Various nutraceuticals are available that claim to be effective in treating EGUS in horses, however to date none of the manufacturers claims have been evaluated scientifically (Murray 2004).

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. Importantly it should be noted that individual horses have different requirements for effective treatment (Murray 1994b) and thus it is necessary that treatment be tailored for each horse. In patients where clinical signs have resolved and risk factors for recurrence are absent, it may be expected that remaining ulcers will heal spontaneously (MacAllister 1999). However, given the fact that race training has been shown to be a significant risk factors some racehorses may need to be maintained on therapy while ever they are in training. It is important to note that the

disappearance of clinical signs themselves may not indicate complete healing, rather it may be a reflection of decreased gastric pH and thus decreased irritation of lesions.

Treatment summary

Current research indicates treatment of horses with EGUS using orally administered omeprazole is the most effective treatment for EGUS (Haven *et al.* 1999; Johnson *et al.* 2001; McClure, White, Sifferman, Bernard, Doucet *et al.* 2005; McClure, White, Sifferman, Bernard, Hughes *et al.* 2005; Orsini *et al.* 2003). Treatment at 4mg/kg PO SID for 28 days followed by treatment with 1mg/kg SID is effective in both treating the ulceration and preventing recurrence (McClure, White, Sifferman, Bernard, Hughes *et al.* 2005). Other drugs such as H₂ receptor antagonists, sucralfate, synthetic prostaglandins have had variable reports of success, although the treatment regimes have largely been based on anecdotal evidence and extrapolation from human studies.

Conclusion

Equine Gastric Ulcer Syndrome is a condition that affects a large proportion of racing horses. The prevalence of EGUS within New Zealand racing horses is unknown, although a review of the literature suggests that daily access to pasture, as given to most New Zealand racehorses, may result in a lower prevalence. Due to the large number of different grading systems used by various authors it is difficult to compare efficacy of various treatments between studies. The recently proposed scoring system by the Equine Gastric Ulcer Council has yet to be properly validated, but establishment of a standard scoring system is important as it allows for comparison between studies and operators. There is uncertainty in the literature about whether there is a site predilection for location and severity of EGUS lesions within the squamous mucosa. 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 a cause for this condition, though it is likely that other factors such as exercise and dietary change contribute to the development of the excess acidity. However, until more is understood about this disease, its pathogenesis, and its significance, treatment will continue to be symptomatic in nature.

References

- Andrews, FM, Doherty, TJ, Blackford, JT, Nadeau, JA and Saxton, AM** (1999) Effects of Orally Administered Enteric-Coated Omeprazole on Gastric Acid Secretion in Horses. *American Journal of Veterinary Research* 60, 929-931.
- Andrews, FM and Nadeau, JA** (1999) Clinical Syndromes of Gastric Ulceration in Foals and Mature Horses. *Equine Veterinary Journal* Supplement 29, 30-33.
- Andrews, FM, Reinemeyer, CR, McCracken, MD, Blackford, JT, Nadeau, JA, Saabye, L, Sotell, M and Saxton, A** (2002) Comparison of Endoscopic, Necropsy and Histology Scoring of Equine Gastric Ulcers. *Equine Veterinary Journal* 34, 475-478.
- Andrews, FM, Sifferman, RL, Bernard, W, Hughes, FE, Holste, JE, Daurio, CP, Alva, R and Cox, JL** (1999) Efficacy of Omeprazole Paste in the Treatment and Prevention of Gastric Ulcers in Horses. *Equine Veterinary Journal* Supplement 29, 81-86.
- Argenzio, RA** (1999) Comparative Pathophysiology of Nonglandular Ulcer Disease: A Review of Experimental Studies. *Equine Veterinary Journal* Supplement 29, 19-23.
- Argenzio, RA, Lowe, JE, Pickard, DW and Stevens, CE** (1974) Digesta Passage and Water Exchange in the Equine Large Intestine. *American Journal Of Physiology* 226, 1035-1042.
- Baker, SJ and Gerring, EL** (1993a) Effects of Single Intravenously Administered Doses of Omeprazole and Ranitidine on Intragastric Ph and Plasma Gastrin-Concentration in Non-Fed Ponies. *American Journal of Veterinary Research* 54, 2068-2074.
- Baker, SJ and Gerring, EL** (1993b) Technique for Prolonged, Minimally Invasive Monitoring of Intragastric Ph in Ponies. *American Journal of Veterinary Research* 54, 1725-1734.
- Baker, SJ, Gerring, EL and Fox, MT** (1993) 24-Hour Gastric Ph Monitoring and Blood Gastrin-Concentrations in Fasted Ponies. *Research in Veterinary Science* 55, 261-264.

- Begg, LM and O'Sullivan, CB** (2003) The Prevalence and Distribution of Gastric Ulceration in 345 Racehorses. *Australian Veterinary Journal* 81, 199-201.
- Berschneider, HM, Blikslager, AT and Roberts, MC** (1999) Role of Duodenal Reflux in Nonglandular Gastric Ulcer Disease of the Mature Horse. *Equine Veterinary Journal* Supplement 29, 24-29.
- Borne, AT and MacAllister, CG** (1993) Effect of Sucralfate on Healing of Subclinical Gastric Ulcers in Foals. *Journal of the American Veterinary Medical Association* 202, 1465-1468.
- Brunton, LL** Agents for the Control of Gastric Acidity and Treatment of Peptic Ulcers In: *Goodman & Gilman's the Pharmacological Basis of Therapeutics* 9edn., Eds: J.G. Hardman, L.E. Limbird, P.B. Molinoff, R.W. Ruddon and A.G. Gilman. pp 905-915. McGraw-Hill, New York, (1996)
- Buchanan, BR and Andrews, FM** (2003) Treatment and Prevention of Equine Gastric Ulcer Syndrome. *Veterinary Clinics of North America-Equine Practice* 19, 575-597.
- Bullimore, SR, Corfield, AP, Hicks, SJ, Goodall, C and Carrington, SD** (2001) Surface Mucus in the Non-Glandular Region of the Equine Stomach. *Research in Veterinary Science* 70, 149-155.
- Campbell-Thompson, ML and Merritt, AM** (1990) Basal and Pentagastrin-Stimulated Gastric-Secretion in Young Horses. *American Journal Of Physiology* 259, R1259-R1266.
- Campbell-Thompson, ML and Merritt, AM** (1987a) Effect of Ranitidine on Gastric-Acid Secretion in Young Male Horses. *American Journal of Veterinary Research* 48, 1511-1515.
- Campbell-Thompson, ML and Merritt, AM** (1987b) Gastric-Acid and Pepsin Secretion in the Horse. *Veterinary Surgery* 16, 85-85.
- Cargile, JL, Burrow, JA, Kim, I, Cohen, ND and Merritt, AM** (2004) Effect of Dietary Corn Oil Supplementation on Equine Gastric Fluid Acid, Sodium, and Prostaglandin E-2 Content before and During Pentagastrin Infusion. *Journal of Veterinary Internal Medicine* 18, 545-549.
- Clark, CK, Merritt, AM, Burrow, JA and Steible, CK** (1996) Effect of Aluminum Hydroxide Magnesium Hydroxide Antacid and Bismuth Subsalicylate on Gastric Ph in Horses. *Journal of the American Veterinary Medical Association* 208, 1687-1691.
- Collier, DS and Stoneham, SJ** (1997) Gastro-Oesophageal Ulcers in Man and Horse: Semblance and Dissemblance. *Equine Veterinary Journal* 29, 410-412.

- Collins, LG and Tyler, DE** (1985) Experimentally Induced Phenylbutazone Toxicosis in Ponies - Description of the Syndrome and Its Prevention with Synthetic Prostaglandin-E2. *American Journal of Veterinary Research* 46, 1605-1615.
- Daurio, CP, Holste, JE, Andrews, FM, Merritt, AM, Blackford, JT, Dolz, F and Thompson, DR** (1999) Effect of Omeprazole Paste on Gastric Acid Secretion in Horses. *Equine Veterinary Journal* Supplement 29, 59-62.
- Defilippi, C, Mamani, N and Gomez, E** (1987) Relationship between Antropyloric and Intestinal Motility and Duodenogastric Reflux in Fasting Dogs. *Digestive Diseases and Sciences* 32, 171-176.
- Dionne, RM, Vrins, A, Doucet, MY and Pare, J** (2003) Gastric Ulcers in Standardbred Racehorses: Prevalence, Lesion Description, and Risk Factors. *Journal of Veterinary Internal Medicine* 17, 218-222.
- Doherty, TJ, Andrews, FM, Provenza, MK and Frazier, DL** (1998) Acetaminophen as a Marker of Gastric Emptying in Ponies. *Equine Veterinary Journal* 30, 349-351.
- Doucet, MY, Vrins, AA, Dionne, R, Alva, R and Ericsson, G** (2003) Efficacy of a Paste Formulation of Omeprazole for the Treatment of Naturally Occurring Gastric Ulcers in Training Standardbred Racehorses in Canada. *Canadian Veterinary Journal* 44, 581-585.
- Dowling, PM** (1995) Therapy of Gastrointestinal Ulcers. *Canadian Veterinary Journal* 36, 276-277.
- Duran, S, Ravis, W and Smyth, GB** (1993) Comparative Pharmacokinetics of H₂ Antagonists in Horses. *Proceedings of the 11th Annual Veterinary Medical Forum ACVIM*, 687-690.
- Duran, SH** (1999) Famotidine. *Compendium on Continuing Education for the Practicing Veterinarian* 21, 424-425.
- E.G.U.C.** (1999) Recommendations for the Diagnosis and Treatment of Equine Gastric Ulcer Syndrome (Egus) - the Equine Gastric Ulcer Council. *Equine Veterinary Education* 11, 262-272.
- Ethell, MT, Hodgson, DR and Hills, BA** (2000) Evidence for Surfactant Contributing to the Gastric Mucosal Barrier of the Horse. *Equine Veterinary Journal* 32, 470-474.
- Ferrucci, F, Zucca, E, Croci, C, Di Fabio, V and Ferro, E** (2003) Treatment of Gastric Ulceration in 10 Standardbred Racehorses with a Pectin-Lecithin Complex. *Veterinary Record* 152, 679-681.

- Ferrucci, F, Zucca, E, Di Fabio, V, Croci, C and Tradati, F** (2003) Gastroscopic Findings in 63 Standardbred Racehorses in Training. *Veterinary Research Communications* 27, 759-762.
- Furr, M, Taylor, L and Kronfeld, D** (1994) The Effects of Exercise Training on Serum Gastrin Responses in the Horse. *Cornell Veterinarian* 84, 41-45.
- Furr, MO and Murray, MJ** (1989) Treatment of Gastric Ulcers in Horses with Histamine Type 2 Receptor Antagonists. *Equine Veterinary Journal Supplement* 7, 77-79.
- Furr, MO, Murray, MJ and Ferguson, DC** (1992) The Effects of Stress on Gastric-Ulceration, T3, T4, Reverse T3 and Cortisol in Neonatal Foals. *Equine Veterinary Journal* 24, 37-40.
- Geor, RJ** (2000) Gastric Surface Active Phospholipid - a Role in Protection of the Squamous Epithelial Mucosa? *Equine Veterinary Journal* 32, 458-459.
- Geor, RJ, Petrie, L, Papich, MG and Rousseaux, C** (1989) The Protective Effects of Sucralfate and Ranitidine in Foals Experimentally Intoxicated with Phenylbutazone. *Canadian Journal of Veterinary Research* 53, 231-238.
- Hammond, CJ** (1990) A Study of Gastric-Mucosal Ph and Its Correlation with Gastric-Ulcers in Adult Horses. *Journal of Equine Veterinary Science* 10, 404-408.
- Hammond, CJ, Mason, DK and Watkins, KL** (1986) Gastric-Ulceration in Mature Thoroughbred Horses. *Equine Veterinary Journal* 18, 284-287.
- Hartmann, AM and Frankeny, RL** (2003) A Preliminary Investigation into the Association between Competition and Gastric Ulcer Formation in Non-Racing Performance Horses. *Journal of Equine Veterinary Science* 23, 560-561.
- Haven, ML, Dave, K, Burrow, JA, Merritt, AM, Harris, D, Zhang, D and Hickey, GJ** (1999) 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, 54-58.
- Higgins, A** (2004) Endurance Horses and Gastric Ulceration - a Sore Point. *Veterinary Journal* 167, 1-2.
- Holbrook, TC, Simmons, RD, Payton, ME and MacAllister, CG** (2005) Effect of Repeated Oral Administration of Hypertonic Electrolyte Solution on Equine Gastric Mucosa. *Equine Veterinary Journal* 37, 501-504.
- Holland, PS, Ruoff, WW, Brumbaugh, GW and Brown, SA** (1997) Plasma Pharmacokinetics of Ranitidine Hcl in Adult Horses. *Journal Of Veterinary Pharmacology And Therapeutics* 20, 145-152.

- Jeffrey, SC, Murray, MJ and Eichorn, ES** (2001) Distribution of Epidermal Growth Factor Receptor (Egfr) in Normal and Acute Peptic-Injured Equine Gastric Squamous Epithelium. *Equine Veterinary Journal* 33, 562-569.
- Jenkins, CC, Blackford, JT, Andrews, F, Frazier, DL, Mattsson, H, Olovsson, SG and Peterson, A** (1992) Duration of Antisecretory Effects of Oral Omeprazole in Horses with Chronic Gastric Cannulae. *Equine Veterinary Journal* Supplement 13, 89-92.
- Johnson, JH, Vatisstas, N, Castro, L, Fischer, T, Pipers, FS and Maye, D** (2001) Field Survey of the Prevalence of Gastric Ulcers in Thoroughbred Racehorses and on Response to Treatment of Affected Horses with Omeprazole Paste. *Equine Veterinary Education* 13, 221-224.
- Kitchen, DL, Burrow, JA, Heartless, CS and Merritt, AM** (2000) Effect of Pyloric Blockade and Infusion of Histamine or Pentagastrin on Gastric Secretion in Horses. *American Journal of Veterinary Research* 61, 1133-1139.
- Kitchen, DL, Merritt, AM and Burrow, JA** (1998) Histamine-Induced Gastric Acid Secretion in Horses. *American Journal of Veterinary Research* 59, 1303-1306.
- Lloyd, KC** (1993) Ontogeny of Gastric Function Vs the 'Stress Syndrome'. *Equine Veterinary Journal* 25, 179.
- Lorenzo-Figueras, M and Merritt, AM** (2002) Effects of Exercise on Gastric Volume and Ph in the Proximal Portion of the Stomach of Horses. *American Journal of Veterinary Research* 63, 1481-1487.
- Lorenzo, M, Burrow, JA and Merritt, AM** (2001) Barostatic Evaluation of the Effect of Exercise on the Equine Proximal Stomach. *Gastroenterology* 120, A149-A150.
- MacAllister, CG** (1999) A Review of Medical Treatment for Peptic Ulcer Disease. *Equine Veterinary Journal* Supplement 29, 45-49.
- Macallister, CG, Andrews, FM, Deegan, E, Ruoff, W and Olovson, SG** (1997) A Scoring System for Gastric Ulcers in the Horse. *Equine Veterinary Journal* 29, 430-433.
- Macallister, CG, Lowrey, F, Stebbins, M, Newman, MS and Young, B** (1994) Transendoscopic Electrocautery-Induced Gastric-Ulcers as a Model for Gastric Healing Studies in Ponies. *Equine Veterinary Journal* 26, 100-103.
- Macallister, CG, Morgan, SJ, Borne, AT and Pollet, RA** (1993) Comparison of Adverse-Effects of Phenylbutazone, Flunixin Meglumine, and Ketoprofen in Horses. *Journal of the American Veterinary Medical Association* 202, 71-77.
- Macallister, CG and Sangiah, S** (1993) Effect of Ranitidine on Healing of Experimentally-Induced Gastric-Ulcers in Ponies. *American Journal of Veterinary Research* 54, 1103-1107.

- Macallister, CG, Sangiah, S and Mauromoustakos, A** (1992) Effect of a Histamine H-2 Type Receptor Antagonist (Wy-45, 727) on the Healing of Gastric-Ulcers in Ponies. *Journal of Veterinary Internal Medicine* 6, 271-275.
- MacAllister, CG, Sifferman, RL, McClure, SR, White, GW, Vatistas, NJ, Holste, JE, Ericsson, GF and Cox, JL** (1999) Effects of Omeprazole Paste on Healing of Spontaneous Gastric Ulcers in Horses and Foals: A Field Trial. *Equine Veterinary Journal Supplement* 29, 77-80.
- McClure, SR, Carithers, DS, Gross, SJ and Murray, MJ** (2005) Gastric Ulcer Development in Horses in a Simulated Show or Training Environment. *Journal of the American Veterinary Medical Association* 227, 775-777.
- McClure, SR, Glickman, LT and Glickman, NW** (1999) Prevalence of Gastric Ulcers in Show Horses. *Journal of the American Veterinary Medical Association* 215, 1130-1133.
- McClure, SR, White, GW, Sifferman, RL, Bernard, W, Doucet, MY, Vrins, A, Holste, JE, Fleishman, C, Alva, R and Cramer, LG** (2005) Efficacy of Omeprazole Paste for Prevention of Gastric Ulcers in Horses in Race Training. *Journal of the American Veterinary Medical Association* 226, 1681-1684.
- McClure, SR, White, GW, Sifferman, RL, Bernard, W, Hughes, FE, Holste, JE, Fleishman, C, Alva, R and Cramer, LG** (2005) Efficacy of Omeprazole Paste for Prevention of Recurrence of Gastric Ulcers in Horses in Race Training. *Journal of the American Veterinary Medical Association* 226, 1685-1688.
- Merritt, AM** (2003) The Equine Stomach: A Personal Perspective (1963-2003). *Proceedings of the 49th Annual Convention of American Association of Equine Practitioners*. 49, pp75-102.
- Merritt, AM** (1999) Normal Equine Gastroduodenal Secretion and Motility. *Equine Veterinary Journal Supplement* 29, 7-13.
- Merritt, AM, Campbell-Thompson, ML and Lowrey, S** (1989) Effect of Xylazine Treatment on Equine Proximal Gastrointestinal Tract Myoelectrical Activity. *American Journal of Veterinary Research* 50, 945-949.
- Merritt, AM, Sanchez, LC, Burrow, JA, Church, M and Ludzia, S** (2003) Effect of Gastrogard and Three Compounded Oral Omeprazole Preparations on 24 H Intra-gastric Ph in Gastrically Cannulated Mature Horses. *Equine Veterinary Journal* 35, 691-695.
- Miller, TA** (1983) Protective Effects of Prostaglandins against Gastric Mucosal Damage: Current Knowledge and Proposed Mechanisms. *American Journal Of Physiology* 245, G601-623.

- Moore, EW and Scarlata, RW** (1965) The Determination of Gastric Acidity by the Glass Electrode. *Gastroenterology* 49, 178-188.
- Murray, MJ** (1992a) Aetiopathogenesis and Treatment of Peptic Ulcer in the Horse: A Comparative Review. *Equine Veterinary Journal Supplement* 13, 63-74.
- Murray, MJ** (1991a) Diagnosing and Treating Gastric-Ulcers in Foals and Horses. *Veterinary Medicine* 86, 820-827.
- Murray, MJ** Drugs Acting on the Gastrointestinal System. In: *Equine Pharmacology*, Eds: J.B. Bertone and L.J.L. Horspool. pp 85-120. Saunders, London, (2004)
- Murray, MJ** (1989) Endoscopic Appearance of Gastric-Lesions in Foals - 94 Cases (1987-1988). *Journal of the American Veterinary Medical Association* 195, 1135-1141.
- Murray, MJ** (1994a) Equine Model of Inducing Ulceration in Alimentary Squamous Epithelial Mucosa. *Digestive Diseases and Sciences* 39, 2530-2535.
- Murray, MJ** (1994b) Gastric-Ulcers in Adult Horses. *Compendium on Continuing Education for the Practicing Veterinarian* 16, 792-794.
- Murray, MJ** (1992b) Gastric Ulceration in Horses - 91 Cases (1987-1990). *Journal of the American Veterinary Medical Association* 201, 117-120.
- Murray, MJ** (1992c) Gastric Ulceration in Horses: Pathologic and Therapeutic Considerations. *Proceedings of the Annual Convention of the American Association of Equine Practitioners* 38, 557-569.
- Murray, MJ** (1999a) Gastroduodenal Ulceration in Foals. *Equine Veterinary Education* 11, 199-207.
- Murray, MJ** (1991b) The Pathogenesis and Prevalence of Gastric-Ulceration in Foals and Horses. *Veterinary Medicine* 86, 815-819.
- Murray, MJ** (1999b) Pathophysiology of Peptic Disorders in Foals and Horses: A Review. *Equine Veterinary Journal Supplement* 29, 14-18.
- Murray, MJ** (1997) Suppression of Gastric Acidity in Horses. *Journal of the American Veterinary Medical Association* 211, 37-40.
- Murray, MJ and Eichorn, ES** (1996) Effects of Intermittent Feed Deprivation, Intermittent Feed Deprivation with Ranitidine Administration, and Stall Confinement with Ad Libitum Access to Hay on Gastric Ulceration in Horses. *American Journal of Veterinary Research* 57, 1599-1603.
- Murray, MJ, Eichorn, ES, Holste, JE, Cox, JL, Stanier, WB, Cooper, WL and Cooper, VA** (1999) Safety, Acceptability and Endoscopic Findings in Foals and Yearling Horses Treated with a Paste Formulation of Omeprazole for Twenty-Eight Days. *Equine Veterinary Journal Supplement* 29, 67-70.

- Murray, MJ, Eichorn, ES and Jeffrey, SC** (2001) Histological Characteristics of Induced Acute Peptic Injury in Equine Gastric Squamous Epithelium. *Equine Veterinary Journal* 33, 554-560.
- Murray, MJ and Grodinsky, C** (1992) The Effects of Famotidine, Ranitidine and Magnesium Hydroxide/Aluminium Hydroxide on Gastric Fluid Ph in Adult Horses. *Equine Veterinary Journal* Supplement 11, 52-55.
- Murray, MJ and Grodinsky, C** (1989) Regional Gastric Ph Measurement in Horses and Foals. *Equine Veterinary Journal* Supplement 7, 73-76.
- Murray, MJ, Grodinsky, C, Anderson, CW, Radue, PF and Schmidt, GR** (1989) Gastric Ulcers in Horses: A Comparison of Endoscopic Findings in Horses with and without Clinical Signs. *Equine Veterinary Journal* Supplement 7, 68-72.
- Murray, MJ, Haven, ML, Eichorn, ES, Zhang, DH, Eagleson, J and Hickey, GJ** (1997) Effects of Omeprazole on Healing of Naturally-Occurring Gastric Ulcers in Thoroughbred Racehorses. *Equine Veterinary Journal* 29, 425-429.
- Murray, MJ and Mahaffey, EA** (1993) Age-Related Characteristics of Gastric Squamous Epithelial Mucosa in Foals. *Equine Veterinary Journal* 25, 514-517.
- Murray, MJ, Murray, CM, Sweeney, HJ, Weld, J, Digby, NJ and Stoneham, SJ** (1990) Prevalence of Gastric Lesions in Foals without Signs of Gastric Disease: An Endoscopic Survey. *Equine Veterinary Journal* 22, 6-8.
- Murray, MJ, Nout, YS and Ward, DL** (2001) Endoscopic Findings of the Gastric Antrum and Pylorus in Horses: 162 Cases (1996-2000). *Journal of Veterinary Internal Medicine* 15, 401-406.
- Murray, MJ and Schusser, GF** (1993) Measurement of 24-H Gastric Ph Using an Indwelling Ph Electrode in Horses Unfed, Fed and Treated with Ranitidine. *Equine Veterinary Journal* 25, 417-421.
- Murray, MJ, Schusser, GF, Pipers, FS and Gross, SJ** (1996) Factors Associated with Gastric Lesions in Thoroughbred Racehorses. *Equine Veterinary Journal* 28, 368-374.
- Nadeau, JA, Andrews, FM, Mathew, AG, Argenzio, RA and Blackford, JT** (1998) The Effect of Diet on Severity of Gastric Ulcers in Horses. *Gastroenterology* 114, A238-A238.
- Nadeau, JA, Andrews, FM, Mathew, AG, Argenzio, RA, Blackford, JT, Sohtell, M and Saxton, AM** (2000) Evaluation of Diet as a Cause of Gastric Ulcers in Horses. *American Journal of Veterinary Research* 61, 784-790.

- Nadeau, JA, Andrews, FM, Patton, CS, Argenzio, RA, Mathew, AG and Saxton, AM** (2003a) Effects of Hydrochloric, Acetic, Butyric, and Propionic Acids on Pathogenesis of Ulcers in the Nonglandular Portion of the Stomach of Horses. *American Journal of Veterinary Research* 64, 404-412.
- Nadeau, JA, Andrews, FM, Patton, CS, Argenzio, RA, Mathew, AG and Saxton, AM** (2003b) Effects of Hydrochloric, Valeric, and Other Volatile Fatty Acids on Pathogenesis of Ulcers in the Nonglandular Portion of the Stomach of Horses. *American Journal of Veterinary Research* 64, 413-417.
- Nicol, CJ, Davidson, HPD, Harris, PA, Waters, AJ and Wilson, AD** (2002) Study of Crib-Biting and Gastric Inflammation and Ulceration in Young Horses. *Veterinary Record* 151, 658-662.
- Nieto, JE, Snyder, JR, Beldomenico, P, Aleman, M, Kerr, JW and Spier, SJ** (2004) Prevalence of Gastric Ulcers in Endurance Horses - a Preliminary Report. *Veterinary Journal* 167, 33-37.
- Nieto, JE, Spier, S, Pipers, FS, Stanley, S, Aleman, MR, Smith, DC and Snyder, JR** (2002) Comparison of Paste and Suspension Formulations of Omeprazole in the Healing of Gastric Ulcers in Racehorses in Active Training. *Journal of the American Veterinary Medical Association* 221, 1139-1143.
- Nieto, JE, Spier, SJ, van Hoogmoed, L, Pipers, F, Timmerman, B and Snyder, JR** (2001) Comparison of Omeprazole and Cimetidine in Healing of Gastric Ulcers and Prevention of Recurrence in Horses. *Equine Veterinary Education* 13, 260-264.
- O'Connor, MS, Steiner, JM, Roussel, AJ, Williams, DA, Meddings, JB, Pipers, F and Cohen, ND** (2004) Evaluation of Urine Sucrose Concentration for Detection of Gastric Ulcers in Horses. *American Journal of Veterinary Research* 65, 31-39.
- Orsini, J** (2000) Gastric Ulceration in the Mature Horse: A Review. *Equine Veterinary Education* 12, 24-27.
- Orsini, J and Pipers, FS** (1997) Endoscopic Evaluation of the Relationship between Training, Racing and Gastric Ulcers. *Veterinary Surgery* 26, 424.
- Orsini, JA, Dreyfuss, DJ, Vecchione, J, Spencer, PA and Uhlman, R** (1991) Effects of a Histamine Type-2 Receptor Antagonist (Bmy-25368) on Gastric-Secretion in Horses. *American Journal of Veterinary Research* 52, 108-110.
- Orsini, JA, Haddock, M, Stine, L, Sullivan, EK, Rabuffo, TS and Smith, G** (2003) Odds of Moderate or Severe Gastric Ulceration in Racehorses Receiving Antiulcer Medications. *Journal of the American Veterinary Medical Association* 223, 336-339.

- Plue, RE, Wall, HG, Daurio, C, Attebery, DK, Cox, JL and Wallace, DH** (1999) Safety of Omeprazole Paste in Foals and Mature Horses. *Equine Veterinary Journal Supplement* 29, 63-66.
- Rabuffo, TS, Orsini, JA, Sullivan, E, Engiles, J, Norman, T and Boston, R** (2002) Associations between Age or Sex and Prevalence of Gastric Ulceration in Standardbred Racehorses in Training. *Journal of the American Veterinary Medical Association* 221, 1156-1159.
- Ringger, NC, Lester, GD, Neuwirth, L, Merritt, AM, Vetro, T and Harrison, J** (1996) Effect of Bethanechol or Erythromycin on Gastric Emptying in Horses. *American Journal of Veterinary Research* 57, 1771-1775.
- Sams, RA, Gerken, DF, Dyke, TM, Reed, SM and Ashcraft, SM** (1997) Pharmacokinetics of Intravenous and Intragastric Cimetidine in Horses.1. Effects of Intravenous Cimetidine on Pharmacokinetics of Intravenous Phenylbutazone. *Journal Of Veterinary Pharmacology And Therapeutics* 20, 355-361.
- Sanchez, LC, Murray, MJ and Merritt, AM** (2004) Effect of Omeprazole Paste on Intragastric Ph in Clinically Normal Neonatal Foals. *American Journal of Veterinary Research* 65, 1039-1041.
- Sandin, A, Andrews, FM, Nadeau, JA, Doherty, TJ and Nilsson, G** (1999) Effects of Intramuscular Omeprazole on Gastric Acid Secretion in Horses over a Twenty-Four Hour Period. *Equine Veterinary Journal Supplement* 29, 50-53.
- Sandin, A, Skidell, J, Haggstrom, J and Nilsson, G** (2000) Postmortem Findings of Gastric Ulcers in Swedish Horses Older Than Age One Year: A Retrospective Study of 3715 Horses (1924-1996). *Equine Veterinary Journal* 32, 36-42.
- Sangiah, S, MacAllister, CC and Amouzadeh, HR** (1989) Effects of Misoprostol and Omeprazole on Basal Gastric Ph and Free Acid Content in Horses. *Research in Veterinary Science* 47, 350-354.
- Sangiah, S, McAllister, CC and Amouzadeh, HR** (1988) Effects of Cimetidine and Ranitidine on Basal Gastric Ph, Free and Total Acid Contents in Horses. *Research in Veterinary Science* 45, 291-295.
- Sisson, S and Grossman, JD** Sisson and Grossman's the Anatomy of the Domestic Animals. P 481. Saunders, Philadelphia, (1975)
- Smyth, GB, Duran, S, Ravis, W and Clark, CR** (1990) Pharmacokinetic Studies of Cimetidine Hydrochloride in Adult Horses. *Equine Veterinary Journal* 22, 48-50.
- Smyth, GB, Young, DW and Hammond, LS** (1989) Effects of Diet and Feeding on Postprandial Serum Gastrin and Insulin Concentration in Adult Horses. *Equine Veterinary Journal Supplement* 7, 56-59.

- Sojka, JE, Weiss, JS, Samuels, ML and You, GM** (1992) Effect of the Somatostatin Analog Octreotide on Gastric Fluid Ph in Ponies. *American Journal of Veterinary Research* 53, 1818-1821.
- Sutton, DG, Bahr, A, Preston, T, Christley, RM, Love, S and Roussel, AJ** (2003) Validation of the ¹³C-Octanoic Acid Breath Test for Measurement of Equine Gastric Emptying Rate of Solids Using Radioscintigraphy. *Equine Veterinary Journal* 35, 27-33.
- Sutton, DG, Preston, T, Christley, RM, Cohen, ND, Love, S and Roussel, AJ** (2002) The Effects of Xylazine, Detomidine, Acepromazine and Butorphanol on Equine Solid Phase Gastric Emptying Rate. *Equine Veterinary Journal* 34, 486-492.
- Vatistas, NJ, Nieto, JE, Snyder, JR and Thompson, D** (1999) Clinical Trial to Determine the Effect of Omeprazole Given Once or Twice Daily on Gastric Ulceration. *Equine Veterinary Journal Supplement* 29, 87-90.
- Vatistas, NJ, Sifferman, RL, Holste, J, Cox, JL, Pinalto, G and Schultz, KT** (1999) Induction and Maintenance of Gastric Ulceration in Horses in Simulated Race Training. *Equine Veterinary Journal Supplement* 29, 40-44.
- Vatistas, NJ, Snyder, JR, Carlson, G, Johnson, B, Arthur, RM, Thurmond, M, Zhou, H and Lloyd, KL** (1999) Cross-Sectional Study of Gastric Ulcers of the Squamous Mucosa in Thoroughbred Racehorses. *Equine Veterinary Journal Supplement* 29, 34-39.
- Vatistas, NJ, Snyder, JR, Carlson, G, Johnson, B, Arthur, RM, Thurmond, M, Zhou, H and Lloyd, KL** (1994) Epidemiological Study of Gastric Ulceration in the Thoroughbred Race Horse: 202 Horses 1992-1993. *Proceedings of the Annual Convention of the American Association of Equine Practitioners* 40, 125-126.
- Vatistas, NJ, Snyder, JR, Nieto, J, Thompson, D, Pollmeier, M and Holste, J** (1999) Acceptability of a Paste Formulation and Efficacy of High Dose Omeprazole in Healing Gastric Ulcers in Horses Maintained in Race Training. *Equine Veterinary Journal Supplement* 29, 71-76.
- Venner, M, Lauffs, S and Deegen, E** (1999) Treatment of Gastric Lesions in Horses with Pectin-Lecithin Complex. *Equine Veterinary Journal Supplement* 29, 91-96.
- Wallace, JL** (2001) Nonsteroidal Anti-Inflammatory Drugs and the Gastrointestinal Tract. Mechanisms of Protection and Healing: Current Knowledge and Future Research. *The American Journal of Medicine* 110, 19-23S.
- Widenhouse, TV, Lester, GD and Merritt, AM** (2002) Effect of Hydrochloric Acid, Pepsin, or Taurocholate on Bioelectric Properties of Gastric Squamous Mucosa in Horses. *American Journal of Veterinary Research* 63, 744-749.

Zimmerman, TW and Schenker, S (1985) A Comparative Evaluation of Cimetidine and Ranitidine. *Rational Drug Therapy* 19, 1-7.

Chapter 3

The prevalence of gastric ulceration in New Zealand racehorses.

The prevalence of gastric ulceration in New Zealand racehorses.
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Abstract

Aims

To establish the prevalence of gastric ulcers in New Zealand racehorses.

Methods

A prevalence study was conducted during 2003 and 2004 in New Zealand. One hundred and seventy one horses from 24 trainers across New Zealand were examined with gastroscopy as part of the study. Images of the examination were recorded and reviewed. The stomachs were assigned an ordinal score based on the severity of the gastric ulceration present.

Results

There were 171 horses in the study: 133 Thoroughbreds and 38 Standardbreds. One hundred and fifty one (88.3%) of these had evidence of EGUS. There was no significant difference in the prevalence of ulceration between the two breeds ($p=0.51$) or between horses of differing ages ($p=0.56$). There were 141 horses kept at pasture for at least four hours per day, of these 125 (89%) had EGUS. Thirteen horses were kept at pasture full time and all of these had EGUS. Seventeen horses were stabled full time and 16 (94.1%) of these had EGUS. There was no significant difference between the different housing groups and the prevalence or severity of EGUS ($p=0.33$ and 0.13 respectively), and there was no significant difference in the severity of gastric ulceration ($p=0.12$) between the horses grazed on different pasture qualities. There was no significant difference in the prevalence ($p=0.26$) or severity ($p=0.49$) of gastric ulceration based on the duration of training.

Conclusions

The prevalence of EGUS in New Zealand racehorses is similar to that reported elsewhere for horses in active race training. The type of turnout that these horses receive does not appear to be protective for EGUS.

Clinical relevance

Pasture turnout alone may not be protective against EGUS in racehorses that are in active training.

Key words

Horse, equine, gastric ulceration, pasture, prevalence

Abbreviations

EGUC Equine Gastric Ulcer Council

EGUS Equine Gastric Ulcer Syndrome

Introduction

Gastric ulceration is a problem that frequently affects adult horses in active training. The term equine gastric ulcer syndrome (EGUS) has been used to describe this disease due to its complicated and multifactorial nature. As there are no pathognomonic clinical signs, definitive diagnosis of EGUS currently relies on oesophagogastroscopy. Clinical signs of gastric ulceration are non-specific and include: lack of appetite, weight loss/poor body condition, low grade or recurrent colic and loose faeces.

Until recently there has been no standard scoring system for gastric ulceration in the horse (E.G.U.C. 1999) and no reports to date have illustrated a definite relationship between ulcer score and severity of clinical signs (Dionne, Vrins, Doucet *et al.* 2003; Macallister, Andrews, Deegan *et al.* 1997). Between 58 and 100% of adult horses in training may be affected by EGUS (Bezdekova, Jahn, Vyskocil *et al.* 2005; Hammond, Mason and Watkins 1986; Murray, Grodinsky, Anderson *et al.* 1989; Murray, Schusser, Pipers *et al.* 1996; Orsini and Pipers 1997; Roy, Vrins, Beauchamp *et al.* 2005; Vatistas, Snyder, Carlson *et al.* 1994). Most horses will develop gastric ulceration at some time in their careers although not all horses with ulceration will show clinical signs (Murray 1994).

Despite the high prevalence, the aetiology of gastric ulcers in adult racehorses 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 client owned animals (Vatistas, Sifferman, Hoste *et al.* 1999).

The horse is a grazing animal and it is postulated that the constant flow of saliva and feed material into the stomach acts as a buffer for gastric acid. When horses are put

into training they are usually stabled for prolonged periods and have no access to grazing, which may remove this important buffering mechanism (Buchanan and Andrews 2003). “It would therefore be interesting to study horses in training whose trainer allowed them to spend time in the paddock grazing” (Collier 1999). Racehorses in New Zealand are typically turned out into a paddock for at least part of the day and allowed to graze. Some horses are trained out of the paddock without being stabled at all.

The present study was performed to establish the prevalence of gastric ulceration in New Zealand racehorses. We hypothesised that daily access to pasture and grazing would be protective against gastric ulceration, lowering the prevalence in comparison to elsewhere in the world where racehorses are housed more intensively.

Materials and Methods

Study design

A prevalence study was conducted during 2003 and 2004 in New Zealand. The study population comprised 175 horses (137 Thoroughbreds and 38 Standardbreds) in race training from 24 different trainers. Veterinarians from eight different regions in both the North and South Island were contacted, and trainers were selected by these veterinarians on the basis of the trainer’s willingness to participate in the study and provide access to randomly selected horses that met the selection criteria. The horses were in active training, had either raced or trialled in the current preparation and were not nominated to race for five days after examination. Horses were either picked from a list of horses that met the selection criteria by the primary author (11 stables) or all horses that met the inclusion criteria in a stable were examined (13 stables).

Information about age, gender, time in training, number of starts in the current preparation, housing, time at pasture, quality of pasture (the pasture was average if the paddock was fully grass covered and the horse could graze all day, and it was good if the pasture was sufficient to sustain a horse out of training without supplemental feeding and poor if there was insufficient pasture to provide grazing), appetite (good/poor), weight loss (yes/no), lameness history (yes/no), faecal consistency (firm/loose), colic (yes/no), and the use of anti-ulcer medications or other drugs was collected for each horse at the time of examination.

The study was conducted with approval from the Massey University Animal Ethics Committee (protocol number 03/88).

Endoscopic examination

All food was withheld for 8 hours before examination, and water was withdrawn 30 minutes prior to examination. Horses were sedated with detomidine hydrochloride (0.01mg/kg) intravenously (IV) (Dormosedan®: Novartis Animal Health Auckland New Zealand) and butorphanol tartrate (0.01mg/kg) IV (Butorphanol®: Lloyd Laboratories Papkura New Zealand) and a nose twitch applied. A shortened (80cm) nasogastric tube was passed via the nostril and into the proximal oesophagus and a 3m (9.8mm diameter) flexible video endoscope (Olympus SIF100-3000: Auckland New Zealand) was passed through the tube into the stomach. The stomach was insufflated with air and any feed material adherent to the surface of the gastric mucosa was removed with water via the endoscope biopsy channel. Each examination was recorded onto videotape for review and grading. For each gastroscopy the stomach was examined systematically. The greater curvature along the margo plicatus was visualised initially, the squamous fundus was examined, and the endoscope was then

advanced around the greater curvature until the lesser curvature and the cardia of the stomach were observed. Attempts were then made to examine the pylorus. In some horses the pylorus was unable to be visualised because of the presence of residual feed material. Still images were obtained of the greater curvature, lesser curvature and cardia, dorsal squamous fundus and pylorus. The distal oesophagus was imaged upon conclusion of the examination.

Classification Of Ulcers

All lesions were graded by the primary author (RB). For this study the grading system proposed by the Equine Gastric Ulcer Council (EGUC) was used (Table 3.1) (E.G.U.C. 1999). Horses were deemed to have ulcers if they were EGUC grade 2 or above.

Table 3.1: Equine Gastric Ulcer Council (E.G.U.C.) grading system for grading of Equine Gastric Ulcer Syndrome lesions in horses. (E.G.U.C. 1999)

Grade 0	Intact epithelium
Grade 1	Intact mucosa, evidence of hyperkeratosis or hyperaemia
Grade 2	Small, single, or multifocal lesions
Grade 3	Large, single or multifocal lesions or extensive superficial lesions
Grade 4	Extensive lesions with areas of apparent deep ulceration

Statistical Analysis

Univariate associations were examined between the outcome variable, which was the presence of gastric ulcers, and the categoric variables clinical signs, age, time in training and housing. Chi squared analysis was used to test for any significant association between sex or time in training and the presence of ulceration. The Fisher's exact test was used to test for any significant association between breed,

housing, age, clinical signs, geographical location and the presence of gastric ulceration. The Kruskal-Wallis test was used to test for significant association between pasture quality and severity of gastric ulceration. A significance level of $p < 0.05$ was set for all tests. These tests were performed using SPSS 12.0.1 for Windows (SPSS inc Chicago IL USA). The GLIMMIX macro in SAS 8.2 was used to perform an intercept-only random effects, logistic regression model, with trainer added as a random effect to test whether there was any significant variation between trainers.

Results

Of the 175 horses examined 4 were excluded either because of incomplete examination due to excess feed material in the stomach (2 horses) or equipment malfunction (2 horses). The study population was composed of 133 Thoroughbreds and 38 Standardbreds. The geographic distribution of these horses is shown in Table 3.2.

Table 3.2: Number of horses and trainers from each region across New Zealand as part of a prevalence study for Equine Gastric Ulcer Syndrome in racehorses.

Region	Number of horses	Number of Trainers
Manawatu	10 Thoroughbreds	2 trainers
Rangateiki	8 Thoroughbreds	1 trainer
Wairarapa	12 Thoroughbreds	1 trainer
Waikato	59 Thoroughbreds	6 trainers
Auckland	20 Thoroughbreds	3 trainers
Bay of Plenty	11 Thoroughbreds	1 trainer
Taranaki	8 Thoroughbreds	1 trainer
Canterbury	9 Thoroughbreds	2 trainers
	38 Standardbreds	7 trainers

Of these 151 (88.3%) had evidence of gastric ulceration (115/133 Thoroughbreds and 36/38 Standardbreds). The prevalence of gastric ulceration between the different groups of horses is presented in Table 3.3. There was no significant difference between breeds ($p = 0.51$). There were 39 two-year-olds, 71 three-year-olds, 40 four-year-olds, and 21 horses five years or older. No significant difference in the prevalence of EGUS between the different age groups was detected ($p = 0.56$). There was a trend for the severity of the gastric ulceration between horses three years and those older than five years to be more severe than in two-year-olds though this was not statistically significant ($p = 0.09$). There were 66 females, 101 geldings and 4 intact males. There was no significant difference in the prevalence of EGUS between males (geldings and intact males) and females ($p = 0.93$).

Table 3.3: Prevalence of Equine Gastric Ulcer Syndrome (EGUS) in 171 New Zealand racehorses and comparisons between breeds, age and sex

	Number of horses	Prevalence	Lower 95% CI	Upper 95%CI
Combined	171	88.3%	82.6%	92.3%
Thoroughbreds	133	86.5%	79.6%	91.2%
Standardbreds	38	94.7%	82.7%	98.5%
2 year olds	39	87.2%	73.2%	94.4%
3 year olds	71	93.0%	84.6%	97.0%
4 year olds	40	92.5%	80.1%	97.4%
≥5 years old	21	85.7%	65.4%	95.0%
Female	66	90.9%	81.5%	95.8%
Male	105	90.5%	83.4%	94.7%

Information on housing, pasture quality and prevalence of gastric ulceration is presented in tables 3.4 and 3.5.

Table 3.4: Gastric ulceration and housing

Housing	Number of horses	Number of horses with ulceration (%)
Stabled full time	17	16 (94%)
Pasture at least 4 hours	141	126 (89%)
Paddock trained	13	13 (100%)

Table 3.5: Comparison of quality of pasture, time at pasture and presence of gastric ulceration (number of horses with ulceration).

	Average quality pasture	Good quality pasture	Poor quality pasture
Pasture at least 4 hours	46 (38)	59(54)	36(34)
Paddock trained	5 (5)	6 (6)	2 (2)

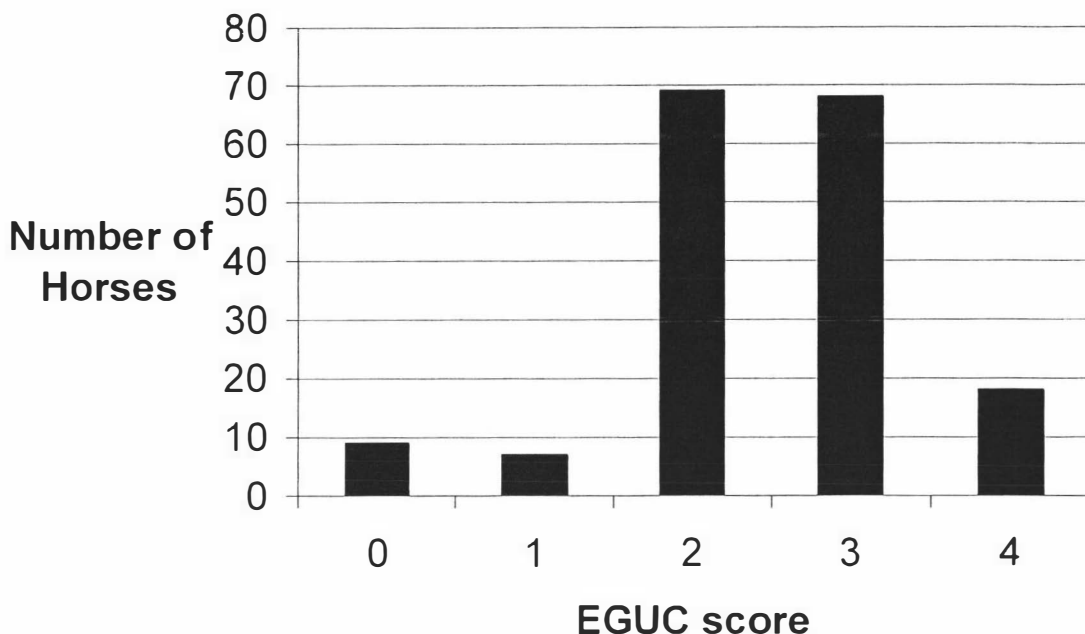
There was no significant difference in the prevalence or severity of gastric ulceration between these pasture groups ($p=0.23$ and 0.12 respectively). There was no significant difference between the prevalence of gastric ulceration in the different housing groups ($p=0.33$) or the severity of ulceration between housing groups ($p=0.13$). The distribution of the specific clinical signs and the proportion of horses that had gastric ulceration are shown in Table 3.6

There was no significant difference in the presence of gastric ulceration between those horses with clinical signs and those without ($p=0.95$). All horses in training for 6 weeks had EGUS, compared to 24/29 horses in training for 8 weeks, 43/48 of those in training for 12 weeks and 68/74 of those in training for 16 or more weeks. These differences were not significant ($p=0.26$). There was no significant difference in the severity of ulceration and the time in training ($p=0.49$). The distribution of ulcer grades is shown in Figure 3.1.

Table 3.6: Presence or absence of clinical signs and prevalence of Equine Gastric Ulcer Syndrome in 171 horses

	Number of horses (% of total)	Number with ulceration (prevalence, 95% CI)	p value; affected vs non-affected
No clinical signs	122 (71%)	111 (0.91, 0.85-0.95)	0.50
One clinical sign	33 (20%)	30 (0.91, 0.76-0.97)	
Two clinical signs	16 (9%)	14 (0.88, 0.64-0.97)	
Appetite			
Poor	18 (11%)	15 (0.83, 0.61-0.94)	0.38
Good	153 (89%)	140 (0.92, 0.86-0.95)	
Weight loss			
Present	24 (14%)	21 (0.88, 0.69-0.96)	0.51
Absent	147 (86%)	134 (0.91, 0.94-0.99)	
Faecal consistency			
Firm	143 (84%)	130 (0.91, 0.86-0.95)	0.40
Loose	28 (16%)	25 (0.89, 0.73-0.96)	

Figure 3.1: Distribution of Equine Gastric Ulcer Council (EGUC) grades in 171 horses



No horses were being treated with anti-ulcer medications. There was no significant difference in the prevalence of gastric ulceration between the 8 different geographic locations within New Zealand ($p=0.73$). The logistic regression model showed that the trainer level variance was not different from 0 ($p>0.05$), which indicates that there was no trainer effect on the prevalence of EGUS in horses in this study.

Discussion

This study illustrates that the prevalence of gastric ulceration in New Zealand racehorses is similar to that reported in previous studies from other countries (Begg and O'Sullivan 2003; Ferrucci, Zucca, Di Fabio *et al.* 2003; Roy *et al.* 2005; Vatistas *et al.* 1994). Because of the possibility of selection bias in stables where true random selection was not possible (i.e. in small stables), all horses that met the selection criteria in such stables were examined. The remainder of horses were selected randomly from those that met the criteria within the stables. This differs from a

number of other studies where the horses have either been selected by the trainers or animals that presented with clinical signs suggestive of gastric ulceration were examined (Begg and O'Sullivan 2003; Ferrucci *et al.* 2003; Johnson, Vatis, Castro *et al.* 2001; Roy *et al.* 2005). These methods introduce a significant bias, as Murray (1992) showed that 100% of horses in training with clinical signs consistent with gastric ulceration had EGUS. Since not all horses with EGUS exhibit clinical signs, it is necessary to examine a representative sample of the study population not just those horses with clinical signs.

The prevalence in our study was higher than that reported by some authors (Bezdekova *et al.* 2005; Dionne *et al.* 2003; Hammond *et al.* 1986; Sandin, Skidell, Haggstrom *et al.* 2000), however these studies included horses at all levels of training, not just those that were in the intensive stages of training (i.e. racing) as in our study. This was highlighted by Roy *et al.* 2005, who found a significantly higher prevalence of EGUS than was reported by other authors (Dionne *et al.* 2003) in a similar population of Standardbreds when stages of training differed.

It has been speculated that keeping racehorses at pasture may provide protection from the development of gastric ulceration (Dionne *et al.* 2003; Ferrucci *et al.* 2003; Murray *et al.* 1996; Orsini and Pipers 1997), either due to a protective factor in the grass itself or through the buffering effect of constant grazing activity. In our study there was no evidence to support this hypothesis, as all horses kept at pasture full time showed evidence of gastric ulceration and there was no difference in the prevalence or severity of gastric ulceration between the differing types of housing. The majority of horses within this study were kept at pasture for at least some portion of the day. Most horses also had access cut grass while ever they were stabled and all horses had

access to hay while stabled, this hay was pasture/clover type hay for the majority of horses. All horses were fed concentrates, this was a mix of whole or crushed oats and one of eight proprietary feeds. Horses were fed consistent diets within each training establishment. The majority of horses in the study were kept in paddocks where the pasture quality was subjectively assessed as either average or good. It should be noted that in most stables only a few horses were kept out at pasture full time, these were often those horses that are 'poor doers' when stabled and in training, and thus may already be affected by gastric ulceration.

These results suggest that pasture alone in these horses is not protective against EGUS, and suggest that the physiologic stresses of training may be sufficient cause for gastric ulceration in racehorses (Lorenzo-Figueras and Merritt 2002). Additionally, horses in this study were receiving significant amounts of grain and supplemental feedstuffs, which may have reduced the amount of time that they spent grazing when they were out at pasture. Horses often preferentially eat these highly palatable feedstuffs, and it has been shown that horses fed grain have an increase in the gastric concentration of volatile fatty acids, which without sufficient buffering may cause a decrease in gastric pH and thus an increase in gastric ulceration (Nadeau, Andrews, Patton *et al.* 2003).

There was no significant difference between different ages of horses with regard to the presence or severity of EGUS. This finding is consistent with that reported elsewhere (Bezdekova *et al.* 2005; Rabuffo, Orsini, Sullivan *et al.* 2002; Roy *et al.* 2005). There was a trend towards a greater EGUC score in horses older than two years, but this was not significant. A comparison of the prevalence of gastric ulceration in horses with clinical signs compared to horses without was performed.

There was no significant difference between the two populations. Other studies have illustrated an increased prevalence of gastric ulceration in horses with clinical signs (Murray 1992; Murray *et al.* 1989; Vatistas, Snyder, Carlson *et al.* 1999). A more recent report, however, showed that only poor body condition was related to an increased severity or prevalence of gastric ulceration (Dionne *et al.* 2003). The fact that a large number of horses without clinical signs had EGUS in our study is important as it reinforces the need for random selection in order to gain a true estimate of the prevalence of EGUS in a population of racehorses.

The amount of time that the horses had been in training did not affect the prevalence of gastric ulceration. Interestingly, those horses in training the shortest period of time had the highest prevalence of gastric ulceration. All horses in training for 6 weeks were affected, whereas only 81% of horses in training for 16 weeks had gastric ulceration. This difference while not statistically significant may be due to the horses acclimatising to the training environment over time. One study showed that serum cortisol levels actually decreased as the horse's time in training increased, suggesting that the horse's levels of stress declined over time (Vatistas, Snyder *et al.* 1999). However, it is apparent that the psychological stress of a new environment is not the only cause of ulceration due to the continued high prevalence of EGUS in these horses.

There are many different scoring systems in the literature for grading EGUS (Andrews, Reinemeyer, McCracken *et al.* 2002). This is partly due to the multifactorial nature of the disease, and partly due to the differing aims of the studies (clinical trials versus prevalence studies). Recently a standard scoring system was proposed by the Equine Gastric Ulcer Council (E.G.U.C. 1999). We used that system

in our study. The EGUC system assigns a horse with a single small ulcer the same grade as one with multiple lesions. We did not class horses with EGUC grade 1 lesions (hyperaemia or hyperkeratosis) as having EGUS, as these animals actually had intact mucosa at the time of examination. Indeed, some authors question the significance of one isolated small gastric ulcer or localised mild hyperkeratosis and feel that such horses are likely to not be significantly affected (Murray 1991). Comparison of the severity of gastric ulceration in this study to those reported elsewhere is difficult due to the lack of a standardised scoring system. However, the severity of the lesions in this study is similar to results reported elsewhere (Rabuffo *et al.* 2002; Vatistas *et al.* 1994) with the majority of horses in our study having grades 2 or 3 and a small number having the most severe grade (grade 4).

The fact that horses from across the whole of New Zealand were examined as part of the study is different to many other studies which have examined horses that present to a single clinic or are present within a small number of training centres (Begg and O'Sullivan 2003; Bezdekova *et al.* 2005; Dionne *et al.* 2003; Johnson *et al.* 2001; Rabuffo *et al.* 2002; Roy *et al.* 2005; Vatistas *et al.* 1994). The wide geographical distribution of trainers participating in the study helps us to be confident that we have a representative sample from across New Zealand. The breakdown of breed of horse and location is roughly representative of the New Zealand horse population. However, the selection of trainers on the basis of their willingness to participate in the study in conjunction with their veterinary surgeon could potentially have led to selection bias towards those trainers that felt that gastric ulceration was a problem in their stables. The fact that there was no effect of trainer on the prevalence of gastric ulceration is important as this makes it unlikely that the methods used by any one trainer in terms

of training techniques, feeding or housing regimens, are the cause of the gastric ulceration.

This study illustrates that the prevalence of EGUS is similar in New Zealand racehorses as that reported elsewhere. The type of pasture turnout that these horses receive is not protective against gastric ulceration. The fact that all horses that were kept at pasture full time were affected by gastric ulceration suggests that housing racehorses in stables alone does not cause the development of EGUS. As there was no effect of geographic location or trainer on the prevalence of gastric ulceration it is likely that there is a common factor to all horses in the study that contributes to the development of gastric ulceration. This finding may serve to focus future research away from individual trainer effects and to look for a common factor among racehorses. More work is needed to elicit the exact aetiopathogenesis of this syndrome.

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References

- Andrews, FM, Reinemeyer, CR, McCracken, MD, Blackford, JT, Nadeau, JA, Saabye, L, Sotell, M and Saxton, A** (2002) Comparison of endoscopic, necropsy and histology scoring of equine gastric ulcers. *Equine Veterinary Journal* 34, 475-478.
- Begg, LM and O'Sullivan, CB** (2003) The prevalence and distribution of gastric ulceration in 345 racehorses. *Australian Veterinary Journal* 81, 199-201.
- Bezdekova, B, Jahn, P, Vyskocil, M and Plachy, J** (2005) Prevalence of equine gastric ulceration in standardbred racehorses in czech republic. *Acta Veterinaria Brno* 74, 59-65.

- Buchanan, BR and Andrews, FM** (2003) Treatment and prevention of equine gastric ulcer syndrome. *Veterinary Clinics Of North America-Equine Practice* 19, 575-597.
- Collier, DS** (1999) Gastric ulceration: Response to an unnatural environment. *Equine Veterinary Journal Supplement* 29, 5-6.
- Dionne, RM, Vrins, A, Doucet, MY and Pare, J** (2003) Gastric ulcers in standardbred racehorses: Prevalence, lesion description, and risk factors. *Journal of Veterinary Internal Medicine* 17, 218-222.
- E.G.U.C.** (1999) Recommendations for the diagnosis and treatment of equine gastric ulcer syndrome (egus) - the equine gastric ulcer council. *Equine Veterinary Education* 11, 262-272.
- Ferrucci, F, Zucca, E, Di Fabio, V, Croci, C and Tradati, F** (2003) Gastroscopic findings in 63 standardbred racehorses in training. *Veterinary Research Communications* 27, 759-762.
- Hammond, CJ, Mason, DK and Watkins, KL** (1986) Gastric-ulceration in mature thoroughbred horses. *Equine Veterinary Journal* 18, 284-287.
- Johnson, JH, Vatistas, N, Castro, L, Fischer, T, Pipers, FS and Maye, D** (2001) Field survey of the prevalence of gastric ulcers in thoroughbred racehorses and on response to treatment of affected horses with omeprazole paste. *Equine Veterinary Education* 13, 221-224.
- Lorenzo-Figueras, M and Merritt, AM** (2002) Effects of exercise on gastric volume and ph in the proximal portion of the stomach of horses. *American Journal of Veterinary Research* 63, 1481-1487.
- Macallister, CG, Andrews, FM, Deegan, E, Ruoff, W and Olovson, SG** (1997) A scoring system for gastric ulcers in the horse. *Equine Veterinary Journal* 29, 430-433.
- Murray, MJ** (1994) Gastric-ulcers in adult horses. *Compendium on Continuing Education for the Practicing Veterinarian* 16, 792-794.
- Murray, MJ** (1992) Gastric ulceration in horses - 91 cases (1987-1990). *Journal of the American Veterinary Medical Association* 201, 117-120.
- Murray, MJ** (1991) The pathogenesis and prevalence of gastric-ulceration in foals and horses. *Veterinary Medicine* 86, 815-819.
- Murray, MJ, Grodinsky, C, Anderson, CW, Radue, PF and Schmidt, GR** (1989) Gastric ulcers in horses: A comparison of endoscopic findings in horses with and without clinical signs. *Equine Veterinary Journal Supplement* 7, 68-72.

- Murray, MJ, Schusser, GF, Pipers, FS and Gross, SJ** (1996) Factors associated with gastric lesions in thoroughbred racehorses. *Equine Veterinary Journal* 28, 368-374.
- Nadeau, JA, Andrews, FM, Patton, CS, Argenzio, RA, Mathew, AG and Saxton, AM** (2003) Effects of hydrochloric, valeric, and other volatile fatty acids on pathogenesis of ulcers in the nonglandular portion of the stomach of horses. *American Journal of Veterinary Research* 64, 413-417.
- Orsini, J and Pipers, FS** (1997) Endoscopic evaluation of the relationship between training, racing and gastric ulcers. *Veterinary Surgery* 26, 424.
- Rabuffo, TS, Orsini, JA, Sullivan, E, Engiles, J, Norman, T and Boston, R** (2002) Associations between age or sex and prevalence of gastric ulceration in standardbred racehorses in training. *Journal of the American Veterinary Medical Association* 221, 1156-1159.
- Roy, MA, Vrins, A, Beauchamp, G and Doucet, MY** (2005) Prevalence of ulcers of the squamous gastric mucosa in standardbred horses. *Journal of Veterinary Internal Medicine* 19, 744-750.
- Sandin, A, Skidell, J, Haggstrom, J and Nilsson, G** (2000) Postmortem findings of gastric ulcers in swedish horses older than age one year: A retrospective study of 3715 horses (1924-1996). *Equine Veterinary Journal* 32, 36-42.
- Vatistas, NJ, Sifferman, RL, Hoste, J, Cox, JL, Pinalto, G and Schultz, KT** (1999) Induction and maintenance of gastric ulceration in horses in simulated race training. . *Equine Veterinary Journal* Supplement 29, 40-42.
- Vatistas, NJ, Snyder, JR, Carlson, G, Johnson, B, Arthur, RM, Thurmond, M, Zhou, H and Lloyd, KL** (1999) Cross-sectional study of gastric ulcers of the squamous mucosa in thoroughbred racehorses. *Equine Veterinary Journal* Supplement 29, 34-39.
- Vatistas, NJ, Snyder, JR, Carlson, G, Johnson, B, Arthur, RM, Thurmond, M, Zhou, H and Lloyd, KL** (1994) Epidemiological study of gastric ulceration in the thoroughbred race horse: 202 horses 1992-1993. *Proceedings of the Annual Convention of the American Association of Equine Practitioners* 40, 125-126.

Chapter 4

A comparison of two scoring systems for endoscopic grading of gastric ulceration in horses.

A comparison of two scoring systems for endoscopic grading of gastric ulceration in horses.

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Abstract

Aims

To compare two scoring systems for grading gastric ulcers in adult horses.

Methods

Digitised recordings of 22 horses that were part of a prevalence study into gastric ulceration in New Zealand racehorses were reviewed independently by 3 examiners. All stomachs were graded using two different systems, the Equine Gastric Ulcer Council (EGUC) system and the Number Severity (N/S) system.

Results

All examiners commented that the EGUC system was the quickest and easiest to use. There was no significant difference between examiners using the EGUC system ($p=0.31$) and the agreement between observers was high with Kappa values of 0.85_{1vs2} , 0.88_{1vs3} and 0.80_{2vs3} . There was a significant difference between grades assigned by examiners with the severity component of the N/S system ($p_{severity}=0.005$).

Conclusions

The EGUC system has better repeatability between examiners and is faster and easier to use than the N/S system.

Clinical relevance

The EGUC system is suitable as a standard scoring system due to its ease of use, and the repeatability and correlation of grades assigned between independent examiners. Use of a standard scoring system will more easily allow comparisons to be made between different research groups and clinicians.

Introduction

Equine Gastric Ulcer Syndrome (EGUS) is a common disease that reportedly affects between 44%-100% of adult racehorses (Begg and O'Sullivan 2003; Dionne, Vrins, Doucet *et al.* 2003; Murray, Schusser, Pipers *et al.* 1996; Rabuffo, Orsini, Sullivan *et al.* 2002). Clinical signs of EGUS are non-specific, and due to the lack of any pathognomonic signs, diagnosis relies on oesophagogastroscopy. Lesions visualised with gastroscopy are usually subjectively scored according to their number and severity. Objective measurement of the size and depth of the lesions is ideal but impractical due to the irregularity of the lesions and the inherent difficulty involved with assessing true depth from a two dimensional image (Macallister, Andrews, Deegan *et al.* 1997).

The lack of a standardised scoring system limits the ability of researchers to compare results between studies and hinders the assessment of clinical cases between clinicians. There are many different scoring systems published with scoring scales ranging from 0-3 (Dionne *et al.* 2003; MacAllister, Sifferman, McClure *et al.* 1999; Vatistas, Sifferman, Holste *et al.* 1999), 0-4 (Andrews, Reinemeyer, McCracken *et al.* 2002; Furr and Murray 1989), 0-5 (Vatistas, Snyder, Nieto *et al.* 1999), 0-6 (McClure, Glickman and Glickman 1999) and 0-10 (Murray *et al.* 1996). The variety of scoring systems in the literature is such that even separate studies by the same investigators have used different scoring systems (Murray and Eichorn 1996; Murray, Eichorn, Holste *et al.* 1999; Murray, Grodinsky, Anderson *et al.* 1989; Murray *et al.* 1996; Vatistas, Nieto, Snyder *et al.* 1999; Vatistas, Sifferman *et al.* 1999; Vatistas, Snyder *et al.* 1999).

Although the Equine Gastric Ulcer Council proposed a standardised scoring system for the classification of EGUS lesions in 1999, this has not been validated and subsequent studies have continued to use their own scoring systems (Andrews *et al.* 2002; Begg and O'Sullivan 2003; Dionne *et al.* 2003; Ferrucci, Zucca, Croci *et al.* 2003; McClure, White, Sifferman *et al.* 2005; Nieto, Snyder, Beldomenico *et al.* 2004; Orsini, Haddock, Stine *et al.* 2003; Rabuffo *et al.* 2002).

The objective of this study was to compare the EGUC grading system to another system that has already been validated (N/S) (Macallister *et al.* 1997), and to assess the ease of use and repeatability of scores between observers when using the EGUC system. The hypothesis was that the EGUC scoring system would be easy to use and have less variation between observers than the N/S system.

Materials And Methods

Study design

The digitised gastroscopic examinations of 22 horses randomly selected (random number generator) from a prevalence study of EGUS in New Zealand were used. The number of horses is similar to that used in a previous study comparing two grading systems (Andrews *et al.* 2002). The use of animals in the prevalence study was approved by the Massey University Animal Ethics Committee.

Scoring of lesions

The gastroscopic images were reviewed and scored by three separate examiners independently and without collusion. Both the EGUC system and the N/S system were used to assign a score to each stomach based upon the severity of the gastric ulceration present (Table 4.1, Table 4.2) (E.G.U.C. 1999; Macallister *et al.* 1997).

Table 4.1: Equine Gastric Ulcer Council (E.G.U.C.) grading system for grading of Equine gastric ulcer syndrome lesions in horses (E.G.U.C. 1999)

Grade 0	Intact epithelium
Grade 1	Intact mucosa, evidence of hyperkeratosis or hyperaemia
Grade 2	Small, single, or multifocal lesions
Grade 3	Large, single or multifocal lesions or extensive superficial lesions
Grade 4	Extensive lesions with areas of apparent deep ulceration

Table 4.2: Number Severity scoring system for grading of equine gastric ulcer syndrome lesions in horses (Macallister *et al.* 1997)

<u>Gastric Ulcer Number Score</u>	
Grade	Description
0	No lesions
1	1-2 localised lesions
2	3-5 localised lesions
3	6-10 lesions
4	> 10 lesions
<u>Gastric Ulcer Severity Score</u>	
Grade	Description
0	Normal
1	Appears superficial
2	Deeper structures involved
3	Multiple lesions and variable severity
4	Same as grade 2 though with an active appearance
5	Same as 4 though with active haemorrhage or blood clot adherent

Statistical analysis

Due to the possibility of bias from the one examiner that was not blinded (examiner 3) the initial statistical analysis was performed using only the 2 blinded examiners. This consisted of generating scatter plots according to previously described techniques (Bland and Altman 1986). Mean mucosal ulceration scores were compared between examiners 1 and 2 using a two-way ANOVA and the Friedman chi-square (Macallister *et al.* 1997). Squamous mucosal ulceration scores with both the EGUC and N/S systems for all examiners were compared using a two-way random effects model to calculate the intra-class correlation coefficient (ICC) (2,1) (Shrout and Fleiss 1979). The agreement between different examiners' scores for each horse was compared using a weighted Kappa test for agreement (Jakobsson and Westergren 2005). The significance level for all tests was $p < 0.05$. The statistical analyses were performed using SPSS 12.0.1 for Windows (SPSS Inc. Chicago IL USA).

Results

The study group comprised 8 females and 14 geldings from 10 different trainers. Horses ranged from 2 to 8 years old. Both grading systems were readily applicable to the digitised images. The examiners all subjectively commented that the EGUC grading system was faster and easier to use than the N/S system.

Nineteen horses had evidence of gastric ulceration with an EGUC grade of 2 or above and a number severity grade of 2/1 or above. Two horses had evidence of hyperkeratosis without ulcerative changes and one horse was normal. Six horses had evidence of glandular gastric ulceration, however the pylorus was only visualised in 7 horses. The mean, median and standard deviation for each examiner in each scoring system are displayed in Table 4.3.

Table 4.3: Ulcer grades assigned by different examiners to 22 horses examined gastroscopically with both the Equine Gastric Ulcer Council (EGUC) grading system and the Number Severity (N/S) grading system

EGUC	Examiner 1 EGUC	Examiner 2 EGUC	Examiner 3 EGUC
Number of horses	22	22	22
Mean	2.45	2.55	2.41
Median	3.00	3.00	3.00
Std. Deviation	1.18	1.10	1.05
N/S Number	Examiner 1 Number	Examiner 2 Number	Examiner 3 Number
Number of horses	22	22	22
Mean	2.68	2.73	3.14
Median	3.00	4.00	4.00
Std Deviation	1.55	1.61	1.52
N/S Severity	Examiner 1 Severity	Examiner 2 Severity	Examiner 3 Severity
Number of horses	22	22	22
Mean	2.55	1.95	2.05
Median	2.5	2	2
Std Deviation	1.59	1.39	1.31

Scatter plots comparing mean score with difference between observers 1 and 2 are presented for each system in Figures 4.1-4.3. These graphs show good agreement between the two observers for both the EGUC system and the number portion of the N/S system. There is poorer agreement for the severity portion of the N/S system.

Figure 4.1: Scatter diagram of the average Equine Gastric Ulcer Council grading system score for 22 horses against the difference of the scores by two examiners

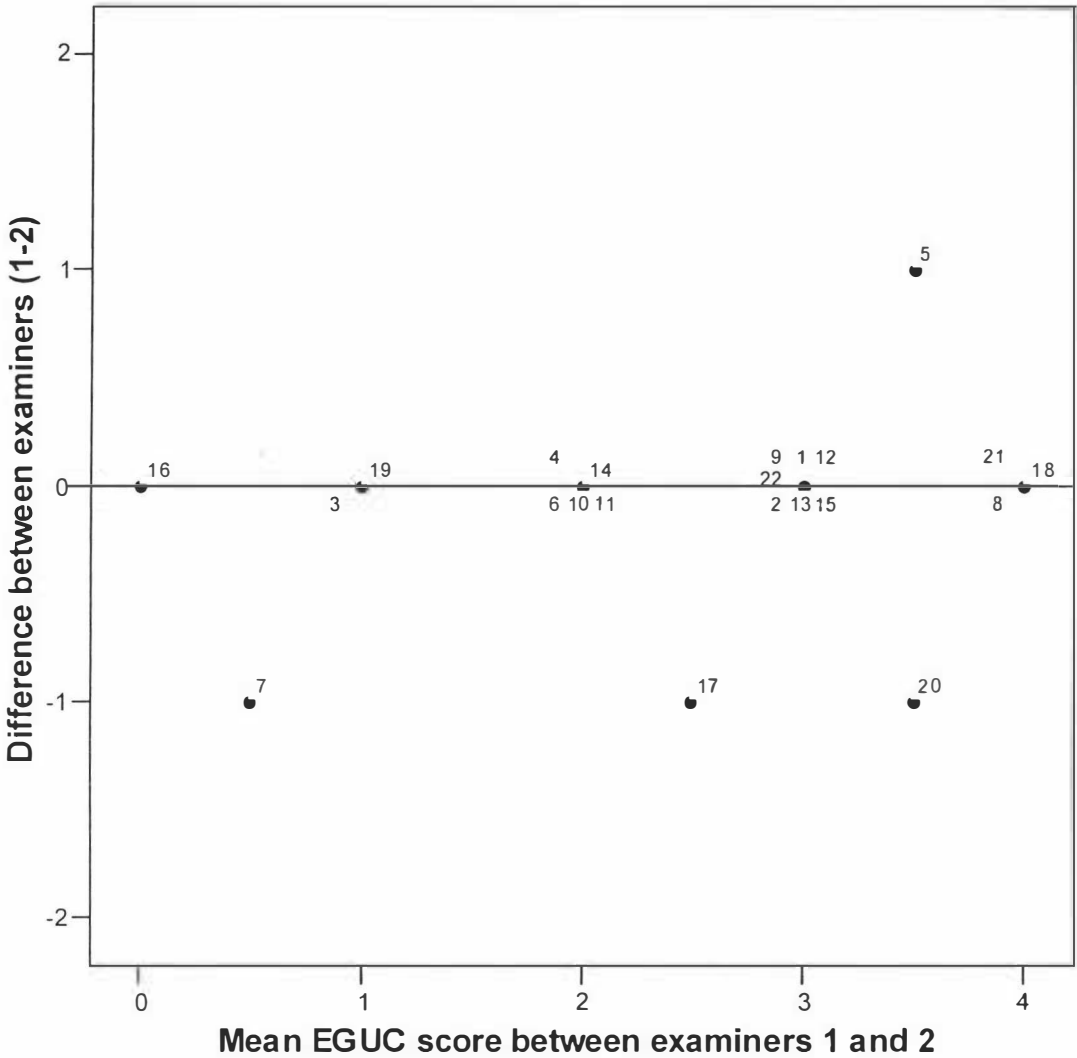


Figure 4.2: Scatter diagram of the average Number Severity grading system number score for 22 horses against the difference of the scores by two examiners

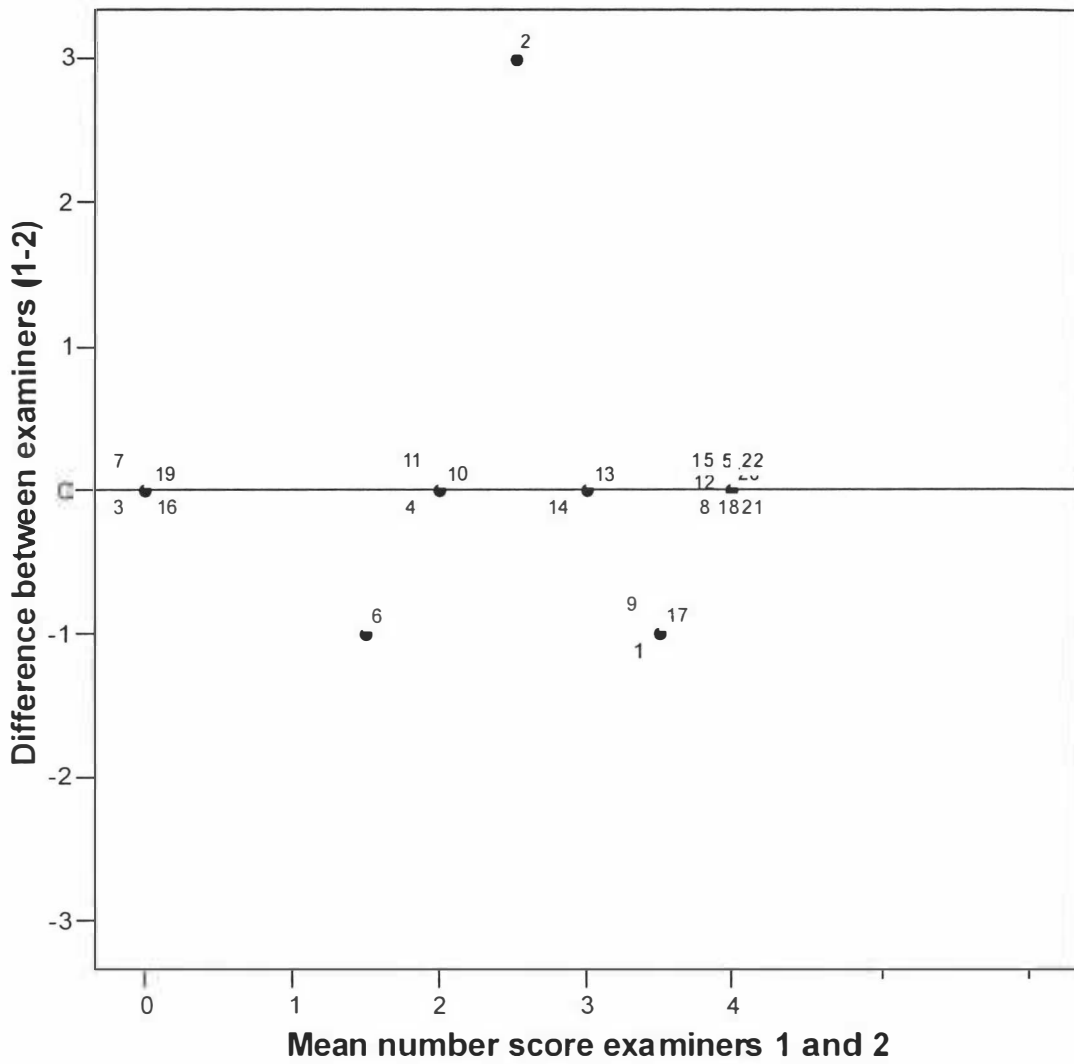
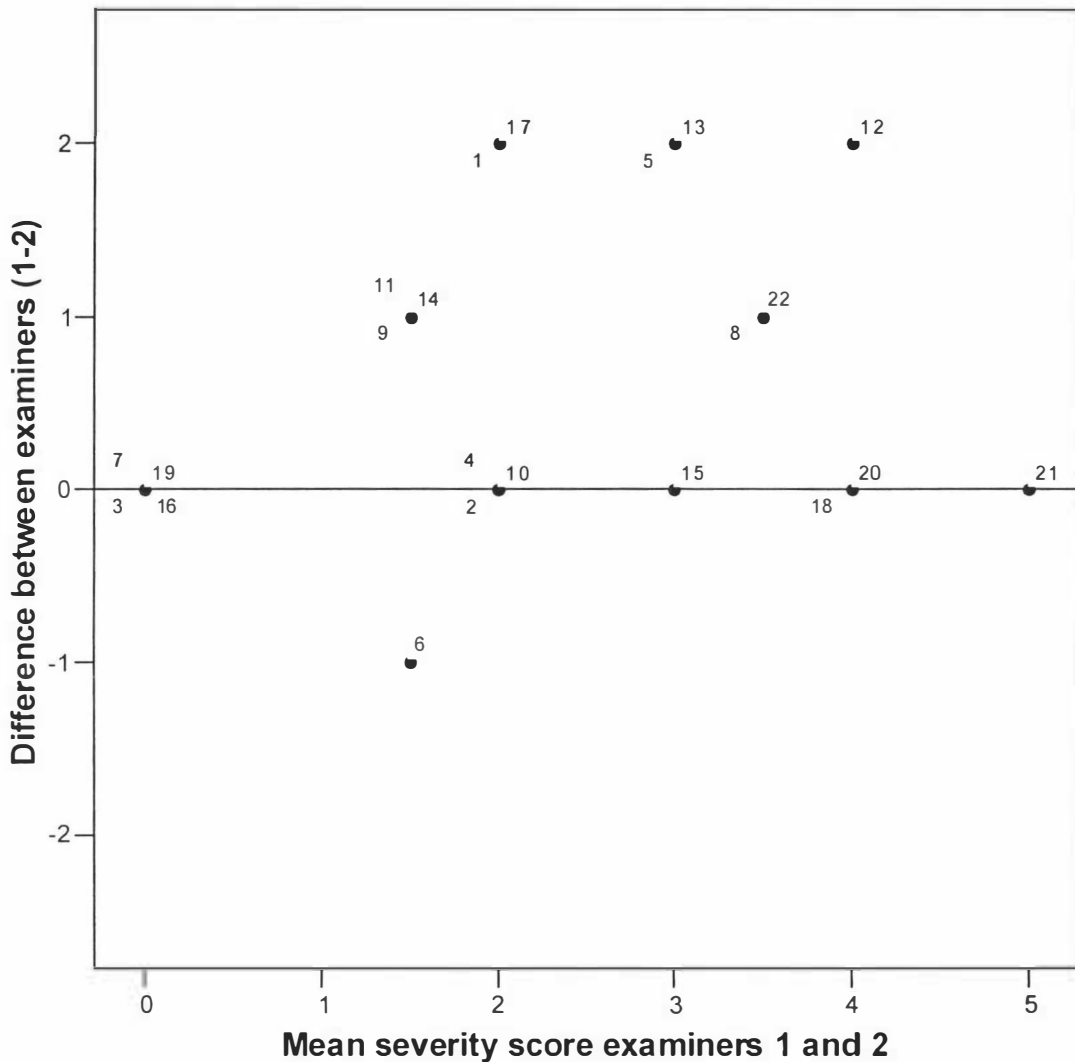


Figure 4.3: Scatter diagram of the average Number Severity grading system number score for 22 horses against the difference of the scores by two examiners



The ICC for all examiners with the EGUC system was 0.97 (95%CI 0.95-0.99). There was no significant difference between scores assigned by examiners 1 and 2 when using the EGUC grading system ($p=0.31$) and a high level of agreement between those scores (Kappa values of 0.85_{1vs2}, 0.88_{1vs3} and 0.80_{2vs3}). There was a significant difference between examiners 1 and 2 when the horses were scored using the N/S system (Number $p=0.18$, Severity $p=0.007$). The ICC for all examiners with the

number portion of the N/S system was 0.94 (95%CI 0.868-0.972). Agreement between examiners was lower for the number portion of the N/S system than the EGUC system when examiners 1 and 2 were compared to examiner 3 (Kappa values of 0.88_{1vs2}, 0.65_{1vs3} and 0.68_{2vs3}). The ICC for the severity portion of the N/S system was 0.927 (95%CI 0.83-0.97). In the severity scores examiner 1 graded lesions significantly more severely than examiner 2 (p=0.008) or examiner 3 (p=0.01), and there was moderate agreement between examiner 1 and examiners 2 or 3 (Kappa values 0.59_{1vs2}, 0.60_{1vs3} and 0.72_{2vs3}).

Discussion

The Equine Gastric Ulcer Council proposed the use of a standardised scoring system that was designed to be simple and straightforward to use by both researchers and practitioners (E.G.U.C. 1999). The use of a standardised scoring system would more readily enable the comparison of results between researchers and clinicians. The EGUC scoring system was the easiest to use in this study, in part due to more generalised descriptions of EGUS lesions for each grade compared to the specifics needed for the N/S system, and also due to the use of just 5 gradations as opposed to 9 in the N/S system. The fact that there was no significant difference between mean EGUC scores assigned by the two blinded independent examiners indicates that this grading system has good repeatability and the high ICC and Kappa values indicate that there is good agreement between grades assigned by different examiners to individual cases (a value of 0 represents no agreement and 1 perfect agreement for both Kappa and ICC).

Haemorrhage from gastric ulcers at the time of examination is assigned significance in the N/S system but not the EGUC system. Some authors believe that haemorrhage

is an indicator of an active (and thus more severe) lesion (Nieto *et al.* 2004). Others suggest that the haemorrhage may be iatrogenic in nature, resulting from stretching of the mucosa during gastric insufflation, or through trauma from passage of the endoscope (Macallister *et al.* 1997). Additionally, superficial erosions may bleed, and deep ulcers may not show any signs of haemorrhage at the time of examination (E.G.U.C. 1999). Thus, the depth of gastric ulcers may be a better indicator of their severity, as deeper ulcers may be expected to result in slower healing than more superficial lesions. However, predicting ulcer depth based upon endoscopic examination is difficult and lesions that are thought to be superficial may actually be much deeper than is apparent endoscopically (Andrews *et al.* 2002).

There was a statistically significant difference between grades assigned by the examiners using the N/S system in this study. This difference was most evident in the severity components of the grading system, which is not surprising considering the wholly subjective nature of the assessment of severity of these lesions. The variation between observers seen with the number portion of the grading system could be explained by the difficulties assessing whether small mild lesions are erosions or true ulcers. Additionally, it is easier to observe ulcer size than to count individual ulcers (Andrews *et al.* 2002) and failing to observe or misclassifying one or two mild ulcers may result in an increase of 1-2 grades with the N/S system. The differences between observers seen with the N/S system are large enough that they would also have an effect in a clinical setting (the median values vary by up to one full grade between examiners).

One potential advantage of the N/S grading system is that it allows for discrimination between horses that have one or two superficial lesions and horses that have multiple

superficial lesions; in the EGUC system both of these groups would be grade 2. This may be important as some authors question the clinical relevance of 1 or 2 superficial lesions in the squamous mucosa (Murray 1991). However, that advantage is probably outweighed by the complexity of the scoring system and difference in grades assigned between observers as illustrated by this study.

The agreement between the grades assigned by the different examiners was good for both scoring systems when using the ICC, although it was better for the EGUC system than either the number or severity portions of the N/S system. The Kappa values for agreement were considered to be moderate to substantial for the N/S system compared to almost perfect for the EGUC system (Landis and Koch 1977). Kappa values are influenced by the number of categories and the prevalence within a category, so a direct comparison between methods using a different number of categories is difficult (Maclure and Willett 1987). For this reason the ICC was also calculated, although this statistic tends to increase as the number of categories increases and this data set may not be truly continuous (Jakobsson and Westergren 2005).

The EGUC grading system was quick and easy to use when reviewing the digitised images of gastroscopic examinations. The high Kappa and ICC values indicate that the EGUC system will readily allow assignment of a grade for the severity of EGUS that is repeatable between different examiners. Use of such a system would facilitate comparison and interpretation of results between different research groups, and allow assessment of clinical progress over multiple examinations or discussion of cases between clinicians. Agreement between grades assigned by different examiners with this system is as good or better than N/S system. This system appears to be suitable

for adoption as a standard scoring system for the grading of gastric ulceration in adult horses.

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References

- Andrews, FM, Reinemeyer, CR, McCracken, MD, Blackford, JT, Nadeau, JA, Saabye, L, Sotell, M and Saxton, A** (2002) Comparison of endoscopic, necropsy and histology scoring of equine gastric ulcers. *Equine Veterinary Journal* 34, 475-478.
- Begg, LM and O'Sullivan, CB** (2003) The prevalence and distribution of gastric ulceration in 345 racehorses. *Australian Veterinary Journal* 81, 199-201.
- Bland, JM and Altman, DG** (1986) Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1, 307-310.
- Dionne, RM, Vrins, A, Doucet, MY and Pare, J** (2003) Gastric ulcers in standardbred racehorses: Prevalence, lesion description, and risk factors. *Journal of Veterinary Internal Medicine* 17, 218-222.
- E.G.U.C.** (1999) Recommendations for the diagnosis and treatment of equine gastric ulcer syndrome (egus) - the equine gastric ulcer council. *Equine Veterinary Education* 11, 262-272.
- Ferrucci, F, Zucca, E, Croci, C, Di Fabio, V and Ferro, E** (2003) Treatment of gastric ulceration in 10 standardbred racehorses with a pectin-lecithin complex. *Veterinary Record* 152, 679-681.
- Furr, MO and Murray, MJ** (1989) Treatment of gastric ulcers in horses with histamine type 2 receptor antagonists. *Equine Veterinary Journal Supplement* 7, 77-79.
- Jakobsson, U and Westergren, A** (2005) Statistical methods for assessing agreement for ordinal data. *Scand. J. Caring Sci.* 19, 427-431.
- Landis, JR and Koch, GG** (1977) The measurement of observer agreement for categorical data. *Biometrics* 33, 159-174.

- Macallister, CG, Andrews, FM, Deegan, E, Ruoff, W and Olovson, SG** (1997) A scoring system for gastric ulcers in the horse. *Equine Veterinary Journal* 29, 430-433.
- MacAllister, CG, Sifferman, RL, McClure, SR, White, GW, Vatistas, NJ, Holste, JE, Ericsson, GF and Cox, JL** (1999) Effects of omeprazole paste on healing of spontaneous gastric ulcers in horses and foals: A field trial. *Equine Veterinary Journal Supplement* 29, 77-80.
- Maclure, M and Willett, WC** (1987) Misinterpretation and misuse of the kappa-statistic. *Am. J. Epidemiol.* 126, 161-169.
- McClure, SR, Glickman, LT and Glickman, NW** (1999) Prevalence of gastric ulcers in show horses. *Journal of the American Veterinary Medical Association* 215, 1130-1133.
- McClure, SR, White, GW, Sifferman, RL, Bernard, W, Doucet, MY, Vrins, A, Holste, JE, Fleishman, C, Alva, R and Cramer, LG** (2005) Efficacy of omeprazole paste for prevention of gastric ulcers in horses in race training. *Journal of the American Veterinary Medical Association* 226, 1681-1684.
- Murray, MJ** (1991) The pathogenesis and prevalence of gastric-ulceration in foals and horses. *Veterinary Medicine* 86, 815-819.
- Murray, MJ and Eichorn, ES** (1996) Effects of intermittent feed deprivation, intermittent feed deprivation with ranitidine administration, and stall confinement with ad libitum access to hay on gastric ulceration in horses. *American Journal of Veterinary Research* 57, 1599-1603.
- Murray, MJ, Eichorn, ES, Holste, JE, Cox, JL, Stanier, WB, Cooper, WL and Cooper, VA** (1999) Safety, acceptability and endoscopic findings in foals and yearling horses treated with a paste formulation of omeprazole for twenty-eight days. *Equine Veterinary Journal Supplement* 29, 67-70.
- Murray, MJ, Grodinsky, C, Anderson, CW, Radue, PF and Schmidt, GR** (1989) Gastric ulcers in horses: A comparison of endoscopic findings in horses with and without clinical signs. *Equine Veterinary Journal Supplement* 7, 68-72.
- Murray, MJ, Schusser, GF, Pipers, FS and Gross, SJ** (1996) Factors associated with gastric lesions in thoroughbred racehorses. *Equine Veterinary Journal* 28, 368-374.
- Nieto, JE, Snyder, JR, Beldomenico, P, Aleman, M, Kerr, JW and Spier, SJ** (2004) Prevalence of gastric ulcers in endurance horses - a preliminary report. *Veterinary Journal* 167, 33-37.
- Orsini, JA, Haddock, M, Stine, L, Sullivan, EK, Rabuffo, TS and Smith, G** (2003) Odds of moderate or severe gastric ulceration in racehorses receiving antiulcer medications. *Journal of the American Veterinary Medical Association* 223, 336-339.

- Rabuffo, TS, Orsini, JA, Sullivan, E, Engiles, J, Norman, T and Boston, R (2002)**
Associations between age or sex and prevalence of gastric ulceration in standardbred racehorses in training. *Journal of the American Veterinary Medical Association* 221, 1156-1159.
- Shrout, PE and Fleiss, JL (1979)** Intraclass correlations - uses in assessing rater reliability. *Psychol. Bull.* 86, 420-428.
- Vatistas, NJ, Nieto, JE, Snyder, JR and Thompson, D (1999)** Clinical trial to determine the effect of omeprazole given once or twice daily on gastric ulceration. *Equine Veterinary Journal* Supplement 29, 87-90.
- Vatistas, NJ, Sifferman, RL, Holste, J, Cox, JL, Pinalto, G and Schultz, KT (1999)** Induction and maintenance of gastric ulceration in horses in simulated race training. *Equine Veterinary Journal* Supplement 29, 40-44.
- Vatistas, NJ, Snyder, JR, Nieto, J, Thompson, D, Pollmeier, M and Holste, J (1999)** Acceptability of a paste formulation and efficacy of high dose omeprazole in healing gastric ulcers in horses maintained in race training. *Equine Veterinary Journal* Supplement 29, 71-76.

Chapter 5

Gastric ulceration in New Zealand Racehorses: lesion location and severity.

Gastric ulceration in New Zealand Racehorses: lesion location and severity.
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Abstract

Aim

To determine whether there is a lesion site predilection for gastric ulceration in New Zealand racehorses affected by Equine Gastric Ulcer Syndrome.

Methods

Video recordings of the gastroscopic examinations of 163 horses were reviewed. The squamous mucosa of the stomach was divided subjectively into regions; the greater curvature adjacent to the margo plicatus (GC), the lesser curvature/cardia (LC), the squamous fundus (fundus) and the pylorus (Pyl). The stomach of each horse was assigned an ordinal score based upon the severity of the gastric ulceration present.

Results

There was a higher prevalence of gastric ulceration at the LC and GC than at the fundus ($p < 0.01$). Gastric ulceration at the LC was more severe than that seen at either the GC ($p = 0.02$) or the fundus ($p < 0.001$). There was no significant difference in lesion severity at the different locations between horses of different ages, sex or times in training. Standardbred horses had significantly less severe ulceration than Thoroughbred horses at the fundus.

Conclusions

The squamous mucosa at the lesser curvature adjacent to the margo plicatus was the most commonly and severely ulcerated portion of the stomach in horses within this study.

Clinical relevance

Exercise may result in greater surface exposure of the lesser curvature to acidic gastric contents. This may explain the higher frequency of more severe lesions seen at this site in a population of athletic horses.

Key words

Horse, Equine, Gastric Ulceration, Location, Severity

Abbreviations

EGUC: Equine Gastric Ulcer Council

EGUS: Equine Gastric Ulcer Syndrome

Fundus: Squamous fundus

GC: Greater curvature of the stomach

LC: Lesser curvature of the stomach

NSAID: Non-steroidal anti-inflammatory drugs

Pyl: Pylorus

Introduction

Equine Gastric Ulcer Syndrome (EGUS) is a problem that reportedly affects a large proportion of racehorses in active training (Begg and O'Sullivan 2003; Dionne, Vrins, Doucet *et al.* 2003; Ferrucci, Zucca, Di Fabio *et al.* 2003; Roy, Vrins, Beauchamp *et al.* 2005). Diagnosis of this condition relies on oesophagogastroscopy due to the non-specific nature of the clinical signs.

The exact aetiology of the condition is currently unknown, but is most likely related to exposure of the gastric mucosa to excess acidity (Andrews and Nadeau 1999). The severity of the lesions appears to be related to the amount of time that the squamous mucosa is exposed to hydrochloric acid (Furr, Murray and Ferguson 1992). Lesions visualised gastroscopically are graded subjectively, according to their number and apparent severity. The majority of squamous ulcers are located along the margo plicatus (Macallister, Andrews, Deegan *et al.* 1997; Sandin, Skidell, Haggstrom *et al.* 2000), although they are also commonly found in the squamous fundus, the squamous mucosa along the lesser curvature, the greater curvature and the cardia.

A higher prevalence and greater severity of gastric ulceration at the lesser curvature along the margo plicatus has been reported (Murray and Eichorn 1996) although other authors report no such site dependent variation in severity (Andrews and Nadeau 1999). Glandular and duodenal ulcers are less common in mature horses than ulceration of the squamous mucosa (Sandin *et al.* 2000).

We hypothesised that there would be more severe gastric ulcer lesions at specific sites in the squamous mucosa in New Zealand racehorses, namely at the lesser curvature adjacent to the margo plicatus, similar to results reported elsewhere.

Materials and Methods

Study design

Video-recordings of gastroscopic examinations of 171 horses obtained as part of a prevalence study into gastric ulceration were reviewed. The stomach was divided subjectively into regions, the greater curvature adjacent to the margo plicatus (GC), the lesser curvature/cardia (LC), the squamous fundus (fundus) and the pylorus.

Lesions were graded according to the EGUC grading system (E.G.U.C. 1999). Grade 0 has intact epithelium. Grade 1 has intact mucosa with evidence of hyperkeratosis or hyperaemia. Grade 2 has small single or multi-focal lesions. Grade 3 has large single or multi-focal lesions or extensive superficial lesions. Grade 4 has extensive lesions with areas of apparent deep ulceration.

Statistical analysis

The prevalence of gastric ulceration at the LC, GC and fundus was compared using the McNemar Test for related variables. Squamous mucosal ulceration scores were compared between the lesser curvature/cardia, greater curvature and squamous fundus using a Wilcoxin Signed rank test for two related samples (Murray and Eichorn 1996). Squamous mucosal ulceration scores were also compared between the different age groups, sex and location using a Kruskal Wallis test and the median test. The squamous mucosal ulceration scores at each of the regions of the stomach were compared between breeds using the Kruskal Wallis test and the Mann Whitney U test. These tests were performed using SPSS 12.0.1 for Windows (SPSS Inc. Chicago IL USA) using a significance of $P < 0.05$.

Results

Eight horses were excluded due to incomplete examination of one or more regions of the stomach. Of the remaining 163 horses the sex and age distributions are shown in Figures 5.1. and 5.2.

Figure 5.1: Age distribution in a study of lesion location and severity of Equine Gastric Ulcer Syndrome in 163 horses

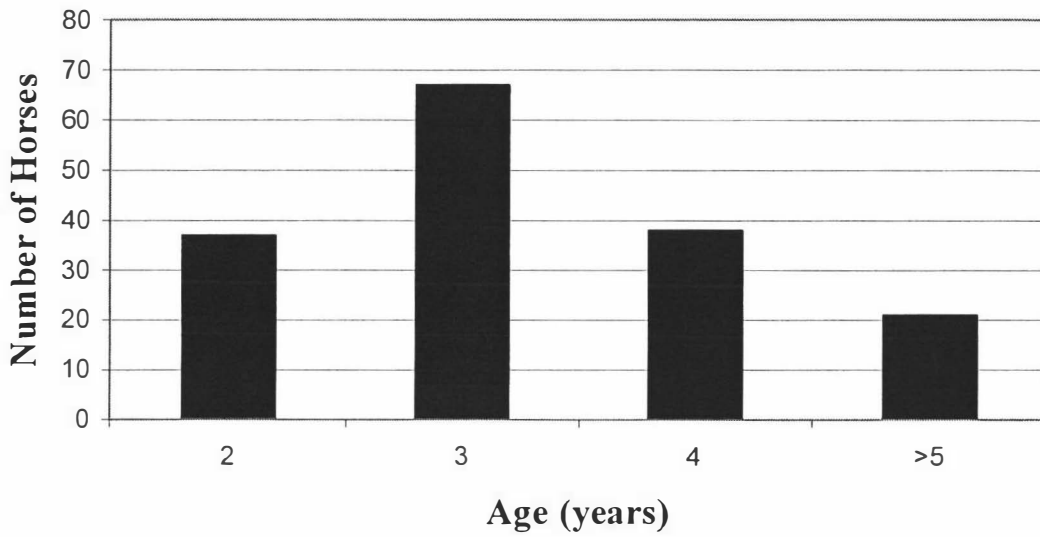
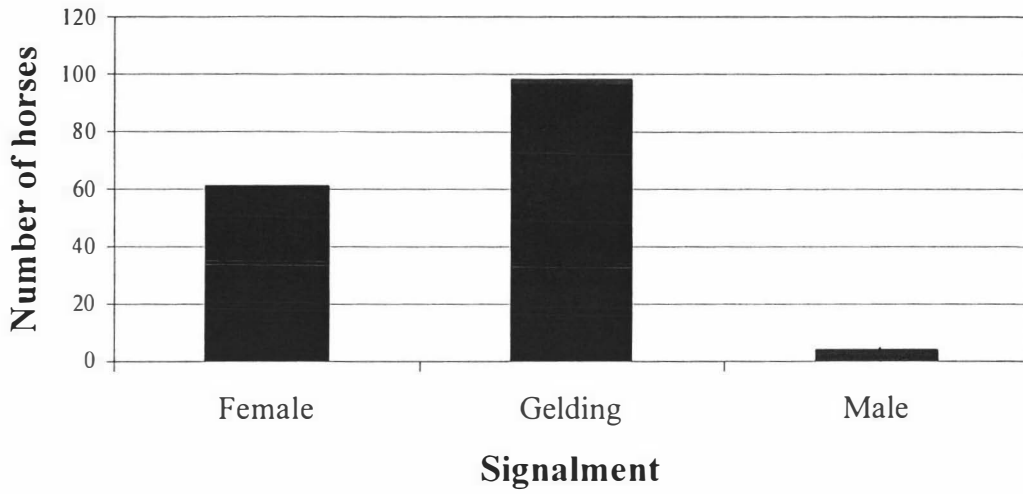


Figure 5.2: Sex distribution in a study of lesion severity and location of Equine Gastric Ulcer syndrome in 163 horses



EGUC grades for the individual squamous locations are presented in Table 5.1.

Table 5.1: Location of squamous gastric ulceration and distribution of Equine Gastric Ulcer Council grades in 163 racehorses

Grade	Lesser Curvature (%)	Greater Curvature (%)	Squamous Fundus (%)
0	21(12.9)	22(13.5)	111(68.1)
1	9 (5.5)	17(10.4)	26(16.0)
2	68 (41.7)	77(47.2)	17(10.4)
3	49 (30.1)	40(24.5)	7(4.3)
4	16 (9.8)	7(4.3)	2(1.2)
Total	163	163	163
Mean Grade	2.18	1.96	0.55
Std. Deviation	1.112	1.032	0.931

The pylorus was visualised in 61 horses and there was evidence of glandular ulceration in 34 of these horses. There was a significantly higher prevalence of gastric ulceration at the LC and GC than at the squamous fundus ($p<0.001$). There was no

significant difference in the prevalence of gastric ulceration at the LC and the GC ($p=0.18$). A comparison of the severity at each location is presented in Table 5.2.

Table 5.2: Comparison of Equine Gastric Ulcer Council (EGUC) grades by location in 163 horses. Horses with lesions of identical severity at each location are found along the diagonal of the table

a) Greater curvature EGUC (GC) ulceration scores versus lesser curvature EGUC ulceration scores

		Lesser curvature EGUC score					Total
		0	1	2	3	4	
GC	0	9	1	7	3	2	22
EGUC	1	2	5	6	2	2	17
score	2	10	2	44	18	3	77
	3	0	1	11	25	3	40
	4	0	0	0	1	6	7
Total		21	9	68	49	16	163

b) Lesser curvature (LC) EGUC ulceration scores versus fundus EGUC ulceration scores

		LC EGUC score					Total
		0	1	2	3	4	
Fundus	0	20	7	46	28	10	111
EGUC	1	0	1	11	12	2	26
score	2	1	0	9	6	1	17
	3	0	1	2	3	1	7
	4	0	0	0	0	2	2
Total		21	9	68	49	16	163

c) Greater curvature EGUC ulceration scores versus fundus EGUC ulceration scores

		Greater curvature EGUC score					Total
		0	1	2	3	4	
Fundus	0	21	14	55	19	2	111
EGUC	1	0	2	15	8	1	26
score	2	1	1	6	7	2	17
	3	0	0	1	6	0	7
	4	0	0	0	0	2	2
Total		22	17	77	40	7	163

There was a significant difference in mean severity between the three locations ($p<0.001$) with the lesser curvature of the stomach having significantly more severe ulceration than the greater curvature ($p=0.02$) or the fundus ($p<0.001$). There was no significant difference in the ulcer severity at the differing locations between horses of

different ages (p values: LC=0.38, GC=0.49, fundus=0.50). There was no significant difference between male and female horses and the severity of the ulceration at differing locations (p values: LC=0.91, GC=0.83, fundus=0.61). There was no significant difference between ulcer grades at either the lesser curvature (p=0.32) or greater curvature (p=0.08) between Standardbred and Thoroughbred horses. Thoroughbred horses had significantly higher gastric ulcer scores at the fundus than Standardbred horses (p=0.02).

Discussion

The squamous fundus had a lower prevalence of gastric ulceration than either the lesser curvature or the greater curvature. The squamous mucosa at the lesser curvature of the stomach directly adjacent to the margo plicatus was the most severely affected portion of the stomach. Examination of the data in Table 5.2 illustrates this increased severity. If the regions within the stomach had lesions of identical severity then all the grades would lie along the diagonal of the table. The fact that they do not indicates that there is a difference in severity between these regions, and in some cases that ulceration may occur in one region whilst the others remain normal.

This increased severity at the LC is similar to other studies, and it has been suggested that increased exposure of this region to gastric acid combined with the absence of the protective barriers afforded the glandular mucosa may be the inciting cause of the ulceration (Furr and Murray 1989; Hammond, Mason and Watkins 1986; Macallister *et al.* 1997; Sandin *et al.* 2000). It is thought that such regionally increased exposure to gastric acid may be induced by strenuous exercise. Gastric pH has been shown to decrease significantly in the proximal portion of the stomach at gaits faster than a walk, most likely due to the substantial decrease in gastric volume seen as exercise

intensity increases (Lorenzo-Figueras and Merritt 2002). The decrease in gastric volume means that the gastric contents are effectively displaced proximally, and combined with the movement effects of the gastric contents associated with locomotion at high speeds, means that the squamous mucosa is increasingly exposed to excess acidity. This would also explain why the majority of gastric ulcers are seen along the margo plicatus (E.G.U.C. 1999) and why the squamous fundus was significantly less affected by gastric ulceration than the other regions of the stomach in our study.

The pylorus was unable to be visualised in all horses, because of residual feed material remaining within the stomach. The proportion of horses in which the pylorus was visualised is lower than previously reported (Begg and O'Sullivan 2003; Murray, Nout and Ward 2001). Possible explanations for this discrepancy include a shorter fasting period (the maximum period of fasting was eight hours in this study), and because the use of a small diameter, flexible endoscope occasionally made passage into the pylorus difficult (Murray 2002). Ulceration was present in 47% of horses in which the pylorus was seen, which is identical to one study (Begg and O'Sullivan 2003) and lower than another (Murray *et al.* 2001). The significance of this finding or indeed any glandular gastric ulceration is unknown in EGUS due to the differing mucosal defences in squamous as compared to glandular mucosa. In this study all horses with gastric glandular ulceration also had squamous gastric ulceration. This is not always the case as it has been reported that ulceration of the pylorus can occur independently to ulceration of the squamous mucosa (Murray *et al.* 2001), leading those authors to speculate on the possibility for a separate cause for the pyloric ulceration.

Different authors have reported varying associations between age and the incidence and severity of EGUS (Bezdekova, Jahn, Vyskocil *et al.* 2005; Dionne *et al.* 2003; Rabuffo, Orsini, Sullivan *et al.* 2002; Roy *et al.* 2005). There were no significant differences between horses of different ages and the presence or severity of ulceration in various locations within the stomach in our study which agrees with results from other authors (Dionne *et al.* 2003; Roy *et al.* 2005). Murray *et al.* (1996) reported that 2-year-old horses had less severe ulceration than older horses, but the majority of those 2-year-olds had not raced. In those 2-year-olds that were examined twice, there was a significant increase in the lesion severity at the second examination (Murray, Schusser, Pipers *et al.* 1996). An association between age and the severity of lesions has been reported, with younger horses tending to have milder lesions than older horses (Rabuffo *et al.* 2002).

There was no significant difference between sex and the severity of the gastric ulceration within the stomach, which is similar to results reported elsewhere (Begg and O'Sullivan 2003; Bezdekova *et al.* 2005; Dionne *et al.* 2003; Murray and Eichorn 1996). Rabuffo *et al.* (2002) also reported that castrated males had a higher relative risk for gastric ulceration as their age increased. It is possible that this difference is not truly sex related as none of the youngest horses in their study were geldings, and mares and stallions may often be retired for breeding rather than continuing to race for as long as geldings.

Breed of horse did not affect the severity of gastric ulceration at two of the locations within the stomach, but there was a statistically significant difference in the severity of ulceration at the squamous fundus with Thoroughbreds having more severe lesions in their squamous fundus compared to Standardbreds. Although unproven, it is

possible that the different gaits may result in a difference in the amount of compression of the stomach and the amount of movement of the gastric contents during exercise, thus influencing the gastric pH experienced by the gastric squamous mucosa. However, it should be noted that the changes in the mean ulcer scores between breeds was low (0.26 vs 0.63) and the median values were identical, making it unlikely that this difference is actually clinically significant.

No previous reports have examined both Standardbred and Thoroughbred racehorses, but the prevalence and relative severity of gastric ulceration in our study is similar to that reported for each separate breed (Ferrucci *et al.* 2003; Murray, Grodinsky, Anderson *et al.* 1989; Murray *et al.* 1996; Roy *et al.* 2005; Vatistas, Snyder, Carlson *et al.* 1999). There are no reports on the prevalence of gastric ulceration in other high speed racing horses such as Quarterhorses, however, a recent report into endurance horses showed that these horses developed gastric ulceration during exercise, though this was primarily glandular (Nieto, Snyder, Beldomenico *et al.* 2004).

In conclusion, EGUS is found in a large proportion of horses in active race training. There is a site dependent difference in the prevalence and severity of gastric ulceration in these racehorses with the squamous mucosa of the lesser curvature of the stomach having the most severe ulceration. This may be consistent with a greater exposure of this region to highly acidic gastric contents during high intensity exercise (Lorenzo-Figueras and Merritt 2002).

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References

- Andrews, FM and Nadeau, JA** (1999) Clinical syndromes of gastric ulceration in foals and mature horses. *Equine Veterinary Journal* Supplement 29, 30-33.
- Begg, LM and O'Sullivan, CB** (2003) The prevalence and distribution of gastric ulceration in 345 racehorses. *Australian Veterinary Journal* 81, 199-201.
- Bezdekova, B, Jahn, P, Vyskocil, M and Plachy, J** (2005) Prevalence of equine gastric ulceration in standardbred racehorses in czech republic. *Acta Veterinaria Brno* 74, 59-65.
- Dionne, RM, Vrins, A, Doucet, MY and Pare, J** (2003) Gastric ulcers in standardbred racehorses: Prevalence, lesion description, and risk factors. *Journal of Veterinary Internal Medicine* 17, 218-222.
- E.G.U.C.** (1999) Recommendations for the diagnosis and treatment of equine gastric ulcer syndrome (egus) - the equine gastric ulcer council. *Equine Veterinary Education* 11, 262-272.
- Ferrucci, F, Zucca, E, Di Fabio, V, Croci, C and Tradati, F** (2003) Gastroscopic findings in 63 standardbred racehorses in training. *Veterinary Research Communications* 27, 759-762.
- Furr, MO and Murray, MJ** (1989) Treatment of gastric ulcers in horses with histamine type 2 receptor antagonists. *Equine Veterinary Journal* Supplement 7, 77-79.
- Furr, MO, Murray, MJ and Ferguson, DC** (1992) The effects of stress on gastric-ulceration, t3, t4, reverse t3 and cortisol in neonatal foals. *Equine Veterinary Journal* 24, 37-40.
- Hammond, CJ, Mason, DK and Watkins, KL** (1986) Gastric-ulceration in mature thoroughbred horses. *Equine Veterinary Journal* 18, 284-287.
- Lorenzo-Figueras, M and Merritt, AM** (2002) Effects of exercise on gastric volume and ph in the proximal portion of the stomach of horses. *American Journal of Veterinary Research* 63, 1481-1487.
- Macallister, CG, Andrews, FM, Deegan, E, Ruoff, W and Olovson, SG** (1997) A scoring system for gastric ulcers in the horse. *Equine Veterinary Journal* 29, 430-433.
- Murray, MJ** (2002) How to perform gastroduodenoscopy. *Proceedings of the American Association of Equine Practitioners* 48, 282-286.
- Murray, MJ and Eichorn, ES** (1996) Effects of intermittent feed deprivation, intermittent feed deprivation with ranitidine administration, and stall confinement with ad libitum access to hay on gastric ulceration in horses. *American Journal of Veterinary Research* 57, 1599-1603.

- Murray, MJ, Grodinsky, C, Anderson, CW, Radue, PF and Schmidt, GR** (1989) Gastric ulcers in horses: A comparison of endoscopic findings in horses with and without clinical signs. *Equine Veterinary Journal Supplement* 7, 68-72.
- Murray, MJ, Nout, YS and Ward, DL** (2001) Endoscopic findings of the gastric antrum and pylorus in horses: 162 cases (1996-2000). *Journal of Veterinary Internal Medicine* 15, 401-406.
- Murray, MJ, Schusser, GF, Pipers, FS and Gross, SJ** (1996) Factors associated with gastric lesions in thoroughbred racehorses. *Equine Veterinary Journal* 28, 368-374.
- Nieto, JE, Snyder, JR, Beldomenico, P, Aleman, M, Kerr, JW and Spier, SJ** (2004) Prevalence of gastric ulcers in endurance horses - a preliminary report. *Veterinary Journal* 167, 33-37.
- Rabuffo, TS, Orsini, JA, Sullivan, E, Engiles, J, Norman, T and Boston, R** (2002) Associations between age or sex and prevalence of gastric ulceration in standardbred racehorses in training. *Journal of the American Veterinary Medical Association* 221, 1156-1159.
- Roy, MA, Vrins, A, Beauchamp, G and Doucet, MY** (2005) Prevalence of ulcers of the squamous gastric mucosa in standardbred horses. *Journal of Veterinary Internal Medicine* 19, 744-750.
- Sandin, A, Skidell, J, Haggstrom, J and Nilsson, G** (2000) Postmortem findings of gastric ulcers in swedish horses older than age one year: A retrospective study of 3715 horses (1924-1996). *Equine Veterinary Journal* 32, 36-42.
- Vatistas, NJ, Snyder, JR, Carlson, G, Johnson, B, Arthur, RM, Thurmond, M, Zhou, H and Lloyd, KL** (1999) Cross-sectional study of gastric ulcers of the squamous mucosa in thoroughbred racehorses. *Equine Veterinary Journal Supplement* 29, 34-39.

Chapter 6

Conclusion

Conclusion

The prevalence of EGUS in New Zealand racehorses is similar to or higher than that reported elsewhere in the world. These results were unexpected, as we had hypothesised that allowing racehorses access to pasture would be protective against gastric ulceration, and result in a lower prevalence in New Zealand racehorses. The increased prevalence compared to other studies is likely due to the fact that all horses within this study were in high intensity work, whereas other studies have included horses from all stages of training.

This study provided a sample of the racing population from across the country, whereas other studies have been limited to isolated training facilities or hospital populations. The high prevalence of EGUS in New Zealand racehorses is especially pertinent given that there currently is no product registered for the treatment of EGUS in horses in New Zealand.

As there is currently no standard scoring system for grading EGUS lesions it is difficult to compare the severity of gastric ulceration seen in this study to that reported elsewhere. A consensus scoring system was proposed by the Equine Gastric Ulcer Council, however this system has not been widely used, nor validated. Our results revealed that this system is suitable for use in grading EGUS lesions as it is quick and easy to use and scores assigned by independent examiners have a high level of agreement. Use of this system as the accepted standard would facilitate better research into EGUS, as it would more readily allow comparisons to be made between different studies. It would also be of benefit in a clinical setting, facilitating communications between clinicians.

The majority of horses examined were assigned low scores of gastric ulceration under the EGUC grading system, with a few horses having the most severe grade of ulceration. The most severe lesions seen in this study were in the squamous mucosa along the margo plicatus at the lesser curvature. There was a higher prevalence of gastric ulceration at both the lesser curvature and the greater curvature of the stomach when compared to the squamous fundus. These findings are similar to other studies, and it is hypothesised that the squamous mucosa at the lesser curvature of the stomach has greater exposure to the acidic contents of the stomach than other regions.

It is possible that the high prevalence of EGUS in racehorses is due to the physiological stress of exercise rather than the changes in housing or feeding management associated with racehorse training. It has been shown that both the gastric volume and the pH of the squamous mucosa decrease at gaits faster than a trot. This would also explain the increased severity of lesions at the lesser curvature of the stomach, as the level of the gastric juices rises due to the decrease in volume and the movement of the liquid gastric contents during exercise.

Most importantly this study challenges the previously held notion that grazing is protective against gastric ulceration in racehorses, although it may merely indicate that the limited grazing these horses receive is not protective against EGUS. Furthermore, it has identified a widespread and potentially performance limiting problem in the New Zealand racing population, for which therapeutic options are currently limited due to the unavailability of anti-ulcer medications with proven efficacy. Further work is necessary to differentiate between the effects of high-energy feedstuffs, change in housing management and the physiologic stresses of exercise as the cause of EGUS.