Equine Gastric Ulcer Syndrome in Horses

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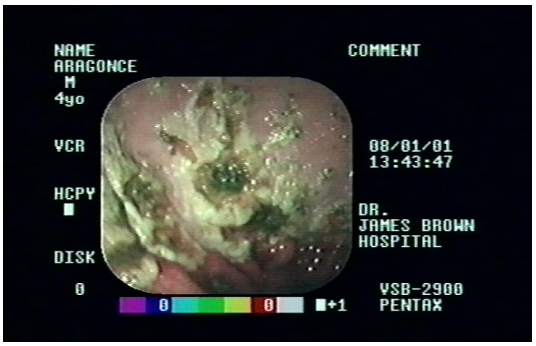
Equine gastric ulcer syndrome is caused by exposure of the stomach to inorganic and organic acids. Many factors including feeding, management, and stress allow increased production of these stomach acids that act synergistically to product gastric ulcers.

Background:

- Gastric ulceration is a problem frequently seen in both foals and adult horses, especially sick foals and adult horses in active training.
- The term equine gastric ulcer syndrome (or EGUS) is commonly used to describe this disease.
- There are two main subsets of the disease
  - The primarily glandular disease seen in neonates and foals;
  - The predominantly squamous form seen in adult horses
- Definitive diagnosis of EGUS currently relies on **gastroscopy**. The procedure requires the use of a 3m endoscope to allow visualisation of the pylorus. Ulcers are then graded based on anatomical location, number and severity. In the absence of gastroscopy, the clinician may elect to treat animals empirically and use response to treatment as a means of indirectly diagnosing EGUS.



Clinical Signs:

- Clinical signs are non-specific and include:
  - Lack of appetite;
  - Weight loss/poor body condition;
  - Dullness of coat;
  - Mild or recurrent colic;
  - Loose faeces.

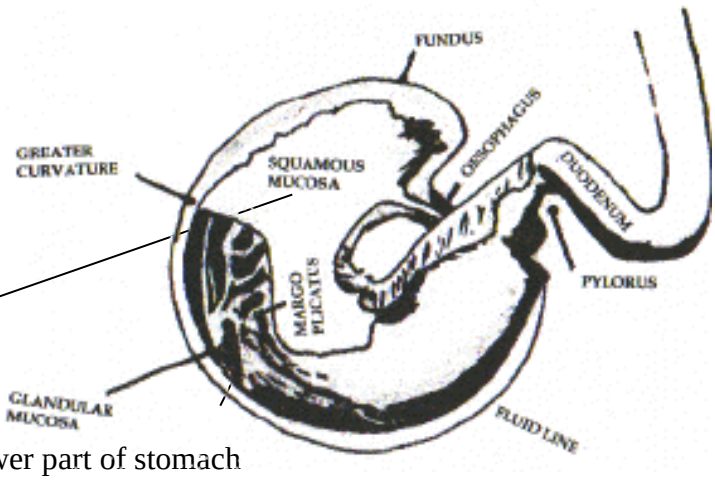
- Foals tend to show a separate more specific set of clinical signs including:
  - Less time spent suckling;
  - Poor body condition;
  - Diarrhoea;
  - Bruxism (teeth grinding);
  - Ptyalism (excessive saliva);
  - Intermittent colic.

Prevalence:

- EGUS affects between 58% and 100% of adult horses in training. It appears that most young racehorses have normal stomachs but once they begin training up to 90% develop EGUS. This occurs after as little as 3 months in work.
- Most racehorses will develop gastric ulceration at some point in their careers although not all horses with ulceration will show clinical signs of disease.
- Prevalence figures for horses in training/racing:
    - Hammond et al., 1986: 66% racehorses, Hong Kong
    - Murray et al., 1996 : 100% racehorses
    - Vatistas et al., 1999: 86% horses in race training
    - Murray et al., 1989: 89% horses in training
    - Rabuffo et al., 2002: 87% horses in training
    - Dionne et al., 2003: 63.3% standardbreds in training, Canada
    - Begg and O'Sullivan, 2003: 86% Thoroughbreds, Australia
    - Murray, 1992: 100% horses in training
- EGUS is not confined to race horses:
    - McClure et al., 1999: 58% show horses
    - Murray et al., 1989: 37% horses used for pleasure/showing
    - Nieto et al., 2004: 67% endurance horses
    - Murray et al., 1989: 52% clinically normal yearlings
    - Murray et al., 1989: 59% horses not in training
    - Dionne et al., 2003: 44% all horses, Canada

Anatomy:

- 75-80% of ulcers are found in the squamous portion of the stomach especially along the margo plicatus.
- Ulcers occurring within the squamous mucosa are similar to gastro-oesophageal reflux disease in humans.



The majority of ulcers associated with EGUS are found in the proximal half of the stomach

The lower part of stomach has protective lining of mucous and bicarbonate

Cause of Gastric Ulcers:

- The development of gastric ulceration may be viewed as an imbalance between aggressive and protective factors on the mucosa.
- Horses continuously secrete gastric acid (even without the presence of feed material in the stomach) and **exposure to acid is currently thought to be the major cause of EGUS**.
- Several different acids have been implicated in damaging the equine gastric squamous mucosa. Hydrochloric acid (HCl) has a corrosive effect and in combination with volatile fatty acids (VFAs) causes inhibition of cellular transport of sodium, cellular swelling and eventual ulceration.
- Performance horses which are more at risk of EGUS are usually fed relatively low roughage, high hydrolysable carbohydrate diets. Hay and grain contain variable concentrations of fermentable carbohydrates, which may be converted by bacteria to volatile fatty acids (VFAs). At low pH, these VFAs may become non-ionised and penetrate the squamous mucosa of the stomach causing local acidification, uncoupling of sodium transport, cellular swelling, inflammation, and ulcers.
- Experimentally, HCl alone and in combination with VFA caused eventual ulceration when exposed to the nonglandular squamous mucosa at pH <4.
- Pepsinogen is thought to play a role by acting in a synergistic fashion with HCl to cause damage to the mucosa.
- Several species of Lactobacillus have also been isolated from the stomach of horses.
- While HCl and stomach pH have been implicated as causes of EGUS, it is likely that a combination of HCl, organic acids, and pepsin act synergistically to cause EGUS.

Risk Factors in Horses:

- Exercise Intensity
    - It has been shown that horses running on a high-speed treadmill have increased abdominal pressure and decreased stomach volume and it has been speculated that stomach contractions allow acid from the glandular mucosa to reflux into the non-glandular mucosa leading to acid injury.
    - Daily exercise may increase the exposure of the nonglandular mucosa to acid, explaining the increased prevalence of gastric ulcers in horses in race training.
    - An increase in serum gastrin concentration has been shown to occur in exercising horses, which may stimulate an increase in HCl secretion and lower stomach pH.
- Intermittent vs Continuous Feeding
    - As little as 48 hours of feed deprivation has been shown to induce gastric ulceration.
    - Horses grazing at pasture have decreased prevalence of EGUS. Feeding has a buffering effect on gastric pH, mainly through the buffering effects of increased saliva. During grazing there is a continuous flow of saliva and ingesta that buffers stomach acid, with stomach pH > 4 for a large portion of the day. When feed is withheld

from horses, before racing or in managed stables, gastric pH drops rapidly and the nonglandular mucosa is exposed to an acid environment. This intermittent feeding has been reproduced experimentally and shown to produce EGUS. The nonglandular mucosa is the most susceptible to ulceration in horses due to its lack of mucosal protective factors.

- Diet
  - **Saliva** plays an important role in buffering gastric pH and it is thought that low forage diets may decrease its production, thus decreasing the buffering provided by saliva and causing an increase in gastric pH.
  - Serum gastrin concentrations are high in horses fed high-concentrate diets. Concentrate diets are high in hydrolysable carbohydrates and are fermented by resident bacteria resulting in the production of VFA which in the presence of low stomach pH (≤ 4) cause damage to the nonglandular squamous mucosa.
  - The prevalence of ulcers has been shown to be lower in horses fed a diet of alfalfa hay compared to grassy hay, despite higher concentrations of VFAs in alfalfa hay. This was thought to be related to the **high protein and calcium content** of the alfalfa hay, which provides buffering for up to 6 hours after ingestion.
- Transport Stress
  - During transportation, water and feed consumption is usually decreased which may cause an increased incidence of EGUS.
- Stall Confinement
  - Horses that are kept on pastures have a decreased prevalence of gastric ulcers compared with horses in boxes.
  - In one study, confinement in stalls for 7 days with *ad-libitum* access to hay resulted in gastric ulceration in 10/11 horses. It was suggested that despite constant access to roughage, confinement in stalls 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 the horses' energy requirements are met by concentrated feeds.
- Nonsteroidal Antiinflammatory Drugs (NSAIDs)
  - The NSAIDs phenylbutazone and flunixin megulamine have been shown to induce gastric ulcers in horses and are thought to cause more severe ulcers in the glandular stomach mucosa because of their effect on prostaglandin inhibition. Prostaglandin inhibition by NSAID results in decreased mucosal blood flow, decreased mucus production and increased HCl secretion. NSAIDs are not considered to be a major cause of EGUS.
- *Helicobacter Species*
  - As *Helicobacter* spp are primarily associated with glandular ulceration, they are less likely to be important in EGUS.
  - While *Helicobacter*-specific DNA was isolated from the glandular and nonglandular mucosa of seven horses, there are no reports to date documenting the presence of *Helicobacter* spp in horses.
  - However, one paper states that "Horses with chronic recurring gastric ulcers may benefit from antibiotic and antacid treatment in much the same way people with *Helicobacter pylori* infections have".

Healing of gastric ulcers:

- Healing of ulcers commences immediately following mucosal injury and the rate of healing is affected by both the size and depth of the lesions. Superficial lesions may take as little as 7 days to heal while deeper lesions may take as long as 3 months. Spontaneous healing of gastric ulcers in horses that are actively being worked is rare. In one study, a slight improvement in ulcers was seen in 6/35 horses after 2-3 months, but none healed completely and lesions tended to worsen as the horses continued in training.

Treatment:

- Treatment current focuses on suppressions of acid secretion using H_2-receptor antagonists and proton pump inhibitors.
- Other drug therapies include synthetic protaglandins, antacids and mucosal protectants

H_2-receptor antagonists:

- Act by blocking the interaction of histamine with H_2-receptors on the parietal cell and thus decrease the basal secretion of HCl.
- There appears to be significant inter-horse variation in the response to H_2-receptor antagonists particularly at lower doses most likely because of the relatively poor oral bioavailability of these drugs in horses thus dosing needs to be at the high end of the dosing scale.
- H_2-receptor antagonists are not beneficial in preventing ulcers when glucocorticoids or NSAIDs are used concurrently.

Proton pump inhibitors:

- Drugs (e.g. omeprazole) which are designed to block gastric acid secretion through irreversible inhibition of hydrogen-potassium adenosine triphosphatase.
- The anti-secretory effects are prolonged allowing for once daily dosing.
- The efficacy of oral omeprazole in decreasing gastric pH varies between products.

Only ranitidine and omeprazole have been registered in Australia by the APVMA for use in horses.