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New Insights Into the Management of Equine Gastric Glandular Disease

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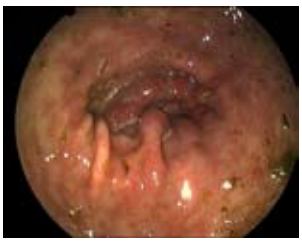

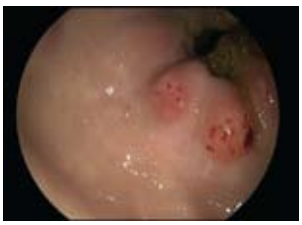

Equine Glandular Gastric Disease (EGGD) is a distinct disease entity to Equine Squamous Gastric Disease (ESGD) with differences in prevalence, risk factors, pathophysiology and response to treatment. Although the treatment of ESGD remains relatively straightforward (think Omeprazole and appropriate management practices), treatment of EGGD is more problematical. Three recent publications have given a clearer understanding of the aetiology, management and treatment of this common problem[1,2,3].

Aetilogy

EGGD may occur anywhere in the glandular mucosa but is predominantly focussed around the pylorus and pyloric antrum. Although true ulceration may occur, it is usually superficial and rarely deep enough to involve the lamina propria. Glandular lesions are more typically inflammatory in nature and more accurately described as a glandular gastritis. When pyloric lesions are evident on gastroscopy, inflammation is usually histologically demonstratable throughout the entire glandular mucosa and not just restricted to the macroscopic lesions.

None of the experimental models for replicating ESGD produce EGGD. It is most likely that compromised mucosal barrier function is the primary cause of EGGD and that acid injury may then perpetuate mucosal damage, inhibit epithelial restitution and is integral in causing clinical signs. In humans it is known that acid exposure on an inflamed/ulcerated mucosa is responsible for clinical symptoms and symptoms may resolve following treatment with proton pump inhibitors (such as omeprazole) prior to resolution of lesions on gastroscopy.

Helicobacter spp, the most common cause of EGGD in man (who only has a glandular stomach) and other species, have not been implicated in the horse. Bacteria are unlikely to have a primary role in the development of EGGD although certain species may have the capacity to colonise the damaged mucosa and inhibit healing.

NSAID's are a rare cause of gastric ulceration in the horse, a fact that was again confirmed in one of the recent studies[1].

Stress appears to play an important role in the pathogenesis of EGGD. Horses with severe EGGD have been shown to exhibit greater increases in cortisol in response to novel stimuli and in response to exogenous ACTH indicating that they may be more sensitive to stress. Stress may also influence gastrin production and blood supply to the glandular mucosa and may be a factor in both initiation and perpetuation of glandular lesions.

Warmblood showjumpers at international level are less likely to have EGGD than lower level jumpers, probably because they are better adapted to the competition environment and consequently adapted to physiological stress as evidenced by lower circulating cortisol concentrations. Same applies to experienced polo ponies. Alternatively, this may reflect selection of those more 'experienced' animals or selection for animals that do not succumb to EGGD as they rise through the ranks.

Stress minimisation may play a pivotal role in reducing EGGD.

Prevalence

Unlike ESGD, the prevalence of EGGD does not increase with increased exercise intensity/duration and is approximately 55% across all disciplines. A composite graph of the relative prevalence of EGGD vs ESGD across equestrian disciplines is shown in Figure 1.

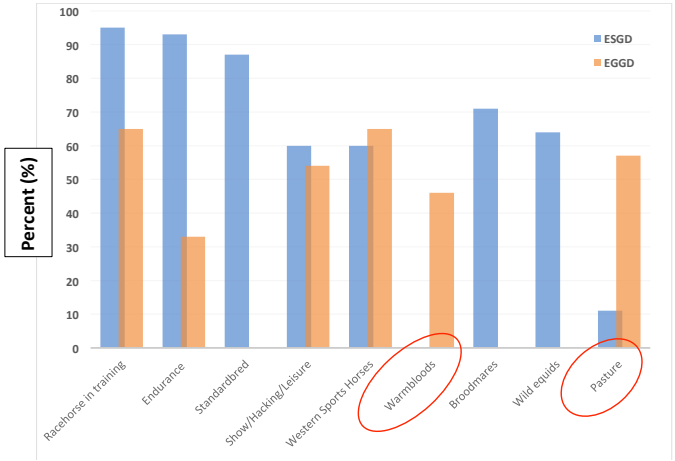

Figure 1: Composite chart showing the prevalence of EGSD (blue bars) and EGGD (orange bars) according to various disciplines.

Clinical Signs

Clinical signs of EGGD are generally reported to be the same as for ESGD.

In two recent studies the most commonly reported sign was poor performance (65%)[3]/racing below expectations[1]. Other commonly reported signs were behavioural changes (33%), girth pain (32%), poor body condition (9.5%), poor appetitie (6.3%) and abdominal pain (7.9%), with 68% of cases having two or more of the above signs.

Diagnosis

Gastroscopy is the only reliable way of diagnosing and monitoring gastic ulcers. The sucrose blood test and faecal tests for haemoglobin and protein are unrelaible and should not be used diagnostically.

As the association between severity of EGGD lesions on gastroscopy and clinical significance has not been established, it has been suggested that EGGD lesions should be described using a combination of the following descriptors:

DESCRIPTOR	
Location	pylorus, pyloric antrum, glandular fundus, cardia
Distribution	focal, multi-focal, diffuse
Severity	mild, moderate, severe
Topography	nodular, raised, flat or depressed
Appearance	erythematous, haemrorrhagic, fibrinosuppurative

Table 1: Suggested descriptions of gastric glandular lesions

Risk Factors

In a recent study, Sykes et al[1] used a comprehensive trainer-completed questionnaire looking at management, feeding and exercise practices and compared results to gastroscopy findings. Results were available for 109 flat racing Thoroughbreds from eight training yards (3 in UK, 5 in Australia). The main findings are summarised in Table 2.

Interestingly, in this study, the prevalence of EGGD was only 25%. In previous studies, the prevalence of EGGD in Australian thoroughbreds has been variously reported as between 47% and 65%.

	ESGD	EGGD	95% Confidence Intervals
Prevalence	72% (64-80%)	25% (16-32%)	
Exercise ≥ 5 days/ week	10.0x	10.4x	1.3-26.9
Racing below expectations		3.7x	1.1-16.7
Trainer		Yes	
Time in work ≤ 6 weeks	0.3 (less likely)		0.1-0.99
Aggressive towards humans	0.12 (less likely)		0.03-0.54
Stereotypies	5.0		1.6-15.9
Presence of other type of ulcers (either EGGD or ESGD)	6.3x	6.6x	(1.5-30.0)/ (2.4-17.0)
High grain diets	Increased risk	No association	
Nonsteroidal anti-inflammatories	No association	No association	
Colic		No association	
Weight loss		No association	

Table 2: Summary of significant risk factors for EGGD and ESGD

The total amount of exercise, and particularly the number of days of exercise per week, are likely to be more relevant to the risk of EGGD than the intensity or duration of exercise.

Management

- **Provide a minimum of two rest days from work per week.**
- **Turn out where possible, provided horse is not stressed by turn out.**
- **Minimise management changes and other potential stressors.**
- **Minimise changes in equine companions and human carers.**
- **Minimise the number of human handlers/riders per horse.**
- **Feed 2L of chaff or an equivalent volume of forage 30 min prior to exercise.**

Treatment

ESGD is expected to resolve with the treatment of any of the recommended treatment regimens for EGGD. Therefore, wherever ESGD and EGGD exist concurrently, treatment decisions should be based on the effective treatment of EGGD.

Although acid injury is not thought to be primary cause of EGGD, a low pH may perpetuate mucosal damage, cause clinical signs and inhibit mucosal healing.

The pH of the gastric fluid in the pyloric region is typically lower (pH=1.0-2.0) than in the rest of the stomach. Therefore, it is likely that additional acid suppression therapy would be required to achieve a more neutral pH necessary for healing.

Anecdotally, nodular and fibrinosuppurative lesions are more difficult to treat than flat or erythematous lesions. Some horses appear to have peristent focal erythema in the peri-pyloric region in absence of clinical signs, whilst others will show marked clinical improvement in response to treatment.

Response to treatment is the best means of assessing the clinial relevance of lesions which are of questionable significance.

Table 3 shows current recommendations for treatment of EGGD

Oral omeprazole montherapy results in rates of healing of EGGD lesions <32%. Efficacy is increased if it used in combination with sucralfate with resolution as high as 63% and improvement in 89% of cases.

A recent publication in 40 sports horses[3], suggested that misoprostol (Cytotec), a PG E1 analogue that suppresses acid production and inhibitis neutrophilic inflammation, may be more effective in both resolving and improving glandular ulcers than omeprazole+sucralfate (73% vs 20% for healing and 98% vs 65% for improvement). However, in this study, treatments were only given for 28-35 days, which is only about half the currently recommended treatment course for omeprazole+sucralfate.

The healing and improvement rates for omeprazole+sucralfate In this study, were lower than has previously been reported. Hepburn reported 80% improvement and 63% healing (grade ≤1) of EGGD lesions (grades ≥2) in 204 sport and leisure horses treated with both omeprazole and sucralfate[4].

In addition in the recent study[3], treatments were not randomised and were assigned according to the study centre which may have resulted in an unidentified inherent bias and the person responsible for the horse who completed the symptoms questionnaires was not blinded to the treatment which may have provided a further source of bias.

"Triple therapy" with misoprostol+omeprazole+sucralfate has also been emperically favoured by some specialist for treatment of EGGD. The effectiveness of "triple therapy" was not examined in the current study[3].

DRUG	TRADE NAME	DOSE	Duration	SPECIAL REQUIREMENTS
Omeprazole (buffered paste)	**Ulcershield** (Omoguard)	4mg/kg PO sid over tongue	> 56 days	Should be used in conjunction with sucralfate. To be administered on a relatively empty stomach and at least 60 min prior to feeding.
Omeprazole (enteric coated)	**Gastropell** (Gastrozol)	2mg/kg PO sid over tongue	> 56 days	Should be used in conjunction with sucralfate. To be administered on a relatively empty stomach and at least 60 min prior to feeding. Avoid chewing of enteric coated pastes.
Sucralfate	Sucralfate Powder, Carafate tablets	12-20 mg/kg PO bd-qid (can be in feed)	> 56 days	Use in conjunction with Omeprazole. Must be administered at least 60 min post omeprazole administration. No registered APVMA product available.
Misoprostol	Cytotec Tablets	5µg/kg bd PO	14 days	Avoid direct handling. May cause vomiting, diarrhoea and abortion in humans. Although misoprostol is commonly given in the feed or immediately prior to feeding, the effect of feed on misoprostol pharmacokinectics has not been established. No currently registered APVMA product available.
Antibiotics	Doxycycline or TMPS	Doxy 10mg/kg bd PO.	28 days	hould only be used for chronic or recalcitrant EGGD and when supported by appropriate histopathological and bacteriology findings. The anti-inflammatory properties of Doxycycline may be of additional benefit.

Table 3: Current recommendations for pharmaceutical treatment of EGGD

There are some concerns that misoprostol and omeprazole should not be used in combination as misoprostol may reduce the activation of the proton pumps and therefore the efficacy of omeprazole, which requires proton pump activation to work. The significance of this redundancy has not been established.

Some precautions should be taken in administering misoprostol (wear gloves) due to human health considerations including diarrhoea, vomiting, abdominal pain and abortion. Misoprostol should also not be used in early pregnant mares, where it may also cause abortion.

As misoprostol may cause early abortion in women, approprate guidance should be given to clients regarding handling and storage of misoprostol, along with appropriate informed consent and client infromation sheets.

A small subset of EGGD cases that have previously failed to respond to other treatemt may resond to glucocorticoid treatment, given the majority of cases will have some lymphocytic inflammation.

There is no evidence to support the use of the following treatments for EGGD; ranitidine, aloe vera, pectin/lecithin complexes, polysaccharides, kaolin, bismuth subsalicylate, Sea buckthorn, acupuncture, homeopathy. Their use should be avoided[2].

Monitoring Treatment

Glandular mucosal lesions may heal within 2-4 weeks but frequently may take longer (months). Horses with EGGD should be monitored by gastroscopy every 4-6 weeks with complete resolution of lesions desirable before ceasing treatment to prevent recrudesence.

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1) Sykes BW, Bowen M, Habershon-Butcher JL, Green M, Hallowell GD. Management factors and clinical implications of glandular and squamous gastric disease in horses. J Vet Intern Med. 2019 Jan;33(1):233-240. doi: 10.1111/jvim.15350. Epub 2018 Nov 29. Free download here: https://onlinelibrary.wiley.com/doi/epdf/10.1111/jvim.15350

2) David Rendle, Mark Bowen, Tim Brazil, Rachael Conwell, Gayle Hallowell, Richard Hepburn, Michael Hewetson, Ben Sykes. UK-Vet Equine 2018 2:Sup1, 2-11. EGGD consensus statement. Recommendations for the management of equine glandular gastric disease. Free download here: https://www.magonlinelibrary.com/doi/pdf/10.12968/ukve.2018.2.S1.3

3) Varley G, Bowen IM, Habershon-Butcher JL, Nicholls V, Hallowell GD. Misoprostol is superior to combined omeprazole-sucralfate for the treatment of equine gastric glandular disease. Equine Vet J. 2019 Feb 26. doi: 10.1111/evj.13087. [Epub ahead of print].

4) Hepburn RJ. Treatment of ulceration of the gastric glandular mucosa: Retrospective evaluation of omeprazole and sucralfate combination therapy in 204 sport and leisure horses (Abstract), Proc 11th Int Equine Colic Res Symp, Dublin. 2014.

The "Regumate" Debate Update

December saw a spate of public comments on social media from prominent racing identities following a number of significant form improvements by mares in major races. Differences in local rules of racing allowed these mares to race on altrenogest to supress their oestrous behaviour.

There needs to become unification between @racing_nsw and @RacingInsider. @OTIRacing owned #Aloisia displayed enormous improvement to storm home for 2nd in @royalrandwick G2 Villiers which favours her to remain racing in NSW #unification #regumate.

The Principal Racing Authorities (including Racing Australia) have made no further announcements regarding the future use of altrenogest products and the status quo remains the same as reported in the Randlab Summer Newsletter (http://www.randlab.com.au/assets/randlab-newsletter-summer-2018.pdf).

Meanwhile there have been no further reports of positve swabs related to trenbolone or trendione since the two original Victorian swabs in late 2017 and early 2018, despite continued widespread useage of oral Altrenogest in some juristications.