Current Thoughts on EGUS Prevention Feeding Strategies

A.M. Merritt

Professor Emeritus, Department of Large Animal Clinical Sciences, College of Veterinary Medicine, University of Florida, Gainesville Florida, USA 32610
E-mail: merritta@ufl.edu

Equine Gastric Ulcer Syndrome (EGUS)

In contrast to most mammals with a simple stomach where the majority of the organ is lined with varying types of glandular mucosas, the top half of the equine stomach is lined with a non-glandular mucosa structured similarly to that lining the esophagus. This is critical to remember when considering the Equine Gastric Ulcer Syndrome (EGUS).

The EGUS term was coined in 1999 by the Equine Gastric Ulcer Council to refer to “…the disease complex that is associated with ulceration of the esophageal, gastric or duodenal mucosa”, with the proviso that, “While the name does not adequately describe all manifestations of the syndrome, adaptation into conventional vocabulary suggests that the reference be maintained” (Andrews et al., 1999). Put more succinctly: EGUS is not one disease. Rather, it refers to a number of conditions of differing etiopathogenesis that cause erosive and ulcerative lesions of the non-glandular (squamous) and/or glandular mucosa. In the subsequent years, developments in endoscopic technology and procedure have made documentation easier with increasing awareness that observation of both squamous and glandular regions is required for a complete procedure.

Non-glandular (Squamous) Mucosal Ulceration

A. Definition of the Problem – It’s the Acid

In most monogastric animals, including the neonatal foal, the gastric contents are quite acidic throughout because of the uniform semi-liquid to liquid consistency of the ingesta. In contrast, the contents of an adult equid on a regular hay/grain diet, where the roughage is available on a free-choice basis, vary in their pH depending upon site within the stomach. It is the roughage component of the diet that determines this since, as in the rumen, the lower density/larger particle size components tend to remain at the top of the mat of ingesta where they are minimally exposed to acid produced in the lower glandular region and maximally exposed to swallowed saliva. Adult horses may secrete up to 35-40 liters of saliva per day, the majority of which is parotid in origin, which has a pH of approximately 7.4 (Eckersall et al., 1985). The greater the dry matter content the food, the greater the amount of saliva secreted due in part to the physical composition of the meal and in part to the time needed for adequate mastication (Meyer et al., 1985).
Thus, during the day when available roughage intake on a free-choice basis is the highest, the mean pH of the gastric contents just inside the lower esophageal sphincter vacillates between 5-7, whereas the contents within the more distal part of the stomach, where the acid is secreted, are consistently within pH 2.0-3.0 (Husted et al., 2008; Merritt et al., 2003). When roughage intake is decreased either because it is withheld or because horses eat less during the early morning hours even if it is available, the mean pH in the upper part of the stomach drops markedly to 4.0 or less (Husted et al., 2008; Husted et al., 2009). When the pH drops below 4.0 for any reason, the integrity of the squamous mucosa in the proximal stomach is challenged since it does not contain the elaborate mechanisms to protect it against HCl that are found within the glandular mucosa (Andrews et al., 2006; Widenhouse et al., 2002). There is convincing evidence that squamous lesions are induced by mucosal exposure to acidic gastric contents since effective antacid therapy results in lesion reduction/disappearance (Andrews et al., 1999; MacAllister et al., 1999).

B. Current Knowledge Concerning Risk Factors with Emphasis on Putative Dietary Factors

A high incidence of squamous ulceration, with or without any associated glandular ulceration, has been described in horses in training, irrespective of breed or activity. Typical complaints/clinical signs include failure to finish grain meals, progressive weight loss and underperformance. The role of exercise in the pathogenesis is supported by a study showing a marked reduction in pH within proximal stomach during treadmill exercise, attributed to increased intra-abdominal pressure that pushed more fluid acidic contents within the distal stomach proximally during the exercise period (Lorenzo-Figueras & Merritt, 2002). Then, there is the question of "stress". Although classic stress ulcer is described only in glandular mucosa, there could be a number of factors in a training environment, over and above the direct effects of the exercise itself, that might result in excessive or prolonged exposure of the squamous mucosa to contents of pH < 4.0, including conditions that make a horse unusually tense with secondary increase in intra-abdominal pressure. Accordingly, early studies reported that removing an afflicted horse from the training environment and turning it out to pasture would result in healing, without medication. {REFS} However, recent studies report a notable incidence in pastured animals as well, indicating the multi-factorial aspects of the etiopathogenesis (Bell et al., 2007; Luthersson et al., 2009a).

As mentioned, a drop in proximal intragastric pH to <4.0 occurs during extended periods of reduced hay ingestion, suggesting a possible role of feeding frequency in both sedentary horses and those in training and this is most probably the basis for the squamous ulcer model described by Murray 1994). The implication here for the risk potential of meal feeding programs is obvious. In fact, Luthersson et al. (2009b), in an epidemiological study of 201 Danish horses, report a significantly greater odds ratio for squamous ulcer disease in animals meal fed forage at >6 hour intervals vs. those that had access to forage on a free choice basis.
Diets high in soluble carbohydrate have been suggested as a potential risk factor. This is based upon the finding that a certain portion of ingested non-structural CHO is broken down and converted into volatile fatty acids (VFA) by intra-gastric bacterial flora (Argenzio et al., 1974; Varloud et al., 2004; Varloud et al., 2009) (Fig. 1). Nadeau et al. (2000) were the first to apply the question of possible dietary influences on squamous ulcerogenesis to scientific scrutiny. Using a 3X3 randomized cross-over design, they fed gastrically cannulated horses either a grain (type not specified)/alfalfa or a bromegrass diet, on a 2 times a day feeding schedule for 14 days. On day 14 they collected gastric contents hourly for 8 hours, and then at 10 and 12 hours, post-feeding for measurement of pH and analysis of total VFA concentration. Gastric endoscopy was done prior to and at day 14 of the feeding trial to look for and score any ulcers within the squamous mucosa. What they found was that although the grain/alfalfa feeding resulted in higher VFA concentration within the contents, but the contents pH was also higher and ulcer scores significantly lower than when the animals were fed the bromegrass combination. The interpretation of these unexpected results was that the alfalfa may have actually been protective by virtue of its higher calcium and protein content that acted as buffers of the gastric acid.
Figure 1: The pH gradient of contents within the stomach of an adult horse fed forage ad libitum. The higher density, most recently swallowed food at the top maintains a median pH between 5-7 due to the fact that it has continuing exposure to saliva and, being in the region of the non-glandular mucosa, has not been exposed to acid. The lower density contents and liquid within the lower part of the stomach, near where the acid is secreted, maintain a pH between 1-2. The microbes involved in fermentative activity survive best where the pH is higher.
These same investigators have subsequently followed up with a series of *in vitro* studies that involved measuring squamous mucosal integrity in Ussing chambers while it is exposed to the various VFA’s added to a bathing solution of varying pH, with the pH adjusted by HCl which is the acid produced by the stomach. Essentially, the results indicated that a VFA may have some corrosive effects on the mucosa *but only if the bathing solution pH is <4.0* (Andrews et al., 2006). Thus, exercise and forage type and intake frequency discussed above would still be critical determinants in this process *in vivo*. This is why it remains very important that additional controlled feeding trials involving high vs. low non-structural CHO diets combined with different forages need to be done to address this question more adequately. Accordingly, in the previously mentioned study of 201 Danish horses, Luthersson et al. (2009b) found a significantly greater odds ratio for squamous ulcer development in those animals fed straw only vs. hay or haylage as roughage, or if they received more than 1 gm/kg bwt/meal of starch equivalent in the grain ration. This could be due not only because more starch in the diet could result in more intra-gastric VFA production, but also because increasing the starch slows gastric emptying (Métayer et al., 2004) which could prolong exposure time of the VFA and HCl to the squamous mucosa.

Concerning the potential protective effect of alfalfa mentioned above, Lybbert et al. (2007) performed a 28 day crossover feeding trial that compared squamous ulcer score in horses meal fed twice a day either alfalfa or Bermuda grass in a 1:1 weight ratio with a 15% protein pelleted concentrate; during the 21 day crossover period the animals were pastured and fed the same pelleted ration twice a day. Ulcer scores were significantly lower in the alfalfa fed groups, which was consistent with the earlier findings of Nadeau et al. (2000).

**C. Putative ameliorative feeding strategies**

With the above discussion in mind, what is the level of our knowledge concerning nutritional strategies aimed at severity reduction or even prevention of squamous ulcer disease? The short answer is, it is not very advanced. Nonetheless, using the information we do have provides some management considerations:

1. Provide forage on a free choice basis. If some of that forage is alfalfa…..even better.

2. Put the supplemental forage in a “nibble bag” where the horse has to work at getting a mouthful because of the relatively small holes in the bag and thus must eat more continuously to satiate itself. This provokes more salivary secretion which, in turn, results in more buffering of the gastric contents covering the squamous mucosa. There are a number of designs commercially available from various manufacturers.

3. Provide more fat-based and fewer non-structural carbohydrate-based calories in the concentrate portion of the diet. There is now considerable evidence, from both physiological and nutritional studies,
that horses can tolerate much more dietary fat than has been traditionally supplied in the various concentrate formulations that have been devised for the beast (Delobel et al., 2008; Harris et al., 1999; Harris, 2009; Kronfeld et al., 2004; Lorenzo-Figueras et al., 2005; Meyer et al., 1997; Meyers et al., 1989; O’Connor et al., 2004; Sales & Homolka, 2011). For instance, Harris et al. (1999) found that feeding either saturated or unsaturated fat at ~20% of DE intake for 6 months to active Thoroughbreds after they had been acclimatized at a 12% of DE intake for 10 months. Likewise, O’Connor et al. (2004) reported that high omega-3 FA fish oil supplementation at 325 mg/kg BW/d for 63 days to exercising horses had, if anything, beneficial effects on numerous exercise-related metabolic parameters. Unfortunately, neither of these studies recorded squamous ulcer incidence and/or severity during the trial.

4. According to some studies, putting the horses on pasture/paddock turnout between working sessions is indicated (Lester, 2007; Reese & Andrews, 2009), although Husted et al. (2008) did not record any difference in proximal gastric pH between stall and paddock environments in horses allowed hay free choice ad libitum.

A number of nutriceutical products that have been marketed over the last 10 years that claim to reduce squamous ulcer incidence and/or severity, but, to date, the efficacy of none of these has been subjected to strict scientific scrutiny.

**Glandular Mucosal Ulceration**

**A. Definition of the Problem**

It is generally accepted that ulcers occur within the gastric glandular mucosa of any species because of disruption of the endogenous mechanism within the mucosa that protects it against corrosion by gastric acid. A classic example is a direct assault by the non-steroidal anti-inflammatory drugs (NSAID’s) such as phenylbutazone and flunixin that disrupt cyclooxygenase activity which is a critical component of the protective mechanism (Peskar, 2001a). Another example in humans and some animals, but as yet not found in the horse, is colonization of the pyloric (antral) glandular mucosa by certain *Helicobacter* species, notably *H. pylori* in humans. Interestingly, to date the majority on the spontaneously occurring glandular lesions in the horse have been found in the pyloric mucosa, in contrast to the fundic mucosa where the acid is produced and secreted (Martineau et al., 2009; Murray et al., 2001). There are only a few reports concerning their histopathological investigation, with the most systematic being by Martineau et al. (2009) whose results indicate that what is called an ulcer when seen on endoscopy may, in fact, only be an erosion when examined histologically. They did find, however, a mild chronic inflammation of parts of the glandular mucosa in a number of animals, the etiology of which was not determined. Suffice to say that the etiopathogenesis of glandular
mucosal lesions in the horse, except those associated with NSAID therapy, is currently poorly understood.

B. Current Knowledge Concerning Risk Factors
There is also a paucity of knowledge concerning risk factors for the development of glandular ulcers aside from NSAID treatment. Luthersson et al (2009b), in the study of Danish horses mentioned above, reported that, as with the squamous disease alone, the feeding of straw rather than hay or haylage and amounts of starch equivalent of >1 gm/kg bwt/meal were significant risk factors for the development of ulcers within any part of the stomach but unfortunately, in contrast to squamous disease, they did not look at glandular disease as its own entity so we do not know how much influence the incidence of the former had on the results. In an abstract of a presentation at the 2012 ACVIM forum, Habershon-Butcher et al. (2012) list a number of risk factors for glandular disease; the nutritionally-related ones include feeding of unprocessed grains, infrequent feeding of a complete diet, lack of haylage feeding and no grass turnout - in short, not much different than what is talked about with respect to squamous ulceration. Hopefully, this study will appear as a full paper that contains further details about experimental design and the character of the glandular lesions that they saw.

C. Putative ameliorative feeding strategies
Based upon what we know at present, the strategies would mimic those concerning squamous ulceration presented above, particularly with respect to providing free-choice roughage and reducing non-structural CHO intake. However, it is not as easy to rationalize why these approaches might be effective here as it is for the squamous disease. Furthermore, Huff et al. (2012) recently reported that sea buckthorn berries and pulp (SeaBuckSBT Gastro Plus™) given twice daily to horses on a complete pelleted feed diet significantly reduced glandular but not squamous ulcer scores. As the authors admit, it would be interesting to see whether such a difference would be seen in animals that had roughage available *ad libitum*.

Finally, Cargile et al. (2004) have shown that daily supplementation of corn oil at ~10 ml/50 kg bwt/d for 30 days significantly increased the prostaglandin E₁ (PGE₁) and decreased the HCl concentrations in response to pentagastrin stimulation in ponies. This indicated that there had been an up-regulation of mucosal PGE₁ which is also an important component of the gastric mucosal protective mechanism (Peskar, 2001b) and suggests that corn oil supplementation might be useful in prevention and treatment of glandular ulcers.
References


