Gastric Ulcers In Adult Horses: Current Situation, Prevention and Improvements Observed with the Use of Fermented Soya

*Practical cases for the use of Fermaid®Ease 187 in horses.*
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1- State of play with regard to ulcers

The gastric ulcer is an alteration in the stomach mucosa, with varying degrees of severity from gastritis (superficial erosion) to deeper lesions that may be accompanied by haemorrhages. Extreme cases, where the ulcer perforates the wall, are often fatal for the animal. The degree of seriousness of an ulcer will therefore depend on its size, on the number of lesions, on the degree of haemorrhaging, or on the appearance of necrotic areas. Ulcers are not exclusively “gastric”; the duodenum may also be affected (see opposite: photograph of deep grade 3 duodenal ulcerations, in significant numbers, associated with hyperkeratosis).

1-1 The Horse’s Stomach

Its anatomy and physiology go a long way to explaining the heightened sensitivity of horses to gastric ulcers. The adult horse has a small stomach of approximately 15 litres with a usable volume of 12 litres. This consists of two distinct parts: a non-glandular part (dorsal part: the highest part of the stomach including the cardia) and a glandular part (ventral part: the lowest part of the stomach including the pylorus). An irregular projecting sutural line, also called the margo plicatus, separates these two zones (Figure 1).

The glandular part varies in color from yellowy-pink in the pyloric area to a darker purplish-red in the fundic region. These mucosae are composed of large parallel folds (gastric folds) that meet at the pylorus. The glandular region secretes digestive agents [hydrochloric acid, enzymes (pepsin, etc)] and hormones that regulate their secretion (gastrin, somatostatin, etc). The special characteristic of the glandular mucosa of Equidae lies in the continuous production of gastric juices by the parietal cells. Under normal conditions, this zone is covered by a layer of mucus containing bicarbonates, giving it a fatty appearance. The buffering effect of this mucus therefore protects it from attack by the corrosive digestive agents that it produces.

The non-glandular part represents almost one-third of the total surface area. This proventricular mucosa, smooth and pinkish-white, is rather dry, and resembles that of the esophagus. The non-glandular mucosa, also called squamous, is not covered with this mucus, but possesses numerous protective layers of keratinised cells.

Figure 1: Anatomy of the horse stomach.
The outlet from the esophagus into the stomach is called the cardiac ostium. In horses, the cardia forms a very narrow sphincter, rich in muscular fibres, which prevents any regurgitation or vomiting.

The majority of ulcers observed in adult horses are situated in the least protected area of the stomach: the stratified squamous epithelial mucosa (non-glandular part).

### 1-2 Origins of Ulcers

These are summarised in Figure 2. At pasture, a horse spends more than two-thirds of its time feeding. Thus, the alimentary bolus and the buffering agents contained in the saliva protect the mucosae from the continuous production of gastric enzymes and acids.

Today, due to the effects of life in a stall and human activities, the horse receives its food in a fragmented way, in two or three daily meals, so its stomach is regularly empty on a continuous basis. The digestive agents are therefore in prolonged contact with the poorly protected digestive mucosae, leading to their erosion. Thus, measurement of gastric acidity shows significant variation depending on whether the stomach pH is measured in a horse with an empty stomach (pH<2) or after a meal (pH>6). This is further aggravated by the rapidity of gastric emptying observed with products rich in cereals (half an hour), as opposed to more fibrous rations (e.g. hay), where it takes several hours.

However, the ulcers detected, even in horses in stalls receiving hay on demand, raise the question of the actual effect of confinement and modification to food intake (nature, frequency, and physical presentation of food, etc). In a stall, the quantity consumed, the speed of ingestion and low level of mastication limit the production of salivary bicarbonates. It takes slightly less than 15 minutes to masticate 1kg of concentrate as opposed to 40 minutes for 1kg of hay, and saliva production is reduced by two (production estimated at 2 litres of saliva for 1kg of concentrate against 4 litres for 1kg of hay).

What is more, physical activity, and the associated contraction of the abdominal muscles, leads to a reduction in the volume of the stomach while working. The gastric juices are therefore moved to the upper part of the stomach, which is not protected against acidity, causing irritation of the mucosa, and, in the longer term, the formation of an ulcer.

Acids from the co-products of microbial fermentations (volatile fatty acids: V.F.A.) in the stomach also pose the question of their contribution to the increase in stomach acidity and their role in the formation of ulcers. These V.F.A. (lactic, acetic, propionic and butyric acids) arise in particular from the rapid fermentation of rations that are rich in soluble carbohydrates (fast starch, simple sugars, etc).

The modern horse is also an animal that is highly sensitive to stress, and it seems that, as in humans, simple changes in routine (transport, competitions, etc), and solitude, etc, may trigger off ulcerous lesions.

The ulcer appears during an imbalance between factors that are aggressive towards the mucosa (pepsin, acid secretions...)

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**Figure 2: Modern horses’ breeding practices are sources of numerous factors that lead to gastric ulcer.**
and cellular hypoxia) and protective factors (mucus, secretion of bicarbonates, blood flow and cell renewal).

This imbalance has many causes but they are basically linked to physiological stresses aggravated by:

- imbalances in diet;
- overwork (period of intensive training);
- change of environment (stalls, different types of transport, competitions, etc);
- rations that are over-rich in protein and/or highly fermentable carbohydrates, certain medications (N.A.I.D.), poor mastication (over-voracious horses), insufficient size of fibrous particles, cereals ground too fine;
- stomach parasites (bot fly infestation).

1-3 Signs Of An Ulcer

There are a number of external clinical signs, more or less direct, associated with the presence of an ulcer, which may alert the owner. These signs are in no way “specific symptoms”, and may not be the basis for a sure diagnosis; however, they remain excellent indicators of this type of problem.

- Health: episodes of colic (often repeated, with or without displacement of the colon), abdominal pains (which may be observed at girding or occurring during meals)
- Feeding behaviour: not finishing meals, emaciation, aerophagy, etc
- Modifications to behavior: stress, development of stereotypy
- Activity: lack of form when working, lack of obedience when jumping, deterioration in physical condition and poor performance
- Posture and attitude: grinding of teeth, dorsal decubitus, eructation, yawning.
- Quality of coat: dull, patchy
- Appearance of faeces: presence of digested black blood, odorous, etc.

However, diagnosis of an ulcer may not be made exclusively on the basis of these external signs. Besides, many ulcerous attacks remain mute and asymptomatic.

1-4 Stages of Gastric Ulcers

Only gastroscopy makes formal diagnosis of an ulcer possible. This direct examination of the stomach or duodenal wall precisely describes the reality and severity of the disorder. Its degree of seriousness is assessed depending on the appearance and extent of the lesions, and is generally graded on a scale of 0 to 4. A few examples are illustrated below:

Grade 0: Mucosa intact, no lesions

Grade 1: Acute gastritis, epithelium intact with zones of erosion present

Grade 2: Superficial ulcers, not very deep and few in number. The photograph on the left shows a case of chronic gastritis associated with hyperkeratosis of the non-glandular part. The one on the right shows superficial ulceration.

Grade 3: Established ulcers, extensive ulcerous lesions in a ‘fingernail mark’ pattern, accompanied by hyperkeratosis or not (depending on the age of the lesion)

Grade 4: Severe ulcer, numerous reactive lesions, in a ‘volcanic crater’ pattern with deep zones or extensive superficial areas of ulceration
1-5 Frequency

All horses may one day suffer an ulcerous episode: any sex or breed, and horses from all equestrian disciplines are affected, with the frequency of the attacks increasing with the level of physical activity and stress.

In 2010, the horses from two racing stables at the Newmarket course in England, that were not receiving any treatment for gastric conditions, were subjected to gastroscopy (n=48 horses): 94% of the working horses presented lesions of varying severity! The grades most frequently encountered were grades 2 (33%) and 1 (27%) (Figure 3).

The ulcer is a somewhat insidious disorder: the majority of the affected horses displayed no symptoms, or just non-specific signs of stomach problems.

One month after this gastroscopy, and still during their training period, all these horses were subjected to a second gastroscopy. All the horses from grade 0 had progressed to grade 1. Of the grade 1 horses, 9 – or 69% of all grade 1 – had an ulcer that had got worse, 38% of grade 2, and 20% of grade 3. It should be noted that 83% of the grade 4 horses went back to grade 3 in a month (Figure 4).

In conclusion, without treatment or preventive measures, a lesion diagnosed as low-grade very often moves into the more severe grades. It is therefore important to take rapid action, even for the least disturbing lesions, which most often become serious in the short or medium term.
2- Use of Fermaid®Ease 187 to fight against the pathology of the ulcer

Fermaid®Ease 187 is a natural food supplement, adapted to the physiology of the horse. Non-GMO micronised soya is fermented by a specific lactic bacteria Lactobacillus delbrueckii lactis Rosell-187, deactivated at the end of the manufacturing process. Fermaid®Ease 187 has been developed to prevent the formation of ulcers. It was used successfully for the first time in human medicine to relieve pain associated with ulcers. Numerous publications bear witness to its efficacy (clinical trials carried out on over 600 patients). These studies reveal the very good tolerance of Fermaid®Ease 187 and conclude that it reduces the symptoms associated with ulcers. Furthermore, a radioscopic examination using X-rays reveals signs of healing extending right to the complete disappearance of the ulcer, with the stomach mucosa returning to normal. Members of the horse family are happy to eat Fermaid®Ease 187, which makes it easy to use. In addition, it has no doping effect which means it can be used throughout the horse’s period of activity.

2- 1 Acts in a Very Original Way

At the moment its method of action has not been fully explained. However, several in vitro trials, on cell cultures, have shown that the inactivated bacteria and its metabolites are able to reduce inflammation and spontaneously repair cells which have been attacked. By interacting with the immune system of human cells, Fermaid®Ease 187 stimulates regeneration of the epithelium, increases the anti-inflammatory IL-6 interleukins produced by the epithelial cells and the lymphocytes (apart from macrophages) and slows down the synthesis of the pro-inflammatory cytokines TNF-α and IL-8 (see boxed text page 7).

In addition to this modulation of the inflammatory response via the action of prostaglandins and cytokines, there is a direct buffer effect, an effect on blood flow (oxygenation of the epithelial cells) and on the secretion volume of bicarbonates. The production of gastric acid is also slowed down by inhibiting competition with histamine, thus reducing irritation of the mucosa. The chemical analysis of the end product also shows the presence of several trypsin inhibitors, which mean that Fermaid®Ease 187 has a direct effect on the production of hydrochloric acid.

By maintaining the integrity of the gastric tract, these effects therefore justify using Fermaid®Ease 187 in the prevention and treatment of ulcers.

2- 2 Results and Efficacy

Between 2005 and 2007, several studies were conducted at the Clinique des Bréviaires with the protocols conventionally used in the field by equine veterinary surgeons. Fermaid®Ease 187 is generally given for one month prior to a period involving stress and activity for the horse. Depending on the severity of the level, Fermaid®Ease 187 can be used alone, or for high levels of severity, as an accompaniment to traditional therapeutic treatment prescribed by the veterinary surgeon: 10 days of Omeprazole, followed by at least one month of Fermaid®Ease 187 (at a rate of 25g/day/horse).

These trials were conducted on horses carrying out work in order to obtain data about subjects under situations of real stress and exercise, unlike certain studies in existence which dealt with sedentary animals or those whose activity was reduced (hospitalised).

Trial # 1

An initial trial was conducted on 8 horses which did not receive a gastroscopy, for which Fermaid®Ease 187 was prescribed on the basis of signs particularly suggestive of this disorder. These horses showed a clinical improvement within the 4 to 7 days after starting to administer the product. Five of them were then able to undergo endoscopy with signs of healing of the gastritis or of ulcers of a level below 2: in principal this examination thus justifies the diagnosis and initial treatment.

Trial # 2

A second protocol involved 59 horses who came in for consultation after their owner had observed clinical signs...
renowned for being associated with ulcers. The horses were divided into 3 groups depending on the assumed gravity of the disorder:

- Group A: 23 horses which did not receive a gastroscopy with clinical signs associated with the disorder and receiving Fermaid®Ease 187 for one month;
- Group B: 17 horses which received a gastroscopy as well as Fermaid®Ease 187 for one month;
- Group C: 19 horses which received a gastroscopy as well as an « antacid » medicinal product (Omeprazole) for 15 days (7/19 horses) to 30 days (12/19 horses). Fermaid®Ease 187 was then prescribed for one month.

The horses were checked twice, after 1 and 2 months (+ 1 week) after the initial diagnosis. At the time of these consultations, the four major clinical signs indicating the potential presence of the ulcer were evaluated for each of these 59 horses who came for a consultation, with it being possible for each horse to present 1 to 4 of these symptoms. For the three groups, the graphs show the individual total of these criteria.

**Group A:**
After 1 month of treatment, 81% of the initial symptoms had disappeared (83% after 2 months) (Figure 5).

So, in spite of the lack of endoscopic documentation, Fermaid®Ease 187 seems to have been effective in 81% of cases after only one month of supplementation with regard to the main clinical signs (loss of appetite or general condition). It should also be pointed out that this improvement was confirmed at the third examination after 2 months, i.e. 1 month after ceasing distribution of Fermaid®Ease 187 whose effect seems to be able to be prolonged.

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**Laboratory studies: analyses of the effects of deactivated lactic bacteria on the production of cytokines**

The intestinal epithelial cells are able to respond to numerous stimuli including the presence of lactic bacteria, for example by producing cytokines. The cytokine profile of these epithelial cells is represented by IL-6 (cytokine stimulating the production of antibodies), IL-8 (chemoattractant pro-inflammatory cytokine: chemokine) and RANTES (cytokine involved in the immune response).

In order to compare the immunomodulating activity of different lactic bacteria and their influence on different aspects of the immune response (production of antibodies and activation of lymphocytes and macrophages), 5 strains, after inactivation by heat, were brought into contact with human intestinal epithelial cells (cell line HT-29) using 2 types of preparation (commercial product or strains cultivated in the laboratory on Mann Rogosa Sharpe medium). The supernatants were collected and quantified using ELISA.

The IL-6 produced in the presence of Lactobacillus delbrukii ssp lactis (noted as R0187 on the green histogram) are significantly higher in numbers than the 3 other strains tested, particularly for commercial industrial preparation. The deactivated bacteria therefore caused an increase in the production of IL-6 (p=0.004, n=3). On the other hand, R0187 tends to reduce the production of IL-8. Finally, the bacteria R0187 is the one which seems to have the least effect on the production of RANTES. Optimum induction of RANTES by epithelial cells requires the presence of TNFα (Tumour Necrosis Factor) and Interferon γ (IFNγ).

The bacteria R0187 leads to a reduction in the secretion of TNFα. TNFα is involved in various biological processes, in particular in those with a pro-inflammatory role: it has the ability to stimulate neutrophils and macrophages, and to increase the secretion of IL-8 by endothelial cells, thus attracting and activating the neutrophils. The production of cytokines by the intestinal epithelial cells has a dual effect. Although on the one hand the production of pro-inflammatory cytokines may be beneficial in certain situations, their production may also be involved in causing local damage to the tissues and inflaming them. Significant expressions of IL-8, RANTES and TNFα were noted in the intestinal mucosa of patients suffering from intestinal inflammation.

This in vitro data shows that production of cytokines IL-6, IL-8, TNFα and RANTES are thus potentially affected by lactic bacteria depending on the strain and the conditions of the culture medium. In view of these elements, the oral ingestion of specific lactic bacteria represents an important way of changing the microenvironment of the mucosa and of interaction with the immune response, particularly in situations of cytokine irregularities in the mucosa leading to tissue damage and pain.
Group B:
The results obtained for these horses, mainly presenting low level lesions (1 and 2), confirm the results obtained on the subjects in group A and justifies the therapeutic choice of only using Fermaid®Ease 187 (figure 6).

After 1 month of treatment, the clinical signs of the horses in group B were reduced by 69% (72% reduction at the 3rd examination, i.e. after going for 1 month without Fermaid®Ease 187).

Group C:
The principle of this complete therapeutic protocol (Omeprazole + Fermaid®Ease 187) was to quickly calm down the ulcerous pathology and to gradually bring down the lesion to a lower level (figure 7). This is able to confirm the advantage of Fermaid®Ease 187, used to take over from Omeprazole, firstly in order to limit the risk of recurrence. The reduction of clinical signs was 83% in the first month, with this continuing for the second month (93%). Recurrences appeared in certain horses 4 months after stopping the medication, confirmed by a gastroscopic examination (3 horses out of 19): this justifies the practical recommendation of maintaining the distribution of Fermaid®Ease 187 continuously during the period of stress in order to avoid these recurrences.

The following should be noted: the horses in group C, suffering more severely with regard to their mucosa, present fewer clinical signs than the subjects in group B after one month. These results confirm that the severity of the ulcer is not strictly correlated with the observation of symptoms, and that Omeprazole is fully justified as the “attacking” part of the treatment. These results also confirm those of the preliminary study (trial 1) which show the efficacy of Fermaid®Ease 187 used on horses with moderate-level gastritis (fli 2).

Trial # 3
The third study concerned 11 horses involved in sport with clinical signs of gastritis. 8 (72%) underwent at least 2 endoscopic examinations. The first examination took place between 1 and 2 months after the diagnosis (i.e. at the end of treatment with Fermaid®Ease 187). The other examinations took place at 2-month intervals on average (Figure 8). At the time of the 1st control gastroscopy, 7 horses (63%) presented an improvement in the condition of their stomach mucosa. Only 4 horses showed little or no improvement. At the 2nd gastroscopy, on 3 horses, only 1 single horse improved, with the levels of the other 2 having deteriorated. At the 3rd examination, the levels of the last two horses had improved.

Relapses were considered as being due to recurring ulcers, requiring longer treatment with Omeprazole.

The mean grade at the first gastroscopy was 2.25 (±1.03). At the second gastroscopy, the reduction of one unit in level was noted with a mean of 1.25 (±1.03).

The horses which only had one gastroscopy presented a significant clinical improvement, consequently the owners did not want any control gastroscopy.
In the case of level 3 and level 4 ulceration, Omeprazole (proton pump inhibitor) was prescribed for a 15-day period, followed by 1 month’s treatment with Fermaid®Ease 187 alone. The horses were then kept on Fermaid®Ease 187 permanently (except when they were in the pasture or were felt to be in a period of limited stress without any change of environment or not competing).

In conclusion, this trial underlines that the risk of recurrence in horses without any therapeutic or nutritional accompaniment, was fairly important in levels of lesion of over 2.

With the use of Fermaid®Ease 187, prescribed for one month, 10 days more than Omeprazole, horses with serious lesions did not present recurrence. In the case of milder lesions, associated with symptoms, Fermaid®Ease 187 produced a significant clinical improvement without medication.

Prospects And General Conclusion

Recent studies (Newmarket) confirm the conclusions of previous studies and reveal the large number of horses with ulcers that are often not diagnosed. In most cases, these ulcerous attacks (often below or equal to level 2) justify its use to prevent solutions which can be used at a lower cost and without any risk of doping. However, the advantage of Omeprazole, used as first intention, on recurring or more severe ulcers is confirmed.

To sum up, Fermaid®Ease 187 helps to:

- Restore the epithelium of the stomach and maintain its integrity;
- Reduce pain (by modulating cytokine profiles);
- Improve the horse’s general condition (by increasing its appetite and ensuring better digestive health).

This nutritional supplement is therefore part of the system for monitoring horses involved in sport or leisure, which have to undergo changes in diet and stresses of various types (confinement, transport, change of environment, etc). Fermaid®Ease 187 forms part of an effective veterinary prescription. It provides an effective and economical addition to the therapeutic arsenal available to the practitioner for preventing and relieving conditions of gastritis and ulcerous lesions of the proximal intestinal tract and to accompany established medicinal treatments for treating ulcers. The frequency of genuine yet undiagnosed lesions fully justifies the distribution of Fermaid®Ease 187 in the preparation of horses, during periods of stress, competition or intense work.

SUMMARY

The pathology of the ulcer increasingly affects the modern horse which spends little time in the pasture. Whether this is a passing phenomenon or the real situation, this study brings us up to date on current knowledge of ulcers, their formation and development. This data has been taken from internal studies and from a recent trial conducted in 2 major racing stables (Newmarket, UK, 2010) in order to evaluate the importance of this disorder and its development. First of all it confirms the high frequency of the number of horses affected: 45 of the 48 horses (i.e. 94%) chosen at random presented a change of varying degrees of severity in the stomach mucosa. The majority of ulcers are of level 2, followed by 1. After 1 month, these same horses were given a gastroscopy a second time by the same veterinary surgeon. The lesions mainly became worse (mostly levels 2 and 3 in identical frequency) inversely proportional to the initial level: the lower the horse’s initial level, the greater the risk of these lesions worsening. These original data underline the impact of stress and human activity on the horse's health, as well as the importance of solutions for preventing and supplementing benign lesions at an early stage.

The second part of this study revealed the advantage of a preventive and improving nutritional solution, Fermaid®Ease 187, on levels 2 or under which can be used to accompany treatment for severe lesions. Its success in human medicine in relieving conditions of gastric burning and ulcers and the number of publications justified its advantage in the equine species, which is also extremely sensitive to this disorder. Its very original method of action (immune effect via anti-inflammatory cytokines and its effect on blood flow) explains the essential information from the conclusions of the 3 trials in the field conducted between 2005 and 2007 at the Clinique des Bréviaires on horses affected by this disorder (n1=8; n2=59; n3=11). Different protocols were tested, systematically providing a daily supplement of Fermaid®Ease 187 for 1 month. Depending on the severity of the ulcer, initial treatment with Omeprazole was administered if necessary. The results show a significant improvement in the 4 clinical signs studied, associated with the ulcer: loss of appetite, loss of condition, recurrent colic and softening of faeces. The gastroscopies carried out after these treatments lasting 1 month generally show signs of healing and a return to degrees lower than 2 in the horses which were initially most affected. The final trial, in which gastroscopies were conducted before and after supplementation with Fermaid®Ease 187 also show an improvement in the health of the mucosa. The horses did not relapse in the 2 months following the trials. In conclusion to these trials, Fermaid®Ease 187 improves the clinical signs associated with ulcers without medication, contributes to maintaining the integrity of the mucosa and stimulates the cell regeneration involved in the horse regaining its condition.

This study confirms the growing presence of the ulcer, alongside growing requirements for a working horse. Without any real pathognomonic symptoms and only being truly diagnosed by gastroscopy, the frequency and presence of this disorder, which is not always obvious, are extremely under-estimated. This observation that recent, non-extensive ulcerous lesions, worsen almost systematically over time, justifies the implementation of systematic or early preventive measures.
Bibliography

Andrews F. M. Ulcers in the Stomach and Colon; Diagnosis and Treatment: A Pain in the Gut! American Association of Equine Practitioners - AAEP - Focus Meeting- Québec, QC, Canada, 2005.


Lafargue De Oliveira Cruz. La Gastroscopie chez le Cheval, thèse pour le doctorat vétérinaire ENVA 2008.

Les Ulcères Gastriques. L’EPERON spécial santé 2007

Lester G. D., Robertson I., and Secombe C. Risk factors for Gastric Ulceration in Thoroughbred racehorses. RIRDC publication number 08/061, Australian Government.


Marqués F. J. Le Syndrome des Ulcères Gastriques du Cheval. La Médecine Vétérinaire des Grands Animaux, Vol. 7 (3). Published by Western College of Veterinary Medicine, University of Saskhewan. Mars 2007.


Murray M. J. Overview of Equine Gastroduodenal Ulceration. AAEP PROCEEDINGS Vol. 43 / 1997 pp 382-387


Pohfunghfung W. Effet du lait du germe de soja dans la cicatrisation des ulcères gastriques. MED. J. AUSTRAL. 1975, 1, 23, p. 717-718


Pratt S. E. Equine Gastric Ulcer Syndrome. Horse-Canada July-August 2003

