GASTRIC ULCERS in the athletic horse

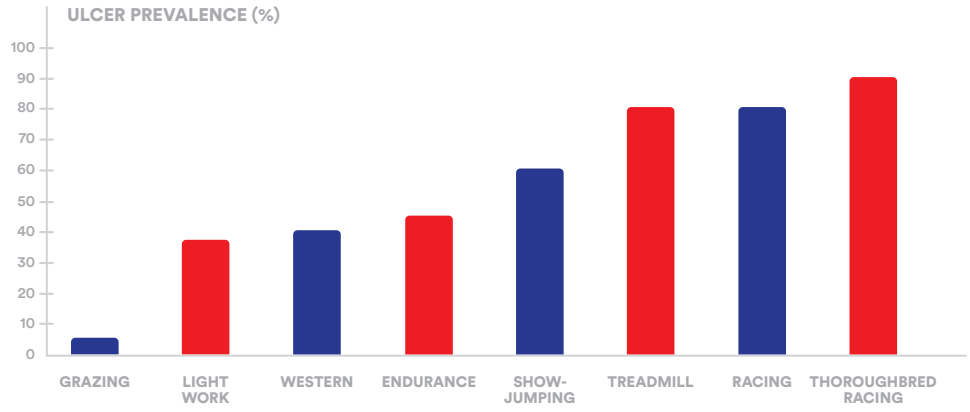
Man imposes living conditions on the horse that can have a negative impact on his health by using him for racing or other equestrian sports. The digestive sphere being the Achilles heel of equines, it is often here that the first disorders appear. Amongst the digestive disorders observed in horses in training, gastric ulcers hold the first place.

I. PREVALENCE

Whilst gastric ulcers are observed in 5% of horses at grass or at rest, up to 93% of racehorses suffer from this pathology during training. (source 1)

The relationship between exercise and gastric-intestinal function is the subject of more and more research given that poor performance caused by ulcers, and their impact on well-being, are of non-negligible economic importance.

PREVALENCE OF GASTRIC ULCERS DEPENDING ON THE DISCIPLINE (1)



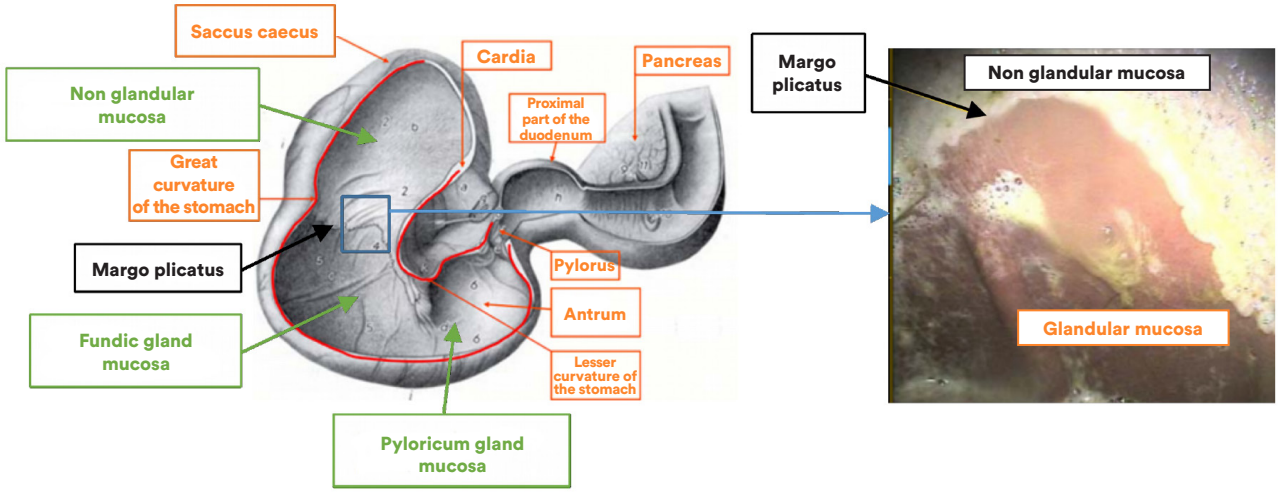
II. ANATOMY OF THE STOMACH

The stomach of the horse is divided into two distinct regions:

- The non-glandular squamous region, white in colour. It is located at the top (proximal) of the stomach and represents about a third of the organ. The squamous mucosa has a stratified epithelium composed of 4 layers of cells, similar, on a histological basis to the oesophagus. The most superficial layer has a keratinized surface.

- The glandular region, pink in colour with a shiny aspect. It represents the remaining two-thirds of the stomach. As indicated by its name, this part has a mucosa that secretes. It is composed of cells secreting mucus and bicarbonates as well as gastric glands housing different cell types.
  Each type of cells produces one of the following compounds: pepsinogen, hydrochloric acid, histamine or gastrin.

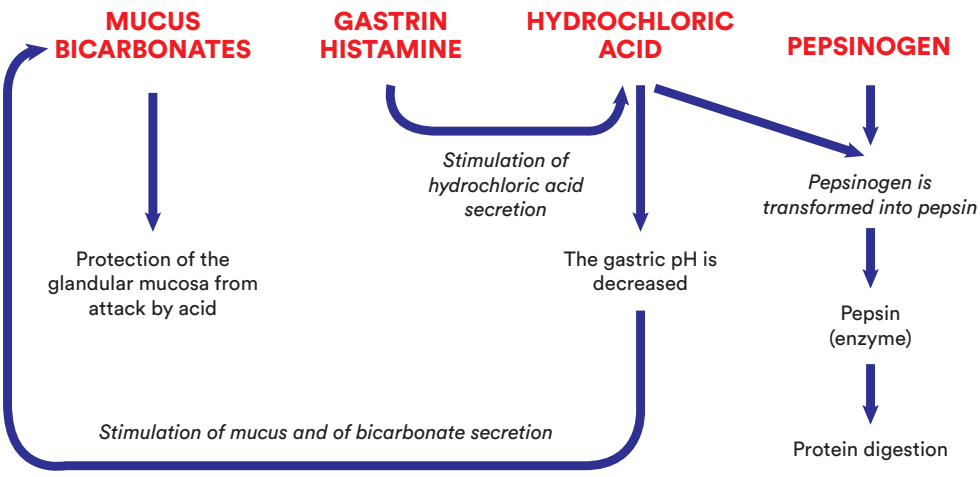
These two parts are separated by a demarcation line that can be seen by the naked eye: the margo plicatus. (1)



III. PHYSIOLOGY OF GASTRIC SECRETIONS

Only the glandular mucosa is composed from cells secreting substances whose role is described below:

In the horse, acid is continuously secreted, even when the stomach is empty. The pH of the gastric contents, which are permanently acid, show however a gradient from the top (proximal) towards the bottom (distal), the lowest pH is found in the distal region (1).



IV. DEFENCE MECHANISMS OF THE GASTRIC MUCOSA

1. GLANDULAR MUCOSA

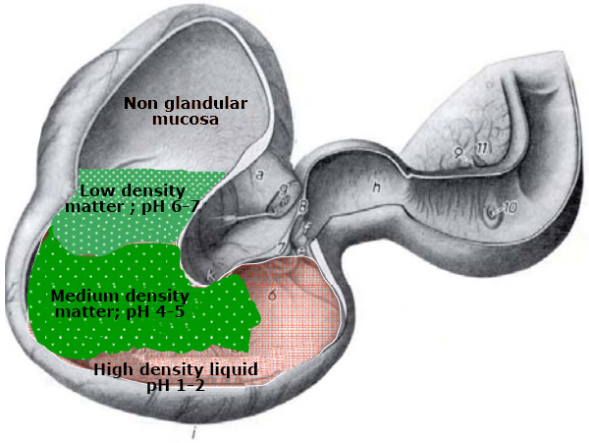
As can be seen on the below diagram, the glandular mucosa is permanently exposed to acid stomach contents. However, it possesses a number of protection mechanisms that preserve integrity (source 2):

- Mucus and bicarbonate secretions form a protective film on the surface of the mucosa. This barrier allows the acid secretions and pepsinogen to pass only one way and thus obtain a neutral pH under the protective layer. This mucus and bicarbonate production is principally induced by prostaglandin E2 (PGE2). This locally acting hormone exerts a positive action on vasodilatation and has the direct effect of inhibiting acid secretion.

- Rapid cell renewal.

- The mucosa is highly vascularised which permits a supply of nutritive substances, oxygen and reparation factors.

CHARACTERISTICS (DENSITY AND PH) OF STRATIFIED GASTRIC CONTENT, IN NORMAL CONDITIONS (1)



2. NON GLANDULAR SQUAMOUS MUCOSA (2)

On the other hand, until proved to the contrary, the squamous mucosa is not protected by a film of mucus. Maintaining integrity is principally dependant on limited exposure to the acid contents of the stomach. The cells present at the surface of the mucosa renew rapidly and are keratinized. When the squamous region is subjected to aggression by the acid contents of the stomach the keratin layer thickens. Nevertheless, these protection mechanisms are quickly exceeded when faced with excessive exposition to acid contents.

NB: Two recent studies carried out on deceased horses have shown the existence of a layer of mucus on the surface of the squamous mucosa. However, this interesting discovery must still be confirmed in live subjects.

When the mucosa is damaged, EGF (Epidermal Growth Factor) receptors appear, who, once stimulated, contribute to inhibiting acid secretion and stimulating the regeneration and protection of the mucosa.

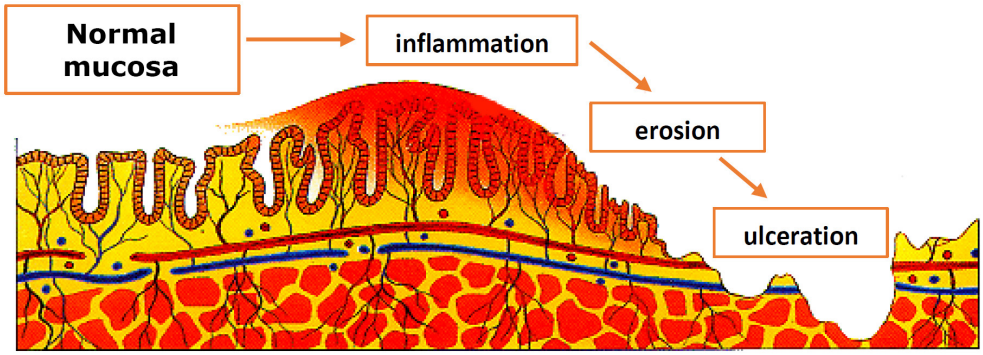
Finally, must be added to these protection mechanisms of the squamous and glandular mucosa, the production of saliva, secreted in the oral cavity during mastication. It contains an important quantity of bicarbonates that once in the stomach contribute to neutralising acid secretions.

V. EQUINE GASTRIC ULCER SYNDROME

1. DEFINITION

Equine gastric ulcer syndrome (EGUS) gathers together different disorders which accompany erosions or ulcers of the mucosa of the stomach, oesophagus or the first part of the small intestine (duodenum) (2). To start with, the lesions are characterised by a local inflammation (erythema) or a thickening of the squamous epithelium (hyperkeratosis) without rupture in the integrity of the surface epithelium. However, they can progress to more or less superficial erosion of the mucosa epithelium, and even penetrate more deeply. Thus, when all the cellular layers of the epithelium are affected and the lesions reach the underlying loose connective tissue, called the lamina propria, we talk about ulcers (source 3).

THE DIFFERENT STAGES OF EQUINE GASTRIC ULCER SYNDROME (EGUS) (3)



2. THE DIFFERENT TYPES OF ULCERS

EGUS gathers different types of lesions, classified depending on their localisation (2):

- Primary squamous lesions, which above all affect adult horses in intensive training, without any discrimination regarding age, breed or sex.

- Glandular lesions and/or primary proximal duodenal mucosa lesions, as the result of an alteration or a failure of the protection mechanisms of the glandular mucosa. The toxicity of non steroidal anti-inflammatory drugs (NSAIDs) is implicated, in particular in the case of individual sensibility or overdosing. The lesions being in preference localised in the pylorus region.

- Secondary squamous lesions, above all seen in the foal (under the mother or shortly after weaning) following a gastric-duodenal ulcerous condition.

- Primary lesions of the cardial glandular mucosa (under the margo plicatus), met with in the new born subjected to intense stress following a severe infection or trauma.

Thus, principally met with in the horse athlete are primary squamous lesions.

VI. PRIMARY SQUAMOUS ULCEROUS DISEASE

1. CLINICAL SYMPTOMS

A wide range of clinical signs is associated with gastric ulcers (1, 2):

- **Fickle appetite**: slow eating, selective or reduced appetite.
- **Reduced drinking**.
- **Reduced overall condition**: weight loss, staring coat.
- **Intolerance to effort, under performing**.
- **Behavioural changes**: lack of enthusiasm when exercised, handling and training difficulties,
- **Low-grade colics**, notably after feeds.

Clinical symptoms associated with pain can also be observed in the case of acute lesions. This pain is notably provoked by mechanical stimulation applied to the damaged mucosa (such as the arrival of water or feed, or during an increase in the intra-abdominal pressure).

If the presence of clinical signs orientates diagnosis, the absence of symptoms cannot on the other hand allow the hypothesis of gastric ulceration to be excluded. Indeed, some animals can have ulcers without showing any clinical signs, which is why EGUS is often under diagnosed (source 4).

A scoring system proposed in 1999 allows lesions to be classified on a scale of 0 to 4:

The majority of primary squamous lesions are situated at the level of the margo plicatus, on the lesser curvature of the stomach, where the squamous mucosa finds itself the most easily exposed to acid contents, even in animals at rest.

SCORING SYSTEM FOR GASTRIC-INTESTINAL ULCERS IN THE HORSE (2)

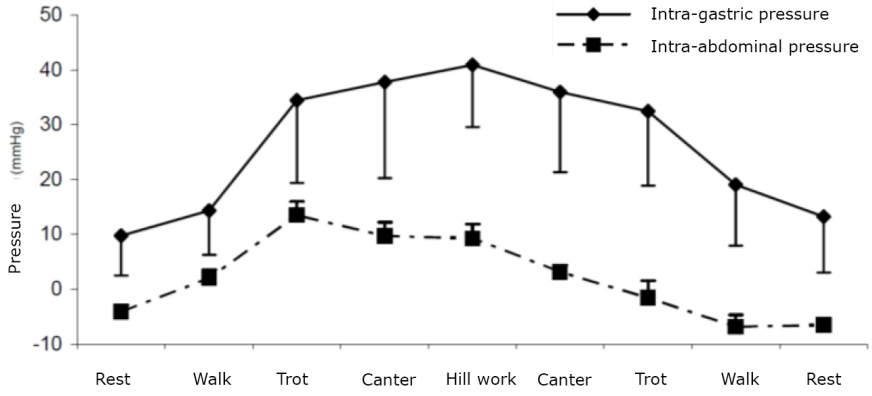
SCORE	DESCRIPTION
0	The epithelium is intact and the mucous membrane does not appear hyperemic (red) nor hyperkeratoic (yellow in the squamous region)
1	The mucosa is intact, but certain regions are red or hyperkeratoic (scaly)
2	Lesions are shallow and isolated or multi-focal
3	Lesions are severe, isolated, multi-focal or widespread and superficial
4	Lesions are widespread, with areas of deep ulceration

2. CAUSES FOR THE APPEARANCE OF ULCERS OF THE SQUAMOUS MUCOSA (NON-GLANDULAR)

a - Exercise

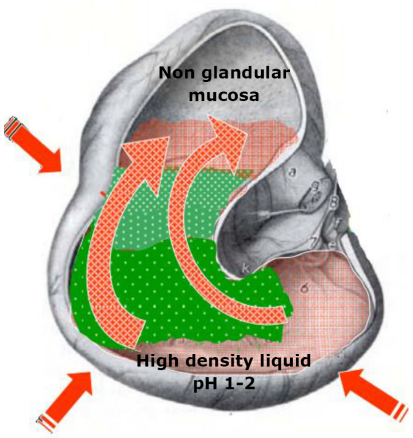
Primary squamous disorders are above all seen in the adult horse in training. During exertion, excessive exposure by the squamous mucosa to the contents is, by a purely mechanical phenomena, responsible for the formation of squamous ulcers. Indeed, when the horses moves at a faster pace than walk, the abdominal muscles contract and increase the intra-abdominal pressure, which is responsible for an increase in the pressure inside the stomach (experimentally proven, cf. the diagram next page) (2).

THE EFFECT OF EXERCISE ON INTER-GASTRIC AND INTRA-ABDOMINAL PRESSURES (2)



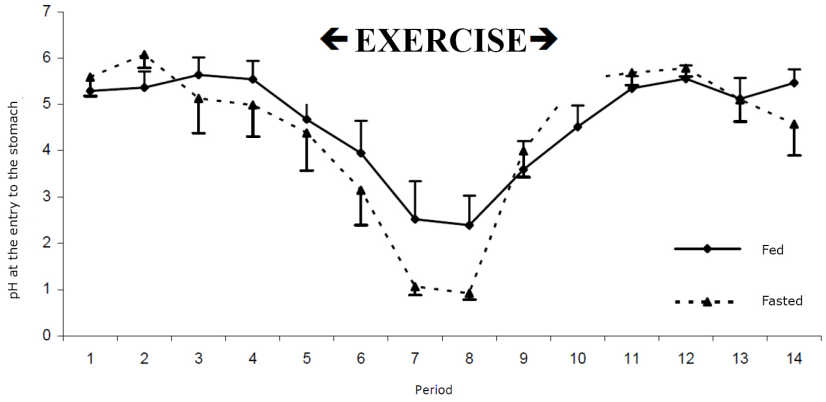
The pressure exerted on the walls of the stomach is at the root of a rise of the gastric contents towards the proximal region (top) of the stomach, thus modifying the normal stratification of the gastric contents (cf. the diagram below). The acid secretions and enzymes then damage the non-glandular mucosa, devoid of a protective barrier.

ABNORMAL STRATIFICATION OF THE GASTRIC CONTENTS FOLLOWING ABDOMINAL MUSCULAR CONTRACTIONS (1)



This hypothesis is supported by the fact that during exertion (trot, canter), the pH measured at the entrance to the stomach is significantly lower (it can reach 1.0) than when the horse is halted or at walk (where it is between 5.0 and 6.0). It should be noted that this drop in pH is even larger when the horse has a completely empty stomach (see the diagram on the next page).

VARIATION IN THE PH AT THE ENTRY TO THE STOMACH DEPENDING ON EXERCISE, IN HORSES FED BEFOREHAND OR FASTED (2)



The squamous portion of the stomach thus finds itself excessively exposed to the gastric contents. In particular the squamous mucosa close to the margo plicatus situated at the length of the lesser curvature, is more or less constantly exposed to the gastric contents, sometimes even at rest because of the anatomical disposition.

To resume, exercise is therefore directly responsible, by a purely mechanical effect, to the squamous mucosa being excessively exposed to the acid stomach contents. Also certain persons also put forward other situations that cause the horse to contract his abdominal musculature during prolonged periods (stressful environment, wind sucking) as being able to lead to a rise in the acid contents onto the squamous mucosa (source 5).

Furthermore, exercise also indirectly favours the appearance of squamous ulcers. Indeed, it has been proven that hydrochloric acid production is greater in horses in training than those at rest.

On the other hand, during punctual exercise, we observe a decrease in blood flow to the stomach mucosa. Blood is directed in preference towards muscles to the detriment of other organs. Also this drop in blood flow to the gastric mucosa rends it more vulnerable to factors of aggression.

b - Feeding

In competition horses, highly digestible and therefore quickly fermented carbohydrates (cereal flakes, wheat, oats) are often fed in large quantities. The latter are easily fermented by the flora of the stomach into volatile fatty acids and lead to a drop in the gastric pH. In an acid environment, the volatile fatty acids can easily penetrate into the cells of the mucosa even if they are not in any way damaged. Thus they acidify the cell contents bringing about necrosis (death of the cell), leading to an ulcer (source 6).

Equally of importance are methods of feeding. In his natural state, that is to say grazing, the horse does not completely fill his stomach, so the greater part of the squamous mucosa is never exposed to the acid and corrosive contents (source 7). On the other hand, current feeding practices do not always go in this direction:

- Concentrate feeds are often very few in number (2 or 3 a day) and are in consequence more voluminous: the stomach is therefore fuller, and consequently the squamous mucous membrane risks being more easily exposed to the corrosive and acid contents (7). Furthermore, it has been proven that the more voluminous and low in fibre the feed, the longer it will stay in the stomach (2). Thus, whilst eating large, high starch, low fibre concentrate feeds, the stomach becomes over full, intense volatile fatty acid producing bacterial fermentations take place and emptying of the gastric contents is retarded. The result is a prolonged contact with the very acid gastric contents by the squamous mucosa. Thus all conditions are bought together for the formation of squamous ulcers.

- If hay is not made available between feeds, prolonged periods of fasting can occur, notably at night. Now fasting leads to a rapid drop in the gastric pH and leads to prolonged exposure to acid contents by the squamous mucosa. Indeed, the continuous acid secretion of acid must be permanently neutralised by bicarbonate rich saliva and by the intrinsic buffer ability of fibre rich forage, and regarding “legume” hays (alfalfa), in calcium and in proteins. So, when forage is lacking, the continuous acidity produced in the stomach is not buffered from where there is a sharp drop in pH and ulcers are formed in a few days at the squamous mucosa level (1). Furthermore the stomach being empty is likely to favour a gastric-duodenal reflux containing biliary acids which, associated with hydrochloric acid are very corrosive to the non glandular mucosa.

These problems due to going without food are in the majority seen in stabled horses or during transport over a long distance. In this case, the long intervals between feeding favours gastric acidity. In the same way, horses turned out into sand or earth paddocks, without access to any source of forage for a good number of hours, are equally exposed to this problem.

3. PREVENTION

The objective is to fight against favouring elements by providing environmental and feeding solutions.

a - Avoid periods without food

To do this, the best means is to distribute ad-lib hay, including at night. Indeed, if a horse hasn’t got hay available during the night (frequent in yards where the last hay feed is distributed around 4 to 5pm), he is quite likely to be without food for 12 hours, so half a day! To make sure this type of situation doesn’t arise, it’s advisable to make hay available in a haynet (hung outside the stable), or a Hayball ND. It is equally possible to use a Haybar ND which can be installed in the corner of the stable.

HAYBALL

HAYBAR

b - Feed a concentrate ration that limits the acidification of the gastric contents.

In the performance horse, distributing cereals is unavoidable. However, depending on the type of starch they contain, these cereals are more or less liable to acidify the gastric contents.

Therefore, if we wish to minimise this phenomena, it is recommended to feed:

- Either a ration composed of a moderate quantity of slow releasing starch (barley) associated with a very small fraction of highly digestible, so easily fermented starch (flaked cereals, oats).
- Or a ration composed from a small quantity of very easily digested starch (oats), mixed with raw ingredients possessing important buffer qualities such as alfalfa (lucerne) (source 8). The latter possesses a strong buffer effect due to its' high levels of calcium, protein and fibre. However, it is not advisable to feed alfalfa hay ad-lib, otherwise we risk upsetting the calcium to phosphorus ratio in the overall ration, and provide excess protein, with all the harmful consequences that this can have in the horse at work (hepatic overload, excessive sweating, dehydration, etc.).

The opposite, rations composed exclusively from oats or containing important quantities of wheat, flaked cereals and molasses are totally inadvisable, being very ulcerogenic.

Next, providing fats and oils is of interest, as they participate in preventing ulcers in many different ways:

- Lipids are above all very high in energy. They increase the energy density of the ration and therefore allow provision of sufficient energy in a limited volume of feed. Thus, for a given energy value, incorporating lipids allows for a reduction in the cereal portion of the ration.
- By covering the mucous membrane, providing oil reinforces the protective barrier against attack from acid. Furthermore, if they are rich in essential fatty acids, that is to say in linolenic acid (omega 3) and in Linoleic acid (omega 6), the oil also plays a part in the nutrition of the cell membranes of the gastric wall.
- Linoleic acid (omega 6) contained in corn (maize) oil (REVERDY OMEGA OIL contains 40 %) or in extruded soya beans, is a precursor of arachidonic acid, a component from which E2 prostaglandins are synthesised.

In this way, as was proved by a study undertaken by Cargile *et al.* (source 9), providing 20 ml / 100 kg / day of maize oil rich in omega 6s (or 50 ml / 100 kg / day of REVERDY OMEGA OIL) allows an increase in stomach prostaglandins PGE2, the principal inductive agent for the production of mucus and of bicarbonates at a glandular level and also contributes to inhibiting acid secretion.

Finally, associated with a well balanced concentrate ration, the use of REVERDY CARE is of interest to limit the acidification of the gastric contents:

- The clays it contains participate in neutralising acid secretions in the stomach.
- The prebiotics contribute to limiting undesirable, volatile fatty acid and lactic acid producing, bacterial fermentations.

Furthermore, the clays plays a part in protecting the gastric mucosa.

c - Avoid the stomach becoming overfull and shorten the time the feed spends in the stomach

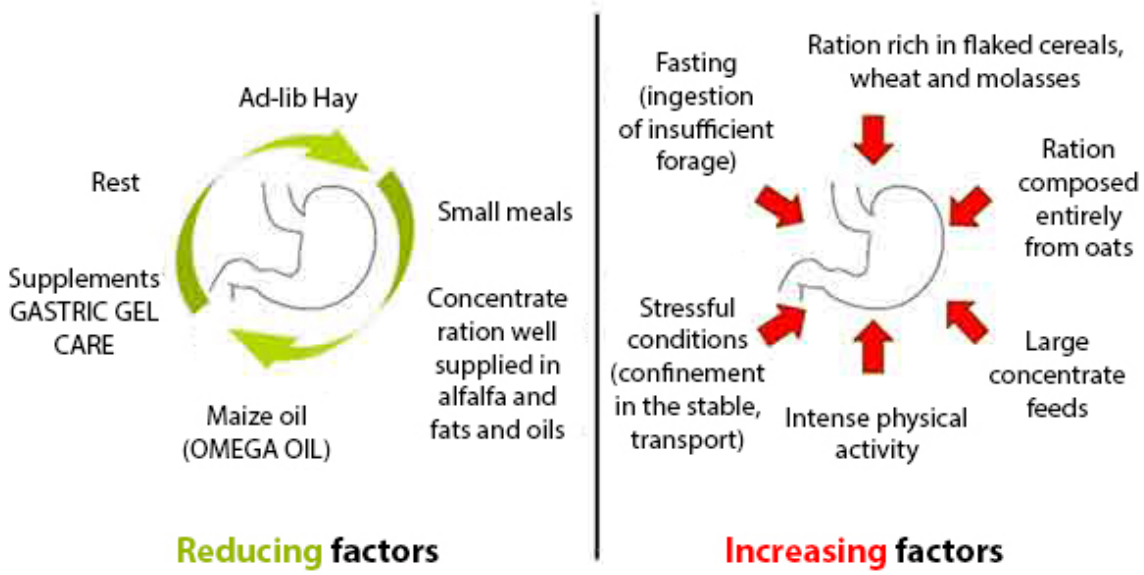
It is advisable to fraction the daily ration the maximum possible in order to feed a little each time. Feeding 3 times a day is the strict minimum in the sporting horse, knowing that the ideal is to feed via an automatic feed distributor able to provide up to 10 to 12 small feeds a day.

d - Protect the squamous mucosa against acid projections that occur during physical effort

For this, it's advisable not to work a horse on an empty stomach. Consuming forage before work, which, in addition to its' intrinsic qualities, leads to twice the saliva production than an equal quantity of a concentrate feed (8), allows effective buffering of the gastric contents acidity. In the same way, just before entering the track or the arena, administering a syringe of REVERDY GASTRIC GEL contributes to protecting the squamous mucosa from acid projections.
Indeed, when they arrive in the stomach, the aluminium phosphate and the aloe vera from which this nutritional supplement is composed will on one hand cover a part of the squamous mucous membrane and on the other settle on the surface of the gastric contents. Thus, these two digestive protectors will be projected during effort with the gastric contents onto the squamous mucosa. Because of their covering ability and cytoprotective action, they contribute to protecting the non-glandular portion of the stomach from attack by acid.

Associated with these feeding measures, turnout in lightly grassed paddocks equipped with hay racks and hay contributes to reducing the stress of being confined to the stable which increases the risk of the onset of gastric ulcers. However, completely bare sand or earth paddocks, lacking a system for forage distribution, are more harmful than beneficial for gastric disorders. Time spent in this type of paddock will be imposed fasting time for the horse.

RISK OF INJURY OF SQUAMOUS MUCOSA



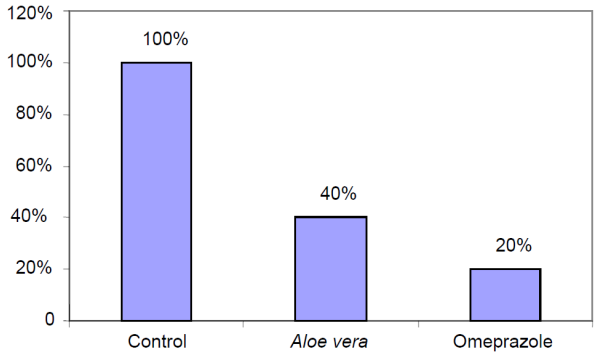
4. TREATMENT

Treatment for gastric ulcers must eliminate the clinical symptoms, promote healing, prevent recurrence and complications. It is essentially based on the use of inhibitors of the proton pump (omeprazole, lansoprazole) specifically stopping the secretion of hydrochloric acid. This family of molecules joins in a covalent fashion to this pump and for the entire lifespan of the cell. Thus, all the while the cell does not synthesise new pumps, acid secretion cannot resume. This explains why a single daily dose of proton inhibitors is sufficient (source 10).

Associated with this medical treatment, applying the measures described in Part 3. "Prevention" will contribute to accelerating the healing of non glandular squamous ulcers and then help avoid their recurrence. More particularly, the daily use of GASTRIC GEL will act as reinforcement to the action of omeprazole. It is composed from four active ingredients each with complementary properties:

- Principal ingredient, **Aloe vera gel**, contains lectins which inhibit acid secretions of the stomach by acting directly on the parietal cells. The tannins, saponins and flavonoids which it contains can be responsible for its' cytoprotective action and anti-inflammatory properties on digestive mucosa. A study (11) undertaken in rats showed that aloe vera possessed significantly comparative antiulcer activity to the "reference" treatment omeprazole (at a therapeutic dose). On the diagram below, the number of lesions induced by the administration of non-steroidal anti-inflammatory drugs in the control group represents the reference and has the score of 100 %. Even if omeprazole remains the most effective treatment with 80 % less ulcers, preliminary oral administration of Aloe vera is very interesting as 60 % less lesions are obtained compared to the control group.

THE EFFECT OF ALOE VERA AND OF OMEPRAZOLE IN PREVENTING ULCERS FOLLOWING THE ADMINISTRATION OF A NON-STEROIDAL ANTI-INFLAMMATORY DRUG, COMPARED TO A CONTROL GROUP (source 11)



- **Aluminium phosphate** has strong covering ability and lines the gastric mucous membrane. Indeed, it has been scientifically proven that this cytoprotector stimulates the synthesis of endogenous prostaglandins which, in addition to favouring mucus and bicarbonate secretion, reduce acid secretion and increase mucosa blood flow, thus aiding healing. It also leads to the liberation of sulfhydryl radicals, maintaining the integrity of the mucous membrane (source 12).

- **Glutamine** represents an important energy source for fast renewing cells, such as the cells in the digestive tract. This amino acid thus participates in maintaining the integrity of the gastric mucous membrane and helps heal ulcerous lesions.

- Playing the role of prebiotics, **fructo-oligosaccharides (FOS)** contribute to maintaining healthy conditions in the stomach.

TO SUM UP

The use of the horse for racing and equestrian sport associated with changes to feeding habits, goes a long way to explaining the high prevalence of gastric ulcers in the athletic horse. This pathology is a big problem as in addition to being detrimental to the well being of the horse, it is responsible for poor performances that have important economic repercussions.

Thus the management of gastric ulcers necessitates the putting into place of environmental preventative measures, limiting stressful conditions such as being confined to a stable, and above all nutritional measures. Amongst these latter, we retain, ad-lib forage, small concentrate feeds containing plenty of alfalfa (lucerne), oils and fats rich in essential fatty acids, and containing moderate quantities of slow releasing starch or small quantities of easily digested starch. The daily ration can be given further security by feeding nutritional supplements, REVERDY CARE and REVERDY GASTRIC GEL.

Finally, it is interesting to note that the bacteria Helicobacter pilori recognised as being responsible for gastric ulcers in Man has, to this day, an undetermined pathogenic role in the horse. Certain persons such as, Scott *et al.* (source 13), advocate in favour of the existence of a Helicobacter in the horse but further research needs to be undertaken.

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