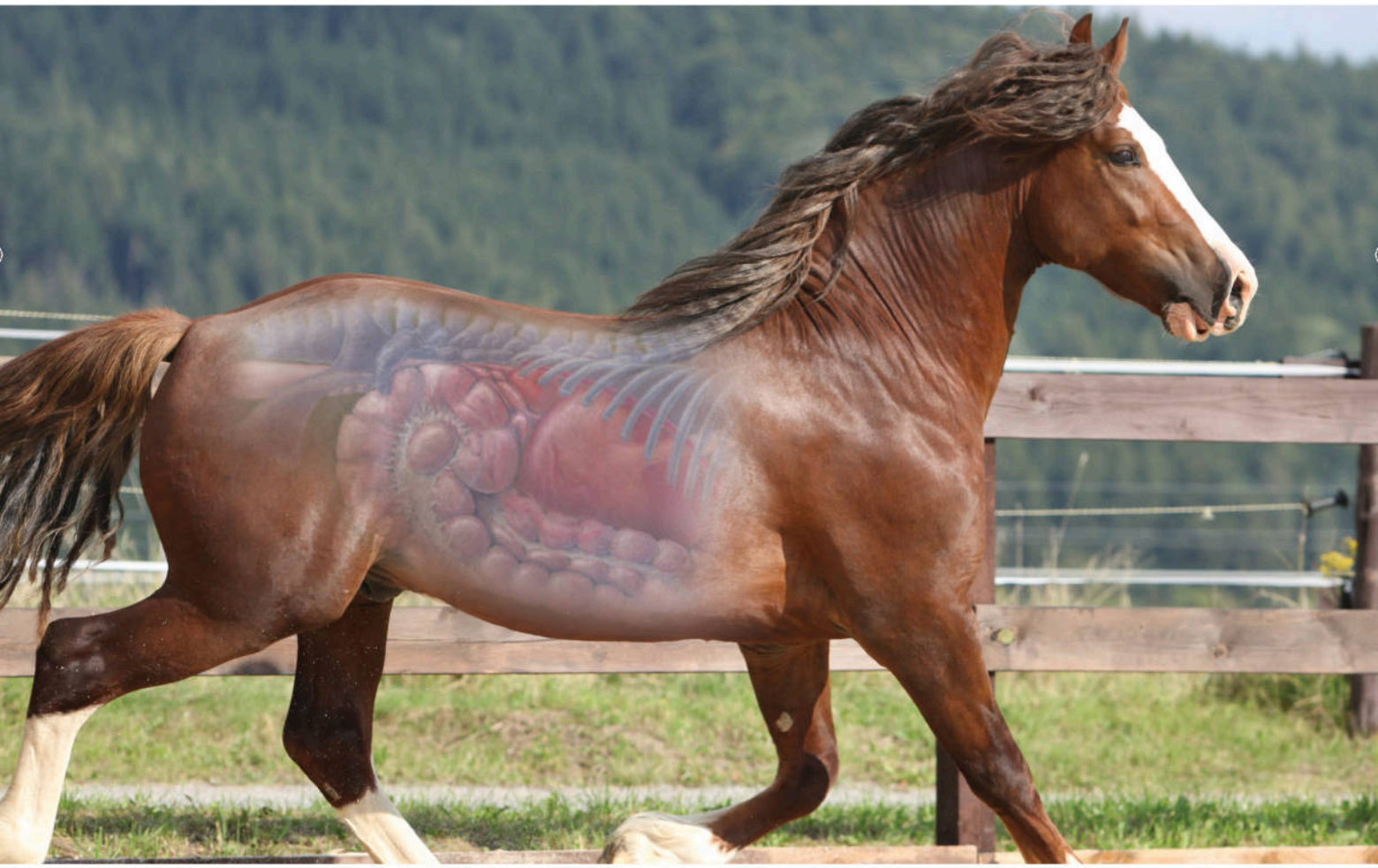
equine HEALTH

Digestive health and the modern horse

Exploring current research and methods of diagnosis, care and management



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Introduction

By Professor Derek Knottenbelt

Gastric ulceration appears to have increased in incidence over the last 90 years with a significant increase in the clinical recognition, treatment and welfare implication of the condition in horses, particularly over the last 20 years. This has coincided almost exactly with the availability of high-quality endoscopes capable of reaching the stomach and the duodenum even of large horses. Historically gastric ulcers were recognised post-mortem but were widely viewed as either 'incidental' or of no significant clinical importance. In modern equine practice this is far from the case where there are large numbers of publications relating to the grading of squamous and glandular ulceration.

Gastric ulcer syndrome

There is strong evidence to suggest that gastric ulcers have become increasingly prevalent in the horse population to the point now where up to 80 to 90% of stabled horses and indeed a significant proportion of grazing horses, have detectable ulceration. The reason for this ulceration is by no means clear. The ECEIM Consensus statement (Sykes et al. 2014) makes it clear that the causes are conjectural rather than definitive, but that excessive gastric acidity is an incontrovertible aspect of the disease. It is however, not clear what else could be involved nor indeed why gastric acidity and the consequent ulceration, develops so quickly.

A paper presented by Andrews (2014) at the American Association of Equine Practitioners Convention, identified that within a day or two of moving ostensibly normal horses from a pasture circumstance to a stabled circumstance, ulceration was found in the large majority of the horses. This very dramatic onset of ulceration is a well-recognised feature in Thoroughbred and other performance horses where ulceration is now accepted as being almost "normal" for them. This in turn means that they require medication to control the condition. Given that we still have no really convincing evidence for any specific cause for this dramatic change, and given that long-term proton pump blocking medication is now regarded as a necessary component of race horse management, there has to be something wrong. There is clearly a bias towards the diagnosis and treatment of a condition that does not commonly occur in normal, natural grazing horses. A study carried out by Vatistas et al. (1999) showed that the severity of ulceration in the horses given active omeprazole was significantly reduced at 13-17 days and 27-31 days. However, ulcers that had been completely eliminated subsequently returned when re-examined between 7 and 14 days after removal of the medication. Ulcers seem to be a more or less inevitable consequence of the management of racing Thoroughbred horses. Grazing horses have a very low incidence of gastric ulceration, but within a very short time of commencing performance training, they became almost a natural event.

Routine medication

Why do gastric ulcers develop in the first place and, is there any way in which we can prevent their occurrence so that horses in high performance training can be viewed as healthy, as opposed to unhealthy and 'under medication'? In some parts of the world, it has become common practice to accept the use of proton pump blockers in performance animals and withdrawal is not required; this simply condones the ongoing welfare concerns of the management methods of performance horses in particular. The counter argument to this is of course that gastric ulcers are 'normal' - at least to some degree but it is certainly true that the vast majority of non-performance horses maintained under completely natural circumstances, do not develop significant gastric ulceration.

We also know that long-term medication is almost essential – even short-term withdrawal of the medication results in a significant deterioration in the ulceration grade, since some of the drugs used to control gastric ulceration have to be withdrawn before racing or other performance events, the management of high-performance horses in particular becomes a welfare concern. The effect of long-term reduction of gastric acidity in a mono gastric animal is unknown, but is certainly abnormal in terms of the evolutionary development of the dietary process in horses. It is time that rather than looking at ways of medicating ulcers in horses, we spent more time looking at the reason why they develop in the first place, and try to find ways of avoiding the need for continuing medication.

The intestinal tract

The next big issue relating to the current management process of horses is the fact that, although much attention has been focused upon the stomach, very little is known about the rest of the intestinal tract. There are however, some very well recognised syndromes that relate to overt symptoms of intestine or malfunction, such as salmonella or clostridial colitis. These also include various forms of inflammatory bowel disease such as idiopathic focal eosinophilic enteritis and right dorsal colitis, and of course,

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the almost ubiquitous, parasite related inflammatory bowel diseases. Although the serious acute pathologies are recognised, the diagnosis of most these conditions however remains problematic. Even the serious forms of cyathostominosis are largely diagnosed on the basis of clinical signs and history alone. The definitive diagnosis may rely on access to the bowel for biopsy - the large majority of the commoner conditions diagnosed either by inference or by exclusion, or by direct examination during laparotomy or laparoscopy, and histological examination of samples of the bowel wall. Rectal biopsy has been used widely but it is subject to variation, error and misinterpretation (Sloet and Grinwis, 2014). Many of the more subtle disorders are not easily diagnosed even with all the current endoscopic / laparoscopic or ultrasonographic technology. Diagnosis of the conditions are however, also only identified at necropsy and this is clearly a major challenge for the veterinary profession.

The rather vague and non-specific signs that are involved in large colon disease in particular make the diagnostic process even more complicated and, there is an element of "out of sight, out of mind" for both owners and vets. As an example of the difficulty of clinical diagnosis, the term spasmodic colic is used when mild or sometimes even moderate colic responds to simple analgesic or antispasmodic drugs. The problem is that there is no REAL diagnosis in the disease – what is it and is it always the same? How many of these so-called drug-responsives are for example, focal eosinophilic enteritis and how many are partial non-strangulating obstructions? What actually is spasmodic colic? Would we be able to identify the condition if all such colic cases were subjected to immediate laparotomy? The same could be said for the condition that is recognised as right dorsal colitis - what exactly is it and why does it develop? Is it possible that these conditions are a result of our very unnatural management of horses? How many wild or feral horses will be affected by right dorsal colitis or eosinophilic enteritis?

Diagnostic limitations

Since our management of horses clearly results in significant gastric pathology, we have to expect that the management also has an influence on the rest of the alimentary tract. The proportion of the tract that is examinable by any means is very small – the remaining 23m of small intestine and the whole of the large intestine and caecum as well as the small colon is largely a diagnostic black hole. The diagnostic options include ultrasonography per rectum or transcutaneous or auscultation, rectal biopsy and palpation per rectum. As a result of this difficulty, few conditions are recognised as affecting the large colon in particular, and even fewer have been accepted as being of clinical significance – is this because we don't really want to complicate an already difficult situation? We need better and more convenient indicators of intestinal pathology.

As a diagnostic test, the feacal occult blood test can be compared to the thermometer, which has proved invaluable in identifying patients with fever and remains one of the most significant tests in clinical examinations. It does not however, by itself, make any further contribution to the diagnosis but, is frequently used to monitor the progress of a disease once a diagnosis had been established by clinical acumen. The thermometer has absolute sensitivity but a very low specificity. Finding an elevated body temperature stimulates the clinician to investigate the possible causes of fever. The same diagnostic implications and limitations are inherent in the use of the faecal occult blood test from Freedom Health (SUCCEED™ Equine Fecal Blood Test™). It can be viewed as a broad screening test and, under no circumstances, should it be used to establish a categoric diagnosis of a specific disorder. This is a highly sensitive but non-specific test which leads the clinician to the application of clinical acumen in the exploration of the clinical circumstance and hopefully, to a specific diagnosis. Once the diagnosis has been made the test can perhaps be used again as a means for monitoring the effect of treatment or management measures.

The possibility of large colon disease should always be considered – there is more pathology to be found in the intestine or tract beyond the stomach than there is in the stomach itself, and yet there is so much focus on the stomach. We need to broaden our diagnostic horizons and we need to explore the range of pathologies in the large colon in particular, since the horse is highly reliant upon the large colon for much of its digestive efficiency. This also becomes even more important when horses are maintained on persistent medication for gastric ulcers. It is almost inconceivable that there would be no implication from the sustained (possibly even life-time) reduction in gastric acidity. The more important issue here is that prevention of gastric ulcers would probably lead to a more healthy intestinal tract in general, and probably fewer pathological states. There is little published information regarding 98% of the alimentary tract, and an enormous and burgeoning body of information and data regarding the stomach. Surely this is the wrong way round.

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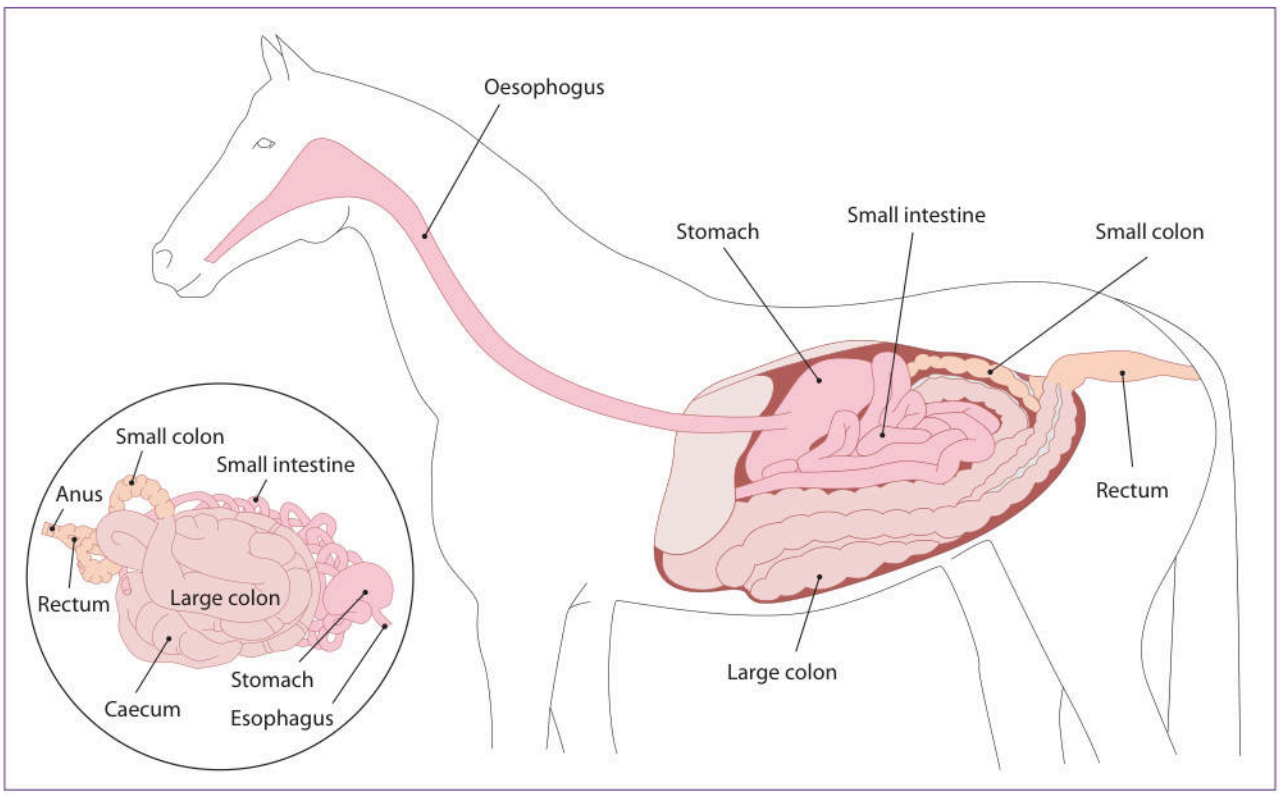
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The equine digestive system and the importance of the hindgut

By Dr Helen Warren



The equine digestive system - inset shows view of the right side to reveal the caecum

The digestive tract of the horse has evolved to digest dietary fibre. It is well adapted to grazing and browsing forage feeds during numerous short feeding periods totalling around 16 to 18 hours a day. This has led to the term 'trickle feeder' being applied to the horse's natural eating behaviour.

The digestive process

The horse is characterised as a hindgut fermenter because the hindgut is where the majority of the digestive processes take place. Rapid gastric passage through a relatively small stomach and limited intestinal enzymatic digestion, precedes a more prolonged and intense microbial fermentation in the large intestine (Santos et al., 2010). The basic anatomy of the gastrointestinal (GI) tract is similar to that of other non-ruminants with prehension of food and water by the lips and mouth, followed by mastication and insalivation. The resultant food bolus is then swallowed. The stomach is relatively small given the size of the horse with a capacity of only around 8 litres. The stomach also secretes acid continuously, accommodating the nearly continuous grazing lifestyle. Another interesting feature is that the stomach will start to empty into the small intestine (SI) when around two thirds full, irrespective of how long the food has been in situ. The horse is ideally adapted to making use of the 'wild-type' or natural diet. Whilst it naturally feeds 'little and often' the modern practice of fewer, larger meals, means that food can enter the SI having been subjected to little or no gastric digestion.

Once ingesta has entered the small intestine (SI) enzymatic digestion of carbohydrates, proteins and lipids is similar to that of other mammals although the nature of the

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food means that there is relatively less value derived from digestive process compared to other species – the horse therefore, has a relatively long small intestine (over 23 metres in length for a 500kg horse).

The lack of a gallbladder is a further adaptation to the 'trickle feeding' phenotype. It is suggested that this results in continued trickling of bile and almost continual passage of small amounts of digesta through the GI tract. Bile is secreted from the liver in response to continued gastric filling – starvation results in the near cessation of secretion of bile and a concomitant increase in the bile pigment, bilirubin, in the blood stream. Various mechanisms for this process have been put forward, including a reduction in bilirubin uptake by the liver (possibly through competition with increased circulating non-esterified fatty acids (hyperlipidaemia) during starvation or fasting) (Engelking, 1993).

Of the nutrients entering the SI, non-structural carbohydrates in the form of starches and sugars have received considerable attention with regards to intestinal health. The natural diet of low quality fibrous grazing contains few of these soluble compounds and the horse therefore, has a limited capacity to digest them at any one time. The small intestine has some difficulty in dealing with concentrate meals (coarse mixes, straights etc) containing more than 3-4g starch 1992); this is commonly known as 'starch overload'. Most modern horse pastures are of higher nutrient quality, suitable for grazing production livestock. These supply high levels of energy and protein, which creates a problem for more native animals that for various reasons, are often under-worked. Further, horses naturally exercised only in short bursts of activity when under threat from predators, for example, so had little need for such high energy food sources. This is in stark contrast to today's modern horse which is often required to carry out sustained intense exercise and is routinely fed 'starchy' meals providing sufficient energy to maintain output. The current recommendation is to feed no more than 1g starch per kg of bodyweight per meal (Vervuert, 2009). The key is 'little and often' - a mantra that has not changed for decades.

Nutrition and energy

Horses can satisfy most of their nutritional requirements from digestion and absorption from the SI, but the hindgut provides a substantial contribution to energy requirements via volatile fatty acids (VFA) generated from microbial fermentation and, represents nearly 70% of the total digestive tract. The colon is around 6 to 7 metres long and has four distinct anatomical sections, each separated by a bend or flexure. These flexures are often implicated in intestinal impaction leading to colic. At the junction between the ileum and large colon lies the caecum. There are differences between the anatomical sections of the hindgut with regards to microbial populations and subsequent fermentation (de Fombelle et al. 2003) but the microbial fermentation of fibrous feed occurs throughout the hindgut. Acetate, propionate and butyrate are produced in the hindgut and diffuse across the LI wall to contribute around 60-70% of the horse's energy requirement - propionate is gluconeogenic and acetate and butyrate are lipogenic. Proportions of these VFA will vary according to the dietary fibre content (Vermorel and Martin-Rosset, 1997). Changes in diet will alter the fermentation pattern in the hindgut environment altering the pH, sometimes with detrimental effects. Cellulolytic bacteria require a near-neutral pH, but large quantities of undigested soluble carbohydrates reaching the hindgut result in abnormal fermentation with lactate production. Lactate has a lower pKa compared with either acetate or propionate and thus, results in a quicker and greater reduction in pH. This can lead to hindgut disturbances, such as colic.

Normal function

The maintenance of normal gut function is dependent upon a combination of management and animal factors, and it is critical to ensure that the supplied feed is as close to its natural feeding pattern as possible. Disruption of normal hindgut function through reduced dietary fibre or increased dietary starch can result in reduced buffering capacity, and a potentially pathological decrease in caecal and blood pH, possibly leading to acidosis. Additionally, much of the caecal microbiota cannot survive in this low pH and as they die, they can release bacterial endotoxins into the blood stream. Acidosis results from a lowering of the blood alkali reserves. Many horses on low forage high energy diets suffer from a sub-clinical form of acidosis; this particularly affects those in hard work with limited access to forage. Gut disturbances, such as acidosis, are one of the many factors implicated in colic.

Acidosis is a symptom of many hindgut perturbations and it is suggested that the prevalence of hindgut conditions is significantly underestimated. Much focus has been placed recently on equine gastric ulcer syndrome (EGUS) and there has been an increasing amount of research into incidence, potential causes and prevention. It is recognised that around 80-90% of racehorses have some form of gastric ulceration (Vatistas et al. 1999; Bell et al. 2007). Acid making its way from the gastric portion of the stomach to the relatively unprotected squamous portion is reported to be the cause of the majority of ulcer cases but, ulcers do also occur in the lower glandular portion. Numerous risk factors for development of gastric ulceration are suggested including dietary management, exercise, stress and, in some cases, prolonged use of non-steroidal anti-inflammatory drugs (NSAIDs). However, some clinical signs commonly ascribed to the presence of gastric ulcers may have their origin elsewhere in the gut, and in particular the hindgut. One such sign is the horse objecting to having the girth tightened.

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Colonic ulcers - overcoming the diagnostic challenge

By Dr Helen Warren

Despite the extensive research in EGUS, very little is known about colonic ulcers and inflammation, their incidence and effective treatment and prevention. Colonic ulceration can lead to similar performance-inhibiting effects as gastric ulcers but are difficult or impossible to diagnose, mainly due to their inaccessible anatomic location.

Diagnostic options

Gastroscopy is a simple and routine procedure but only reaches the duodenum. Colonoscopy is very difficult and seldom used, and in any case, has very limited diagnostic value as it would be limited to the small colon only. This state of affairs has led to the increased detection of gastric ulcers compared with hindgut issues. The stomach just happens to be the part that we can now 'see' easily in a living animal. This point is illustrated by a study carried out by Pellegrini (2005). Subclinical anaemia was being detected in a large number of racehorses, which prompted the first large-scale necropsy study into equine colonic ulcers (Pelligrini, 2005). The digestive tract was examined in 545 horses. Three hundred and sixty five horses were of mixed breed and use, while 180 were classified as performance horses and were accompanied by a standard guaiac-based faecal occult blood test (gFOBT). As expected, the performance horses were more heavily afflicted by gastric ulcers than their more sedentary counterparts (87%, and 55% respectively) but, interestingly, the same trend was found for the incidence of colonic ulcers (63 and44%, respectively). Overall, 97% of the horses necropsied were positive for some form of ulceration and at least 60% displayed colonic pathology.

The correlation of necropsy with the gFOBT demonstrated the potential for a non-invasive test for the detection of non-gastric ulceration/inflammation. Indeed, the specificity for any type of ulceration was 100% (Pellegrini, 2005). Furthermore, the study showed that when there was a positive gFOBT but no gastric ulceration, then colonic ulcers were always present.

The gFOBT detects the haeme portion of the haemoglobin in any occult blood in the faeces. There is no differentiation of where that blood has originated from, therefore, it could be from either gastric or hindgut sources, or both. This test is not a definitive diagnosis per se, but more a valuable aid



Colonic cherry ulcer

in diagnosis. Could this be a useful field-based test that, in combination with other diagnostic tools (such as endoscopy), could support the possible diagnosis of colonic ulcers to be detected and then treated? After all, gastric ulcers only became a real issue after the development of a flexible endoscope long enough to reach the stomach (Knottenbelt, submitted). Why should disturbances elsewhere in the GI tract be ignored simply because we have no definitive diagnostic test? Hindgut aberrations are by their nature difficult to diagnose and are likely to be underestimated, so simple, non-invasive tools that allow veterinarians to piece together some of the symptomatic puzzle should be welcomed.

In humans, the gFOBT is used for the detection of many GI disturbances, including colorectal cancers but its use has been superseded in some regions by more sensitive tests, such as the faecal immunochemical test FIT) (Brenner and Tao, 2013, Carroll et al., 2014), as well as faecal protein markers and faecal DNA/RNA testing (Carroll et al., 2014). Advances have been made in the equine field also.

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In an attempt to improve diagnostic value to the standard FOBT, a test that detects both haemoglobin and albumin has been developed (SUCCEED™ FBT™, Freedom Health, Ohio, USA). The test is designed to differentiate between hindgut and foregut aberrations. Essentially a faecal occult blood test, the SUCCEED™ FBT™ uses ELISA technology as part of a lateral flow assay to detect two proteins within a specified range; albumin and haemoglobin (both equine specific). It is the differentiation between these two components that can be used to identify where the issue is likely located along the gut. Haemoglobin detected in the faeces may have originated from bleeding anywhere along the GI tract, however, proteolytic enzymes released into the duodenum breakdown any albumin present. Therefore, any albumin present in the faeces must have originated from tissue damage within the LI. This differentiation can be used, not only to determine that an issue exists but also to pinpoint roughly where along the GI tract the issue lies. Positive tests for both haemoglobin and albumin indicate a definite hindgut but also possible foregut issue, whereas a positive haemoglobin but negative albumin result indicates foregut aberrations and would indicate other diagnostic tools, such as endoscopy should be employed. Conversely, positives for albumin but not for haemoglobin probably suggest hindgut issues only.

Prevention is always better than cure

The area of animal welfare provides a significant contribution to animal research. Much of this research focuses on behaviour and environmental conditions. However, thought is now also shifting from the treatment to the prevention of disease as a key welfare goal. Historically, the role of the veterinarian has been to simply treat symptoms and disorders with which they are faced but the belief is increasingly that the focus should be on promoting management practices to reduce the incidence of disease. This is particularly evident and effective in the field of nutrition where a greater understanding by horse owners on the critical importance of dietary fibre has been achieved. Despite this, there also seems to be an acceptance of many of the negative aspects of modern horse management without investigation into their cause(s) or mitigation strategies. A case in point would be the gastric ulcer syndrome. The ability to 'see' gastric ulcers, grade their severity then prescribe a seemingly effective drug is obviously a good thing but do we not owe it to the horse to investigate definitive risk factors, causes and aetiology?

A study carried out by Kerbyson et al. (2014) investigated the effect of a nutritional supplement (SUCCEED™) on the development and treatment of squamous gastric ulceration in racing Thoroughbreds. Horses recruited onto the trial had been diagnosed with gastric ulcers (via gastroscopy) but with no clinical signs or history of treatment. Allocated to one of two treatments (omeprazole or SUCCEED™, both administered according to manufacturer's recommendations) horses were scoped again on days 30, 60 and 90 of the trial. By the end of the trial there was no significant difference between the omeprazole and SUCCEED™ treatments. The fact that a nutritional supplement (a combination of polar lipids and β-glucans) had the same effect as a commonly prescribed drug does seem to pose the question as to whether we truly understand the aetiology of gastric ulcers. Was the omeprazole truly effective or was the nutritional supplement providing prophylaxis in some way? What are the implications of long-term use of proton-pump inhibitors? Acid production is a natural part of the digestive process and restricting it for long periods has its own potential negative consequences that so far have not been seriously addressed. More research is needed to answer these questions. What we do know however, is that better management, detection and prevention strategies are required in the war against a wider range of GI tract aberrations.

Drugs undoubtedly work rapidly and results are often seen almost immediately but dietary adjustment takes longer since the GI tract and its associated elements require a longer-term approach to adapt to the available foods. If horses are to be kept and used for performance and enjoyment, should we not look at blueprints for best management practices rather than defaulting to drugs to treat the resultant disturbances? There are, of course practical and economical restrictions in many instances but reducing the over-reliance on prescribed drugs has to be beneficial for all involved.

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The need for a reliable diagnostic test for GI tract disorders

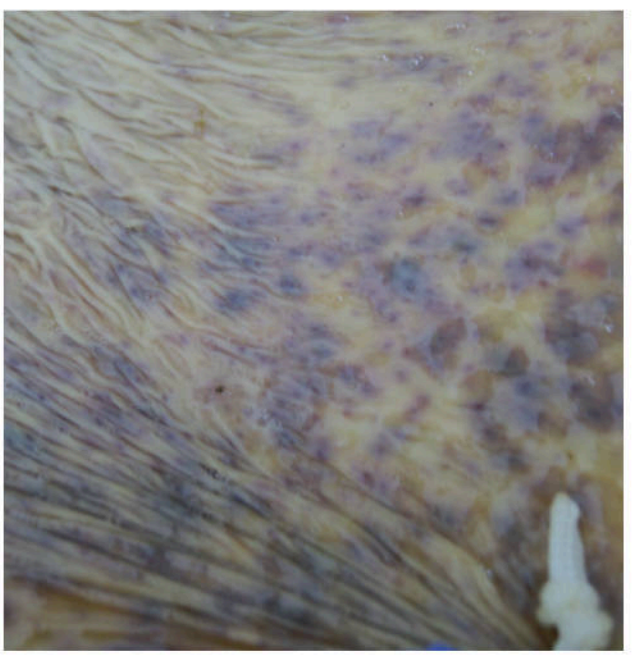
By Dr Emma Hardy

Extensive research conducted by Freedom Health LLC, and independently at the University of Glasgow School of Veterinary Medicine, is shifting the spotlight in equine gastrointestinal (GI) disease towards the hindgut, and specifically disorders of the mucosal lining. Still, these disorders remain largely under-reported. Indeed, the number of published articles relating to gastric ulcer syndrome over the past year number in the region of 900, whilst those published in reference to colonic inflammation and/or ulceration number just nine. This under diagnosis is due in part to limitations on current diagnostic techniques (Pellegrini, 2005):

- Gastroscopy, a now commonplace procedure, allows for visualisation of the stomach and proximal duodenum only, leaving the remaining 70 feet of small intestine plus the caecum and colon unobserved.
- Colonoscopy beyond the distal portion of the colon would carry with it a high risk of mortality, due to its highly invasive nature and the evacuation of the bowel required for this procedure (Kerbyson et al. 2014)
- Abdominal ultrasonography is routine in the diagnosis of colitis, where thickening of the colon wall and submucosal oedema is highly characteristic. However, this remains an in-patient procedure, and the interpretation of the image is very dependent on the experience and skill of the operator (Glavin et al. 2004)
- Rectal biopsy, a particularly invasive procedure, has been found to be useful in the diagnosis of intestinal disorders (Lindberg et al. 1996) but, whether a biopsy might histologically reflect the mucosa/submucosa of the more cranial intestinal tract is questionable (Peek, 2010).

Colonic ulceration and inflammation can elicit a range of symptoms, from hindgut discomfort and recurrent colic to loss of performance and condition and even, behavioural and lameness issues (Pers Comms). Often these symptoms, which are frequently vague and non-specific, are attributed to alternative causes. As a result, by the time consideration is given to a disorder of the GI tract, and specifically of the hindgut, the health of the horse may be at a critical stage with limited treatment options, carrying greater risk to the animal and cost for the owner. By understanding a disease process at an earlier point, and having a reliable method to aid diagnosis, proactive steps can be taken to correct



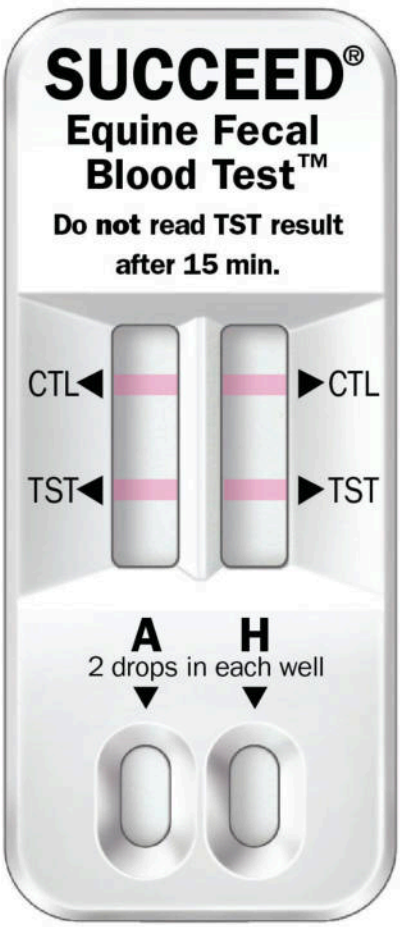


Above; The SUCCEED™ FBT™ can indicate conditions which may otherwise be undetected

Table 1 Interpretation of FBT results

Results	Negative albumin	Positive albumin
Negative haemoglobin	No detectable bleeding	Hind gut bleeding
Positive haemoglobin	Foregut bleeding	Hind gut and possible foregut bleeding

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The SUCCEED ™ FBT includes a test for equine albumin and one for equine haemoglobin

it. This gives rise to the importance of reliable diagnostic methods for gastrointestinal disease.

A faecal test provides an initial screening

The SUCCEED™ Equine Fecal Blood Test (FBT) is a diagnostic aid which, in conjunction with the veterinarian's expertise and other diagnostic measures, helps to achieve a diagnosis for GI tract disorders. The completely non-invasive stable-side test detects occult equine albumin and haemoglobin in a faecal sample. These marker proteins serve as indicators of gastrointestinal conditions, wherein their presence in a faecal sample indicates the presence of inflammation and/or blood loss.

Because of differences in the nature of albumin and heme, the presence or lack of these proteins serves to indicate where in the equine GI tract they originate. Albumin, but not heme, is naturally degraded by acids and proteinases (Carter & Pellegrini, unpublished) which are introduced into the small intestine via the common bile duct at a point just past the stomach. As a result, detection of albumin in a faecal sample serves as a proxy for inflammation in the hindgut. When the two markers are evaluated together they can enable conditions to be pinpointed as foregut, hindgut, or both *Table 1*.

The FBT is highly sensitive but non-specific. Akin to a thermometer, it is intended to be an indicator of disease rather than confirming a specific disorder. It has been developed to initiate the process of diagnosis, which in turn, helps the clinician to select the most appropriate and effective additional investigations and best treatment options for optimal recovery.

How is the FBT used?

The FBT is entirely self-contained, requires no laboratory analysis or additional processing and, has been designed to be easily used at the point of care. This also negates the need for a horse to be transported to a clinic for testing, or even for a vet to attend should a fresh faecal sample be provided to the practice for immediate testing. The FBT takes the form of a two-part test cassette, packed inside a plastic screw top bottle (used for sample collection) along with a pipette, vinyl glove and set of instructions. The cassette contains two wells, and two wicking/viewing windows, one each for detection of albumin and haemoglobin. Two drops of the faecal sample and water solution is placed into each well, and the results appear within 15 minutes.

The FBT detects blood components from any source. While the presence of blood proteins in a faecal sample likely derive from the GI tract, care should be taken to ensure the FBT is not run in situations where blood may be introduced into either the GI tract or the faeces from external sources.

Development and validation

Faecal blood testing originated from human medicine, where guaiac stain was used to detect the pseudoperoxidase activity of the heme portion of haemoglobin, and initial studies investigating the incidence of colonic ulceration in horses employed this

Table 2 PPV, NPV and p value for the FBT as a predictor for gastric or colonic disease

	Positive predictive value	Negative predictive value	p-value
Albumin (predictive for colonic disease)	95.4%	75.0%	0.04
Haemoglobin (predictive for gastric or colonic disease)	96.9%	57.9%	0.03

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method. This technique however lacked sensitivity and some question existed over the possibility of false positives resulting from chlorophyll in the equine diet mimicking peroxidase molecules (Sinatra et al. 1999). The FBT overcomes these limitations by using an immunoassay (ELISA) with highly specific antibodies raised against equine heme and equine albumin.

Several hundred post-mortem examinations were conducted in the process of correlating FBT findings to actual pathology of the gastrointestinal mucosa. The protocol involved collecting and testing faecal balls using the FBT and then correlating the results with independent visual observations of the stomachs and large colons of the subject horses. The statistical reliability of the test was calculated based on the results of the most recent necropsy study in October 2011 with 178 horse subjects *Table 2*.

These data illustrate the highly sensitive, minimally specific nature of the test. Only 11 horses of the 178 investigated did not show some kind of ulcerative, proliferative or haemorrhagic lesion in either the stomach or colon. This low number of true negatives influenced the calculation of the NPV number.

The importance of the FBT as a diagnostic aid is not limited to GI tract ulceration. It can be used to facilitate diagnosis of numerous GI tract disorders, characterised by a loss of protein or whole blood, and to monitor recovery, and even efficacy of treatment options. The FBT is routinely used to help provide more information in horses with suspected colitis, IBD, colic, unexplained loss of weight/condition/performance, changes in temperament, and protein losing enteropathy. The scope of the FBT is also not limited to only faecal testing. In the event of a hypoalbuminaemia, simple FBT testing of both faecal and urinary samples can help identify the presence of an enteropathy or nephropathy.

Due to its supporting role in diagnosis of disease, the SUCCEED™ Equine Fecal Blood Test™ is available only to veterinarians.

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Supporting the digestive system with a nutritional supplement programme

By Dr Emma Hardy



Specific nutrition, feeding and management regimens are required to meet the high demands placed on today's performance horse. A diet high in energy-dense non-structural carbohydrate, but often lacking in sufficient fibre and fed intermittently, combined with prolonged stabling and the stresses that exist alongside training, competing and travel, all pose risks to digestive health.

Although the methods of feeding and management for optimum performance have evolved rapidly over the past few decades, the equine digestive system remains unchanged. Unfortunately, low stress lifestyles, and trickle fed diets exclusive in fibre can be very difficult to implement and, are often not conducive to managing top competition horses. SUCCEED™ Digestive Conditioning Program™ was developed in response to the need to be able to feed and manage for success, while reducing the risks carried with it.

How modern management and feeding can affect the digestive tract

Various aspects of the digestive system and digestive process are negatively affected by modern feed types, feeding and management routines.

Intensive training has long been recognised as posing some risks to digestive health. It is well accepted that race-horses for instance, have the highest prevalence of gastric ulceration (Hammond et al 1986, Vatistas et al 1999).

High intensity work goes hand in hand with stress, and high levels of cortisol that can not only contribute

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to immune dysfunction and pro-inflammatory responses within the gut, but also reduce the positive effects of prostaglandin E (Breazile 1987); an important hormone which helps to produce bicarbonate ions to neutralise gastric acid and, helps to maintain adequate mucosal blood flow and mucus production. Mucosal ischemia may result in tissue necrosis and the development of inflammation and ulceration (Navab & Steingrub, 1995).



Salivary bicarbonate ions are important for digestive health (Konturek et al. 2011) and their abundance is closely associated with mastication. For the horse, the act of chewing is not only important to meet behavioural needs, but also to ensure an adequate production of saliva and, in turn, bicarbonate and sodium chloride to help to buffer digesta. The type of diet becomes a determinant in chewing time, with structural carbohydrates requiring 3 to 4 times longer for the horse to ingest, when compared to the same quantity of non-structural carbohydrate (Frape, 2004). Intermittent feeding poses further problems, particularly if also given in large volumes. Horses fed in this way can have a greater tendency to bolt their feed leading to increased transit rate through the GI tract, and decreased nutrient absorbency (Feige et al 2002).

Gastric acid – good or bad?

Horses produce gastric acid continuously, coinciding with the horse's natural feeding pattern of continuous grazing. When the grazing lifestyle is replaced with intermittent "meals", this continuous flow of acid becomes, in effect, "excessive." The problems with excessive acid are well understood, however, many overlook the important role acid plays within digestion.

- Digestive enzymes, such as pepsins and lipases, function optimally within narrow range of pH: with any deviation affecting activity at either side of the peak (Chiba, 2009).
- Acidification of the duodenum stimulates the release of the hormone secretin, which targets the pancreas to produce bicarbonate rich fluid. This helps to neutralise gastric acid, and establish a pH suitable for the activation of other digestive enzymes.
- A low pH in the stomach may prevent multiplication of ingested bacteria (except *lactobacilli*) so could well be also implicated in maintaining optimal health (Frape, 2004).
- There is some normal fermentation of non-structural carbohydrates in the fundic region of the stomach but, is limited at the pylorus when the drop in pH activates pepsin. This drop in pH is necessary to limit fermentation to prevent an excess production of volatile fatty acids (VFAs). At a low pH (less than 4.0), VFAs are fat-soluble and so they are able to permeate squamous mucosa which inhibits sodium transport functions of the gastric mucosa. When sodium accumulates within the cells of the stomach lining, water is osmotically pulled into the cells which can lead to oedema and mucosal damage, with resulting sloughing and ulceration (Nadeau et al. 2003).

The dangers of hindgut acidosis

The horse struggles to fully digest a diet high in non-structural carbohydrate (NSC). This is primarily due to the very limited production of pancreatic alpha-amylase (Kienzle et al. 1994), the enzyme required to break down starches and sugars in the small intestine but, is also compounded by the way these feedstuffs are often fed; intermittently and in large volumes. This can contribute to an overconsumption and rapid transit rate through the GI tract and, increase the likelihood that poorly digested NSC will reach and subsequently, ferment within the large intestine. As bacterial fermentation of NSC occurs the production of lactic acid overtakes production of energy producing volatile fatty acids, lowering the pH. The fall in pH, particularly below 6.5, causes a bacterial inversion to take place where beneficial, forage-fermenting bacteria such as *Ruminococcus albus* and *Fibrobacter succinogenes* are destroyed and proliferation of pathogenic bacteria such as *Streptococcus bovis* and *lactobacillus* occur. This perpetuates further acidification. Potential consequences of these events include reduction in fibre digestion and release of endotoxins (Clarke et al. 1990) which, when exposed to the colonic mucosa, increases paracellular permeability (Weiss et al. 2000). Ultimately this can reduce the integrity of the mucosal lining, causing lesions and necrosis in the mucosal layer of the intestinal lining. Other risks include endotoxemia, dysmotility, gaseous and displacement colic. Maintaining stability of the hindgut microbial community is of paramount importance to overall gastrointestinal health.

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How can SUCCEED™ Digestive Conditioning Program™ help?

SUCCEED™ is a once daily feed supplement program. The product is a construction of specific ingredients, with constituent nutrients that work together to optimise the health and functioning of the entire gastrointestinal tract.

- Polar lipids – The oat oil in SUCCEED™ is extracted through a proprietary process that retains a high level of polar lipids. Polar lipids play an important role in cellular membranes, helping to maintain tight junctions between the epithelial cells present in GI mucosa. Tight junctions optimise the natural defensive mechanisms within the gut lining to protect against gastric acid, pathogens and toxins (McNeil & Ito, 1989). As a result the risk of inflammation and lesions developing are mini-mised. Oat oil is also naturally high in the anti-oxidant, Vitamin E. Free radicals are formed in response to exercise and have been associated with muscle fatigue; however vitamin E scavenges these products of oxidative stress and helps to protect against damage free radicals can exert on cellular membranes. The bioavailability of water- and fat-soluble molecules is enhanced by using polar lipids as a carrier, improving availability of several vitamins by up to 500%. This helps to maximise uptake of the ingredients in SUCCEED™ into the vascular system and tissues.
- Beta-glucan – The oat flour in SUCCEED™ is produced through a process that retains a large portion of the polysaccharide, beta-glucan. This soluble fibre, when fed alongside hard feed, creates a hydrogel that helps to moderate the transit of starches through the GI tract, helping to ensure a more complete digestion within the small intestine (Bohm & Kulicke, 1999) and to thus minimize the levels entering the large intestine. It has been shown that beta-glucan can reduce post prandial glycaemic peaks by up to 50% (Tappy et al. 1996). This can have positive effects on behaviour, especially in horses being fed high starch diets to meet energy demands. Beta-glucan has a highly stimulatory effect on phagocytosis and macrophages to boost immunity and counteract pathogenic microbes (Czop, 1985).
- L-Arginine – Technically a nonessential amino acid, L-Arginine can be depleted from stress and intensive training. Arginine enhances gut function (Stechmiller et al. 1997), decreases mucosal injury from pathogens, and shortens recovery time following illness or intestinal injury (Sukhotnik et al., 2004). It supports the production of growth hormones and insulin, enhancing strength and stamina (Sureda and Pons, 2012; Schmidt et al., 1992).
- L-Threonine –Threonine is an essential amino acid and an important component of mucin; proteins which are produced by intestinal goblet cells scattered along the intestinal villi to enhance the gut barrier function. A healthy mucus gel layer protects the gut against digestive enzymes and physical damage by digesta. Intestinal inflammation increases threonine uptake by the gut in order to synthesise more mucin. As synthesis is sensitive to dietary threonine supply (Bertolo et al. 1998), the addition of this amino acid is beneficial in promoting optimal health of the tract lining. Threonine is also a main component in immunoglobulins (Cuaron et al. 1984) and so promotes immunity.
- Nucleotides – A healthy intestinal tract requires continuous cell division. To achieve this millions of DNA and RNA molecules must replicate using several billion nucleotides. This process is essential for cell turnover, repair and growth, optimising the natural protective mechanisms of the mucosal lining and, proliferation of beneficial bacteria, to name but a few. The yeast products in SUCCEED™ are sources of nucleotides. By adding dietary nucleotides, the body can down regulate the synthesis of nucleotides, and instead utilise the enzyme HGPRT to scavenge intact nucleotides, thereby improving efficiency of cell repair (Uauy et al. 1990). Indeed it has been shown that nucleotide supplements increase mucosal thickness and protein levels as well as speeding up intestinal recovery after chronic diarrhoea and intestinal damage (Bueno et al. 1994).
- Yeast Products – SUCCEED™ contains two different yeast products.

One is a yeast beta glucan extracted from the inner cell wall of the yeast Saccharomyces cerevisiae. It is a highly efficient mycotoxin adsorbent helping to minimise, decontaminate and thus control the toxicity of mycotoxins produced from ubiquitous fungi and moulds (Raymond et al. 2003). Mycotoxins can exert numerous mutagenic, carcinogenic, oestrogenic and teratogenic effects and most frequently enter the body through unavoidably contaminated grain, forage and feeds.

The second yeast product is a mannan oligosaccharide, extracted from the outer cell wall of Saccharomyces cerevisiae. Its primary role is the competitive blocking of bacterial lectins. Bacterial lectins have an affinity to bind with glycoproteins attached to the membrane of intestinal enterocytes; the first stage of infection (Mirelman and Ofek, 1986). The mannan mimics these glycoproteins, providing an alternative attachment site and essentially "tricks" the pathogenic bacteria into binding with it instead (Swanson et al. 2002). This helps to block colonisation of pathogenic bacteria organisms such as *Clostridium, E.coli* and *salmonella* by adsorbing and safely removing them. The resulting effect is a positive modulation of gut microflora and reduced risk of infection.

Mannan oligosaccharides also aid immune response by enhancing plasma and colostral IgG and bile IgA antibody levels (Bland et al. 2004; O'Quinn et al., 2001; Newman & Newman, 2001). Passive transfer of immunity within

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the first 24 hours of the foal's life is crucial for protection against pathogenic challenges, which may otherwise result in diarrhoea, sepsis and even death.

The nutrients in SUCCEED™ equip the horse to obtain and maintain optimal digestive health when faced with challenging circumstances, whether nutritionally or physically. By directly supporting the structure and functioning of the gut, while also facilitating better nutrient absorption, the horse can cope and thrive even in the face of modern feed, feeding and management routines.

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SUCCEED™ – the opinions



Jamie Gornall
Showjumper and Breeder

My main philosophy is this: simple basics done very well are paramount; then it's the details in the basics that make the difference.

You can easily feed SUCCEED™ and no other supplements for gut health, knowing and trusting full-well that all internal digestive organs will be looked after by a natural product. We use SUCCEED™ on a day-to-day basis as a foundation in the feeding and training regime for all the horses at Gornall Equestrian. We find good gut health is essential in maintaining the horses' optimum health.

The horses are less irritable and sensitive to changes in conditions when they've been on SUCCEED™ long-term. They arrive at competitions relaxed in the body, which isn't always easy to achieve after a journey, new stables, lots of new horses stabled nearby, etc. This is important as we have a lot of stallions, which are very sensitive and can react extremely to these environmental changes.



Tess Carmichael
Showjumper

It's really important to me that my horses get regular access to forage and hard feed. Each horse is completely treated as an individual and has a feed program tailored to their personal needs.

I think for horses to jump and perform their best, they need to feel their best. SUCCEED™ helps maintain overall digestive health, even when traveling and competing.

I recommend SUCCEED™ regularly because it's a product that I genuinely trust. I've had such great results from using it that I never think twice about encouraging other people to use it as well. SUCCEED™ works.



Bill Levett
Eventing

We like bringing horses along slowly and at their own pace, to avoid undue stress. I'm always looking for new ways to support our horses, such as feeding SUCCEED™.

SUCCEED™ ensures that our horses hold their weight well, even when super-fit and competing/traveling a fair amount. It also seems to help one horse with skin problems to stay healthier.

We're really pleased with how our horses have held their weight and muscle over the winter months, thanks in part to the help of SUCCEED™. It really does make our job so much easier, as all of the horses—even the fussy eaters and poor-doers—seem to thrive on SUCCEED™.



Lissa Green
Eventing

My horses and I have really been spoilt in that we have been using SUCCEED™ for a number of years, and I cannot tell you the difference it has made. I had one horse in particular that never seemed to put on weight, was always stressed, banging her stable door and constantly had a nervouse disposition. However, once she was on SUCCEED™ her whole demeanor changed, she relaxed in the stable and when being ridden, her coat improved drmatically and she is now so calm that even un-horsey people flock to her stable to pet her, whereas before they used to leave a wide berth.

For me the most important things about SUCCEED™ is the confidence it gives me throughout the season. With the challenges the stomach and gut go through that are related to travel, stress and competition. I know that SUCCEED™ will help combat any irregularities they may encounter.

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Author biography

Dr Emma Hardy



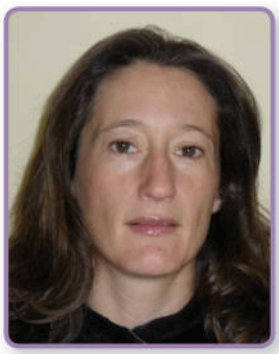
Dr Emma Hardy has been European Regional Manager for Freedom Health LLC since joining the company in 2009. A lifelong interest in keeping and competing horses led to studying a Bachelor of Science in Equine Sports Science at the University of Lincoln, where she was awarded a First Class (Hons) in 2001. Following, she was accepted onto a Research Internship Program with Kentucky Equine Research, USA which involved helping to plan, implement and analyse various equine nutrition and exercise trials. On returning to the UK, Emma undertook her Doctor of Philosophy also at Lincoln, researching equine myopathies, with particular focus on aberrant protein expression in equine skeletal muscle and erythrocytes.

Emma's role at Freedom Health varies widely, from communicating with veterinary professionals and trainers/owners/riders about equine digestive health and the SUCCEED™ products, to attending conferences and CPD, and helping with marketing and writing.

She lives on the North Devon coast with her husband and two young sons, Sam and Ollie.

Dr Helen Warren

HW Consulting



Dr Warren achieved her primary degree in Animal Science from Aberystwyth University, Wales in 1999, followed by her PhD from the Faculty of Medical and Veterinary Sciences at Bristol University. She is a member of the British Society of Animal Science, a qualified lecturer and a registered animal scientist. Previous employment has included lecturing at Nottingham Trent University and Bicton College. She has lectured degree level students in equine nutrition, fitness and training and anatomy and physiology. She currently works as director of HW Consulting, involving initiating European research projects, delivering nutritional education and technical support to animal health and nutrition companies.

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Optimal equine GI health requires accurate **IDENTIFICATION** if a condition is suspected.

The SUCCEED® Equine Fecal Blood Test™ (FBT) allows for the detection of bleeding and inflammation originating from the GI tract, using just a fresh faecal sample. This simple, rapid and affordable, stable side test can be invaluable if you suspect a GI tract condition, or as part of a routine wellness program. The horse's digestive system is the key to overall health, which is why you should have your vet test your horse regularly with the Succeed FBT to ensure targeted treatment, resolution and optimal prevention.



SUCCEED®

Equine Fecal Blood Test™

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The ultimate **SOLUTION** for equine digestive health.

Performance, appearance, temperament and overall health are all significantly influenced by the condition of the GI tract. SUCCEED® Digestive Conditioning Program™ is a daily functional feed which helps optimise the structure and functioning of the entire tract. Ideal for horses facing the rigours of training, performance and related lifestyle factors, it can both aid recovery and help offset the challenges the GI tract can face when under these conditions. It's supported with clinical trials, published research and multiple patents worldwide.



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In the U.K. call or email Dr. Emma Hardy at 01522 309946 / ehardy@freedomhealthllc.com
In Ireland call or email Sandra Hughes at +353 87 3781739 / shughes@freedomhealthllc.com

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