

Equine Cushing's Disease (Pituitary pars Intermedia Dysfunction)

Equine Cushing's disease is a complex hormonal condition involving the abnormal function of the hypothalamus and pituitary gland. These glands sit deep inside the skull at the base of the equine brain and are the primary command centre for the production of hormones.

In a normal horse, these exist in a fine balance, and play an important role in maintaining and controlling bodily functions. In a cushingoid horse or pony, neurons (nerves) in the hypothalamus undergo progressive degeneration and produce insufficient quantities of a nerve transmitter substance called dopamine.

Dopamine is important in controlling the secretions of a part of the pituitary gland called the *pars intermedia*. Insufficient quantities of dopamine causes the *pars intermedia* to enlarge which then produces excessive amounts of a range of hormones important in controlling the body. The hormones in question are known as the *pro-opiomelanocortin-derived peptides* (POMC) and include *melanocyte-stimulating hormone* (MSH), *corticotrophin-like intermediate lobe peptide* (CLIP), *beta-endorphin* (B-END) and *adrenocorticotrophic hormone* (ACTH).

The POMC hormones play a part in controlling a wide range of body functions and the hormonal imbalances caused in Equine Cushings result in a range of clinical abnormalities.

What are the clinical signs?

The average age of a horse or pony with Cushings is 20 years although with the advancement of testing for the disease we are discovering horses much younger with the condition and it now has become a common condition in horses aged 15 years and over. Cases on much younger horses do occur but less commonly.

The clinical signs can vary significantly between horses. If your horse shows one or more of the following symptoms it would be worth considering having them tested for Cushings:

- ◆ Inability to maintain muscle while accumulating fat (especially on the crest)
- ◆ Bulging fat pads above the eye (supraorbital fat pads)
- ◆ A pot bellied appearance
- ◆ Acute or recurrent attacks of laminitis
- ◆ Lethargy
- ◆ Increased thirst and urination (polydipsia and polyuria)
- ◆ Late shedding of winter coat
- ◆ Excessive sweating
- ◆ Weight loss
- ◆ Long curly coat (hirsutism)



EQUINE CUSHING'S DISEASE & EMS

Consequences of laminitis

Equine Cushings cases if left untreated, will inevitably develop laminitis and many of them suffer from liver disease too. Because the condition results in suppression of the immune system, skin and other infections are common. Sometimes lice, ringworm, bacterial dermatitis and internal parasites can be serious complications. Foot abscesses can develop, both from laminitic changes and poor hoof quality as well as reduced body defences. Sinus and dental infections are common and so many affected horses have an infected nasal discharge. The depressed healing responses mean that wounds often fail to heal; even small ulcers in the mouth remain over some months and often enlarge significantly.

How is Cushings diagnosed?

There are various tests designed to diagnose for Equine Cushings Disease. The most commonly (and most effectively) used test is a blood test called an Endogenous ACTH test. This is a single blood test which measures the resting levels of adrenocorticotrophic hormone (ACTH) in a horse. An abnormally high result of this hormone is associated with a positive result for Cushings and treatment is likely to be needed.

The endogenous ACTH test is the newest test to diagnose cushings. It has superseded other tests such as the dexamethasone suppression test due to its more accurate results and ease of use. For accurate results, samples are taken into iced tubes, the plasma promptly separates from the red cells and the sample is kept permanently chilled until it reaches the lab.

Can Equine Cushings Disease be treated

Early identification of horses and ponies with Cushings helps to arrest the disease early in its course. Although there is no "cure" for the problem, appropriate medical treatment and good routine health care can help keep your horse healthy and fit

Prascend is the first licensed medicine for the treatment of Equine Cushings disease. Prascend contains a drug called pergolide which acts directly on the dopamine-producing neurons in the hypothalamus, helping to bring cortisol concentrations in the blood stream back to normal levels.

Prascend is normally given once daily and can be mixed with a small amount of food to ease administration. As Prascend affects cortisol production, there is usually a short lag between beginning treatment and seeing your horse return to normal in terms of clinical signs. It can take up to 6-12 weeks to see the full benefit of treatment.

It may be necessary to re-sample your horse six weeks after beginning treatment to see what affect the Prascend has had on the ACTH levels. If the levels are still high the dose of Prascend may need to be increased.

Can it be prevented?

It is not possible to prevent this condition. However with available blood tests we are now able to recognise and treat more cases earlier and more effectively and many treated horses and ponies go on to live comfortable and active lives for many years after diagnosis and treatment. Indeed many owners comment that the treatment appears to have taken years off their horse!



EQUINE CUSHING'S DISEASE & EMS

What is Equine Metabolic Syndrome?

Equine metabolic syndrome (EMS) is a relatively newly recognised disorder of horses and ponies. It doesn't relate to one particular problem but rather:

"A collection of risk factors that are associated with an increased susceptibility to laminitis."

A horse with EMS is quite often referred to as "a good doer" i.e. It seems to gain weight very easily on very little food intake. Those most susceptible seem to be the native breeds, and ponies in particular. This may be due, in part to an evolutionary trait that enabled them to survive in harsh conditions on poor/sparse pasture.

The idea being that in the spring and summer when there was plenty of food they would gain weight, then in the winter months certain tissues (liver, fat, skeletal muscle) would become insulin resistant in an effort to ensure that their energy resources were used mainly by the important organs of the body.

Insulin resistance:

Insulin resistance is one of the risk factors associated with EMS. Insulin is made and released into the body by an organ called the pancreas.

For cells in the body to work they require energy in the form of glucose. Insulin attaches to the body's cells and allows them to take up glucose from the bloodstream.

If the body becomes insulin resistant then these cells don't remove glucose from the bloodstream, which results in a high blood sugar (hyperglycaemia).

The body then responds to this increase in glucose in the blood by releasing yet more insulin from the pancreas thus causing a high blood insulin level (hyperinsulinaemia).

Diagnosis:

The clinical history of an animal is often highly suggestive of EMS and will lead us to recommend certain blood tests to enable us to come to a definitive diagnosis and hence to then be able to work with you on how to manage the syndrome. As indicated above, these blood tests involve looking at the levels of insulin and glucose in your horse's blood.

The simplest blood test involves a one off sample taken after your horse has been starved for a period of 5-6hrs. However due to the compensatory mechanisms of a horse's physiology this test can sometimes be inconclusive. A better test involves starving the horse overnight and then feeding a set dose of glucose in a low-glycaemic feed (e.g. a bowl of chaff) and then measuring insulin and glucose levels in the blood 2 hours later.



EQUINE CUSHING'S DISEASE & EMS

The type of clinical history that would lead us to recommend a blood test would include:

- ◆ Recurrent bouts of laminitis.
- ◆ enlarged fat deposits such as a large crest, mammary gland, prepuce or tail base.
- ◆ a low level of fitness.

(It should be remembered that horses don't always read the text books so may show all, some or none of these signs. EMS has been recorded in some high-level competition warm bloods).

The role of "fat":

Fat isn't a natural part of a horse's diet. However once we start feeding horses that have been designed to live on sparse moor land, rich, lush, energy rich pasture, they quite quickly convert this to fat (or adipose tissue) in an attempt to store this glut of energy in preparation for the harsh winter and subsequent lack of food that may be on it's way.

However the harsh winter and lack of food never comes as we then put nice warm rugs on our horses, give them stables to shelter in and continue to feed them high-energy concentrate feeds.

Contrary to popular belief, adipose tissue is not just an inactive lump of jelly like material. It produces hormones and inflammatory chemicals called *adipokines* (specifically, leptin, tumour necrosis factor and interleukin-6).

These factors increase the likelihood of insulin resistance by blocking insulin receptors on cells in the body. They can also result in altered blood flow to structures in the foot, impairing nutrient delivery to hoof tissues and a continual state of inflammation, all of which increase the chance of laminitis occurring.

Management of EMS:

Theoretically EMS is a reversible disease, hence with the correct management the problem can be overcome and your horse can continue to enjoy a good quality of life.

- ◆ **Diet:** - It hopefully makes sense that a fat horse that has large stores of energy should receive less energy in the form of feed than it requires for daily maintenance. In adult horses the daily maintenance requirements are approximately 1/8 of their bodyweight expressed as mega joules (MJ) e.g. $400\text{kg}/8 = 50 \text{ MJ}$.

However a horse generally likes to eat 2% of its bodyweight a day e.g. $400\text{kg} \times 2\% = 8\text{kg}$. Therefore the dietary intake should average no more than 6.25MJ per kg of dry matter (50/8).

Thus feeding a hay only diet at 1.5-2% of bodyweight will be maintenance feed levels for most EMS type horses, i.e. a 300kg pony will need 4.5-6kg of hay per day and nothing else!

In addition, you will struggle to manage any dietary restriction unless the horse is stabled on an inedible bed!

The energy content of commercial feeds should be available on the packaging or from the manufacturers. If you compare these to what is actually required you will find that many feeds are well over the 6.25MJ/kgDE and this value is better equated to the energy in very poor quality hay or straw.

High glycaemic feeds (cereals, carrots, apples) should be avoided, as these will cause hyperglycaemia and hyperinsulinaemia potentiating the problem. Likewise fresh grass should also be avoided. The diet should consist of hay that has been soaked for several hours (to remove any laminitis causing nutrients). This can be supplemented with high fibre feeds such as low energy chaffs. A vitamin and mineral supplement is advisable in the absence of fresh feed.

- ◆ **Exercise:** - If laminitis allows it, an increase in energy expenditure will help to reduce obesity with the added benefit that fitter horses are more sensitive to insulin.
- ◆ **Medication:** - Although there is still a lot of research in this area the most suitable treatment is one that increases the body's sensitivity to its own insulin. This treatment is known as Metformin. This drug should not though be considered as the golden bullet that will cure all ills. There is evidence to show that the body can, after varying amounts of time become resistant to its insulin once again despite the medication. As such this treatment should be seen as an opportunity to carry out changes in the management of your horse (increase it's fitness and decrease it's fatness) such that it then has less of the risk factors that may make it susceptible to laminitis.



Appearance of horses suffering with EMS, note the fatty deposits on picture 1.