

Equine Pituitary Pars Intermedia Dysfunction (PPID) vs Equine Metabolic Syndrome (EMS)

Better known as Cushing's disease, equine pituitary pars intermedia dysfunction or PPID is a syndrome where a part of the brain, the pituitary, becomes enlarged and overactive. The pituitary is located at the base of the brain. In PPID the middle lobe, the pars intermedia, becomes enlarged over time into what is often (incorrectly) called a pituitary adenoma and results in the over production of many hormones. In affected horses the pars intermedia produces excessive amounts of pro-opiomelanocortin (POMC) which is broken down into various other hormones, including adrenocorticotropic hormone (ACTH) and melanocyte stimulating hormone (MSH). Normally this function is kept in check by the neighbouring hypothalamus, which is in charge of regulating thirst, hunger, body temperature, water balance, blood pressure and other vital functions via secretion of dopamine.

Pituitary pars intermedia dysfunction disease is one of the most common diseases of horses greater than 15 years of age. The average age of horses diagnosed with PPID is 20 years. PPID affects >20% of horses \geq 15 years of age. Although it is most common in aged horses, PPID has been diagnosed in horses as young as 7 years of age. Though this disease affects countless horses every year, still much needs to be learned about its effects and process.

The clinical signs of PPID vary with each horse. While the exact mechanism that causes these clinical signs is unknown it is thought to be due to the excessive production of POMC derived compounds. The most recognized sign is a long, curly hair coat that fails to shed properly. This is known as hirsutism and is a clinical sign specific to PPID. Other symptoms can include a failure to shed well in the spring, excessive drinking and urination, laminitis, lethargy, excessive sweating, or lack of sweating, muscle mass loss, a sway back, pot belly, loss of hair colour, repeated infections, infertility and redistribution and abnormal accumulation of fat. Horses with PPID may also have hyperinsulinemia, or high blood levels of insulin. Hyperinsulinemia is also known as insulin resistance. This is where the tissues of the horse fail to respond to the natural increase in insulin stimulated by carbohydrate and sugar intake. The lack of response by the body causes the pancreas to continue to secrete insulin in an attempt to deal with higher sugar levels in the blood. The elevation in circulating insulin also contributes to the clinical signs associated with PPID. Essentially some of these horses also have a type II diabetes-like syndrome.

There are a few ways to diagnose PPID. The best indication of the disease is hirsutism in the aged horse. This is the most sensitive test of PPID available, however it only becomes apparent during more advanced disease. Occasionally we see horses that shows clinical signs that may be associated with PPID, but are too early into the clinical course of the disease to detect it without laboratory testing. Unfortunately, no test is 100% accurate. The two most commonly used tests are the resting ACTH test and the overnight dexamethasone suppression test (ODST). Other tests that have been advocated for PPID diagnosis: the thyrotropin releasing hormone test (TRH), fasting insulin concentration and the circadian cortisol test however their diagnostic rates have not been proven and aren't therefore they aren't used regularly. Though testing is not necessary for diagnosis of PPID it is essential for monitoring the response to treatment. Seldom does treatment achieve complete remission of disease, however it does significantly improve the horse's quality of life.

The drug of choice for treatment of PPID is pergolide mesylate or Prascend (made by Boehringer Ingelheim). It is currently the only approved therapy for PPID on the market. This medication works by mimicking the inhibitory action the hypothalamus has on the rest of the body. It helps to reduce the amount of ACTH and other POMC derived hormones produced by the pars pituitary. A good response to therapy is associated with improvement in clinical signs or normalization of the results of an ODST or ACTH test.

In addition to pharmaceutical treatment, horses with PPID will benefit from multiple other management strategies. Since most PPID horses are also insulin resistant they should be fed hay that is less than 10% non-structural carbohydrates (NSC). Non-structural carbohydrates are also known as sugar and starch. If the hay has not, or cannot, be tested it should be soaked for a minimum of 30 minutes in water to reduce the NSC available to the individual. Access to lush green pastures should be monitored closely and should be limited if the high NSC content is known to cause bouts of laminitis. Pelleted or other types of complete feed should be avoided where possible and replaced with diets high in fiber and fats. Many feeds are available that are specifically designed for senior horses and those that are metabolically challenged. Care should be taken to ensure that feeds combined with sugar or molasses are avoided. As with all aged horses, dental care and regular deworming is essential to their longevity. An appropriate schedule should be worked out with your regular veterinarian.

While managing laminitis cases a relationship between you, your farrier and your veterinarian should be established. This way your farrier can trim and shoe appropriately based on x-rays taken by your veterinarian. Your veterinarian can also help manage chronic pain by prescribing one of many different medications. Therapies such as laser therapy, herbs and acupuncture may also be of great help to your horse to manage the pain associated with laminitis.

Equine Metabolic Syndrome (EMS) is a recently described collection of clinical abnormalities which shares some characteristics with PPID. Both of these disorders alter cortisol metabolism. Equine metabolic syndrome has no underlying connection to thyroid gland

dysfunction. It is thought that EMS results from excess production of active cortisol primarily in fat cells, or adipose tissue. The pituitary gland functions normally in patients with this disorder. Understandably, while the underlying causes of EMS and PPID may be different, the resulting clinical problems are very similar, including abnormal fat deposition (along the crest, over the tail head, and in geldings' sheaths) and laminitis. Metabolic syndrome is typically seen in middle-aged horses, perhaps starting at 10-20 years of age. It is also observed more often in various breeds: pony breeds, domesticated Spanish mustangs, Peruvian Pasos, Paso Finos, Andalusians, European Warmbloods, American Saddlebreds, and Morgan horses. This suggests a genetic predisposition is present, but this has not been scientifically proven.

With more recent studies of the syndrome, experts agree that the term EMS should be used only when the following, three diagnostic criteria are met:

1. insulin resistance (IR) – high insulin levels circulating in the blood
2. history of, or current active laminitis – a direct result of the high insulin, cortisol and sugar levels circulating in the blood
3. excess fat depositions in typical regions – this is the most commonly recognized body type, though “skinny” metabolic horses have been identified

Insulin resistance is a term used to describe the condition in which various body tissues fail to respond appropriately to insulin. In a classic scenario, the individual has both abnormally high blood sugar and blood insulin concentrations. Once the pathologic state of IR develops, poor utilization of glucose from the diet and intermittent high blood sugar occurs (similar to Type 2 diabetes mellitus in people). Diets that are higher in carbohydrates exacerbate this state because they stimulate further insulin production when eaten. The possible mechanisms behind IR in horses are numerous and can be discussed with your veterinarian. A major concern with IR is that it appears to be linked to pasture-associated laminitis in horses and ponies. Thus, when IR is identified or suspected in a horse, veterinarians often suggest methods which may help a horse's insulin sensitivity. This typically includes diet changes and an increase in regular exercise. As an aside, although IR is not identified in all horses with PPID, it can be an associated endocrine problem for many equine PPID cases as well.

More recent research in horses with EMS has found that horses can have some of the same medical problems as people with metabolic syndrome. This may include:

- Hyperglycemia
- Altered tissue-level cortisol activity
- Increased leptin concentrations
- Altered lipid metabolism with hypertriglyceridemia
- Increased expression of inflammatory cytokines
- hypertension

Testing options for metabolic syndrome are still debated as the equine medical community learns more about this syndrome. To diagnose EMS, the presence of the previously described clinical changes and blood tests are used. A single test to identify increased cortisol in fat tissue does not yet exist. The primary and most consistent laboratory abnormality is a high serum insulin concentration. In addition, because of the shared traits of EMS and PPID, it is important to rule out a diagnosis of PPID. Also, because laminitis is often the first complaint, assessing coffin bone position with foot radiographs is very important.

Many veterinarians are using their test of choice for PPID combined with serum glucose and serum insulin measurements to evaluate a horse or pony for EMS. While the results can be frustrating and not point to an obvious diagnosis, they are still useful tools. Veterinarians recognize that many horses and ponies fit an “inconclusive” category where PPID or EMS cannot be diagnosed with certainty. That said, it is often suggested to repeat diagnostic tests in horses suspected of having PPID or EMS. It is possible that at certain times, the subject's hormone levels are abnormal, and at other times, they are normal.

Management of horses and ponies with EMS focuses on therapy for laminitis and dietary adjustments with the aim of limiting the stimulus for insulin production. Unfortunately, because of the abundance of high carbohydrate-content commercial feed options, diet supervision can be extremely difficult for owners. In order to decrease this stimulus for insulin secretion, an alternate feeding regimen with a low glycemic index is recommended for these patients.

Glycemic index signifies the degree to which a certain food raises blood sugar and insulin levels in the body. Molasses-based diets, such as sweet and certain senior feeds, oats, and barley have high glycemic indexes. Low glycemic index feeds include Bermuda grass hay, rice bran, and beet pulp. Other hays, such as timothy and alfalfa, have moderate glycemic indexes. An important recommendation is to feed grass hay or other feed sources which are low in water-soluble carbohydrates (WSC) or non-structural carbohydrates (NSC). Forage analysis of your hay is strongly encouraged to accurately determine the WSC/NSC content of one's hay. NSC content below 10% is suggested for IR horses and ponies, in both EMS and PPID patients. Also, if more calories are needed, fat sources, such

as oils or rice bran, are excellent choices instead of grains and feeds with high molasses content. Higher fiber content in the daily diet is also encouraged. This can be found in beet pulp and many commercially produced pelleted feeds. Supplements, such as Insulin Wise, can significantly help with your horses daily insulin regulation.

As said previously, chronic laminitis is the primary, day-to-day effect of EMS – and also the most life-threatening, if not controlled. As with PPID-affected horses and ponies, making a team of people to manage EMS-associated laminitis is critical. Owners must maintain strict control of dietary management and be prepared for acute laminitis episodes during season changes (especially spring pasture) and any disruption to his/her horse's typical daily diet. Managing a horse or pony with EMS requires a long-term commitment, but can be very successful.

References:

<https://aaep.org/horse-owners/horse-health>

<https://sites.tufts.edu/equineendogroup/>

<https://www.kppvvet.com/insulinwise/>