Cushing’s disease and Equine Metabolic Syndrome have been a grey area in the horse community for years because the clinical signs of both diseases overlap in some respects. However, Cushing’s disease and metabolic syndrome have very different medical etiologies.

**What is the difference between Cushing’s disease and Metabolic Syndrome in horses?**

**Cushing’s Disease**

Cushing’s disease, now referred to as “pituitary pars intermedia dysfunction” (PPID), is a disease of aging horses (most ≥ 15 years). It represents hyperplasia of the pars intermedia. This portion of the gland produces a number of vital peptides and hormones that are derived from pro-opiomelanocortin (POMC), including adrenocorticotropic hormone (ACTH), melanocyte stimulating hormone, corticotropin-like intermediate lobe peptide, lipotropins, and beta endorphin. The pars intermedia is innervated by dopaminergic neurons, and dopamine is normally inhibitory to equine pars intermedia activity. PPID is a neurodegenerative disease and occurs when there is loss of dopaminergic inhibitory input to the pars intermedia. As a result, the pars intermedia melanotropes undergo hyperplasia and increased production of POMC-derived hormones. The chronically increased ACTH leads to overstimulation of the adrenal gland, with resultant increase in cortisol production. The clinical signs of PPID include hirsutism, excessive sweating, polyuria/polydipsia, hyperhidrosis, muscle atrophy, increased body fat deposition with a pot-bellied appearance, dental disease, laminitis, and consequences of immune suppression including sinus infections and hoof abscesses. Earlier signs, before the disease has progressed, include delayed shedding and muscle atrophy along the top line.
Equine Metabolic Syndrome

Another endocrine disorder of horses is “equine metabolic syndrome” (EMS). While some of the features may be similar to PPID, they are distinct syndromes. This is a disease of middle-aged to older horses, with most horses first diagnosed between five and 15 years of age. The disease consists of increased adiposity (particularly regionally), hyperinsulinemia, and insulin resistance. This is a complex syndrome caused by genetic, nutritional and environmental factors, whose pathophysiology has not been completely elucidated. Breeds with a predisposition to EMS include ponies, Miniature horses, Morgans, Arabians, Paso Finos, Andalusians, Saddlebreds, Spanish Mustangs, Tennessee Walking horses, Quarter horses, Warmbloods and other breeds.

Clinical signs of the disease include accumulation of regional fat, especially in the crest of the neck, tail head, behind the shoulder, and in front of the prepuce or mammary gland. Many have general obesity and are commonly referred to as “easy keepers”. Other signs include preputial swelling, due not only to adipose tissue expansion but also edema secondary to reduced lymphatic return. Affected horses have a predisposition toward chronic or recurrent laminitis similar to horses with PPID.

How are PPID and EMS diagnosed?

PPID

The diagnosis of PPID relies on measurement of plasma ACTH concentrations, which are increased in affected horses. ACTH concentrations may fall in a “gray zone” in early cases, making a definitive diagnosis difficult. Recent research has shown that ACTH concentrations vary depending on the time of year, with highest levels occurring in the fall in both healthy and PPID horses. Therefore, ACTH concentrations should be interpreted in light of the time of year, against seasonal reference ranges. An endogenous ACTH > 29 pg/mL (6.4 pmol/L) between November and July, or > 47 pg/mL (10.4 pmol/L) between August and October are consistent with PPID. A dexamethasone suppression test (DST) can also be used, and has long been considered the gold standard diagnostic test; however this status has recently been questioned based on research evaluating post mortem examinations. In addition, false positive DST results can also occur during the fall season. Because corticosteroids rarely have been associated with laminitis in horses, the DST should not be used in laminitis horses or those considered at high risk.

EMS

The diagnosis of EMS is through measurement of fasting insulin concentrations as a screening test (generally > 20 µU/mL). Fasting blood glucose concentrations may or may not be increased, but hyperglycemia would support the diagnosis. Fasting consists of leaving a low starch hay (one small flake), such as a low nonstructural carbohydrate (NSC) grass hay, as the sole feed after 10 pm. Blood should be drawn the following morning. Borderline insulin concentrations warrant further testing through an “oral sugar test”, where light Karo corn syrup (0.15 mL/kg, PO) is administered after an overnight fast. A serum insulin concentration is measured 1-1.5 hours later. An insulin concentration > 60 µU/mL at this time point, after the administration of Karo syrup, indicates insulin resistance and supports the diagnosis of EMS.

How are these treated?

PPID

Treatment of PPID is primarily through administration of pergolide, which down regulates the production of ACTH through its dopamine receptor agonism. High quality management, including regular dental care, parasite control, hoof care, and a highly digestible diet are very important for affected horses. Ideally, a high starch or soluble carbohydrate diet should be avoided in horses with secondary insulin resistance.

EMS

Treatment of EMS is primarily through dietary and exercise management. Weight loss and provision of a low starch/soluble carbohydrate diet are the primarily goals. Diet should consist of hay with <10% nonstructural carbohydrates (NSC), which consists of starch, sugar and fructans. In addition, grain, molasses, grass pasture and other sources of simple sugars should be avoided. A vitamin/mineral supplement should be provided unless a low NSC complete or supplemental feed is fed. Exercise should include a gradual increase in intensity and duration, as long as it is tolerated. If tolerated without signs of lameness, the exercise program should ultimately consist of 30-minute daily sessions, and as much turn out time as possible. Some horses with laminitis are not able to be exercised.

For horses with an inadequate response to diet and exercise modifications alone, or those with severe obesity or an inability to exercise, a course of high dose thyroxine (0.1 mg/kg PO daily) is prescribed. Thyroxine aids in weight loss and enhances insulin sensitivity. There are many nutritional supplements available for use in horses with EMS, including chromium, magnesium, cinnamon, and chaste berry. However, these require further research to evaluate for efficacy.

For a more detailed discussion of these topics, including the following important questions and bullet points, we invite you to attend the Pacific Veterinary Conference:

1. Controversies in diagnostic testing of PPID and EMS
2. New potential adjunctive therapies for PPID and EMS
3. Are there any physiological connections between PPID and EMS?