



Pituitary Pars Intermedia Dysfunction (PPID)

Cushing's Disease

Sports Medicine, Lameness, Reproduction and Dentistry

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Cushing's Disease, now more commonly referred to as Pituitary Pars Intermedia Dysfunction (PPID) is an endocrine disease found in a small percentage of horses. The pituitary gland is located at the base of the brain and releases hormones which regulate various aspects of the body. The pituitary gland is activated (controlled) by hormones released from the hypothalamus. The hypothalamus responds to various hormones/peptides circulating in the body. The pituitary is essentially a regulation center for the body. Endocrine diseases are very complicated and very in depth. The point of this paper is to explain the basics of how PPID works, and how it is controlled and managed.

The pituitary gland is separated into two sections, the adenohypophysis and the neurohypophysis. Within the adenohypophysis there are three smaller sections; the pars tuberalis, pars distalis, and pars intermedia. The pars distalis releases the following hormones: POMC, ACTH, Beta-endorphin, and a small amount of alpha-MSH. The release of these hormones is controlled by the diurnal secretion of AVP (anti-diuretic hormone) and CRH (corticotrophic hormone) released by the hypothalamus. ACTH acts on the adrenal glands to release glucocorticoids. The increased levels of glucocorticoids in turn have a negative feedback on the hypothalamus resulting in a decrease in AVP and CRH hormone, which in turn will cause a decrease in ACTH, POMC, Beta-endorphin, and alpha-MSH. The pars intermedia produce and release alpha-MSH, POMC, and small levels of ACTH. The pars intermedia is controlled/regulated by dopamine levels. Increased levels of dopamine will have a negative feedback to the pars intermedia and therefore decrease the release of the alpha-MSH, POMC, and ACTH. When dopamine levels are low, there is a transient increase in the pars intermedia hormones.

PPID causes excessive production of the pars intermedia hormones resulting in increased levels of POMC, ACTH, and alpha-MSH. The excessive increase is from a hormone secreting adenoma/carcinoma of the pars intermedia. Since the pars intermedia is non-responsive to the negative feedback loop of the rising glucocorticoids, the increased levels of ACTH and POMC cause more and more release of the glucocorticoids from the adrenal gland. Adenomas (hormone secreting tumors) of the pituitary are the number one cause of PPID; however, there are some other causes which are less common. Adenomas of the adrenal gland, secretion of ACTH from a non-endocrine secreting tumor, or excessive iatrogenic administration (medications administered to the horse) of ACTH can all lead to Cushing's like disease. Increased

levels of insulin are often associated with PPID, and therefore should be considered when treating the patient.

Clinical signs of PPID include: increased hair coat growth with decreased shedding, increased sweating, muscle wasting, uneven deposits of fat over the crest of the neck and tail head, lethargy, decreased wound healing, poor condition, laminitis, and change in attitude or appetite. The disease is most commonly found in ponies and Morgans, but can affect all breeds of horses. Typically, the horses that are affected are older in age and the onset of the clinical signs are slow.



Figure 1 Google Image of a horse with PPID

Diagnosis of the disease is based on: clinical signs, age of the horse, signs of laminitis, and blood work. There is a loss of diurnal rise and fall of blood cortisol levels, increased plasma concentrations of ACTH, and many times increased levels of blood glucose and insulin. Multiple tests can be performed to diagnose the disease if the clinical signs and basic blood work are inconclusive. The tests include: ACTH stimulation test, twenty four hour dexamethasone suppression test, and Domperidone test. An MRI or CT scan of the brain can also be used to visualize the adenoma, but are not commonly performed.

There is no curative treatment for PPID, but control of the clinical signs is possible. Pergolide is a dopamine agonist that when given orally can help decrease the amount of hormones released by the pars intermedia. As the tumor grows with age, the pergolide will become less effective and may have to be given at higher doses. Cyproheptidine is another medication that can be used on those horses which pergolide is not effective. If there is a subsequent insulin resistance, then the horse will also need to be treated for metabolic syndrome as well (please refer to the metabolic syndrome information sheet). Control of the diet is essential to help maintain a healthier horse. Diets low in carbohydrates and high in protein and fat are recommended. Constant monitoring of the feet is needed. If signs of laminitis are present, radiographs and proper farrier attention are needed immediately to reduce the rotation and sinking of the coffin bone. Again there is no treatment, only control. Eventually all possible treatments will not lower the level of ACTH and stop the onset of clinical signs but this eventual loss of control depends on the growth of the tumor and the progression of the disease. Many horses if monitored and handled properly can live long, happy lives with this disease. It is up to you as an owner to stay informed and monitor your horse's progress and keep your veterinarian and farrier up to date on any changes that need to be examined.