Howdy,

My name is Emma Bender. I am a first-year vet student at Texas A&M University from Plano, Texas. I am primarily interested in small animal medicine but have a special interest in equine. Most of my horse experience is in a nonveterinary setting as I started working at a barn during my undergraduate career at TAMU and have continued through my vet school journey as well.

What started as a job quickly became a passion as I developed good horsemanship skills and came to adore the horses I was caring for. Flash, one of the older geldings, quickly became my favorite (and still is). Not long ago, he was diagnosed with PPID, which at the time I was incredibly unfamiliar with. I just knew I was required to give him a new medication at every meal.

In the endocrine unit of physiology class during my first semester of vet school, we briefly talked about PPID and I was immediately able to connect the dots to Flash. As we talked about clinical signs I pictured Flash's thick coat, remembered the recurring infection that led to the enucleation of his eye, and recalled the pergolide pill he gets at each meal. As I was learning, it was awesome being able to connect these concepts to a horse that I have bonded with and care for regularly.

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The Equine Endocrine Enigma

It is not uncommon for geriatric horses to “slow down”. However, if signs of lethargy are accompanied by other abnormal symptoms such as pot belly, fatty deposits, and delayed shedding, it may be wise to call a veterinarian. Among other symptoms, these are all signs of Pituitary Pars Intermedia Dysregulation, a condition that affects about 25% of horses over the age of 15 and often goes unnoticed.

What is PPID?

Pituitary Pars Intermedia Dysregulation, commonly referred to as equine Cushing's disease, is one of the most common endocrine disorders affecting older horses, usually over the age of fifteen. Although PPID can occur in younger horses as well, it is rarer. PPID is characterized by the dysregulation of the hypothalamic-pituitary-adrenal axis leading to an abnormal metabolic state and dysregulation in various body systems.

The Anatomy and Pathophysiology Behind the Disorder

In the horse, the pituitary gland is suspended just ventral to the hypothalamus via the infundibular stalk. The hypothalamus and pituitary communicate by direct innervation and via the hypophyseal portal system, which delivers hormones released by the hypothalamus directly to the pituitary. The pituitary gland has various lobes that take on different functions and different methods of communication with the hypothalamus.

Unlike in other species, the pathophysiology of pituitary-dependent hyperadrenocorticism is poorly understood as it is marked by an increase in plasma ACTH rather than cortisol, despite the relationship that these two hormones have. PPID is characterized by a hyperplastic pars intermedia lobe of the anterior pituitary caused by the degeneration of dopaminergic neurons that connect the hypothalamus and pars intermedia.

In the normal equine pituitary, corticotropin releasing hormone (CRH) is delivered from the hypothalamus to the pars distalis lobe of the pituitary via the hypophyseal portal vessels. CRH initiates the secretion of adrenocorticotrophin hormone (ACTH) which then acts on the adrenal gland to stimulate synthesis and secretion of glucocorticoids. The pars intermedia is involved in the negative feedback of this axis to prevent the over-secretion of ACTH. Upon a negative feedback signal, the dopaminergic neurons that directly innervate the pars intermedia release dopamine which has an inhibitory effect on the transcription of POMC. POMC is altered by the enzyme prohormone convertase 1 in the pars distalis to produce ACTH, thus the inhibition of POMC by dopamine prevents further release of ACTH from the pituitary.

In PPID horses, this “check” on the pituitary is severely altered due to a lack of dopamine. The dopaminergic neurons of the hypothalamus degenerate, leading to the breakdown of this endocrine axis characterized by the overproduction of POMC derivatives including ACTH. However, the ACTH released by the par intermedia is less biologically active and does not stimulate the adrenal gland.

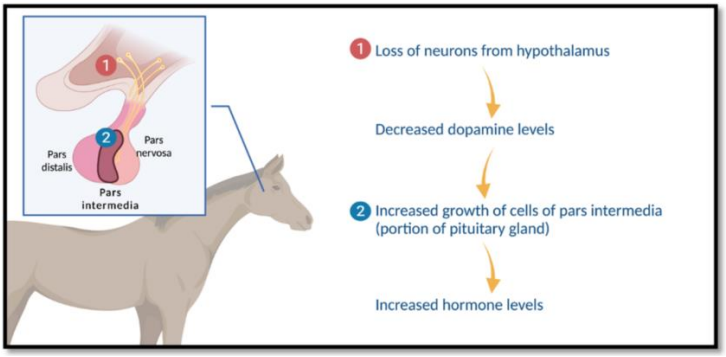

Figure 1:

https://vetmed.umn.edu/equine/research/equine-genetics-and-genomics-laboratory/projects/equine-pituitary-pars-intermedia-dysfunction-ppid

Clinical Signs and Diagnosis

Pituitary Pars Intermedia Dysregulation has a plethora of clinical signs, many of which go unnoticed by owners, especially in mild cases of the disease. Signs include hypertrichosis/delayed shedding, muscle atrophy, polyuria, polydipsia, lethargy, laminitis, recurrent infection, insulin dysregulation, abnormal sweating, and abnormal fat deposition.

Recognition of these clinical signs is incredibly important in diagnosing PPID as it may initiate the process of diagnostic testing to clearly identify the disease. There are a few specific tests used in diagnosing PPID. The first of which is the baseline ACTH test. This test requires a blood sample that is used to determine the amount of ACTH in the patient's plasma. It is necessary for the patient to be restricted from grain for at least 12 hours before acquiring the blood sample. There are numerous factors that influence ACTH levels that must be taken into account when analyzing the results and make this test suitable only for moderate to severe cases of the disease. These factors include seasonal changes, breed differences, stress, diet, illness, and exercise. The TRH stimulation test is a more accurate tool used to diagnose PPID. This test measures plasma ACTH levels before and 10 minutes post administration of IV thyrotropin-releasing hormone. In horses with PPID, ACTH levels post-TRH administration will be elevated whereas in a normal horse, glucocorticoid negative feedback restricts the release of ACTH from the pars distalis. Similar to the baseline ACTH test, seasonal influences on plasma ACTH levels should be considered when interpreting results.

Imaging is another powerful tool to be exploited in diagnosing PPID. CT and MRI technology can be used to evaluate the pituitary gland in great detail making this a great option for early detection. Financial limitations and lack of accessibility make this option less popular, however.

Figure 2: Depiction of hypertrichosis

https://vmc.usask.ca/care/equine-health/resources/ppid.php#Treatmentandmanagement

Is My Horse at Risk?

If you own a horse over the age of 15, PPID is something you should be on the lookout for. Age seems to be the only significant risk factor for PPID. Currently, there are no known predispositions for PPID based on breed or sex.

Treatment

While there is no cure for PPID, it can be treated to manage clinical signs. The only drug that may be used as a treatment is pergolide mesylate, a synthetic dopamine agonist. The dopaminergic inhibition reduces the amount of POMC and its derivatives produced by the pars intermedia, thereby improving clinical signs. The recommended starting dose of pergolide is 1mg per 500kg. After a month of therapy, baseline ACTH levels should be tested to ensure proper dosing.

References

Kirkwood, N. C., Hughes, K. J., & Stewart, A. J. (2022). Pituitary Pars Intermedia Dysfunction (PPID) in Horses. *Veterinary sciences*, *9*(10), 556. https://doi.org/10.3390/vetsci9100556

Morgan, R. A., Keen, J. A., Homer, N., Nixon, M., McKinnon-Garvin, A. M., Moses-Williams, J. A., Davis, S. R., Hadoke, P. W. F., & Walker, B. R. (2018). Dysregulation of Cortisol Metabolism in Equine Pituitary Pars Intermedia Dysfunction. *Endocrinology*, *159*(11), 3791–3800. https://doi.org/10.1210/en.2018-00726

Young, A. (2020, March 23). *Pituitary Pars Intermedia Dysfunction (PPID)*. UC Davis Veterinary Medicine Center for Equine Health. https://ceh.vetmed.ucdavis.edu/health-topics/pituitary-pars-intermedia-dysfunction-ppid