Equine Endocrinology

PPID Review and TRH response Update

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The original assessment of equine pituitary disease centered around the appearance of older horses with delayed coat shedding, and muscle wasting. Initially the condition was labeled as “equine Cushing’s disease” and considered to be the result of a pituitary adenoma. These initial considerations have been discarded. The condition is now considered a neurodegenerative disease that is at least in part due to a loss of dopamine producing neurons within the hypothalamus, which results in persistent over stimulation of the melanotroph cells within the pars intermedia. Overstimulation causes an increase in the prohormone pro-opiomelanocortin (POMC) and all of its associated enzymatic peptide end products. Interestingly, the main products are β-endorphin, corticotropin-lipotropin precursor (CLIP), αMSH and surprisingly less ACTH.

This ACTH is biologically inactive and does not appear to stimulate adrenal cortisol production. Given our better understanding of the pathology the disease is now designated as Pars Pituitary Intermedia disease (PPID)

There are both advances in the pathophysiology of this condition and a greater clinical awareness earlier in the disease process. Diagnosis especially in the early stages of the disease remains problematic. The levels of ACTH that we measure are predominantly of pars distalis origin with only a small component from the pars intermedia. This component does increase with time and over the course of the disease. However, in the early stages of the disease concentrations may be insufficient to result in significant increases in the levels that are measured in the laboratory.

ACTH levels are influenced by age, sex, disease, and most importantly by photoperiod/climate and temperature. There is a pronounced increase in ACTH levels which is very noticeable in August (northern hemisphere) and extends to the end of October. The level starts tapering through November and is at a seasonal low from January through April with gradual increases until the next peak in August. The variation in these values can interfere with diagnosis and are also specific to different photoperiods. There are extensive reviews in the literature regarding photoperiods/temperature and either diagnostic cut-off values (DOCV) or reference intervals which vary by region.

It is important to note that none of the published reference intervals are from the Pacific Northwest which has a significant shift in photoperiod of 7.7 hours shorter daylight in December as compared to the summer solstice in June; and this change in daylight is substantially less in e.g., Sacramento (≈5 hrs) or Lansing Michigan (≈6 hrs).

This difference in daylight has a significant impact on ACTH as well as the chosen DOCV. Our reference intervals were determined from varying breeds of horses native to the lower mainland and all were between 9-13 years of age.

ACTH levels should not be run on horses under 10 years of age as the disease does not occur in this age group, nor on patients of any age without clinical signs that support PPID.

An ACTH level of >11.66 pmol/L in autumn, >10.22 pmol/L the remainder of the year, will have a 95% specificity for PPID if there are clinical signs of this disease.

The equivocal zone ranges from 6.2 -11.6 in autumn, to 5.3 to 10.2 in the remainder of the year.

When to Run a TRH Response Test?

- **If there is a high clinical index of suspicion for PPID and the ACTH value falls in the equivocal range a TRH response test may be helpful to increase the sensitivity of detecting PPID, but there are increased false positives with this test.**

- **From July to December TRH stimulation testing can only be used to identify negative cases in these months to avoid the risk of false positives.**

- **TRH tests can be used to monitor response to therapy. Decreased ACTH levels may occur post therapy however the majority of the horses will still have levels within the equivocal zone or greater than the reference interval.**

For further information see:

Recommendations for the Diagnosis and Treatment of Pituitary Pars Intermedia Dysfunction (PPID) Revised October 2021 by the PPID Working Group Kelsey Hart (Group Coordinator; University of Georgia), Andy Durham (Liphook Equine Hospital), Nicholas Frank (Tufts University), Catherine McGowan (University of Liverpool), Hal Schott (Michigan State University), and Allison Stewart (University of Queensland)

A.E. Durham, The effect of pergolide mesylate on adrenocorticotrophic hormone responses to exogenous thyrotropin releasing hormone in horses, The Veterinary Journal, Volume 285, 2022, 105831, ISSN 1090-0233.

Thane K et al,. Effect of early or late blood sampling on thyrotropin releasing hormone stimulation test results in horses. J Vet Intern Med. 2022 Mar;36(2):770-777. doi: 10.1111/jvim.16362. Epub 2022 Jan 20.