

Pituitary Pars Intermedia Dysfunction: old disease, new tests

Pituitary pars intermedia dysfunction (PPID) is the most common endocrinopathy of horses and ponies with up to 30 per cent of older animals affected (Equine Endocrinology Group booklet), writes Siobhan McAuliffe MVB DACVIM Cert RA. It is predominantly a disease of older animals (> 13 years) but there have been cases in animals as young as seven years

With increasing emphasis on improving productivity and performance length, greater attention is being given to conditions that were previously viewed simply as 'old age' changes.

The clinical signs that are seen are as a result of increased levels of ACTH, α -melanocyte stimulating hormone and β -endorphin, secreted by an adenoma or hypertrophied cells of the pars intermedia of the pituitary gland (Figure 1). The condition has had various names over the years including equine Cushing's Disease but is now termed pituitary pars intermedia dysfunction (PPID).



Figure 1. Adenoma of the pituitary gland. Photo: Author.

Classical clinical signs associated with PPID are hypertrichosis (Figure 2), weight loss and poor muscle tone, abnormal distribution of subcutaneous fat, periorbital swelling in the absence of ocular disease (Figure 3), polyuria and polydipsia, laminitis (Figure 4) and a predisposition to infections. The reproductive cycles of mares are interrupted or abnormal in duration, and some affected mares even produce milk without pregnancy. The signs are insidious in onset or are frequently attributed to old age.



Figure 2. Hypertrichosis. Photo: Author.



Figure 3. Supraorbital fat deposits. Photo: Author.



Figure 4. Laminitic changes to the hoof wall. Photo: Author.

Testing should be considered in all animals over 15 years of age, younger animals showing clinical signs and mares with poor reproductive performance. An ACTH test can be performed free of charge (complimentary laboratory fees only – visit, blood sampling and interpretation fees may be applied by veterinary practices) by downloading a voucher from the 'Talk about laminitis' website (see panel).

A compounding factor in many cases is the presence of concurrent metabolic syndrome (EMS) or insulin

Visit www.talkaboutlaminitis.ie to download vouchers for free* diagnostic ACTH tests for your clients (*free basal ACTH laboratory fees only, terms and conditions apply).

dysregulation. Both PPID and EMS have many clinical signs in common such as laminitis, abnormal fat deposition and irregular cycles or poor reproductive performance (Figure 5). Therefore current recommendations indicate testing for both conditions simultaneously.



Figure 5. Typical phenotype for insulin dysregulation/metabolic syndrome. Photo: Author.

DIAGNOSIS

- Hypertrichosis (abnormally dense, hairy coat) is considered

pathognomonic for PPID. The hair coat is abnormally long, curly, brittle and dense. Normal seasonal shedding of the coat does not occur and the horse remains hirsute in the summer months. Sweating and weight loss may be detectable on close examination, but may be missed under the heavy, shaggy coat. Commonly, it is mistakenly interpreted as a normally long winter coat in small ponies and this may lead to a delay in diagnosis in these cases. Testing of these animals for both PPID and insulin dysregulation is still recommended.

- Measurement of ACTH concentration is the most popular means of diagnosing PPID but care is required in the interpretation of the results and its use as a single stand alone diagnostic test is not suitable in all cases. Measurement of ACTH following the administration of thyropin releasing hormone is more appropriate in horses that do not have obvious clinical signs.

ADRENOCORTICOTROPIC HORMONE - ACTH

The sensitivity and specificity of ACTH measurements alone for the diagnosis of PPID has varied between studies, in many cases influenced by inclusion criteria. In summary, the test works well in horses that are displaying clinical signs.



Other compounding factors such as diet, time of the year and individual fluctuation in pituitary output can also result in test variation.

Day length has a major influence on pituitary activity and, hence, ACTH concentration. This has resulted in laboratories providing varying reference values based on the time of the year the test is performed.

In many instances, the test result may fall into a borderline category and this is more commonly seen in horses that either have minimal or no clinical signs. These are horses that may be selected for testing based on, for example, poor heat cycling in mares. In these cases, a thyrotropin releasing hormone stimulation test (TRHST) is more appropriate.

ACTH MEASUREMENT

Measurement is carried out as follows:

- Use glass or plastic tubes containing EDTA.
- Collect at any time of the day.
- Keep samples cool (ice packs or refrigerator).
- Centrifuge and separate plasma prior to shipping. Centrifuge is preferred to gravity separation.
- Overnight shipping with ice packs.

THYROTROPIN RELEASING HORMONE STIMULATION TEST (TRHST)

The use of TRH to maximally stimulate the pituitary gland reduces the relative importance of compounding factors and increases accuracy. A TRHST is currently considered the most reliable means of diagnosing PPID in horses with minimal clinical signs or those that have fallen within the 'equivocal' ranges. TRH is not licensed in Ireland and must be imported and shipped chilled, while the initial ACTH test can be performed free of charge. This makes an initial single ACTH measurement practical and inexpensive in an Irish setting.

The test is carried out as follows:

- 1mg of TRH is administered IV (0.5mg in ponies weighing less than 250kg)
- A serum sample is taken 10 minutes later for measurement of ACTH.
- Horses that fall in the equivocal range following a TRHST without clinical signs should be retested in six months.

ASSESSING INSULIN DYSREGULATION

Assessing insulin dysregulation should be considered vital in animals displaying signs of laminitis and/or other signs of PPID. They are frequently seen together and in those cases the relative clinical contribution of each component will be impossible to assess if they are not treated simultaneously.

Historical anecdotal claims by vets that treatment of PPID was unrewarding was likely related to a lack of recognition, and therefore lack of treatment, of concurrent insulin dysregulation. Medication may be required in cases of insulin dysregulation especially those that are experiencing an acute laminitic episode but many can be managed long term with dietary and management changes. In most instances, a single insulin measurement is all that is required. Fasting is not required prior to sampling but nothing other than hay should have been fed in the

four hours prior to testing. A single serum sample can be used for both ACTH and insulin measurement. Further diagnostics and treatment of metabolic syndrome are beyond the scope of this article, and some recommended reading is included on the right.

INTERPRETATION OF RESULTS

For recommendations for interpretation of PPID diagnostics tests, see Table 1.

	Negative	Equivocal	Positive
ACTH (MID-NOVEMBER TO MID-JULY)	<30pg/ml	30 - 50pg/ml	>50pg/ml
ACTH (MID-JULY TO MID-NOVEMBER)	<50pg/ml	50 - 100pg/ml	>100pg/ml
ACTH 10 MINS AFTER 1MG OF TRH	<110pg/ml	110 - 200pg/ml	>200pg/ml

Table 1. Recommendations for interpretation of PPID diagnostic tests. Reference ranges from Equine Endocrinology Group based on the Immulite (TM) immunoassay for ACTH (always check with laboratory where test was performed for their reference values as values vary depending on assay used).

TREATMENT OF PPID

Therapy is aimed at increasing dopaminergic tone in the pars intermedia or decreasing circulating cortisol concentration.

- Pergolide is a dopamine agonist and is considered to be the treatment of choice. The initial dose is 0.002mg/kg PO q 24h (1mg per 450kg). It is important to remember that PPID is a slowly progressive disease and the dose may need to be slowly increased if the horse becomes refractory to treatment due to disease progression. Adverse effects of treatment include anorexia, depression and ataxia, and the dose should be decreased if any of these signs are observed.
- Cyroheptadine is a serotonin antagonist that has been widely used to treat PPID. However, reports of efficacy are lacking.
- Another factor in the treatment of horses with PPID is improved general husbandry including: careful feeding, early attention to infections and regular farrier care. It is important to remember that PPID is a progressive disease and as such a 'cure' is not possible but the majority of horses improve dramatically with treatment.

RECOMMENDED READING

PPID: https://sites.tufts.edu/equineendogroup/files/2019/12/2019-PPID_EEGbooklet.pdf

Equine Metabolic syndrome: https://sites.tufts.edu/equineendogroup/files/2020/09/200592_EMS_Recommendations_Bro-FINAL.pdf