

How to Diagnose Equine Pituitary Pars Intermedia Dysfunction

Nat T. Messer IV, DVM

Diagnosis of pituitary pars intermedia dysfunction in horses is based on clinical signs and results of dynamic endocrinological testing. The dexamethasone suppression test is a sensitive diagnostic test and is easy to perform, at moderate expense. Author's address: Department of Veterinary Medicine and Surgery, College of Veterinary Medicine, University of Missouri, 379 E. Campus Dr., Columbia, MO 65211. © 1999 AAEP.

1. Introduction

Pituitary pars intermedia dysfunction (PPID) in the horse is a slowly progressive disorder with a characteristic clinical picture. It is also referred to as equine Cushing's disease because of its similarity to Cushing's disease in humans.¹ Unlike its counterpart in humans, the condition in horses is caused by adenomas or adenomatous hypertrophy of the intermediate lobe of the pituitary gland, thus the designation "pituitary tumor" or "pituitary adenoma."¹⁻⁷

The anterior lobe of the pituitary gland consists of three parts: pars distalis, pars intermedia, and pars tuberalis. The main secretory products of the corticotropes, located in the pars distalis, are adrenocorticotropin (ACTH) and α - and β -lipotropin (LPH) while the main secretory products of the melanotropes, located in the pars intermedia, are α - and β -melanocyte-stimulating hormone (MSH), corticotrophin-like intermediate lobe peptide (CLIP), and β -endorphin-related peptides (β END).⁴ Both corticotropes and melanotropes synthesize the same precursor protein, pro-opiomelanocortin (POMC), but they cleave it into different hormones. Under normal circumstances, adrenocortical steroidogenesis is

maintained by corticotrope secretion of ACTH and corticotropes are inhibited via negative feedback by glucocorticoids. In horses with PPID, hypertrophy and hyperplasia of melanotropes result in a marked increase in POMC synthesis, with release of large amounts of MSH, CLIP, and β END peptides as well as comparatively small but increased amounts of ACTH.^{6,8} The MSH and β END peptides are capable of inducing a sixfold increase in the steroidogenic properties of ACTH.⁶ Therefore, a small increase in ACTH coupled with a large increase in potentiating peptide concentrations is sufficient to stimulate adrenocortical steroidogenesis, resulting in an increase in plasma cortisol concentrations and even more importantly in loss of the circadian pattern of cortisol secretion. The insensitivity of melanotropes to glucocorticoids has diagnostic implications that permit differentiation of melanotrope-maintained steroidogenesis in affected animals from corticotrope-maintained steroidogenesis in normal animals.⁶

Besides dysfunction of the pituitary-adrenocortical axis, studies report some manifestation of peripheral insulin resistance in horses with PPID.^{3-5,9,10}

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This is evidenced by elevated basal insulin concentration,^{5,10} intolerance to intravenous glucose,¹⁰ either decreased¹⁰ or increased⁹ insulin response to glucose loading and failure to reduce hyperglycemia after administration of exogenous insulin.¹¹ In one study, basal insulin concentrations in horses with PPID were the same as those in young horses without PPID,⁹ and not all horses with PPID in other studies^{4,5} had high basal insulin concentrations. These studies point out conflicting evidence regarding glucoregulatory mechanisms in horses with PPID. This may be further confounded in pony breeds because of their apparent insensitivity to insulin, which can be complicated by obesity and laminitis.^{12,13} Three of the studies reporting abnormal glucoregulatory mechanisms included ponies as part of the study population.³⁻⁵

Diagnosis of PPID should be based on clinical signs and dynamic endocrinological testing.

2. Clinical Signs

Affected horses are usually older (>15 years), obese animals with a thick, "cresty" neck and a long, curly haircoat (hirsutism) that fails to shed normally in the summer months.¹⁻³ PPID is the only clinical condition known to cause hirsutism in the horse.⁵ There appears to be a higher incidence in females.¹ Many horses also have signs of chronic laminitis, infertility, chronic infections, hyperhidrosis, bulging supraorbital fat pads, polydipsia and polyuria and are hyperglycemic.¹⁻⁴ This disorder may occur even when these characteristic clinical features are not apparent. Likewise, horses may have some of these characteristic clinical features and not have PPID, but rather some other endocrine disorder.^a

3. Endocrinologic Tests

A. Dexamethasone Suppression Test

Differentiation of melanotrope-maintained steroidogenesis in animals affected with PPID from corticotrope-maintained steroidogenesis in normal animals can be determined by use of the dexamethasone suppression test (DST).⁶ Dexamethasone administration must precede the normal diurnal increase in release of ACTH (early morning hours), and the postdexamethasone blood sample must be collected after the normal time of increased ACTH release.⁶ Prolonged suppression of ACTH by dexamethasone is dose-related, with 40 µg dexamethasone/kg causing maximal blockade.⁶

B. Protocol for overnight DST

1. Begin test between 4 and 6 p.m.
2. Collect a baseline (predexamethasone) sample into a heparinized container.
3. Administer dexamethasone (40 µg/kg or 2 mg/100 lb) IM between 4 and 6 p.m.
4. Collect postdexamethasone samples into heparinized containers at 12 noon the following

day (approximately 19 h after dexamethasone administration).

The heparinized containers should be centrifuged immediately after collection, plasma harvested, and either refrigerated or frozen depending on the time between collection and analysis. Samples are analyzed to determine plasma cortisol concentration.

C. Interpretation

Normal horses will have ≤1 µg/dl cortisol 19 h after dexamethasone administration. Affected animals will have ≥1 µg/dl cortisol after dexamethasone administration.

Other tests that have been used to evaluate pituitary-adrenocortical dysfunction in horses include

1. basal ACTH levels,⁵
2. ACTH stimulation tests,⁵
3. basal insulin levels,^{4,5}
4. TRH stimulation test,¹⁴
5. a combined dexamethasone suppression/TRH stimulation test,⁷ and
6. urinary corticoid/creatinine ratios.⁵

Because PPID is the only known cause of hirsutism in horses, it would appear that a clinical diagnosis based on the presence of hirsutism might be as accurate as laboratory diagnosis. Measurement of basal plasma cortisol concentrations alone is of no use in diagnosing PPID.³⁻⁷ A recent study demonstrated that TRH stimulation alone was not able to distinguish healthy horses from those with PPID.⁷

There might be a risk of induction of laminitis by administration of 40 µg/kg dexamethasone to horses with PPID, especially those with a history or signs of previous laminitis. This risk appears low based on the results of two studies involving 17 horses and 52 horses, respectively, with PPID, in which none of the horses receiving dexamethasone developed signs of laminitis.^{2,6}

Horses with clinical signs suggestive of PPID with suppression of cortisol concentrations after dexamethasone administration may have another endocrine abnormality such as that similar to central obesity syndrome in humans.^a

References and Footnotes

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