As the trend toward maintaining horses well into their senior years continues, understanding the challenges of diagnosing and managing horses with Cushing’s syndrome (pituitary pars intermedia dysfunction [PPID]) can help veterinary technicians contribute to the diagnosis and daily care of these patients.

**Pathophysiology**

The tiny pituitary, which lies at the base of the hypothalamus, plays a key role in maintaining homeostasis and controls many functions of other glands in the endocrine system (FIGURE 1). The pituitary is composed of three lobes: the pars distalis, pars intermedia, and pars nervosa. During normal function, the pars intermedia releases a precursor of adrenocorticotropic hormone (ACTH) that is processed into several different hormones that help regulate many body processes, including skin coloring, appetite/satiety balance, fat metabolism, insulin release, analgesia, behavioral modification, vascular tone, and regulation of glucocorticoid production by the adrenal cortex.

Cushing’s syndrome in horses is unique in that it involves hyperplasia of the pars intermedia rather than adenoma of the pars distalis, which occurs in dogs and humans; therefore, the term PPID is preferred to better describe the equine disease process. PPID is the result of hypertrophy, hyperplasia, and microadenoma formation within the pars intermedia. These conditions contribute to excessive ACTH production, and the enlarged gland places mechanical pressure on adjacent tissues, inhibiting function of the pars distalis and pars nervosa. The resultant functional changes and the excessive release of ACTH into the body result in clinical disease.2

**Signalment**

PPID commonly occurs in geriatric horses (≥20 years of age) but can occur in younger horses. Hirsutism (an over-long, shaggy haircoat) is the most obvious clinical sign, but not all horses with PPID exhibit it. Affected horses may also have moist, greasy skin; hyperhidrosis; a patchy haircoat; slow or late seasonal changes to the haircoat; lethargy; a potbellied appearance; polyuria; polydipsia; poor wound healing; an increased respiratory rate; muscle wasting; insulin resistance; and, in mares, poor reproductive performance. PPID is also strongly linked to an increased incidence of chronic laminitis. In some instances, horses with PPID can present with laminitis as the only obvious clinical sign.4

**Diagnostics**

PPID is often diagnosed based on the presence of hirsutism. In fact, the presence of hirsutism has been found to
have greater diagnostic accuracy than endocrine testing.1,5,6 However, a complete physical examination in conjunction with a complete blood count, a serum chemistry profile, and baseline endocrine testing is recommended as a basis for providing optimal patient care.1 Because direct assessment of the pituitary is difficult, several endocrine testing protocols have been developed and investigated to indirectly identify pituitary abnormalities by assessing endocrine function. Current endocrine testing protocols include dynamic and single sample testing. With this approach to diagnosing endocrine abnormalities, the results may be difficult to interpret because of normal seasonal, and even diurnal, hormonal changes.5 The following diagnostic tests are commonly used in practice.

**Dexamethasone Suppression Test**

Previously described as the gold standard endocrine test for PPID, the dexamethasone suppression test assesses the function of the hypothalamic–pituitary–adrenal (HPA) axis (FIGURE 2). However, recent studies have shown this test to be less reliable than previously thought.7

The overnight dexamethasone suppression test is a dynamic test performed by collecting a blood sample to measure the plasma cortisol level in the late afternoon, administering dexamethasone, and then collecting and testing a second blood sample the next day (~15 to 19 hours later). In a normal horse, hypothalamic exposure to dexamethasone suppresses the endogenous cortisol concentration, causing the serum cortisol level to decrease to <1 µg/dL (~30 pmol/L) by the time the second blood sample is collected. Values higher than this level support a diagnosis of PPID.1,5

This testing protocol involves collection of two samples, requiring two farm visits. Another concern is that early in the disease, a horse may still have partial HPA feedback. An exact range of values indicating partial suppression of HPA feedback remains difficult to define due to seasonal and diurnal variability of normal cortisol levels.1,5 Additionally, treatment using steroids has been associated with an episode of laminitis, so this test may increase the risk of laminitis. Researchers continue to work toward defining this risk.1,3

**Resting Serum Adrenocorticotropic Hormone Test**

An example of a single-sample endocrine test is the measurement of resting serum ACTH. In this instance, glucose and insulin levels are often assessed at the same time to check for insulin resistance. In dogs and humans, ACTH levels in collected samples have been found to be highly
unstable, raising concerns regarding using this test in equine ambulatory practice. However, samples from horses have been found to be considerably more stable than those from dogs or humans. In addition, an increased level of circulating ACTH is strongly linked to the presence of hirsutism, which is clinically very indicative of PPID. While one sample to assess the ACTH level may be sufficient for diagnosis, some researchers suggest that collecting two or three samples over the day and also assessing the glucose and insulin levels to determine if insulin resistance is present can be beneficial in obtaining a more accurate diagnosis. However, seasonal variability may complicate the interpretation of this test as well. For example, one study found that horses and ponies living in Pennsylvania had an increased false-positive testing rate between August and October; therefore, it is recommended to limit this testing to the period between November and June. However, obtaining a negative test result (a normal serum ACTH level) during the period between August and October is considered very strong evidence that a horse does not have PPID.

**Differential Diagnosis: Equine Metabolic Syndrome**

Equine metabolic syndrome (EMS), also known as peripheral Cushing’s disease, may present with clinical signs similar to those of PPID. The main difference is that EMS is not directly related to pituitary dysfunction but is related to obesity and associated insulin resistance. Researchers have found that fat, particularly omental fat, is metabolically active, releasing free fatty acids as well as cortisol, leptin, and resistin—hormonal mediators that may contribute to insulin resistance and worsen obesity and laminitis. Commonly affected breeds include pony breeds, domesticated Spanish Mustangs, Peruvian Pasos, Paso Finos, European Warmbloods, American Saddlebreds, and Morgans. Horses with EMS tend not to exhibit hirsutism and tend to present at a slightly younger age (6 to 20 years); otherwise, their clinical signs are often very similar to those of horses with PPID, with the most worrisome sign being chronic laminitis.

Often described as “easy keepers,” horses with EMS tend to have typical fat deposits, most notably a cresty neck (FIGURE 3) and a thickened gluteal region; geldings may have an enlarged prepuce due to adipose tissue. Reproductive difficulties due to abnormal ovarian cycling have been noted in affected mares. While horses with EMS can have a similar appearance to those with PPID and can develop insulin resistance, horses with EMS do not develop an adenoma of the pars intermedia and, therefore, cannot be expected to respond to medications used in treating PPID. The primary treatment for EMS is improved dietary management and exercise to facilitate weight loss; therefore, it is important to ensure that an accurate diagnosis is made.

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**Glossary**

- **Adenoma**—a small benign tumor in which the cells are derived from glandular epithelium
- **Cortisol**—a major natural glucocorticoid released by the adrenal cortex
- **Diurnal**—pertaining to or occurring during the daytime
- **Endogenous**—caused by factors, or produced, within an organism
- **Exogenous**—caused by factors, or originating, outside of an organism
- **Glycemic**—pertaining to glucose
- **Hirsutism**—abnormal hairiness; an overlong haircoat
- **Homeostasis**—a state of equilibrium within the body
- **Hyperhidrosis**—excessive sweating
- **Hyperplasia**—an increase in the number of normal cells in a tissue or organ
- **Hypertrophy**—an enlargement or overgrowth of an organ or body part
- **Insulin resistance**—reduced glucose uptake by tissues of the body despite an increase in the circulating insulin level
- **Omental**—pertaining to a fold of peritoneum extending from the stomach that supports adjacent abdominal organs
- **Polydipsia**—increased thirst
- **Polyuria**—increased urination

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**FIGURE 3**

This illustration shows the typical body type of ponies with EMS. Note the thick, cresty neck (arrow).
Treatment

Treatment of PPID involves several factors, including management and pharmacologic options. Dietary management is of primary importance in all horses with insulin resistance. The main goal of feeding these horses is to provide a feed that stimulates a low glycemic response. For example, the increased sugar content found in fresh growth of grasses can stimulate a very high glycemic response. Therefore, horses with PPID are often allowed limited pasture grazing or withheld from it altogether. However, grass hay provides a much lower glycemic response. Exclusively feeding grass hay with a <12% total nonstructural carbohydrate (NSC) content at a rate of 1.5% to 2% of body weight along with an adequate vitamin and mineral supplement generally supplies a nutritionally sufficient (“safe”) diet. Owners should be strongly encouraged to periodically weigh feed portions to ensure that their horse is not being overfed or underfed.

As a rule, grain and most concentrates should not be fed because of their high carbohydrate levels, which increase the glycemic response. However, in some instances, more calories are needed (e.g., for working horses or horses with poor dentition). In these instances, feeds with lower NSC values (e.g., feeds containing molasses-free beet pulp, corn oil, canola oil, rice bran oil, or rice bran) can be used for dietary supplementation. Many feed manufacturers have developed pelleted complete feeds that are designed to stimulate a low glycemic response in geriatric horses. However, sometimes it may be necessary to supply grains or other concentrates (e.g., for picky eaters). In these instances, the glycemic response can be reduced if (1) hay is fed 15 to 30 minutes before grains and (2) grains are given throughout the day in three or four small meals rather than in one large meal.

Exercise is an important management strategy to facilitate weight loss in obese horses. However, horses experiencing an episode of laminitis must be rested until the condition of their feet stabilizes. Otherwise, they should be exercised regularly (daily is ideal) in a fashion suitable to their fitness level. Hand walking, lunging, and riding can all increase a horse’s fitness level. Exercise and its associated muscle metabolism can play a role in helping to prevent and even reverse insulin resistance to some degree.

Other management considerations include clipping late-shedding haircoats to help horses thermoregulate during warmer months, addressing dental or hoof issues, and carefully managing any other health concerns. Horses with PPID often require careful management to ensure optimal health.

Horses with PPID benefit from treatment with pergolide. An important factor that owners must understand is that pergolide is supportive, not curative, and is often necessary for the remainder of the horse’s life. However, many horses respond favorably to treatment with pergolide. Usually, within a week of starting treatment, the horse appears more bright and energetic. Many clinical signs (e.g., polyuria/polydipsia, laminitis) improve, but hirsutism is unlikely to resolve.

Conclusion

The tiny pituitary, which lies at the base of the hypothalamus, plays a key role in maintaining health and controls many functions of other glands in the endocrine system. A well-recognized problem in dogs, pituitary dysfunction also commonly affects horses. Therefore, a basic understanding of the function and dysfunction of the equine pituitary is valuable for technicians working in equine practice.

References


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1. “Cushing’s syndrome” in equids is unique in that the
   a. pars intermedia is not involved.
   b. pars intermedia is involved.
   c. pars distalis and pars intermedia are involved.
   d. pituitary is not involved.
2. PPID commonly occurs in
   a. obese horses.
   b. geriatric horses (≥20 years of age).
   c. middle-aged geldings (6 to 20 years of age).
   d. young colts (≤5 years of age).
3. Horses with PPID ________ have hirsutism.
   a. always
   b. often
   c. seldom
   d. never
4. Horses with EMS may exhibit
   a. laminitis and insulin resistance.
   b. obesity.
   c. adenoma of the pars intermedia.
   d. a and b
5. Clinical signs of PPID include
   a. hirsutism and slow to late seasonal changes to the haircoat.
   b. hyperhidrosis and polyuria/polydypsia.
   c. laminitis and insulin resistance.
   d. all of the above
6. An example of endocrine testing for PPID is
   a. measurement of ACTH, insulin, and glucose.
   b. measurement of the serum insulin level after dexamethasone administration.

   c. the ACTH stimulation test.
   d. all of the above
7. Insulin resistance
   a. occurs when the body cannot produce sufficient insulin.
   b. results from increased to excessive insulin production.
   c. involves decreased glucose uptake by muscle and other tissues of the body.
   d. does not occur in horses with PPID.
8. Dietary recommendations for horses with insulin resistance include
   a. a high glycemic feed and ample access to pasture.
   b. a strictly hay diet and adequate vitamin and mineral supplementation.
   c. feed containing >12% total NSC.
   d. b and c
9. Pergolide
   a. can be used to treat horses with insulin resistance.
   b. can be used to cure horses with Cushing’s disease.
   c. can be used to help maintain horses with PPID.
   d. is not beneficial to horses with PPID.
10. Regarding horses with PPID, grains and concentrates
    a. stimulate a high glycemic response and, therefore, must never be fed.
    b. can be fed if the NSC values are high.
    c. can be fed to picky eaters in small quantities throughout the day.
    d. b and c