Endocrine Disorders of the Equine Athlete

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KEYWORDS

• Adiposity • Equine metabolic syndrome • Insulin dysregulation • Laminitis
• Pituitary pars intermedia dysfunction

KEY POINTS

- Laminitis poses the greatest threat to the health of the athletic horse and insulin dysregulation (ID) is an important risk factor for this condition.
- ID is likely to have a genetic basis, and exacerbating factors include obesity, age, lack of exercise, systemic disease, pituitary pars intermedia dysfunction (PPID), and corticosteroid administration.
- Mild ID is managed by lowering the nonstructural carbohydrate content of the diet, reducing body fat mass, and increasing exercise, but medical treatments such as metformin may be required for managing severe ID.
- PPID is a cause of poor performance in athletic horses and may also result in loss of topline muscle mass and delayed shedding of the winter hair coat.
- Pergolide is an effective medical treatment of PPID in horses but may not be permitted during competitions.

INTRODUCTION

Equine athletes are affected by the same endocrine and metabolic disorders as other horses, but conditions affecting performance are of particular concern. Laminitis poses the greatest threat to performance because of the damage that it causes to hoof structures and the pain associated with lengthening and separation of dermal and epidermal laminae. There is mounting evidence that *insulin dysregulation (ID)* is an important cause of laminitis in horses, and this highlights the need for screening tests to identify at-risk horses. This article includes an in-depth discussion of ID and other risk factors for laminitis that are grouped together as *equine metabolic syndrome (EMS)*. As horses age, the risk of *pituitary pars intermedia dysfunction (PPID)* increases, and this endocrine disorder may exacerbate preexisting ID and further increase the risk of laminitis. This form of hyperadrenocorticism also weakens tissues and may increase susceptibility to tendon and ligament injury. Equine athletes that

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develop PPID may be presented because of poor performance and loss of muscle along the topline, and medical treatment with pergolide allows activity levels to increase and muscle mass to return. Use of corticosteroids for the treatment of musculoskeletal problems or medical conditions such as equine asthma may exacerbate ID and increase the likelihood of laminitis developing in high-risk horses.

INSULIN DYSREGULATION IN THE EQUINE ATHLETE

ID manifests as fasting hyperinsulinemia, excessive insulin responses to oral sugars, or insulin resistance in horses,[1] and this endocrine disorder is a major health concern because of its association with laminitis. Insulin became the focus of intense research when laminitis was experimentally induced in healthy ponies and Standardbred horses by infusing insulin intravenously,[2,3] and excessive insulin responses to oral sugars have been detected in equids with naturally occurring laminitis.[4,5] ID is the central feature of EMS, a collection of risk factors for endocrinopathic laminitis that also includes increased adiposity, dyslipidemia, hypertension, and adipokine alterations.[1,6–8]

Genetics are thought to play a major role in ID, but only a few studies have examined this relationship to date. Jeffcott and colleagues[9] detected differences in glucose tolerance and insulin sensitivity between ponies and standardbred horses and attributed this to genetic variability among breeds. Fat and laminitic ponies showed more modest responses to exogenous insulin, indicating that insulin sensitivity was lower in these animals. Treiber and colleagues,[4] detected familial associations after performing pedigree analysis on a group of ponies with laminitis from a closed herd. Differences in postprandial insulin responses to meals have also been detected among standardbred horses, mixed-breed ponies, and Andalusian cross horses, and this provides further evidence of breed-related variability in glucose and insulin dynamics.[10] A more detailed examination of genetics has been performed in Arabian horses using genome-wide association, and an EMS locus has been identified.[11] All of these findings are relevant to equine athletes because Arabians, Morgans, Paso Finos, ponies, and warmbloods appear to be genetically susceptible to ID, and they are often used as performance horses. ID is exacerbated by obesity, age, lack of exercise, systemic disease, PPID, and corticosteroid administration, and these risk factors are discussed later.

Obesity

This problem occurs in athletic horses when they are placed on diets that provide more energy than required. Athletic horses commonly receive grain or other concentrates in their diet because it assumed that additional energy is required to meet the demands of exercise. A diet should ideally be formulated for the individual horse, with body condition scoring performed regularly to assess body fat mass. Unfortunately, this is not always the case, and performance horses become obese as a result of overfeeding. Interestingly, obesity is more difficult to assess through visual examination in performance horses, and increased fat mass is sometimes mistaken for increased muscle mass. In the author's experience, this occurs more frequently in warmblood horses because of their larger stature. Palpation is required to assess body condition score in these animals, or ultrasound examination can be performed to measure the depth of subcutaneous or abdominal fat. Plasma leptin concentrations correlate with body fat mass,[12] and it is sometimes useful to measure this adipokine to convince owners that their horse is obese. Because obesity exacerbates ID and therefore raises the risk of laminitis, all horse owners should be strongly advised to manage obesity in athletic horses.

Some affected horses develop regional adiposity and accumulate fat in the neck region, and this may be referred to as a "cresty neck." Fat may also accumulate in the tail head, prepuce, or mammary gland regions, and subcutaneous fat masses sometimes appear in random locations. The neck should be palpated as part of routine physical examinations, and a cresty neck scoring system can be used to measure of adiposity in this region.[13] A horse with an enlarged neck crest is displayed in Fig. 1.

Age

Racehorses tend to be younger in age, but athletic horses used for other disciplines such as dressage remain in competition until they reach middle age. Age-related insulin resistance may occur in horses as it does in other species,[14] and the risk of PPID developing increases with age. If a horse is already genetically susceptible to ID, then these factors may raise blood insulin concentrations even further and increase the risk of laminitis developing.

Exercise

ID may be exacerbated when horses are laid up because of injuries and kept on a high-energy diet. Fat accumulates in adipose, muscle, and hepatic tissues and lowers insulin sensitivity, which raises insulin concentrations and increases the risk laminitis of laminitis occurring. Accumulation of fat within the liver decreases insulin clearance from the portal blood and causes plasma insulin concentrations to rise. More than 70% of the insulin secreted by pancreatic beta cells is cleared from the portal blood by the liver, so conditions that compromise liver function increase insulin concentrations within the peripheral blood.[15] The risk of hyperinsulinemia is highest in horses and ponies that are genetically predisposed to ID, so it is imperative that at-risk animals be placed on diets that are low in energy and nonstructural carbohydrates (NSC) whenever they are taken out of work.

Systemic Disease

Athletic horses travel more than other horses because they compete at different events, and their risk of acquiring infectious diseases is higher as a result. The stress associated with travel, housing in unfamiliar environments, and competition further increases the risk of infectious disease, and the combination of increased stress hormones and systemic inflammation may increase the risk of laminitis. When considering this group of risk factors, it is important to return to the concept of genetic susceptibility to ID because a Welsh pony with systemic inflammation may be more likely to develop laminitis than a thoroughbred with the same condition.

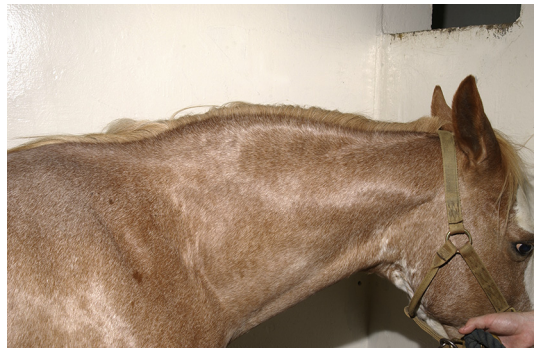

Fig. 1. Enlarged neck crest as an example of regional adiposity in a horse.

Pituitary Pars Intermedia Dysfunction

The risk of this endocrinopathy developing increases with age, and horses older than 10 years of age should be observed closely for clinical signs of muscle loss and delayed shedding of the winter hair coat. Development of PPID in a horse with preexisting ID is more worrisome than the same disease occurring in a horse with normal insulin status, and it is important to consider the breed of the horse being examined. Concurrent ID and PPID raises the risk of laminitis, and Mastro and colleagues[16] reported that some horses with PPID suffer from ID, whereas others have normal insulin sensitivity. Laminitis risk is more closely tied to ID than PPID status. As discussed in greater detail in later discussion, PPID can be seen in middle-aged athletic horses and negatively impacts performance. It is also a concern when managing ID because PPID appears to exacerbate ID and raise the risk of laminitis developing.

Corticosteroids

This controversial topic has been discussed in several articles, and debate continues about the risk of laminitis developing after corticosteroid administration.[17–19] An important piece of evidence was recently provided by an epidemiologic study of pasture- and endocrinopathy-associated laminitis, where an odds ratio of 10 was reported for laminitis developing after corticosteroid administration.[20] In the author's experience, the risk of laminitis after intra-articular or systemic administration of corticosteroids depends on multiple factors, and care should be taken to fully assess the patient before administering these drugs. If the horse has a higher risk of ID because of its breed, and exacerbating factors, such as obesity or systemic inflammation, are also noted, then there is a higher risk of laminitis developing after corticosteroid administration. Other exacerbating factors such as recent reduction in exercise, stall confinement, or the pain of lameness must also be considered. A high-grain diet also increases the risk of laminitis in horses receiving corticosteroid injections, and owners should be advised to lower NSC intake when these drugs are being administered. Corticosteroids lower tissue insulin sensitivity and raise blood insulin concentrations,[21–24] and marked hyperinsulinemia can induce laminitis.

Diagnostic Testing for Insulin Dysregulation

Diagnostic tests for ID are described in **Table 1**. The oral sugar test (OST) is preferred because stimulating insulin release from the pancreas allows mild ID to be detected. If owners raise concerns about inducing or exacerbating laminitis by performing the OST, then resting glucose and insulin concentrations should be measured first. However, it is still important to proceed with the OST if resting concentrations are normal because of the limited sensitivity of this resting measure.

Radiographs of the feet are a diagnostic test for EMS because laminitis may occur at a subclinical level before lameness is first detected. Divergent hoof rings ("founder lines") and widening of the white line are also clues that laminitis has been occurring.

Oral sugar test

This dynamic test assesses the magnitude of postprandial hyperinsulinemia in equids[6] and is a more sensitive diagnostic test than resting insulin concentrations. The test is performed by withholding feed for approximately 6 hours before administering corn syrup (Karo Light; ACH Food Companies, Inc, Cordova, TN, USA) at a dosage of 0.15 mL/kg (75 mL for a 500-kg horse) by mouth. Leave only one flake of hay with the horse after 10 PM and perform the test the next morning, or feed as normal in the morning and then fast the horse for 4 to 6 hours before performing the test in the afternoon. Corn syrup is given by mouth using 60-mL catheter-tip syringes, and

Table 1
Recommended diagnostic tests for insulin dysregulation

Oral Sugar Test		
Normal Insulin <45 μU/mL (radioimmunoassay) at 60 and 90 min	Mild ID Insulin 45–60 μU/mL (radioimmunoassay) at 60 or 90 min	Marked ID Insulin >60 μU/mL (radioimmunoassay) at 60 or 90 min
Excessive glucose response if glucose concentration >125 mg/dL at 60 or 90 min		
Resting (fed) insulin concentration		
Negative Insulin <20 μU/mL (radioimmunoassay)	Mild ID Insulin 20–50 μU/mL (radioimmunoassay)	Marked ID Insulin >50 μU/mL (radioimmunoassay)

Adapted from the 2016 equine endocrinology group recommendations on diagnosis and management of equine metabolic syndome in horses. Available at: http://sites.tufts.edu/equineendogroup. Accessed May 23, 2018; with permission.

blood samples are collected for glucose and insulin measurements 60 and 90 minutes later. Owners can administer corn syrup themselves so that the veterinarian needs only to arrive in time to collect blood at 60 and 90 minutes.

Resting insulin concentrations were previously recommended for assessing insulin status in horses, and this test can still be used to confirm the diagnosis of ID in severely affected animals.[3] Blood is collected under fed conditions with horses having access to hay or grass, but grain must not be fed for 6 hours before blood is collected.

Other diagnostic tests for EMS include measurement of plasma leptin concentrations to assess internal and external fat depots (normal <10 ng/mL; Cornell Animal Health Diagnostic Center). Plasma high-molecular-weight adiponectin concentrations have also been measured in research studies, and it is hoped that diagnostic laboratories will start offering this test soon.[25,26] High-molecular-weight adiponectin concentrations decrease as ID gets worse. An octreotide response test for diagnosing ID is being developed,[27] but additional research is required.

Management of Insulin Dysregulation

When making recommendations for horses with ID, it is important to first assess the severity of ID. OST insulin concentrations greater than 60 μU/mL define marked ID, and patients with values in this range require more intensive management than those with OST insulin values in the 45- to 60-μU/mL range (mild ID). It has recently been shown that oral glucose test results predict the risk of laminitis in ponies,[28] so it can be assumed that animals with severe ID are at high risk for developing laminitis if they are left untreated.

Dietary management of mild insulin dysregulation

When OST insulin results fall within the 45- to 60-μU/mL range, it can be assumed that risk of laminitis is high, and steps should immediately be taken to lower insulin concentrations. Insulin concentrations increase after feeding, and postprandial hyperinsulinemia may induce laminitis, so the main goal of dietary management is to decrease stimulation of insulin release from the pancreas; this is achieved by reducing simple sugars in the diet. As previously mentioned, many athletic horses are on high-NSC

diets because it is assumed that they have a higher energy requirement than other horses. If high-NSC sweet feeds or other grain mixtures are being fed, they should be discontinued right away and replaced with hay. If hay does not provide enough energy to meet the demands of the horse, as determined by body condition scoring, then additional calories can be added in the form of vegetable oil (1–2 cups per day). Low-NSC pelleted feeds are another option, and a wide array of products are available. Horses on hay-only diets require a vitamin-mineral supplement, and some owners provide a ration balancer containing additional protein, although care must be taken to select one with low-NSC content. Access to pasture should be restricted until insulin concentrations return to normal, and this is achieved by placing the horse and a companion in a small (150 ft × 150 ft) grass paddock or enclosed section of the pasture. A grazing muzzle can also be used to limit the amount of grass consumed. It is not necessary to eliminate access to grass altogether when only mild ID is detected, but care must be taken to limit intake because pasture grass is the most variable source of sugars and amino acids in the horse's diet.

Dietary management of severe insulin dysregulation

Horses, ponies, miniature horses, and donkeys with markedly increased insulin concentrations require more intensive dietary management. In these situations, all components of the horse's diet must be closely scrutinized to determine the amounts of sugars and amino acids that are being ingested. A hay diet is recommended, and it is important to analyze the hay that is fed to severely affected horses. Hay samples should be sent to a commercial laboratory for measurement of NSC content, and the greater the severity of ID, the more important it is to feed hay with a low-NSC value. An NSC (water-soluble carbohydrates + starches) value of less than 10% has been previously recommended for horses with ID,[6] but this cutoff value was not determined by research studies. Blood insulin responses to hay are determined by the feed itself, and also the severity of ID in the individual horse, and this can be investigated further by measuring the patient's insulin concentrations 2 and 4 hours after feeding the hay. It is also advisable to soak hay in cold water for 30 to 60 minutes to remove some of the simple sugars, although results vary according to the type of hay selected.[29] Severely affected horses must be removed from pasture and placed in dirt paddocks, but it may be possible to permit grazing again in the future if insulin concentrations return to normal or fall back into the range for mild ID. If hay is not providing enough energy for exercise and the horse is losing body condition, fat or a low-NSC pelleted feed can be added to the diet. Feeding horses smaller amounts of hay more frequently is recommended if ID is severe, and this can be achieved by using slow-feeder bags.

Management of obesity in the horse with mild insulin dysregulation

Increased adiposity manifests as generalized obesity or more subtle expansion of subcutaneous or visceral fat stores. Lipid may also accumulate within the liver, and mildly increased plasma Gamma Glutamyl Transferase activities are sometimes noted in these cases. If increased adiposity is a detected through body condition scoring, ultrasound examination, or measurement of plasma leptin concentrations, then a weight loss plan is required. This plan should consist of decreasing the amount of energy provided in the diet, while increasing exercise to accelerate energy consumption. Energy intake should be incrementally decreased using a stepwise reduction in the amounts of concentrates (grain, pelleted feed, or fat/oil supplement) provided. If obesity persists once concentrates are removed from the diet, hay amounts should be incrementally decreased at 2-week intervals. One approach is to first lower the amount of hay provided to the amount equivalent to 1.5% of current body weight. If

the horse has not started to lose weight after 2 weeks, the amount of hay provided should be lowered to 1.5% of ideal body weight. A further reduction to 1% of ideal body weight can be considered if the horse is still not losing weight after 2 weeks.

Exercise increases consumption of energy, which helps to address the problem of obesity and improve insulin sensitivity,[30,31] and moderate-intensity exercise is recommended whenever possible. As previously mentioned, ID may develop when athletic horses are forced to rest because of lameness or other medical problems. Immediate adjustments in diet are required in these cases, and the horse should be encouraged to exercise if permitted, even when training has been halted. Placing the horse in a small paddock with a companion is one approach, and another strategy is to place feed in different locations within the paddock to encourage exercise. Swimming is an effective form of exercise, and a recent article described the positive effects of swimming on insulin dynamics in horses.[31]

Management of obesity in the horse with severe insulin dysregulation

A more intensive approach is required when ID is severe because the risk of laminitis remains high for as long as insulin concentrations stay elevated. Levothyroxine sodium (Thyro L, Lloyd, Inc, Shenandoah, IA, USA) can be administered at high doses to accelerate weight loss in severely affected horses, and this treatment is also selected for horses that remain obese, even after all diet and exercise strategies have been attempted. The goal of levothyroxine treatment is to induce mild subclinical hyperthyroidism and increase metabolic rate, and a starting dosage of 0.1 mg/kg body weight every 24 hours orally is selected, which is equivalent to approximately 48 mg (4 teaspoons) levothyroxine powder per day for a 500-kg horse, given by mouth or mixed in a handful of low-NSC pellets. Levothyroxine is administered until body fat mass decreases or for a maximum of 6 months, and then the dose is incrementally lowered over 2 weeks before treatment is discontinued. Dietary recommendations must be followed at the same time that levothyroxine is administered; otherwise, horses consume additional feed to compensate for the increase in metabolic rate.

Medical management of the horse with severe insulin dysregulation

Metformin hydrochloride is commonly prescribed for the management of diabetes mellitus in humans, and this drug can be used to manage postprandial hyperinsulinemia in horses. Although metformin is an effective antidiabetic drug in humans, oral bioavailability is low for the formulations of metformin that are currently available for use in horses. Hustace and colleagues[32] reported only 7% oral bioavailability for metformin in horses when feed is withheld, and this value decreased to 4% when the same horses were fed before the drug was administered. Results of one study suggest that metformin administered at a dose of 15 mg/kg every 12 hours orally improves insulin sensitivity in horses and ponies with ID,[33] but in a subsequent study of insulin-resistant ponies, metformin had no effect on insulin dynamics.[34] Another study showed that metformin (30 mg/kg) administered 1 hour before an oral glucose test lowered blood glucose and insulin concentrations, and this suggests that the drug affects glucose absorption from the intestine.[35] On the basis of these results, owners are instructed to administer metformin 30 to 60 minutes before feeding when the drug is prescribed for horses with severe ID. A starting dosage of 30 mg/kg every 8 to 12 hours orally is currently recommended when using metformin in horses, and the author has extended the dose range to 50 mg/kg every 8 to 12 hours orally in some cases. Current formulations of metformin may cause oral irritation when administered at high doses, so horses on treatment should be monitored

closely. Rinsing the mouth with water after administering metformin helps to reduce oral irritation and prevent ulcers from forming. Responses to metformin appear to vary among horses with severe ID, and it is therefore ideal to assess the individual horse by measuring postprandial insulin concentrations 2 hours after the horse is fed, before and after initiating metformin treatment.

Management of refractory insulin dysregulation in horses

Unfortunately a small number of patients with severe ID fail to respond to the management strategies outlined above, and it is possible that they have a different manifestation of ID than other affected animals. All attempts should be made to manage these cases, but only partial responses to management changes may be seen. New antidiabetic drugs are being developed for use in humans and sodium-glucose cotransporter 2 inhibitors show promise as drugs for managing severe ID in horses. These drugs are expensive at present but may be worth considering for short-term management of ID when severely affected horses enter an acute crisis, for example, when a horse with ID is accidentally fed grain, breaks into the feed room, or escapes from its paddock and grazes on pasture. Canagliflozin belongs to this class of drugs, and it is administered orally on a once-daily basis.

PITUITARY PARS INTERMEDIA DYSFUNCTION IN THE EQUINE ATHLETE

Middle-aged (10–20 years) and aged (>20 years) horses are at risk for developing PPID, and this is a relatively common cause of poor performance in athletic horses that fall within these age ranges. Owners may report decreased performance during training sessions and say that affected horses seem duller than normal or lethargic. These signs are subtle to begin with, and it is difficult for the veterinarian to appreciate the shifts in behavior that the owner or trainer is noting. Occasionally, owners report that a horse with a history of being difficult to ride is calmer than before. Over time, horses with PPID show decreased epaxial muscle mass along the topline, and owners report a decrease in body condition, even though exercise and feeding regimens have remained the same. Muscle loss is sometimes attributed to the horse growing older, but aging changes are gradual and muscle loss associated with PPID occurs more rapidly. Delayed shedding of winter hair may also be noted. One of the first signs of PPID in show horses is the need for clipping to be performed more frequently.

Presenting complaints for *early PPID* include the detection of longer hair in certain regions of the body, such as the palmar/plantar aspects of the legs, and this is referred to as regional hypertrichosis. The hair coat may appear duller and feel coarser or thicker than normal, and owners may not have noticed these abnormalities because of their gradual onset. Reproductive performance might also be affected by PPID because dopamine inhibition is involved in regulation of the seasonal anovulatory period,[36] although definitive studies are lacking in this area.

Advanced PPID is easily recognized, and a presumptive diagnosis is reached by taking a history and performing a physical examination. As PPID progresses, horses show year-round retention of the winter hair coat and generalized hypertrichosis. The long curly hair coat detected in horses with advanced disease was previously referred to as hirsutism, and it is sometimes considered a pathognomonic clinical sign for PPID. Other clinical findings of advanced PPID include rounding of the abdomen, polyuria/polydipsia, recurrent bacterial infections, persistent neutrophilia and lymphopenia, infertility, and inappropriate lactation. Sole abscesses occur with greater frequency in horses with PPID, and this problem may be noted in performance horses that are shod on a regular basis.

Suspensory Ligament Degeneration

Older horses with PPID have a higher incidence of suspensory ligament injury, and there is evidence to suggest that increased tissue-specific cortisol action is responsible for weakening these structures.[37,38] Wellness examinations in middle-aged performance horses should therefore include PPID testing, and those with positive test results should be placed on pergolide treatment to prevent further degeneration of suspensory ligaments.

Diagnostic Testing for Pituitary Pars Intermedia Dysfunction

Diagnostic tests for PPID are outlined in **Table 2**, and it is important to select the correct test for the stage of disease and time of the year when testing is performed. The thyrotropin-releasing hormone (TRH) stimulation test is recommended for the diagnosis of early PPID because resting adrenocorticotropic hormone (ACTH) concentrations often fall within reference interval at this stage of the disease. To perform this test, first collect a preinjection baseline blood sample and then administer 1.0 mg TRH (1 mL) via intravenous injection. Compounding pharmacies now supply TRH, and their product elicits the same responses as TRH prepared in research laboratories.[39] A second blood sample is collected 10 minutes later, and both samples are submitted for measurement of ACTH. TRH stimulates ACTH secretion, and higher concentrations are detected in horses with PPID, compared with healthy horses.[40] Melanotrophs possess TRH receptors, and more ACTH is released when hyperplastic or neoplastic cells within the pars intermedia are stimulated. There are some short-term side effects of TRH administration, including yawning and nonproductive coughing, but these problems resolve within a few minutes and are not a major concern.[41] One limitation of the TRH stimulation test is that seasonally adjusted reference intervals have not been established for the late summer and fall, so these times should be avoided until further research is performed.

As PPID advances, resting ACTH concentrations rise above reference interval, and this test becomes more useful. However, ACTH concentrations normally increase in the late summer and fall as animals prepare for winter, so seasonally adjusted

Table 2
Recommended diagnostic tests for pituitary pars intermedia dysfunction

Early PPID	*TRH stimulation test*			
	Non-Fall Mid-November to mid-July	Negative Plasma ACTH <110 pg/mL at 10 min	Equivocal Plasma ACTH 110–200 pg/mL at 10 min	Positive Plasma ACTH >200 pg/mL at 10 min
	Fall Mid-July to mid-November	Reference intervals not available at this time		
Advanced PPID	*Resting ACTH concentration*			
	Non-Fall Mid-November to mid-July	Negative Plasma ACTH <30 pg/mL	Equivocal Plasma ACTH 30–50 pg/mL	Positive Plasma ACTH >50 pg/mL
	Fall Mid-July to mid-November	Negative Plasma ACTH <50 pg/mL	Equivocal Plasma ACTH 50–100 pg/mL	Positive Plasma ACTH >100 pg/mL

Adapted from the 2017 equine endocrinology group recommendations on diagnosis and management of pituitary pars intermedia dysfunction in horses. Available at: http://sites.tufts.edu/equineendogroup. Accessed May 23, 2018; with permission.

reference intervals must be applied when interpreting results during these seasons. It was previously thought that the late summer and fall should be avoided when testing horses for PPID, but the opposite approach is now recommended. Measuring plasma ACTH concentrations when hormonal systems are stimulated increases the likelihood of detecting PPID.

Management of Pituitary Pars Intermedia Dysfunction

Managing pituitary pars intermedia dysfunction to lower laminitis risk in horses with insulin dysregulation

As previously discussed, laminitis is one of the greatest threats to the health of the athletic horse. PPID may exacerbate ID in horses, and this is an important consideration when assessing the risk of laminitis in an individual patient. High insulin concentrations are detected in some, but not all horses and ponies with PPID,[42–44] and laminitis is more closely associated with ID than PPID.[1,43,45] Other risk factors, such as systemic inflammation or corticosteroid administration, are a greater concern in horses with concurrent ID and PPID, and the risk of laminitis is high in these animals.

Medical management of pituitary pars intermedia dysfunction

Pergolide is recommended for the treatment of PPID in horses at an initial dosage of 0.002 mg/kg, and it is available as 1-mg tablets (Prascend; Boehringer Ingelheim Vetmedica Inc, St. Joseph, MO, USA). This ergot alkaloid dopamine receptor agonist is administered to restore dopaminergic inhibition of melanotrophs, and its interaction with D2 receptors inhibits hormone secretion. It has not been determined if pergolide treatment also inhibits the development of pituitary hyperplasia or reduces the size of pituitary adenomas, but these beneficial effects are plausible considering its mechanism of action. Pergolide was available in the past as Permax (previously manufactured by Eli Lilly Co), and it was used in humans for the treatment of Parkinson disease. However, this product was voluntarily withdrawn from the market in March 2007 after the US Food and Drug Administration (FDA) issued a warning that pergolide was associated with increased incidence of valvular regurgitation in people.[46,47] Cardiac problems have not been encountered in horses, and Prascend was introduced in December 2011 as an FDA-approved drug for the treatment of PPID in horses.

If the horse is concurrently affected by ID and PPID, insulin concentrations typically decrease in response to pergolide treatment, and this lowers the likelihood of laminitis reoccurring. Horses with ID can be monitored by measuring resting insulin concentrations under fed conditions or by performing an OST. If insulin concentrations do not decrease after administering pergolide for 2 weeks at the dosage level selected, consider increasing the dose by 0.5 mg/d, even if ACTH concentrations have normalized.

When plasma ACTH concentrations do not decrease in response to pergolide treatment, the drug formulation and dose must be considered. If compounded pergolide is being administered, it may not be effective because of quality control issues and lack of stability. Davis and colleagues[48] demonstrated that pergolide is unstable over a 35-day period when prepared as an aqueous suspension, with higher temperatures and exposure to light-enhancing degradation. The dosage level selected is very important, and the dose should be appropriate for the stage of disease. For example, horses with PPID that have generalized hypertrichosis and muscle wasting may require 3 mg/d pergolide before plasma ACTH concentrations significantly decrease.

Cyproheptadine is also used for the management of PPID, but the author reserves this drug for horses with advanced PPID that are on higher doses of pergolide. This drug inhibits the action of serotonin, an excitatory transmitter that stimulates

melanotrophs. Consider adding cyproheptadine at a dosage of 0.25 mg/kg orally every 12 hours or 0.50 mg/kg every 24 hours orally once the 3-mg pergolide/d level is reached.

Dietary management of pituitary pars intermedia dysfunction

Recommendations should be based on the body condition score of the horse, and glucose and insulin results. If a high OST insulin response is detected or resting hyperinsulinemia (>50 mU/L) is detected, care must be taken to select low-NSC feeds. Commercial low-NSC/low-starch pelleted feeds are recommended, or molasses-free beet pulp can be fed with vegetable oil added as a more economical alternative. Hay with low-NSC content should be provided. It is also important to note that many horses with PPID do not suffer from ID. They are not genetically predisposed to ID and have not suffered from laminitis in the past. Horses in this group have normal OST insulin responses and can be fed senior feeds with higher NSC content.

Medical Treatments and Drug Regulations

Fédération Equestre Internationale (FEI) regulations and rules set by other governing bodies for competitions must be reviewed before drugs recommended in this article are administered. Attempts are being made to have pergolide approved by the FEI for use in horses with documented PPID, but at the time of writing, this drug is still listed as a prohibited substance, and appropriate withdrawal times are required.

SUMMARY

ID and PPID are important endocrine/metabolic disorders in athletic horses because they are associated with laminitis, a condition of the equine foot that significantly impacts performance. Horses that are genetically predisposed to ID as a result of their breed and exhibit regional adiposity should undergo diagnostic testing to assess insulin status and their risk of laminitis. Those with clinical signs of PPID should be tested and placed on long-term pergolide treatment.

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