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EQUINE
ENDOCRINOLOGY
GROUP

Pituitary Pars Intermedia Dysfunction (PPID)

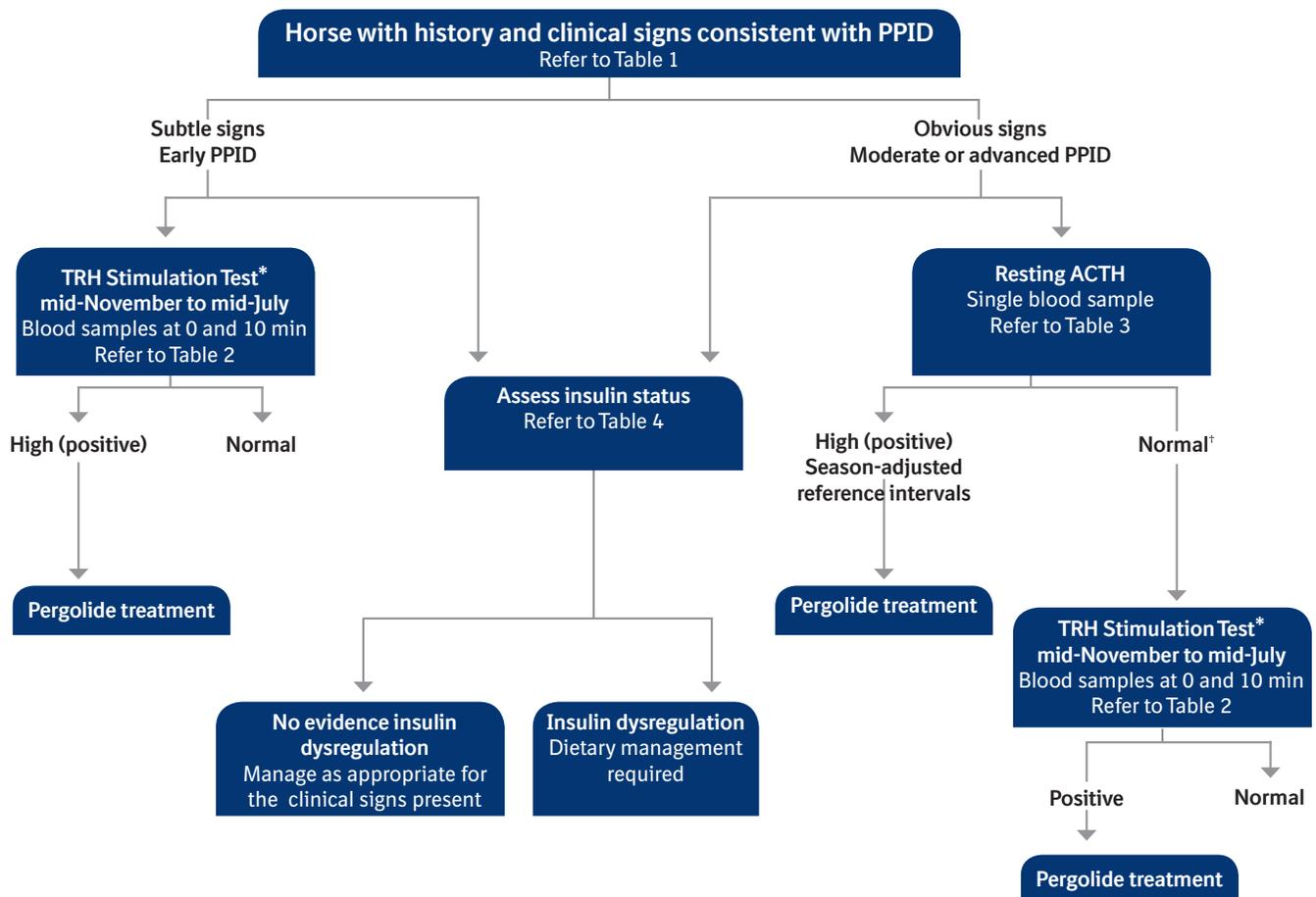
Recommendations for the Diagnosis and Treatment of Pituitary Pars Intermedia Dysfunction (PPID)

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Prepared by

Nicholas Frank (Group Coordinator), Frank Andrews, Andy Durham, Janice Kritchevsky, Dianne McFarlane, and Hal Schott

Figure 1 - Algorithm for the diagnosis and management of PPID

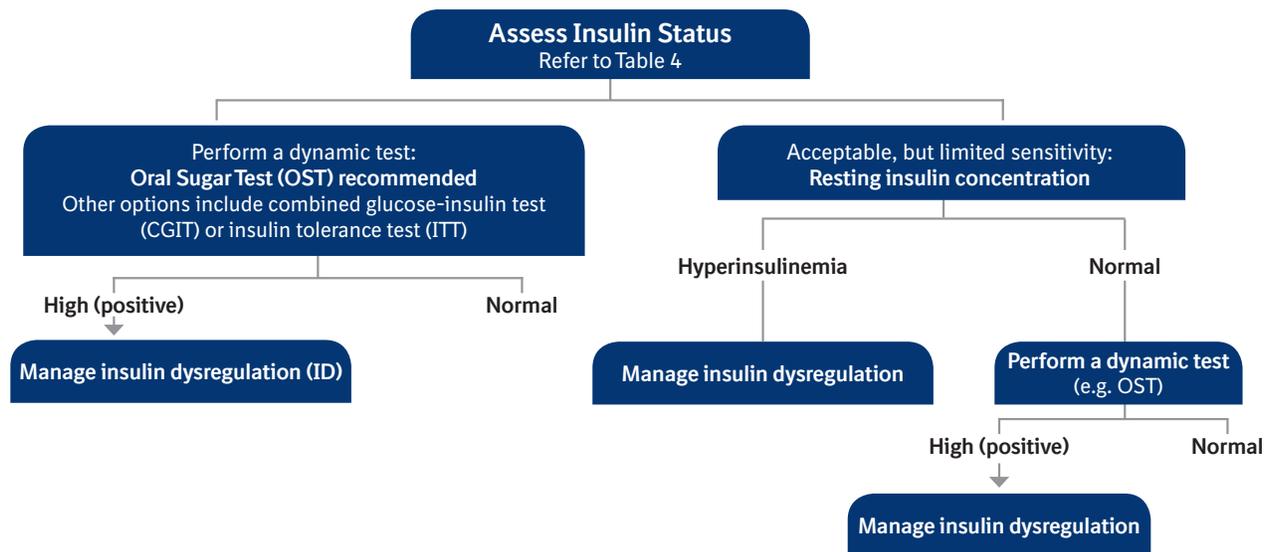


* Only use from mid-November to mid-July; if testing required in late summer/fall, then recommend resting ACTH concentration with seasonally adjusted reference interval.

† Pergolide treatment can be considered even when there is a normal ACTH result if the horse exhibits delayed hair shedding or hypertrichosis, weight loss with normal energy intake, and a dull attitude or depression.

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Figure 2 - Algorithm for assessment of insulin status



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Table 1- Clinical presentation of pituitary pars intermedia dysfunction

Pituitary Pars Intermedia Dysfunction (PPID) clinical presentation	
Early	Advanced
<ul style="list-style-type: none">Decreased athletic performanceChange in attitude/lethargyDelayed hair coat sheddingRegional hypertrichosisLoss of epaxial muscle mass (topline)Regional adiposityLaminitis	<ul style="list-style-type: none">LethargyGeneralized hypertrichosisLoss of seasonal hair coat sheddingSkeletal muscle atrophyRounded abdomen ('hay belly')Abnormal sweating (increased or decreased)Polyuria/polydipsiaRecurrent infections (e.g. sole abscesses)Bulging supraorbital fatAbsent reproductive cycle/infertilityLaminitisSeizure-like activityBlindnessParasitismTendon laxity

Table 2 - Thyrotropin-releasing hormone (TRH) stimulation test

Thyrotropin-releasing hormone stimulation test

Procedure

Testing is only recommended from mid-November to mid-July until seasonally-adjusted reference intervals are established.
Horses can be tested under short-term fasting conditions or after hay is fed, but not grain.
Do not perform immediately after an oral sugar test.
Veterinarian administers 1.0 mg (total dose) thyrotropin-releasing hormone (TRH) intravenously.
Side effects of TRH are transient and include coughing, Flehmen response, mouthing, and yawning.
Blood samples are collected in tubes containing EDTA at 0 and exactly 10 minutes relative to TRH administration.^a
Submit plasma for measurement of adrenocorticotropin hormone (ACTH) (process as per Table 2)

Interpretation of results

mid-November to mid-July		
	Negative (normal)	Positive (PPID)
0 min (pre)	≤ 35 pg/mL ^b	> 35 pg/mL
10 min	≤ 110 pg/mL	> 110 pg/mL
mid-July to mid - November		
Reference intervals not available at this time		

^a Sampling at 30 minutes is also acceptable using a cutoff value of 65 pg/mL. Reference intervals for both time points are the subject of ongoing research.

^b Cornell University Animal Health Diagnostic Laboratory (<http://ahdc.vet.cornell.edu/>). Consult reference intervals for the laboratory used.

Table 3 - Plasma adrenocorticotropin hormone concentrations

Resting adrenocorticotropin hormone (ACTH) concentration test

Procedure

Use glass or plastic tubes containing EDTA (purple top)
 Collect at any time of the day
 Keep samples cool (ice packs or refrigerator) at all times
 Centrifuge prior to shipping or freezing
 Ship via overnight mail with ice packs
 Preservatives (e.g. aprotinin) or freezing are not required
 Samples can be frozen, but only after centrifugation (gravity-separated samples will return falsely high results if frozen)

Interpretation of results^a

mid-November to mid-July	
≤ 35 pg/mL	Negative
Above reference interval	Positive
mid-July to mid-November	
≤ 100 pg/mL	Negative
Above reference interval ^b	Positive

^a Note that resting ACTH concentrations are variable, so another sample should be submitted or a dynamic test for PPID performed if the result falls close to the upper limit of reference interval (i.e. equivocal). Horses with early PPID may fail to demonstrate significant increases in basal ACTH concentrations and retesting between mid-July and mid-November (when test sensitivity is highest) or performing a TRH stimulation test (mid-November to mid-July) is recommended.

^b There is some evidence that breed of horse affects the magnitude of seasonal increases in ACTH; ponies appear to have greater increases in ACTH in the late summer & autumn.

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Table 4 - Recommended tests to assess insulin status

Test	Procedure	Interpretation ^a
<p>ORAL SUGAR TEST (OST)</p> <p>Easily performed in the field and more sensitive than the fasting insulin concentration. Recommended as the first choice for assessing insulin status.</p> <p>If the owner has concerns about this test inducing laminitis despite the absence of reported problems, a two-step approach can be followed. First, measure fasting insulin concentrations. If within reference interval, proceed to the OST to further assess insulin status with a dynamic test.</p>	<p>ORAL SUGAR TEST</p> <p>Fasting required (see below)</p> <p>Owner administers 0.15 mL per kg (approximately 75 mL) Karo Light^a corn syrup orally using 60 mL catheter-tip syringes.</p> <p>Collect blood 60 and 90 minutes after administration of corn syrup. Measure glucose and insulin concentrations.</p>	<p>ORAL SUGAR TEST</p> <p>Normal if the insulin concentration is < 45 µU/mL at 60 and 90 min.</p> <p>Strong support for insulin dysregulation if the insulin concentration is > 60 µU/mL at 60 or 90 min.</p> <p>Weak support for insulin dysregulation if the insulin concentration is 45 to 60 µU/mL at 60 or 90 min. Repeat testing at a later time or consider other tests.</p> <p>Excessive glucose response if glucose concentration > 125 mg/dL at 60 or 90 min.</p>
<p>FASTING INSULIN CONCENTRATION (glucose also measured)</p> <p>This test is easily performed and can be combined with a resting ACTH measurement.</p> <p>Limitation: Lower sensitivity when compared with the oral sugar test.</p>	<p>FASTING INSULIN CONCENTRATION</p> <p>For measurement of fasting insulin concentrations, leave only one flake of hay in the stall for 6-12 hours before testing.</p> <p>For measurement of fed insulin concentrations, sample under normal housing & management conditions, but do not feed grain.</p> <p>Collect blood into a tube containing EDTA or serum tube.</p>	<p>FASTING INSULIN CONCENTRATION</p> <p>When fasted, an insulin concentration > 20 µU/mL (mU/L) is supportive of ID.</p> <p>When fed hay, an insulin concentration > 50 µU/mL is supportive of insulin dysregulation.</p> <p>Persistent hyperglycemia indicates diabetes mellitus (insulin is normal or increased).</p> <p>A high insulin concentration is significant, but a normal (low) insulin is not diagnostically meaningful and can be found in normal horses and many with PPID (the oral sugar test is preferred).</p>

^a Karo Light[®]; ACH Food Companies, Inc, Cordova, TN. ACTH = Adrenocorticotrophic hormone.

Table 5 - Diagnostic tests for pituitary pars intermedia dysfunction (PPID)

Pituitary Pars Intermedia Dysfunction (PPID) Diagnostic Testing

SUPPORTIVE FINDINGS

Relative neutrophilia and lymphopenia
Hyperglycemia
Hyperinsulinemia
Hypertriglyceridemia
High fecal egg count

RECOMMENDED TESTS

Subtle signs (early PPID): thyrotropin-releasing hormone (TRH) stimulation test with ACTH measured*
Obvious signs (moderate-advanced PPID): Resting ACTH concentration

NO LONGER RECOMMENDED

Overnight dexamethasone suppression test (DST)
Oral domperidone challenge test
Combined dexamethasone suppression/TRH stimulation test with cortisol measured
Magnetic resonance imaging (MRI) specific for pars intermedia enlargement

NOT APPROPRIATE FOR PPID DIAGNOSIS

ACTH stimulation test
Resting cortisol concentration
Diurnal cortisol rhythm
TRH stimulation test with cortisol measured (without DST)
Total cortisol concentration (plasma, urine, or saliva)

*Testing should only be performed from mid-November to mid-July until seasonally-adjusted reference intervals are established

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Table 6 - Treatment plans and monitoring for pituitary pars intermedia dysfunction (PPID)

Treatment of PPID and monitoring

Initial treatment plan

The FDA-approved pergolide (Prascend®; Boehringer Ingelheim Vetmedica, Inc.) is recommended at an initial dosage of 0.5 mg for a 250-kg pony and 1.0 mg for a 500-kg horse (approx. 2 µg/kg) q24h orally. Perform baseline diagnostic testing before starting treatment. The test used to diagnose PPID (e.g., plasma ACTH concentration or TRH stimulation test) can be rechecked as early as 30 days to assess the response to treatment. However, 2 months may be required to fully assess changes in clinical signs. Some horses show a transient reduction in appetite. If this occurs, then stop treatment until appetite returns and then reintroduce gradually by giving partial doses for the first 4 days or by administering half the dose morning and evening.

Initial response (first 30 days)

Improved attitude
Improvement in polyuria/polydipsia

Increased activity
Control of hyperglycemia

Long-term response (1-12 months)

Improvement in hair coat abnormalities
Less pronounced rounding of the abdomen
Less likely to develop infections

Increased skeletal muscle mass
Fewer/milder episodes of laminitis

Timeline

The test used to diagnose PPID (e.g., plasma ACTH concentration or TRH stimulation test) should be rechecked after 30 days to assess the response to treatment.

A period of 2 months is required before conclusions should be drawn about changes in clinical signs.

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Table 6 - Treatment plans and monitoring for pituitary pars intermedia dysfunction (PPID) cont.

Treatment strategies

Adequate laboratory response with good clinical response of case

If test results are normal at recheck and clinical signs have improved or are stable, the dosage is held constant and the patient is placed on an every six-month recheck schedule, with one appointment occurring in the mid-July to mid-November season. This allows assessment of the patient during the seasonal increase in ACTH concentrations and ensures that treatment is adequate during this period.

Adequate laboratory response with poor clinical response of case

If test results are normal at recheck, but there has been recurrence or development of new problems (i.e., laminitis, bacterial infection, or weight loss), then reassess patient for additional medical problems including insulin dysregulation before assuming that an increase in pergolide dosage is required.

Inadequate laboratory response with good clinical response

If test results are abnormal at recheck, yet the patient is responding well clinically, the dosage can be held at the same level or increased, according to the veterinarian's preference. This may be observed more commonly when testing is performed mid-July to mid-November.

Inadequate laboratory response with poor clinical response

If test results remain positive at recheck and the patient is not responding well clinically, increase the dosage by 0.5 to 1.0 mg/day for a 500-kg horse (1-2 µg/kg/day) and recheck after 30 days.

Treatment strategies used by the group for refractory cases include gradually increasing the pergolide dosage to 3 mg for a 500-kg horse (6 µg/kg) daily and adding cyproheptadine (0.25 mg/kg PO q12h or 0.5 mg/kg q24h) or gradually increasing the pergolide dosage up to 5 mg for a 500-kg horse (10 µg/kg) daily.

Table 7 - Other considerations when managing horses with pituitary pars intermedia dysfunction (PPID)

Other Considerations

Switching horses from compounded pergolide

It may be possible to reduce the dosage of pergolide when switching from compounded pergolide to Prascend®. First consider the current status of the horse. If PPID is well controlled, consider a lower dosage of Prascend® (maximum recommended reduction of 50%). Retest the horse after 30 days (consider history and physical examination findings) to assess response to treatment.

Removing horses from pergolide treatment

In the event that a horse on pergolide treatment misses a dose or is removed from treatment for exhibition/competition, ACTH concentrations may begin to increase within 48 hours, but the risk of worsening clinical signs is low for this period.

Quality of life

The majority of horses with PPID are aged and therefore susceptible to non-PPID conditions. Therefore, horse owners should be advised that while medical management of PPID improves quality of life, it does not necessarily prolong lifespan.

Wellness care

In addition to medical management, horses with PPID should receive regular wellness care. Special attention should be paid to body condition, dentistry, and parasite control. Adequate water should be available if polyuria/polydipsia are persistent problems. Inadequately controlled PPID horses are at risk for bacterial infections. If insulin dysregulation is also diagnosed, special care should be paid to the horse's diet and access to pasture.

Diet and exercise recommendations

Feed selection should be based upon body condition score and oral sugar test results. Some PPID horses are lean and have normal insulin status, and senior feeds and pasture grazing are appropriate in these cases. Obese ($\geq 7/9$) horses should be placed on a lower energy diet and exercise program, and those with insulin dysregulation require lower non-structural carbohydrate feeds and limited access to pasture. Feed requirements of aged horses, especially those with PPID, are dynamic and monthly monitoring of body condition score by owners is recommended. Dietary supplements have also been suggested for the management of PPID, but to date, scientific evidence for their efficacy is lacking.

