

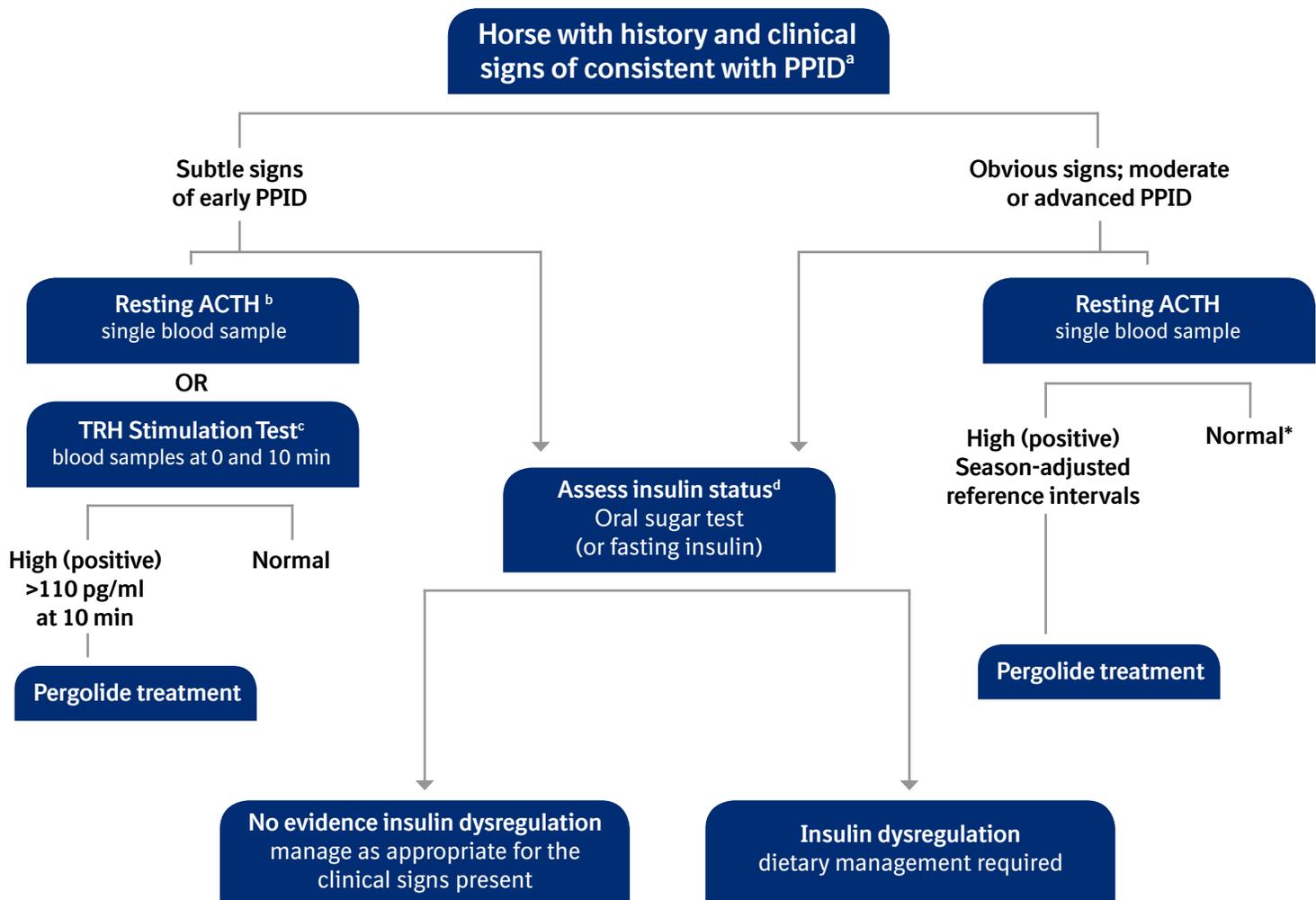
EQUINE
ENDOCRINOLOGY
GROUP

Pituitary Pars Intermedia Dysfunction (PPID)

EQUINE ENDOCRINOLOGY GROUP

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

Prepared by the PPID Working Group
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^{a-d} see Tables 1-4, respectively

* If clinical signs persist or progress, recheck ACTH concentration or perform a TRH stimulation test

Figure 1 - Algorithm for the diagnosis and management of PPID (October 2013)

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 performance Change in attitude/lethargy Delayed haircoat shedding Regional hypertrichosis Change in body conformation Regional adiposity Laminitis 	<ul style="list-style-type: none"> Lethargy Generalized hypertrichosis Loss of seasonal haircoat shedding Skeletal muscle atrophy Rounded abdomen Abnormal sweating (increased or decreased) Polyuria/polydipsia Recurrent infections (e.g., sole abscesses) Regional adiposity Absent reproductive cycle / infertility Laminitis Hyperglycemia Neurologic deficit/blindness

Table 2 - Plasma adrenocorticotropin hormone concentrations

Resting adrenocorticotropin hormone (ACTH) concentration test									
Procedure	<ul style="list-style-type: none"> Plastic tubes containing EDTA (purple top) recommended 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*	<p style="text-align: center;"><i>Use reference intervals provided by the laboratory</i></p> <p style="text-align: center;">NOVEMBER TO JULY</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="padding: 5px;">≤ 29 pg/mL^a ≤ 35 pg/mL^b</td> <td style="text-align: center; padding: 5px;">Negative</td> </tr> <tr> <td style="padding: 5px;">Above reference interval</td> <td style="text-align: center; padding: 5px;">Positive</td> </tr> </table> <p style="text-align: center;">AUGUST TO OCTOBER</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="padding: 5px;">≤ 47 pg/mL^a ≤ 100 pg/mL^b</td> <td style="text-align: center; padding: 5px;">Negative</td> </tr> <tr> <td style="padding: 5px;">Above reference interval</td> <td style="text-align: center; padding: 5px;">Positive</td> </tr> </table>	≤ 29 pg/mL ^a ≤ 35 pg/mL ^b	Negative	Above reference interval	Positive	≤ 47 pg/mL ^a ≤ 100 pg/mL ^b	Negative	Above reference interval	Positive
≤ 29 pg/mL ^a ≤ 35 pg/mL ^b	Negative								
Above reference interval	Positive								
≤ 47 pg/mL ^a ≤ 100 pg/mL ^b	Negative								
Above reference interval	Positive								

*Note that resting ACTH concentrations are variable, so another sample should be submitted or an evocative test performed if the result falls close to the upper limit of reference interval (i.e., equivocal).

Cases with early PPID may fail to demonstrate significant increases in basal ACTH concentrations and retesting between August and October (when test sensitivity is highest) or performing a TRH stimulation test (December to June) is recommended.

^a Liphook Equine Hospital (<http://www.liphookequinehosp.co.uk/>)

^b Estimated cut-off value that requires further research. Based upon information provided on the Cornell University Animal Health Diagnostic Laboratory website (<http://ahdc.vet.cornell.edu/>) where it is stated that "Seasonal elevation of ACTH levels occurs from approximately mid-August to mid-October. Samples taken during this time period may have up to 3 times reference levels of ACTH in normal horses."

Table 3 - Thyrotropin-releasing hormone (TRH) stimulation test

Thyrotropin-releasing hormone stimulation test

Procedure

Testing should only be performed from December to June until seasonally-adjusted reference intervals are established.

Veterinarian administers 1.0 mg (total dose) thyrotropin-releasing hormone (TRH) intravenously.

Blood samples are collected in tubes containing EDTA at 0 and *exactly* 10 minutes relative to TRH administration. Sampling at 30 minutes is also acceptable using a cutoff value of 65 pg/mL. This is a higher value than previously recommended (35 pg/mL) and reference intervals for both time points are the subject of ongoing research.

Submit plasma for measurement of adrenocorticotropin hormone (ACTH).

Interpretation of results*

DECEMBER TO JUNE

	Negative	Positive
0 min (pre)	≤ 35 pg/mL [†]	> 35 pg/mL
10 min	≤ 110 pg/mL	> 110 pg/mL

JULY TO NOVEMBER

Reference intervals not available at this time

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

Table 4 - Recommended tests to assess insulin status

Test	Procedure	Interpretation ^a
<p>ORAL SUGAR TEST</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 range, proceed to the OST to confirm normal insulin status.</p>	<p>ORAL SUGAR TEST</p> <p>Fasting required (see below). 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>Hyperinsulinemia if the insulin concentration is > 60 µU/mL at 60 or 90 min.</p> <p>Equivocal result 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 (OST).</p>	<p>FASTING INSULIN CONCENTRATION</p> <p>Fasting required. Leave only one flake of hay in the stall after 10 p.m. the night before and collect blood in the morning.</p> <p>Collect blood into one EDTA and one serum tube.</p>	<p>FASTING INSULIN CONCENTRATION</p> <p>Hyperinsulinemia if fasting insulin concentration > 20 µU/mL (mU/L) by radioimmunoassay.</p> <p>Persistent hyperglycemia indicates diabetes mellitus (insulin is normal or increased).</p> <p>A high insulin concentration is significant, but a normal (low) fasting insulin is not diagnostically meaningful and can be found in normal horses and many with PPID (the oral sugar test is preferred).</p>

^aKaro Light[®]; ACH Food Companies, Inc, Cordova, TN.
ACTH = Adrenocorticotropin 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

RECOMMENDED TESTS

Subtle signs (early PPID): Thyrotropin-releasing hormone (TRH) stimulation test with ACTH measured or resting adrenocorticotropin hormone (ACTH) concentration
Obvious signs (moderate-advanced PPID): Resting ACTH concentration

OTHER AVAILABLE TESTS WITH LOWER RECOMMENDATION

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

OTHER POTENTIAL TESTS THAT ARE NOT COMMERCIALY AVAILABLE

Alpha melanocyte-stimulating hormone concentrations
Bioactive ACTH concentrations
Pro-opiomelanocortin (POMC) concentrations
Beta endorphin concentrations
Corticotrophin-like intermediate peptide (CLIP) concentrations

NO LONGER RECOMMENDED FOR PPID DIAGNOSIS

ACTH stimulation test
Resting cortisol concentration
Diurnal cortisol rhythm
TRH stimulation test with cortisol measured (without DST)
Urinary cortisol concentration
Salivary cortisol concentration

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 2 µg/kg (0.5 mg for a 250-kg pony; 1.0 mg for a 500-kg horse) q24h orally. Perform baseline diagnostic testing before starting treatment and recheck after 30 days.*

Some horses show a transient reduction in appetite. It is therefore recommended that PRASCEND be introduced gradually by giving partial doses for the first four 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 haircoat abnormalities

Less pronounced rounding of the abdomen

Infections are less likely to develop

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 two months is required before conclusions should be drawn about changes in clinical signs.

Treatment strategies

Adequate laboratory response

If test results are negative at the 30-day recheck, the dosage is held constant and the patient is placed on an every six-month recheck schedule, with one appointment occurring in the August-October season. This allows assessment of the patient during the seasonal increase in ACTH concentrations and ensures that treatment is adequate during this period.

Inadequate laboratory response with good clinical response

If test results remain positive at 30 days, yet the patient is responding well clinically, the dosage can be held at the same level or increased, according to the veterinarian's preference.

Inadequate laboratory response with poor clinical response

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

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

*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%). Response to treatment is assessed by measuring ACTH concentration after 30 days and considering history and physical examination findings.

