2021 EQUINE ENDOCRINOLOGY GROUP

PITUITARY PARS INTERMEDIA DYSFUNCTION (PPID)

The Equine Endocrinology Group (EEG) is composed of experts in the field of equine endocrinology who provide advice in the form of written guidelines to help North American veterinary practitioners diagnose and manage equine endocrine disorders. Guidelines are updated every two years and can be found on the EEG website: **http://sites.tufts.edu/equineendogroup.**

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

Revised October 2021 by the PPID Working Group

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INTRODUCTION

Pituitary pars intermedia dysfunction (PPID) is a slowly progressive degenerative disease of hypothalamic dopaminergic neurons. Loss of dopaminergic inhibitory control of pars intermedia (PI) melanotropes leads to hyperplasia and adenoma formation in the PI. Melanotropes in the enlarged PI produce increased amounts of pro-opiomelanocortin, a large prohormone that is subsequently cleaved into smaller peptides, including adrenocorticotropic hormone (ACTH). PPID is more common in older equids, with a documented prevalence of approximately 20% in equids 15 years and older. Disease prevalence increases to 30% in equids over 30 years of age. There is no apparent breed or sex predilection and the only documented risk factor for development of PPID is advancing age. Hypertrichosis, a long hair coat that often fails to shed, is essentially a pathognomonic clinical sign for PPID. However, PPID can be manifested by a constellation of other clinical signs/syndromes (Figures 1 and 2, Table 1); consequently, PPID should be considered as a potential contributing factor for many disorders in horses 15 years age or older.

Measurement of baseline ACTH concentration is a practical test for diagnosis of PPID, though variation in ACTH concentrations in individuals and over time results in some overlap in ACTH concentrations between normal and PPID populations. As ACTH concentrations increase in the autumn in healthy and PPID animals, interpretation of ACTH testing for PPID diagnosis requires seasonally adjusted values. We have revised our 2019 recommendations to refine this seasonal interpretation and expanded the equivocal zone (Table 2 and Figure 5) to maximize this test's ability to rule in or out PPID for animals with ACTH concentrations outside the equivocal zone. When baseline ACTH concentrations fall in this equivocal zone, veterinarians should use clinical information such as age and severity of signs to decide whether to monitor and re-test, follow-up with dynamic TRH stimulation testing, or in some cases, to treat (Figure 4). Because baseline ACTH is more likely to fall in the equivocal zone in early-stage disease, the TRH stimulation test may also be an appropriate first line test in many cases. PPID can also be accompanied by insulin dysregulation, increasing the risk of hyperinsulinemia-associated laminitis, so assessing insulin dynamics is recommended in concert with PPID testing (see Equine Endocrinology Group's Recommendations for Diagnosis and Treatment of Equine Metabolic Syndrome.

FIGURE 1 - Clinical signs and syndromes with PPID vary in affected equids

Pathognomonic Hypertrichosis

Loss of Topline Musculature

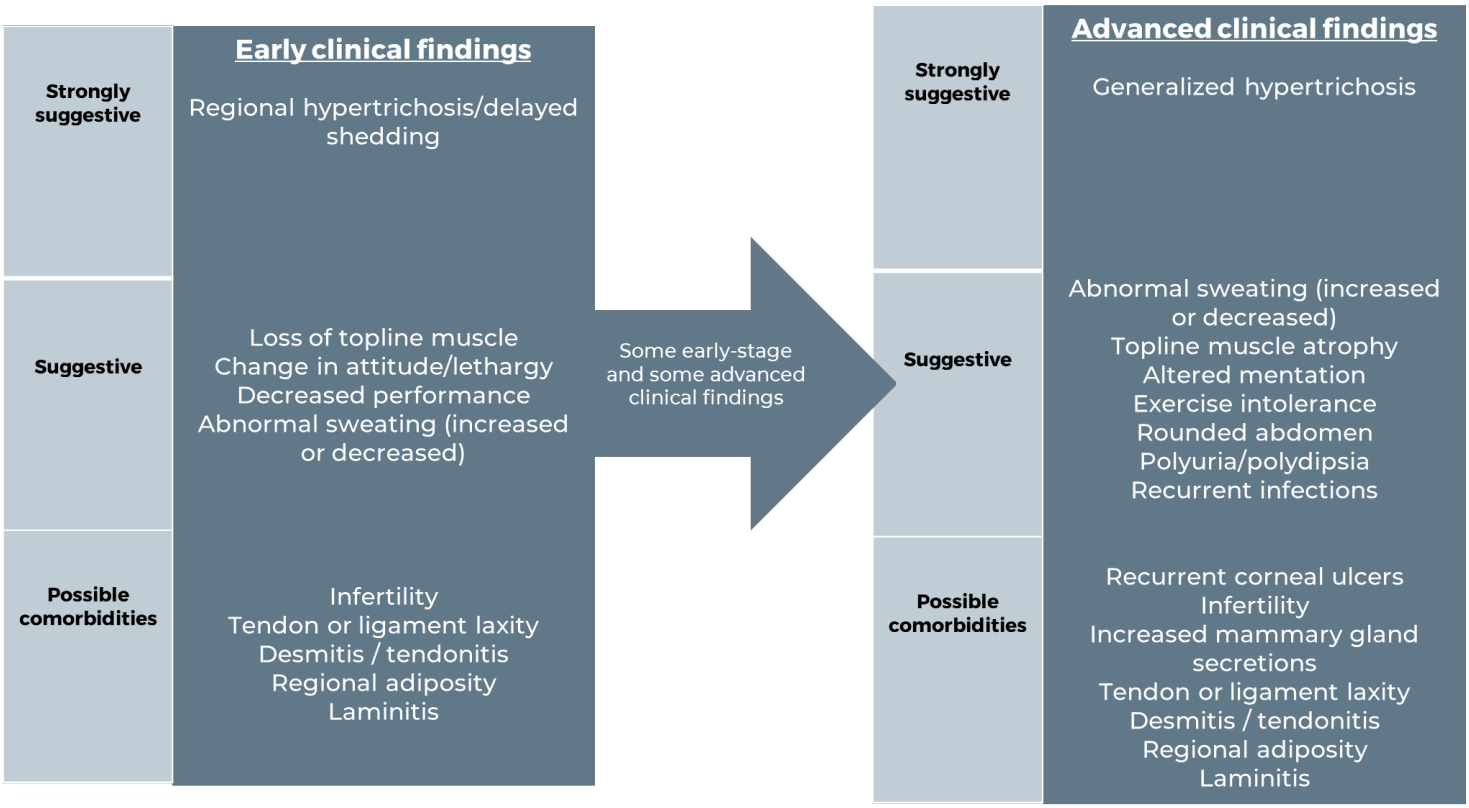
Hair Color Changes & Patchy Shedding

Suspensory Ligament Breakdown

Chronic Laminitis

Figure 2 – Clinical progression of PPID

**Note: affected animals may have only one, several or many of the listed signs*

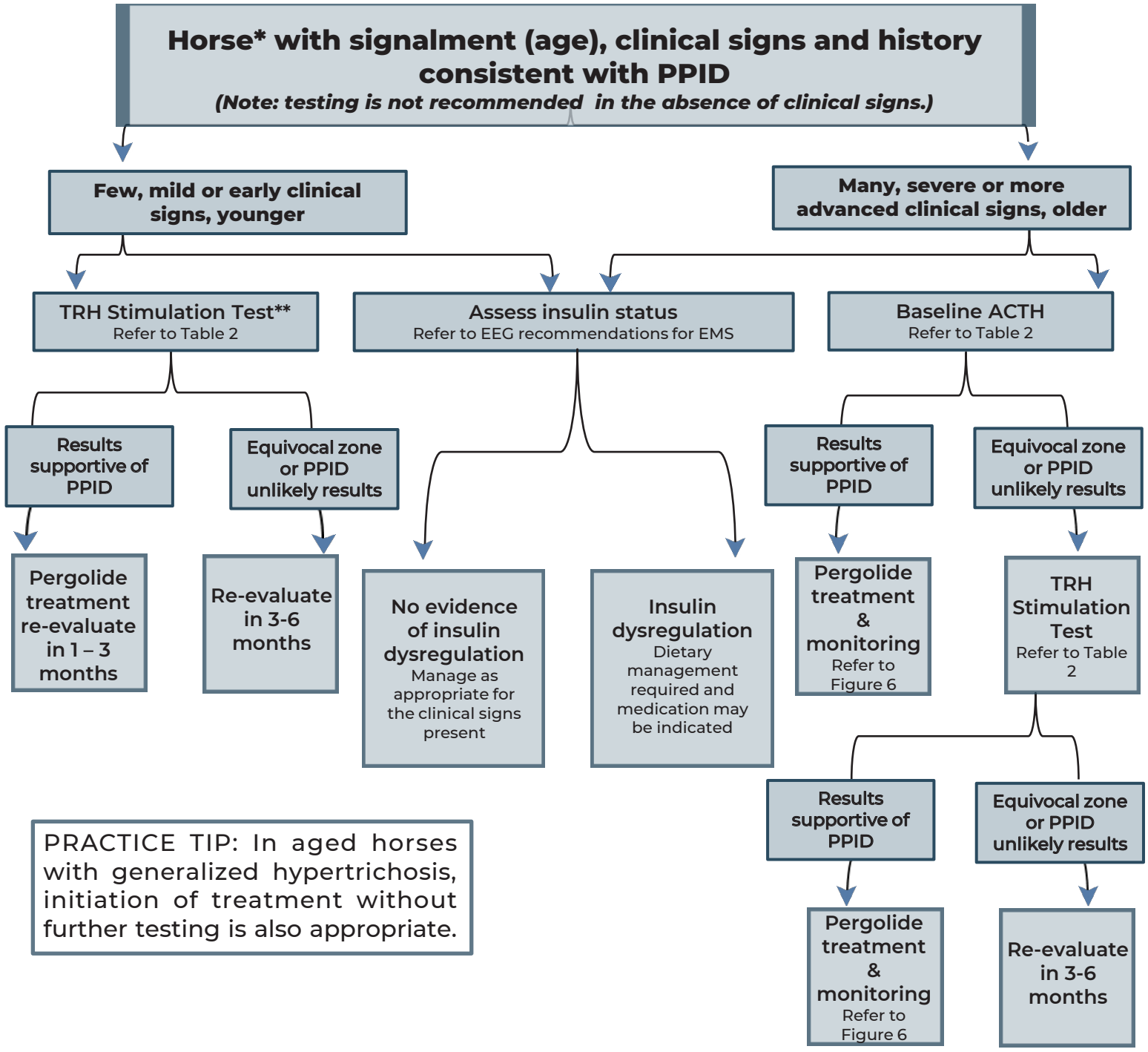


PRACTICE TIP: Increasing animal age and number of concurrent clinical signs increases the likelihood that these clinical signs are truly associated with PPID.

TABLE 1 - Laboratory findings that may accompany PPID

- Hyperglycemia
- Hyperinsulinemia
- Hypertriglyceridemia
- High fecal egg count

FIGURE 3 - Algorithm for the diagnosis and management of PPID



PRACTICE TIP: In aged horses with generalized hypertrichosis, initiation of treatment without further testing is also appropriate.

* At present this algorithm is largely based on data collected in horses but it can be applied to other equids (ponies, donkeys, and mules) until further data becomes available.

** The TRH stimulation test is recommended as a first line test for suspected early-stage PPID in North America. In locations where TRH is not readily available, or use is restricted, initial testing may begin with measurement of baseline ACTH concentration regardless of suspected disease stage. However, baseline ACTH is more likely to be non-supportive of PPID diagnosis in early-stage disease than TRH stimulation testing.

TABLE 2 - Baseline ACTH concentration and TRH stimulation test

Procedure for Baseline ACTH	▪ Collect into EDTA containing tube (purple top) at any time of the day ▪ Keep samples cool (ice packs or refrigerator) at all times ▪ Centrifuge and separate plasma prior to shipping ▪ Ship via overnight mail with ice packs ▪ Plasma can be frozen (centrifuged samples only) but avoid freeze-thaw cycles
Procedure for TRH stimulation test	▪ Horses can be tested after hay is fed, but not within 12 hours after a grain meal. Testing can be performed immediately before an oral sugar test (OST) but do not perform within 12 hours after an OST. ▪ Administer 0.5 mg (equids <250 kg) or 1.0 mg (equids >250 kg) of TRH intravenously. Side effects after administration are transient and include coughing, flehmen response, and yawning. ▪ Collect blood into EDTA containing tubes (purple top) at 0 and **exactly** 10 minutes after TRH administration. ▪ Submit plasma for measurement of ACTH as described above.

Seasonal interpretation of results * (Also refer to Figures 4 and 5)		PPID unlikely	Equivocal* *Requires strong clinical signs, re-testing, or TRH stim to confirm diagnosis*	PPID likely
Baseline ACTH or TRH time 0 (pg/ml) **see important note below*	Dec - Jun	< 15 *	15 – 40*	> 40
	Jul & Nov	< 15 *	15 – 50*	> 50
	Aug	< 20 *	20 – 75*	> 75
	Sept-Oct	<30 *	30-90*	>90
10 min after TRH (pg/ml)	Jan – Jun	< 100	100 – 200	> 200
	Jul – Dec	< 100	TRH stimulation testing can only be used to identify negative cases in these months due to many false positives	

IMPORTANT NOTES:

- The analyzer used to measure ACTH has changed since the 2019 EEG recommendations were released, with the Immulite 2000XPI chemiluminescent immunoassay now used in many laboratories. ACTH values are lower with this method, so ACTH concentrations provided here have been adjusted accordingly.
- In addition, the equivocal zone for baseline ACTH has been expanded to maximize diagnostic accuracy outside of this zone, and to **emphasize the importance of assessing results in the context of the horse's clinical signs.**
  - Current data in a large group of animals with suspected PPID suggests that ***approximately 25% of horses and ponies with PPID, particularly those of certain breeds, may have results that are in this equivocal zone;*** a diagnosis of PPID is still appropriate in an aged animal when strong clinical signs are present. ***Up to 30% of horses may have results that fall within the equivocal zone because of stress, breed, and other factors***, and are unlikely to have PPID if strong clinical signs are not present. Further study to refine these criteria in animals with and without confirmed PPID is needed.
  - Re-evaluation of baseline ACTH concentration in 3-6 months or follow-up TRH stimulation testing is recommended for most animals with results in the equivocal zone (see figure 4).
  - A board-certified internal medicine specialist should be consulted for complicated cases.

FIGURE 4 - Algorithm for interpretation of baseline ACTH concentrations

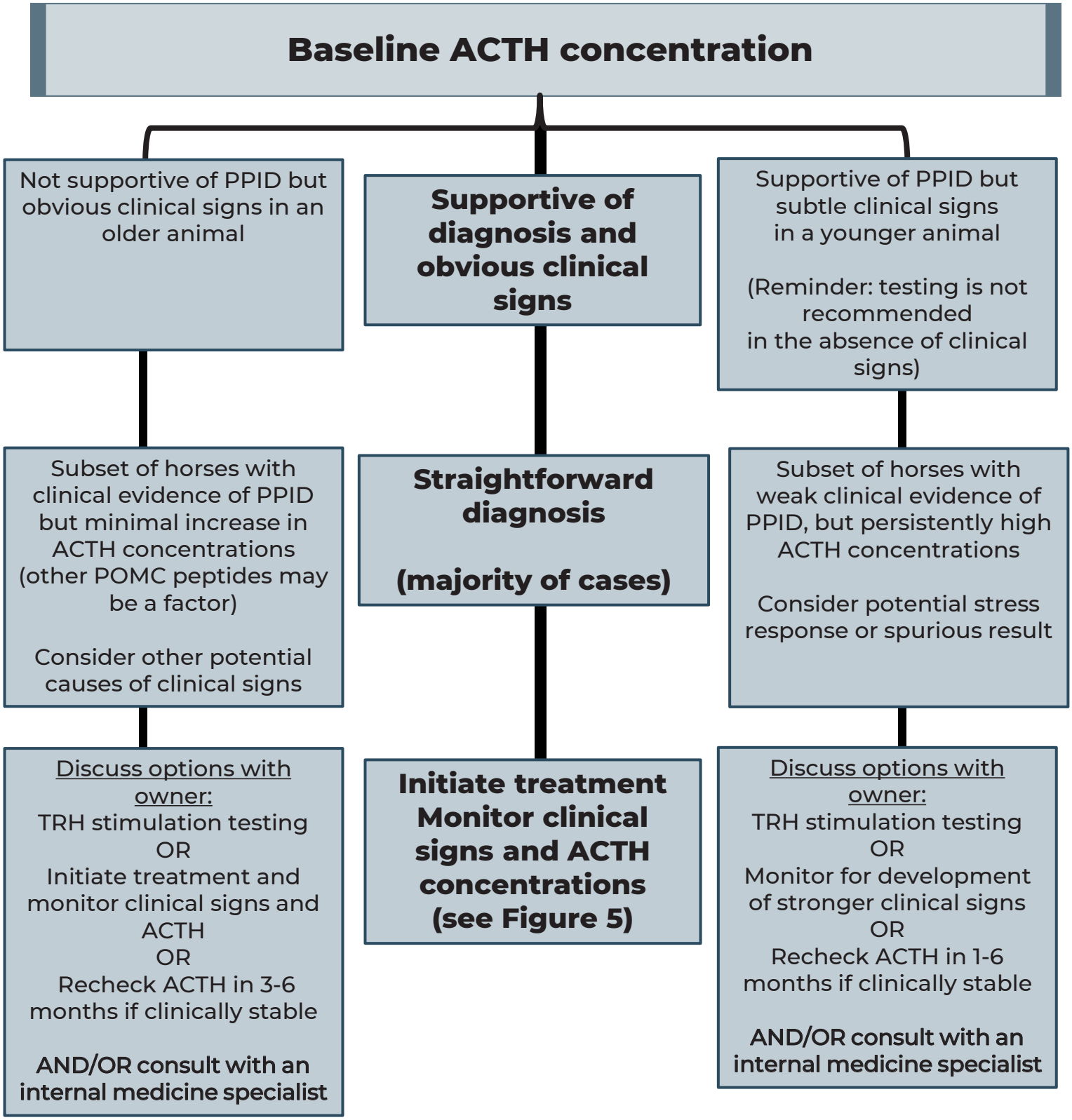
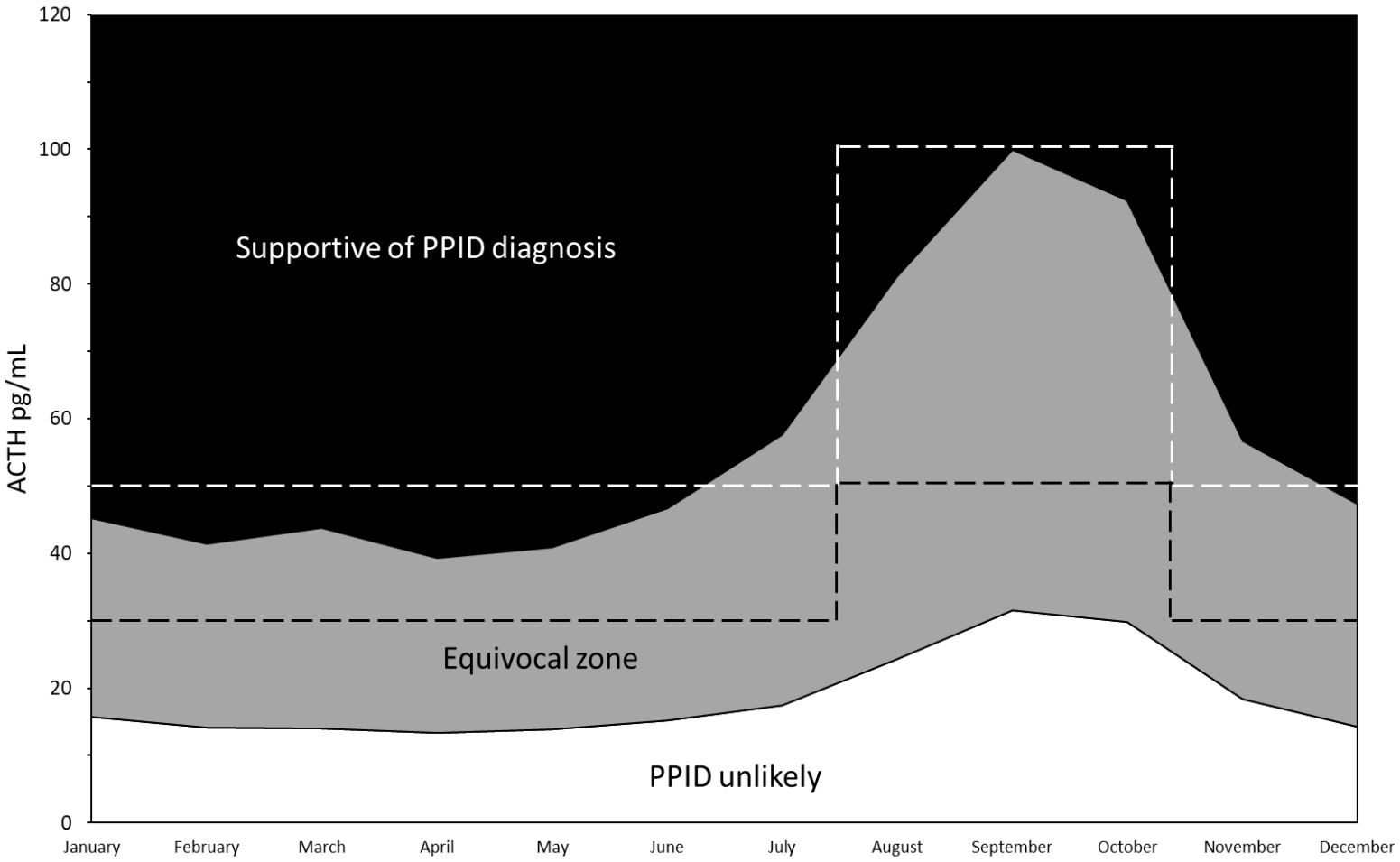


FIGURE 5 - Seasonal interpretation of baseline ACTH concentrations

Notes: ACTH values presented here were determined using the Immulite 2000xpi analyzer. ACTH concentrations falling in the black shaded area are supportive of PPID diagnosis, and those falling in the white shaded area suggest a PPID diagnosis is unlikely at that time. ACTH concentrations falling in the grey shaded area are in the equivocal zone, and require further interpretation based on the clinical picture. The dashed lines denote previous diagnostic cutoff values from the 2019 EEG recommendations (white dashed line = upper values, black dashed line = lower values).



ACTH concentrations throughout the year gradually increase from June to late September / early October, followed by a more rapid fall until December in the Northern hemisphere. ACTH concentrations should only be used to make a diagnosis of PPID in combination with clinical signs, especially when ACTH values fall within the equivocal zone. The equivocal zone is wider and lower than the 2019 recommendations, due to new data and the implementation of the Immulite 2000xpi analyzer in many labs.

TABLE 3 - Diagnostic tests for Pituitary Pars Intermedia Dysfunction (PPID)

RECOMMENDED TESTS

- **Early PPID:** TRH stimulation test with ACTH measured or baseline ACTH if TRH is not readily available
- **Moderate to advanced PPID:** Baseline ACTH concentration or TRH stimulation test with ACTH measured

OTHER POTENTIALLY SUPPORTIVE TESTS

- Overnight dexamethasone suppression test
- Magnetic resonance imaging (MRI) specific for pars intermedia enlargement

NO LONGER RECOMMENDED

- Oral domperidone challenge test
- Combined dexamethasone suppression/TRH stimulation test with cortisol measured

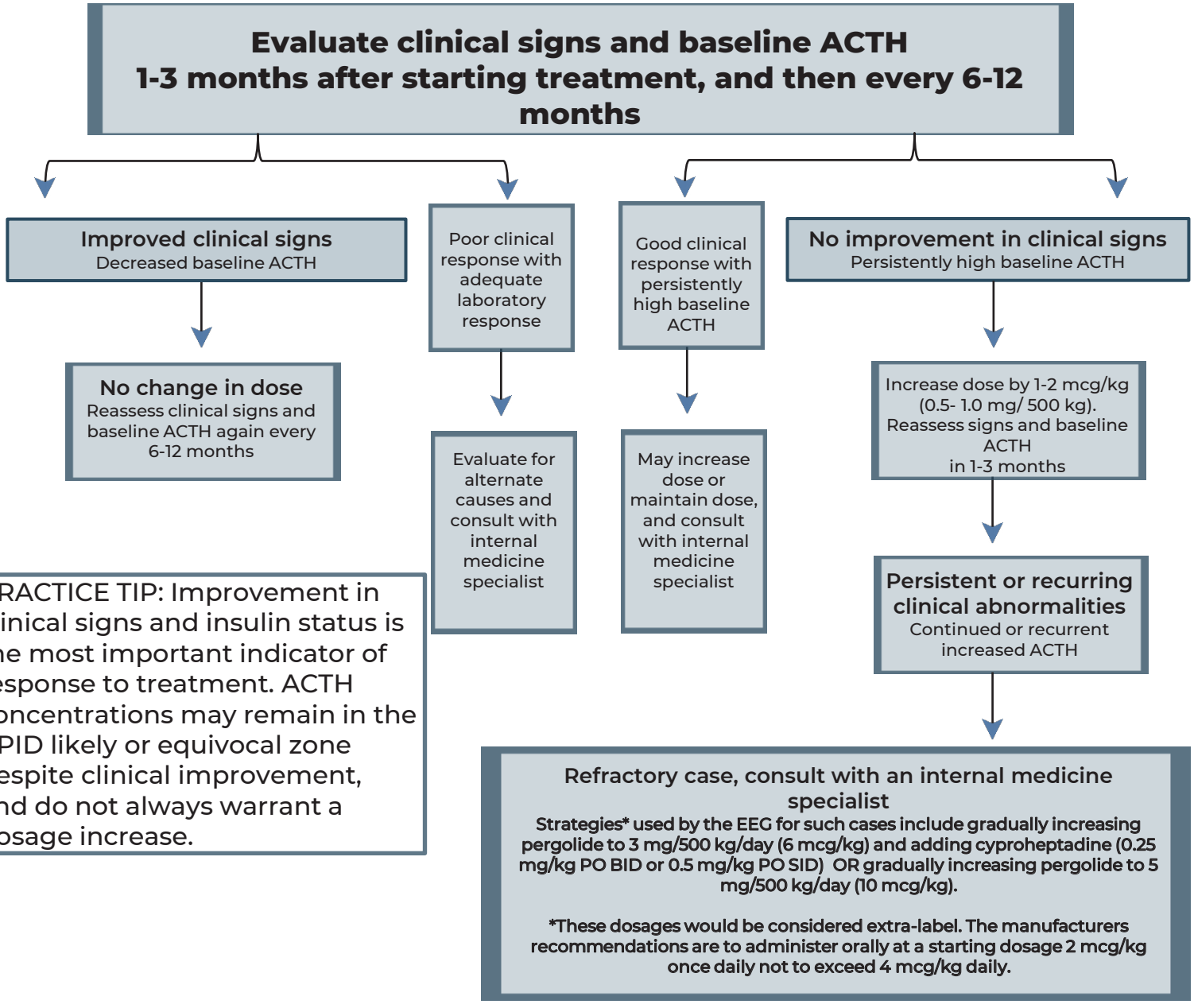
NOT APPROPRIATE FOR PPID DIAGNOSIS

- ACTH stimulation test
- Baseline cortisol concentration
- Diurnal cortisol rhythm

Figure 6 - Treatment and monitoring of PPID

Initial treatment plan

The FDA-approved pergolide Prascend® (pergolide tablets); [Boehringer Ingelheim Animal Health, USA, Inc.] is recommended at an initial dosage of 2 mcg/kg (0.5 mg for a 250-kg pony and 1.0 mg for a 500 kg horse). The dosage is not to exceed 4 mcg/kg bodyweight once daily. Perform baseline diagnostic testing before starting treatment. Some horses show a transient reduction in appetite. To address this problem, stop treatment until appetite returns and or decrease by half for 3 to 5 days and then titrate back up in **0.5 -1** mcg/kg increments every 2 weeks until the desired dose is achieved.



PRACTICE TIP: Improvement in clinical signs and insulin status is the most important indicator of response to treatment. ACTH concentrations may remain in the PPID likely or equivocal zone despite clinical improvement, and do not always warrant a dosage increase.

TABLE 4 - Other considerations for managing horses with PPID

Switching horses from compounded pergolide

It may be possible to reduce the dosage of pergolide when switching from compounded pergolide to Prascend® (pergolide tablets). 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 1 – 2 months (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 clinical signs worsening during this period is low. Drug clearance varies substantially among individual horses and can result in detectable drug levels for much longer than 48 hours in some animals.

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, hoof care, dentistry, and parasite control. Inadequately controlled PPID horses are also at risk for bacterial infections. Adequate water should be available if polydipsia and polyuria are persistent problems.

Diet and exercise recommendations

Feed selection should be based upon body condition score and evidence for insulin dysregulation. Some PPID horses are lean and have normal insulin status, and senior feeds and pasture grazing are appropriate in these cases. Obese horses should be fed a lower energy diet and be encouraged to follow an exercise program if soundness permits. Those with insulin dysregulation require lower non-structural carbohydrate feeds and limited access to pasture. Feed requirements of aged horses, especially those with PPID, may change over time and monthly monitoring of BCS 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.

TABLE 4 cont. - Other considerations for managing horses with PPID

Management of glucose, insulin, and lipid disorders

Assessment for insulin dysregulation should also be pursued in all patients with PPID (see Equine Endocrine Group Recommendations for Diagnosis and Management of Equine Metabolic Syndrome). Insulin dysregulation is detected in approximately one-third of cases and is most likely a result of PPID developing in equids genetically predisposed to EMS. Less commonly, diabetes mellitus develops in horses with PPID and is characterized by persistent hyperglycemia and glucosuria. Hypertriglyceridemia is detected in some horses, and blood lipid concentrations markedly increase if the animal enters negative energy balance. Pergolide treatment has been associated with improved glycemic control and normalization of blood triglyceride concentrations in some of these cases with positive effects often seen within 48-72 hours. Attention should also be paid to the horse's diet and access to pasture (see below).

Testing in the face of laminitis pain and other stress

Stress, excitement, and trailering can result in a transient increase in ACTH concentrations. Samples for PPID diagnosis via baseline ACTH should not be collected within 30 minutes of trailering, or in an animal that is visibly excited. Low to moderate pain of at least 24 hours duration does not appear to impact diagnostic testing with baseline ACTH or TRH stimulation testing. Testing may be performed in laminitic horses, but it is ideal to postpone until severe pain is controlled.

Testing after sedation

Sedation may impact endocrine responses. Diagnostic testing with baseline ACTH concentration only can be performed immediately (within 5-10 minutes) after sedation with xylazine or detomidine, with or without butorphanol, without substantial impact on the test interpretation. TRH stimulation testing and assessment of insulin status are impacted by sedation for at least several hours. Thus, it is ideal to avoid diagnostic testing for PPID and insulin status within 24-48 hours of sedation.

TABLE 5. – Suggested further reading

- Durham AE, Clarke BR, Potier JFN, Hammarstrand R, Malone GL. Clinically and temporally specific diagnostic thresholds for plasma ACTH in the horse. Equine Vet J. 00:1-11. 2020. DOI: 10.1111/evj.13292
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- Horn R, Stewart AJ, Jackson KV, Dryburgh EL, Medina-Torres CE, Bertin FR. Clinical implications of using adrenocorticotropic hormone diagnostic cutoffs or reference intervals to diagnose pituitary pars intermedia dysfunction in mature horses. J Vet Intern Med. 2021 Jan;35(1):560-570. DOI: 10.1111/jvim.16017
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- McFarlane D. Diagnostic testing for equine endocrine diseases: confirmation versus confusion. Vet Clin Equine 35: 327-338. 2019. DOI: 10.1016/j.cveq.2019.03.005
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- Tatum RC, McGowan CM, Ireland JL. Evaluation of the sensitivity and specificity of basal plasma adrenocorticotrophic hormone concentration for diagnosing pituitary pars intermedia dysfunction in horses: A systematic review. Vet J. 2021 May 21:105695. DOI: 10.1016/j.tvjl.2021.105695
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Prascend®

Pergolide (as pergolide mesylate)
1 mg tablets for horses

Veterinary Use Only

DIN 02412217

EN

Boehringer Ingelheim

Description: Prascend® is a dopamine receptor agonist for oral use in horses. Prascend® tablets are rectangular light red colored, half-scored tablets.

Indications: For the control of clinical signs associated with Pituitary Pars Intermedia Dysfunction (Equine Cushing's Disease) in horses.

Active Ingredient: Each tablet contains 1 mg pergolide (as pergolide mesylate).

Dosage and Administration: Administer orally at a starting dose of 2 mcg/kg once daily. Dosage may be adjusted to effect, up to 4 mcg/kg daily (see "Animal Safety" section). To facilitate the administration, one or more tablets may be dissolved with a small amount of water and/or mixed with molasses or other sweetener. In this case, the dissolved tablets should be administered with a syringe. The entire amount should be administered immediately. The tablets should not be crushed.

The tablets are scored and the calculated dosage should be provided to the nearest one-half tablet increment (see Table 1).

Table 1- Dosing Table

Body weight	Starting dose 2 mcg/kg (in tablets)	Dosage range (in mcg/kg)
136 - 340 kg	0.5 tablets	1.5 - 3.7
341 - 567 kg	1 tablets	1.8 - 2.9
568 - 795 kg	1.5 tablets	1.9 - 2.6
796 - 1022 kg	2 tablets	2.0 - 2.5

Appropriate endocrine laboratory tests (e.g., dexamethasone suppression test or ACTH test) should be conducted as well as an evaluation of the clinical signs in order to establish a diagnosis of Pituitary Pars Intermedia Dysfunction (PPID). Following initial diagnosis, repeat the endocrine test at intervals of 4 - 6 weeks for dose titration until results and/or clinical signs have improved or stabilized. Following stabilization, a clinical assessment and endocrine testing should be performed every 6 months to monitor long-term treatment response. Dosing should be titrated according to the individual horse response to achieve the lowest effective dose. Where there is no apparent response to treatment, the diagnosis should be reevaluated.

If signs of dose intolerance develop, treatment should be stopped for 2 - 3 days and re-instated at one-half of the previous dose. The total daily dose can be titrated back up by 0.5 mg increments (half-tablets) every 2 - 4 weeks until the desired clinical effect is achieved.

Contraindications: Prascend® is contraindicated in horses with known hypersensitivity to pergolide mesylate or other ergot derivatives.

Cautions: Do not use in horses younger than 3 years of age, and in breeding, pregnant, or lactating horses, as Prascend® has not been evaluated in these animals. In mice, pergolide mesylate has been shown to inhibit prolactin secretion, a hormone linked to milk and colostrum production.

Pergolide mesylate is approximately 90% associated with plasma proteins in humans and laboratory animals. Use caution if administering Prascend® with other drugs that affect protein binding. Dopamine antagonists, such as neuroleptics (phenothiazines, domperidone) or metoclopramide, should not be administered concurrently with Prascend® (a dopamine agonist) since these agents may diminish the effectiveness of Prascend®.

Warnings: Keep out of reach of children. Prascend® should not be administered by persons who have had adverse reactions to ergotamine or other ergot derivatives. Pregnant or nursing women should wear gloves when administering this product. It has been reported that pergolide tablets may cause eye irritation, an irritating smell, or headache when Prascend® tablets are split or crushed. Prascend® tablets should not be crushed due to the potential for increased human exposure and care should be taken to minimize exposure when splitting tablets. Consult a physician in case of accidental ingestion by humans. In case of contact with skin, wash exposed skin with water. In the event of pergolide exposure to the eye, flush the affected eye immediately with water and get medical advice. Do not use in horses intended for human consumption. Owners and handlers should monitor for any changes in balance or behaviour of horses on this medication.

Adverse Reactions:
Potential adverse reactions in horses include inappetence, lethargy, depression, ataxia, diarrhea and colic.

Although not all adverse reactions are reported, the following adverse reaction information is based on voluntary post-approval drug experience reporting. It is generally recognized that this method of reporting results is significant under-reporting of adverse drug reactions. It should be noted that suspected adverse drug reactions listed here reflect reporting and not causality. The categories of adverse reactions are listed in decreasing order of frequency by body system.

Systemic disorders: anorexia, lethargy

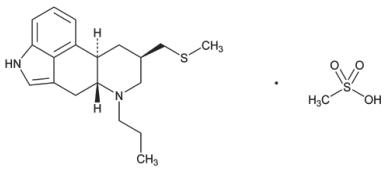
Neurological disorders: ataxia, muscle tremor, hyperesthesia

Digestive tract disorders: diarrhea, colic

On very rare occasions behavioural changes such as aggression and hyperexcitability have been seen.

Clinical Pharmacology: Pergolide mesylate is a synthetic ergot derivative and is a potent dopamine receptor agonist. The chemical name of pergolide mesylate is 8β-[(Methylthio) methyl]-6-propyl-ergoline monomethanesulfonate.

The chemical structure is:



As with other dopamine agonists, pergolide inhibits the release of prolactin which suggests that it may interfere with lactation. In horses with PPID, pergolide is believed to exert its therapeutic effect by stimulating dopamine receptors, and has been shown to decrease the plasma levels of adrenocorticotropic hormone (ACTH), melanocyte stimulating hormone (MSH), and other pro-opiomelanocortin peptides.

Pharmacokinetic information in the horse is based on a study using single oral doses of 10 mcg/kg in six healthy mares between 3 and 17 years of age. Pergolide was rapidly absorbed; the mean maximum concentration (C_{max}) was 2.11 ± 0.38 ng/mL with the median time to maximum concentration (T_{max}) being 0.33 hours. The area under the curve (AUC) was 8.44 ± 1.33 hr·ng/mL. The mean half-life ($T_{1/2}$) was 26.84 ± 10.2 hours; the mean apparent oral clearance (CL/F) was 1417.96 mL/kg/hr; and the mean apparent volume of distribution (V/F) was 39739.01 ± 10285.42 mL/kg.

Safety and Efficacy Study Information:
Animal Safety: In a six month target animal safety study healthy adult horses received Prascend® administered orally, once daily, at doses of either 0 mcg/kg, 4 mcg/kg, 6 mcg/kg, or 8 mcg/kg (0X, 1X, 1.5X, or 2X the maximum recommended dose). There were eight healthy horses (four males and four females) in each treatment group. Doses were prepared by dissolving tablets in approximately 10 mL of a 50% sugar water solution.

Prascend® treated groups had lower mean heart rates than the control group. Mean heart rates were statistically significantly different for geldings in all treated groups (4, 6 and 8 mcg/kg) and for mares in the 2X (8 mcg/kg). Mean heart rate was reduced by approximately 10 (1X group), 18 (1.5X group) and 16 (2X group) beats per minute for geldings and 8 beats per minute for mares in the 2X group.

Mares in the 1X and 1.5X groups also had numerically lower mean heart rates; however, the differences were not statistically significant. The minimum heart rates for individuals in all treated groups were within the normal range (24 - 44 beats per minute). Horses in all treatment groups also had higher mean temperatures when compared to the control group. However, maximum temperatures remained below 101.5°F (38.6°C). One 1.5X horse experienced a mild episode of spasmodic colic on Day 3 that resolved after treatment with flunixin meglumine.

Statistically significant decreases in mean red blood cell counts and hemoglobin values were present in all Prascend® treated groups (4, 6 and 8 mcg/kg) as compared to the control group. Other hematology parameters including hematocrit, white blood cells, absolute neutrophils, and absolute lymphocytes exhibited mild, transient decreases as compared to the control group. The hematology parameters generally decreased over the first 30 to 60 days after treatment initiation and then returned to values similar to pre-treatment levels. No treatment related alterations were identified on histopathology evaluation of bone marrow.

The safety analysis was conducted with the results of all 122 horses included in this field study and treated with Prascend® for six months.

Table 2 - Summary of the most common adverse reactions (N=122)

Clinical sign	# Cases	Cases (%)
Decreased appetite	40	32.8
Lameness	22	18.0
Diarrhea/Loose stool	12	9.8
Colic	12	9.8
Lethargy	12	9.8
Abnormal Weight Loss	11	9.0
Laminitis*	10	8.2
Heart murmur	10	8.2
Death	8	6.6
Tooth disorder	8	6.6
Skin abscess	7	5.7
Musculoskeletal pain	6	4.9
Behavior change	6	4.9

*Three new cases and 7 pre-existing, recurring cases

Inappetance or decreased appetite occurred at one or more meals in 40 of 122 horses treated with Prascend®. At the baseline evaluation 1.6% of owners reported a history of inappetance or decreased appetite as compared to the 32.8% of horses that experienced inappetance or decreased appetite during the study. Most cases of inappetance were transient and occurred during the first month of treatment; however, some horses experienced sporadic inappetance throughout the study. Two horses required a temporary reduction in dose due to inappetance during the first month of the study. Both horses returned to their original dose within 30 days.

Weight loss occurred in more than half of the horses in this study; however, weight loss that was considered abnormal was only reported in 11 horses.

Lethargy was reported in 9.8% of horses during the study, and was not reported in any horses at the baseline evaluation.

Behavioural changes were noted in 6 horses including aggression, kicking, agitation, nervous behaviour and increased activity. One horse required a temporary reduction in dose due to energetic behaviour during the first month of the study and increased back to original dose 9 days later.

Eight horses died or were euthanized during the study due to worsening of pre-existing conditions (laminitis, dental disease, septic tenosynovitis), or colic (strangulating lipomas, large colon volvulus).

One mare was inadvertently enrolled in the study while pregnant and experienced dystocia due to malpositioning resulting in the death of the foal.

Efficacy: An open-label, historical control, field study evaluated the effectiveness of Prascend® for the control of clinical signs of PPID. A total of 122 horses with PPID were enrolled in the study, 113 of which were included in effectiveness evaluations. The success of each horse was based on results of endocrinology testing (dexamethasone suppression test or endogenous ACTH test) and/or improvement in clinical signs related to PPID (hirsutism, hyperhidrosis, polyuria/polydypsia, abnormal fat distribution, and/or muscle wasting) on the Day 180 evaluation. Based on endocrine testing and investigators' clinical assessment scores, 86 (76.1%) of the 113 evaluable cases were treatment successes.

Table 3 - Proportion of Treatment Successes on Day 180

Percent success	Lower bound: one-sided 95% confidence interval
76.1% (86/113)	67.2 %

Enrolled horses were diagnosed with PPID based on the presence of hirsutism and an abnormal pre-study endocrine test result. All horses were treated with 2 mcg/kg Prascend® (to the nearest one-half tablet) orally once daily for the first three months. If the endocrine test result on Day 90 was normal or adequately improved, the horse continued on the same dose through Day 180. If the endocrine test result on Day 90 was abnormal, the dose increased to 4 mcg/kg given once daily through Day 180. Forty-seven (41.6%) of the 113 horses included in the effectiveness database required a dose increase at Day 90.

Improvement was noted in scores for all clinical sign categories and in mean results for endocrine tests.

Table 4 - Percent of Animals with Improvement in Clinical Signs Relative to Baseline Scores

Clinical sign	Day 90±7 (%)	Day 180±7 (%)
Hirsutism	32.7 %	89.2 %
Hyperhidrosis	27.4 %	42.3 %
Polyuria / polydypsia	31.0 %	34.2 %
Abnormal fat distribution	21.2 %	33.3 %
Muscle wasting	36.3 %	46.0 %

Table 5 - Endocrine test results (mean values)

Test	# Animals	Baseline	Day 90	Day 90
ACTH (pg/mL)	20	73.53	51.12	45.08
TSD** (mcg/dL)	93	3.12	1.39	1.47

** Dexamethasone suppression test: Post dexamethasone cortisol concentration

Storage: Store at or below 25°C. Do not freeze. Store the blister in the original carton.

Presentation: Prascend® (pergolide mesylate) tablets are available in 1 mg strength – packaged 10 tablets per blister and 60 or 160 tablets per carton.

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