PPID and Equine Metabolic Syndrome Review & Literature Update

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Cornell Animal Health Diagnostic Center

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Cornell College of Veterinary Medicine

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EQUINE ENDOCRINOLOGY GROUP 2022

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Andy Durham (Liphook Equine Hospital, UK)
Nicholas Frank (Tufts University, USA)
Catherine McGowan (University of Liverpool, UK)
Kelsey Hart (University of Georgia, USA)
Jean-Yin Tan (University of Calgary, CAN)
Francois-Rene Bertin (University of Queensland, AUS)
Julien Delarocque (Tierärztliche Hochschule Hannover, GER)

5th
Global Equine Endocrine Symposium
Bern, National Horse Center Switzerland
January 3rd – 5th 2023

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Pituitary Pars Intermedia Dysfunction (PPID)

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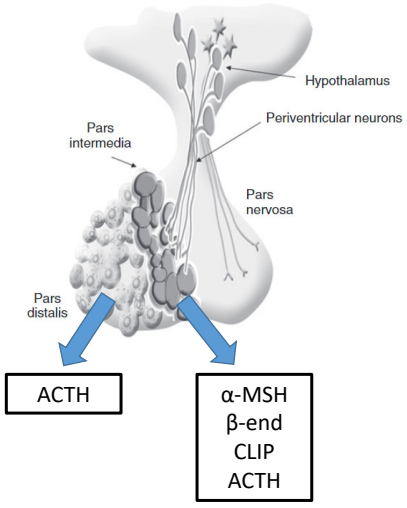
PPID Anatomy and Physiology

Smith et al. Large Animal Internal Medicine, 6th Edition, 2020. Pg. 1353

- Melanotropes of pars intermedia produce the precursor protein <u>proopiomelanocortin</u> (POMC)
- Pars intermedia converts POMC to:
  - ACTH (also produced by corticotropes in pars distalis)
  - α-MSH
  - CLIP
  - β-end



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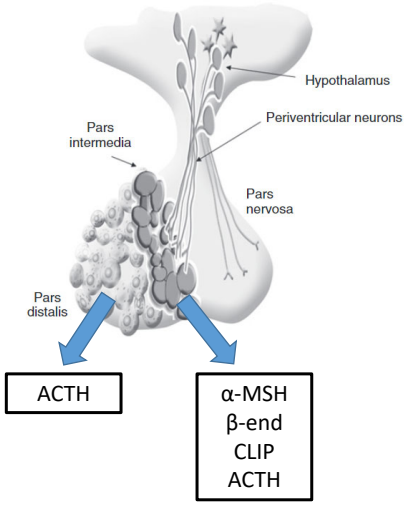
PPID Anatomy and Physiology

Smith et al. Large Animal Internal Medicine, 6th Edition, 2020. Pg. 1353

Function of POMC-derived peptides

- ACTH
  - Stimulates cortisol release by adrenal gland
- α-MSH
  - Coat/skin pigmentation
  - Regulator of energy homeostasis
  - Anti-inflammatory by regulating cytokine response
- β-end
  - Endogenous opioid providing analgesia and behavioral modification
- CLIP
  - Not well understood



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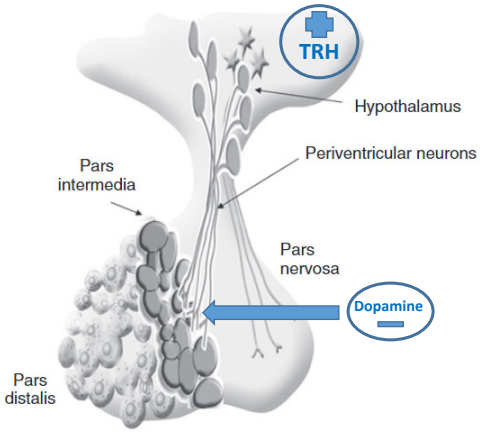
PPID Anatomy and Physiology

- Melanotropes are stimulated to produce POMCs by thyrotropin-releasing hormone (TRH) originating from the hypothalamus
- Periventricular neuron end terminals that originate from the hypothalamus transmit inhibitory dopamine to the pars intermedia, regulating the production of POMCs



Smith et al. Large Animal Internal Medicine, 6th Edition, 2020. Pg. 1353

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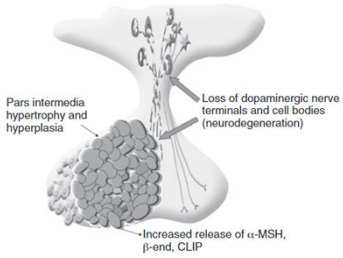
PPID Pathophysiology

1. Degradation of functional dopaminergic periventricular neurons due to oxidative damage
2. Decreased dopamine inhibition to melanotropes in pars intermedia
3. Hypertrophy, hyperplasia and micro- and macroadenoma formation of pars intermedia
4. Compression of nearby pituitary lobes and hypothalamus with loss of function
5. Pars intermedia loss of regulation results in increased POMC peptide secretion



Smith et al. Large Animal Internal Medicine, 6th Edition, 2020. Pg. 1354

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PPID Clinical Signs

- **Laminitis due to insulin dysregulation**
- Hypertrichosis (hirsuitism)
- Muscle atrophy
- Regional fat accumulation
- Polydipsia and Polyuria
- Sweating dysregulation
- Secondary infection
- Lethargy
- Infertility
- Persistent Lactation
- Exercise Intolerance

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PPID Testing Strategies

Baseline ACTH

- Sensitivity 70%, Specificity 80%

- Seasonal rise in ACTH occurs in fall (August-October) in North America

- Seasonal rise reference intervals for United States by latitudinal zone do not exist…are the needed?

  - **Objective:** The goal of this study was to determine whether seasonal variation in plasma ACTH concentrations of healthy horses is affected by latitude in the United States.

New York State Agriculture and Markets

Animal Health Diagnostic Center
Cornell University College of Veterinary Medicine

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Effects of Latitude, Age and Season on Equine Adrenocorticotropic Hormone Concentrations in the United States

Pinn-Woodcock T, **Gonzalo Llanos Soto S**, Ivanek R, Goodrich EL, Frye E, Lamb SV, Wells A, Place NJ

Study Population

- Healthy horses >5 years of age
- Location: United States between latitude 25º-45ºN

Data Collection

- Study conducted between June, 2019 and May, 2020
- EDTA plasma
  - Collected once monthly during non-fall (December – June)
  - Collected twice monthly during fall (July – November)

Map of Sampling Locations

Location	Initial study population (n)	Horses remaining after outlier analysis (n)	Percent (%)
Northern Latitude	**57**	36	23
New York	31	23	15
Wisconsin	13	13	0
Minnesota	13	13	8
Central Latitude	**102**	85	55
California	35	33	21
Colorado	24	19	14
Pennsylvania	43	33	21
Southern Latitude	**48**	33	21
Florida	27	22	14
North Carolina	9	9	6
Arizona	12	2	1

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Effects of Latitude, Age and Season on Equine Adrenocorticotropic Hormone Concentrations in the United States

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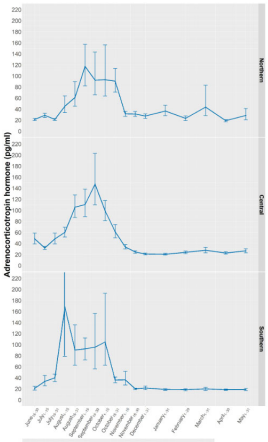

Figure 1. (left). Line plot representing ACTH upper reference limits of apparently healthy horses at three different latitude locations. The upper error bar value for August$_{1\text{-}15}$ in the southern latitude in 626.5 pg/mL.

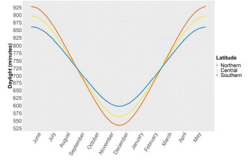

Figure 2. (left) Line plot representing the photoperiods (minutes of daylight per day) during the course of the study from June 2019 to May 2020 for northern, central and southern latitudes in the United States. Data were obtained from NOAA's Global Monitoring Laboratory.

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Effects of Latitude, Age and Season on Equine Adrenocorticotropic Hormone Concentrations in the United States

Pinn-Woodcock T, **Gonzalo Llanos Soto S**, Ivanek R, Goodrich EL, Frye E, Lamb SV, Wells A, Place NJ

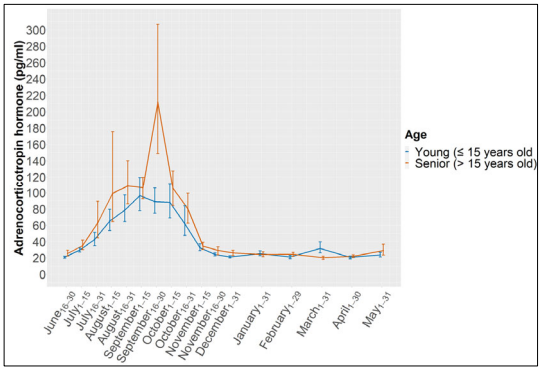

Figure 3. (Above) Line plots representing ACTH upper reference limits generated from Box-Cox-transformed data of apparently healthy horses from two age categories using the bootstrapped robust parametric method

Summary and Conclusions

- **Fall rise in ACTH occurred in all latitude groups (Fig. 1).**
- **The fall rise in ACTH corresponds to the rapidly decreasing photoperiod, which is most pronounced between late July and early October (Fig. 2).**
- **Healthy horses >15 years of age with no clinical signs of PPID have higher ACTH in fall than apparently healthy younger horses (Fig. 3).**
- **Individual horses in this study demonstrated considerable variability in ACTH during both fall and non-fall seasons, which suggests a single baseline ACTH determination at any time of year has limited diagnostic sensitivity for PPID.**

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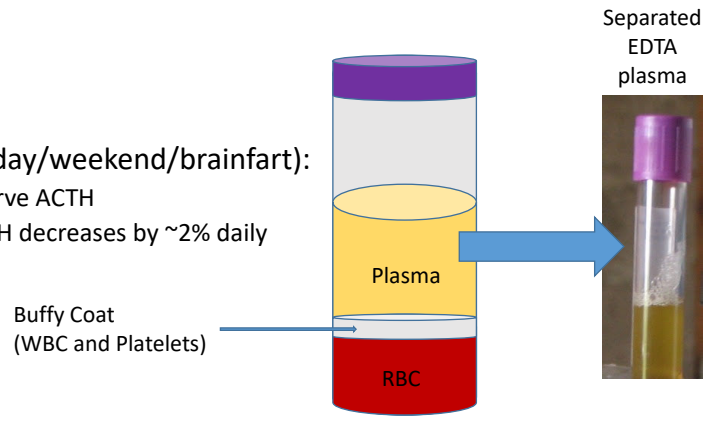
Storage of ACTH Samples

- Spin down and separate EDTA plasma within 4hrs of collection
  - If left on cells >24hrs → ACTH drops ~25%
- Once plasma is separated:
  - Ship overnight with icepacks
  - If delay occurs (weather/holiday/weekend/brainfart):
    - Ideally, freeze plasma to preserve ACTH
    - Ok for 1 week in the frig – ACTH decreases by ~2% daily



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Equine Veterinary Journal ISSN 0425-1644
DOI: 10.1111/j.2042-3306.2011.00444.x

Circannual variation in plasma adrenocorticotropic hormone concentrations in the UK in normal horses and ponies, and those with pituitary *pars intermedia* dysfunction

V. E. N. COPAS* and A. E. DURHAM

The Liphook Equine Hospital, Hampshire, UK.

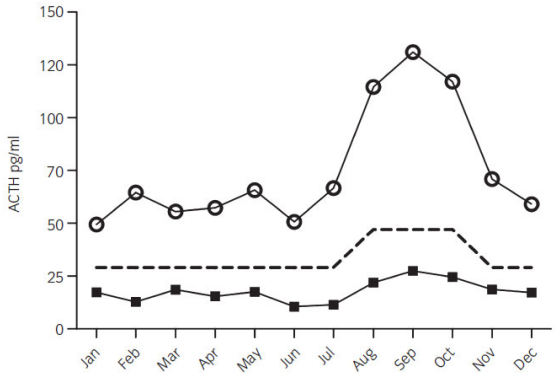

Fig 4: Graphical comparison of the median plasma ACTH concentration (pg/ml) by month for the PPID groups (circles) and non-PPID group (boxes). The dashed line represents the upper limit of the reference interval for plasma ACTH.

Equine Veterinary Journal **44** (2012) 440–443 © 2011 EVJ Ltd

- UK study at similar latitude of Northeastern US
- A significant difference in ACTH between PPID and non-PPID horses occurred during the seasonal rise.

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PPID Testing Strategies

- Dynamic Tests?
- Previously the Dexamethasone Suppression Test (DST) was gold standard
  - PPID horses fail to suppress cortisol following dexamethasone injection due to continued ACTH production from the pars intermedia
  - DST *fails* to diagnose early-stage PPID cases
  - DST is sensitive in the diagnosis of end stage PPID

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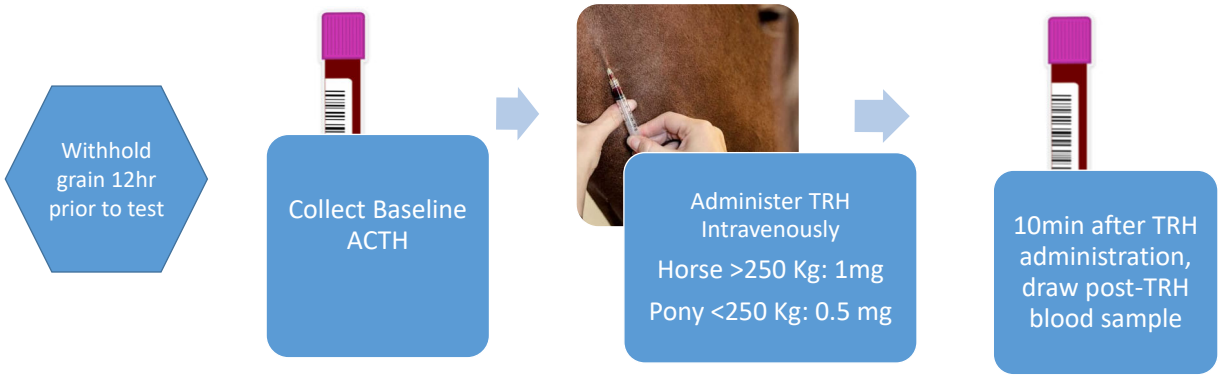
PPID Testing Strategies

Thyrotropin-Releasing Hormone (TRH) Stimulation Test

- Sensitivity 94%, specificity 78%
- PPID horses with lack of dopaminergic inhibition will respond with increased ACTH levels



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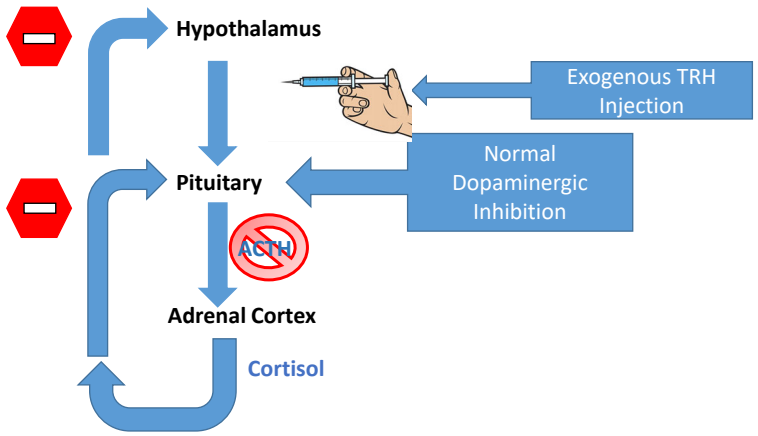
PPID Testing Strategies

TRH Stimulation Test – Normal Horse with intact dopaminergic inhibition of pars intermedia



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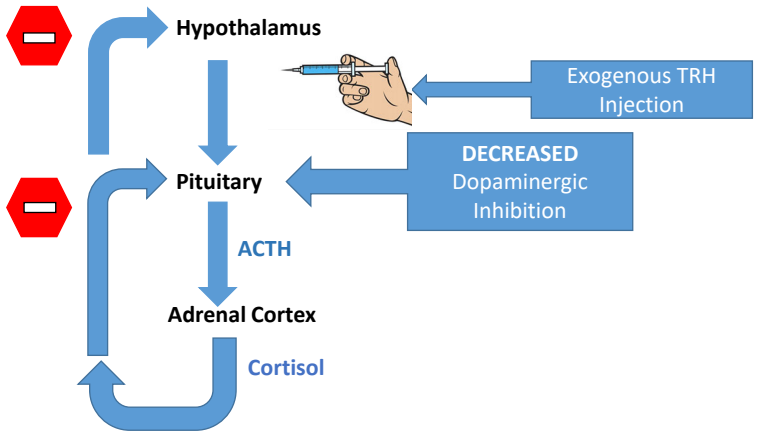
PPID Testing Strategies

TRH Stimulation Test – **PPID** horse with loss of dopaminergic inhibition responds with excessive release of ACTH



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5th Global Equine Endocrine Symposium
Bern, National Horse Center Switzerland
January 3rd–5th 2023

The Effect of Trailering on Thyrotropin Releasing Hormone Stimulation of Adrenocorticotropic Hormone Concentration in Horses

[1]J.C. Haffner, [1]R.M. Hoffman and [2]S.T. Grubbs
[1]Middle Tennessee State University, Murfreesboro, TN
[2] Boehringer Ingelheim Animal Health USA Inc., Duluth, GA

- The aim of this study was to determine if trailering affects ACTH concentrations 10 min after a TRH-stimulation test (T10ACTH).
  - 10 horses rotated through 5 trailer positions
  - TRH-stimulation was performed at 0, 15, 30, 60, and 120-min post-trailering
- A 40-min trailer ride caused false positive PPID diagnosis using baseline ACTH for up to 30min post-trailering
- T10 after TRH-stimulation was not elevated by trailer stress in all but 1 horse at time 0

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Baseline ACTH and TRH Response Test Reference Intervals

- Reference intervals in fall months for post TRH response test are not yet well established in North America

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Interpretation of results[a]	Negative	Equivocal	Positive
Non-fall months: mid-November to mid-July			
basal ACTH or time 0	<30 pg/mL	30-50 pg/mL*	>50 pg/mL
10 min after TRH	<110 pg/mL	110-200 pg/mL	>200 pg/mL**
Fall months: mid-July to mid-November* **			
	Negative	Equivocal	Positive
basal ACTH	<50 pg/mL	50-100 pg/mL	>100 pg/mL

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PPID Treatment

- Pergolide (Prascend)
  - Dopamine agonist
  - Reassess ACTH level 1 month after treatment initiated, and q6-12mo after that

ACTH AFTER TRH STIMULATION IN PPID PATIENTS TREATED WITH PERGOLIDE FOR SIX TO EIGHT WEEKS

Christiane Schorn[1], Klaus Failing[2], Kerstin Fey[1]

EEG Summit 2020

N=11

- Horses with normal baseline ACTH after pergolide treatment continued to have abnormal TRH stimulation tests.
- More research needed. Base decisions regarding pergolide dosing on:
  - Compare serial tests in same horse to establish trend
  - Trend of clinical signs in response to treatment

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PPID Treatment

Cyproheptidine

- Mechanism – anti-seratoninergic
  - May decrease ACTH release from corticotropes in pars distalis of pituitary
- When to use:
  - Adjunct therapy used when horses don't respond to pergolide
  - Alternative treatment in horses that experience significant pergolide side effects
- Side effects – associated with seizures in rodents, do not use in horses with previous history of seizure.

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Additional PPID Management Considerations

- Dietary management
  - Horses with concurrent insulin dysregulation require low starch diet
- Routine fecal egg counts to assess parasite load
- Body clip when necessary to manage hypertrichosis and excessive sweating
- Monitor for infections

'Starshine'

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Equine Metabolic Syndrome

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EMS – Definition of Terms

Hyperinsulinemia-Associated Laminitis (HAL)

- Mild to moderate laminitis due to sustained undetected hyperinsulinemia which leads to laminar hoof damage.
  - Horses with HAL can appear lame or have subclinical laminitis with no obvious lameness
  - Horses with EMS and 30% of horses with PPID develop HAL
- Pasture-Associated Laminitis is an example of HAL
- Mechanism? Two theories:
  1. Hyperinsulinemia induces inappropriate stimulation of insulin-like growth factor-1 receptors on laminar epidermal cells
  2. Decreased lamellar perfusion with altered lamellar energy regulation

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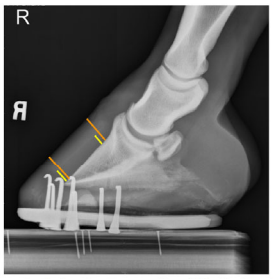
How does hyperinsulinemia cause laminitis?

- Popular working theory:
  - Through inappropriate stimulation of insulin-like growth factor 1 receptors on lamellar epidermal cells
    - Mitosis of lamellar cells → stretching and failure

Effects of an anti-IGF-1 receptor monoclonal antibody on laminitis induced by prolonged hyperinsulinaemia in Standardbred horses

Samira Rahnama, Niveditha Vathsangam, Robert Spence, Carlos E. Medina-Torres, Christopher C. Pollitt, Melody A. de Laat, Simon R. Bailey, Martin N. Sillence

Published: September 29, 2020 • https://doi.org/10.1371/journal.pone.0239261



Grenager VCNA 2018

Fig. 4. Lateral radiograph of a foot showing stretching of the distal hoof-lamellar zone (*yellow lines*) in the absence of significant rotation of the distal phalanx with respect to the hoof wall (*orange lines*). Note the nails in the block, which are a known distance from each other, used to calibrate the image.

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EMS – Definition of Terms

Insulin Resistance (IR)

- Impaired response of the body to insulin, resulting in elevated blood glucose

Insulin Dysregulation (ID)

- Excessive insulin response to sugars, resting and postprandial hyperinsulinemia and insulin resistance
- Associated with EMS, may also occur secondary to PPID, systemic illness, stress, pregnancy and starvation

Nonstructural Carbohydrates (NSC) – Dry Matter Basis

- Starches and sugars in feed
- NSC = WSC + Starch

Sugar (WSC)	10.45
Starch	4.42
NSC	14.87

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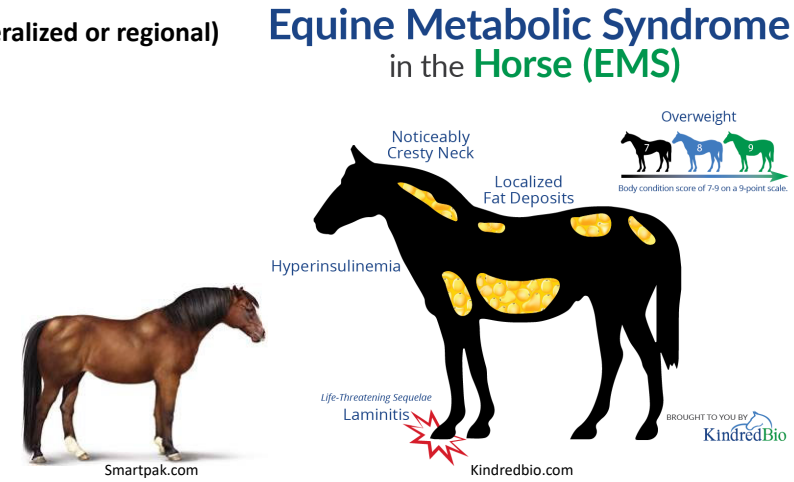
Equine Metabolic Syndrome (EMS)

- EMS is defined as the risk factors associated with HAL development:
  - **Insulin dysregulation**
  - **Increased adiposity (generalized or regional)**
  - Hypertriglyceridemia
  - Hypertension



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EMS Risk Factors

- Genetics
  - High genetic risk animals develop EMS with low environmental influences
    - British native pony breeds
- Environment
  - Diet - Feeds with high NSC (grain, grass)
  - Lack of exercise

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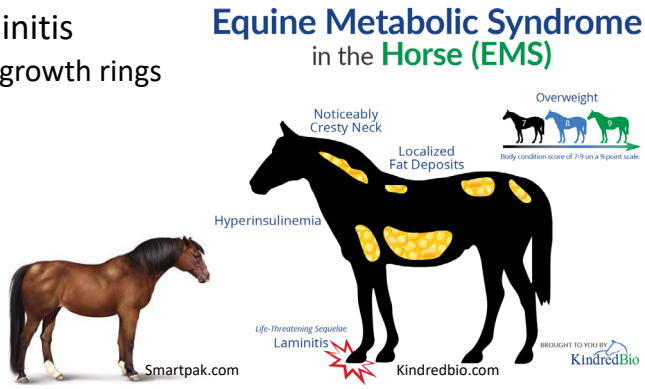
EMS Clinical Signs

- Obese 'easy keeper' with thick neck crest or other regional adiposity
  - BCS>7 (where 1 is emaciated, 5 is ideal and 9 is obese)
- Evidence of subclinical laminitis
  - Divergent hoof capsule growth rings
  - Widening of white line
- Laminitis



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EMS Diagnostic Testing

Pros and Cons of EMS Diagnostics used in the field:

1. **Baseline Insulin**
   - Complete fasting is not required
     - No need to remove hay or pasture, but must wait 4hr after high carb grain meal
   - *Low sensitivity for diagnosis of EMS*
2. **Oral Sugar Test (OST)**
   - Dynamic test that assesses insulin response following sugar ingestion (corn syrup)
   - Requires fasting for 3-6 hrs
   - *Improved sensitivity over insulin baseline*
   - Makes some owners nervous
3. **Insulin Tolerance Test**
   - Dynamic test
   - Fasting not required
   - Baseline glucose → 0.1 IU/kg regular insulin → collect 2nd glucose 30min after insulin, then feed meal to prevent hypoglycemia

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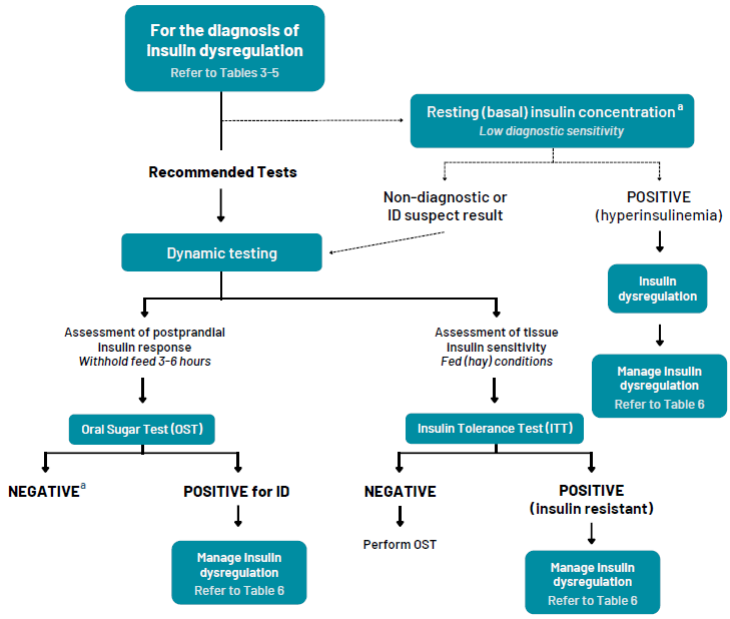
EQUINE ENDOCRINOLOGY GROUP 2022

Figure 3 – Algorithm for detection of insulin dysregulation (June 2022)



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Influence of Feed on Insulin Baseline (RIA)

- Reference ranges created in the context of 2 feeding scenarios:
  - Horses on hay and pasture: 10-40 uIU/ml
  - Horses fasted overnight: <20 uIU/ml
- If grain has been fed, wait 4 hours before sampling insulin baseline
  - Most normal horse's insulin will return to reference range within 2hr of meal

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Validation and method comparison for a point-of-care lateral flow assay measuring equine whole blood insulin concentrations

Emily H Berryhill, Naomi S Urbina, Sam Marton, William Vernau, Flavio H Alonso

Corresponding author: Emily H Berryhill, Department of Medicine and Epidemiology, School of Veterinary Medicine, University of California-Davis, One Garrod Dr, Davis, CA 95616, USA. eberryhill@ucdavis.edu

- Evaluated the Wellness Ready Equine Insulin Test (WRT)
  - Stall-side lateral flow assay that measures insulin in whole blood
  - Compared to radioimmunoassay
- WRT insulin concentrations averaged 10% higher than the RIA
  - Sensitivity ranged 87-95%
  - Specificity ranged 92-96%
- Conclusion – good association with RIA

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Practice Tip: Stall-side/point-of-care insulin analyzers have been recently developed and are now commercially available but have not been critically evaluated at this time. The EEG recommends that referral laboratories be used until further independent research is performed.

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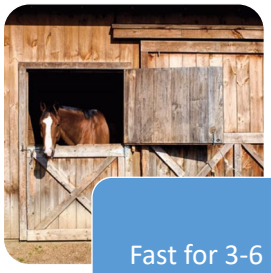
OST Steps



Fast for 3-6 hours
(no hay/grain)

Administer corn syrup with oral dosing syringe
- Karo Syrup Lite

Draw blood for insulin at 60min and 90min
(EDTA or red Top Tube)

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Oral Sugar Test for Diagnosis of EMS (RIA)

- New research suggests that using a higher dose of corn syrup (Karo Lite) is more sensitive for the diagnosis of EMS
  - 0.45 ml/Kg rather than 0.15 ml/Kg

Jocelyn NA, Harris PA, Menzies-Gow NJ. Effect of varying the dose of corn syrup on the insulin and glucose response to the oral sugar test. *Equine Vet J* 2018;50:836-841.

Corn Syrup Dose	Post-OST Insulin Ref. Range
Low Dose 0.15 ml/Kg	<45 IU/ml – no evidence >45 IU/ml – evidence of ID
High Dose 0.45 ml/Kg	<65 IU/ml no evidence >65 IU/ml supportive of EMS

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Oral Sugar Test for Diagnosis of EMS

Jocelyn NA, Harris PA, Menzies-Gow NJ. Effect of varying the dose of corn syrup on the insulin and glucose response to the oral sugar test. *Equine Vet J* 2018;50:836-841.

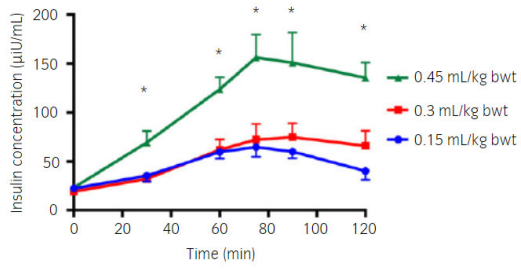

Fig 1: Estimated marginal mean (±1.96 s.e.) serum insulin concentration at single time points in response to three different doses of corn syrup (Karo Light Corn Syrup)[a]. (n = 8) *Values that are significantly different (P<0.05) from the equivalent values from a different dose.

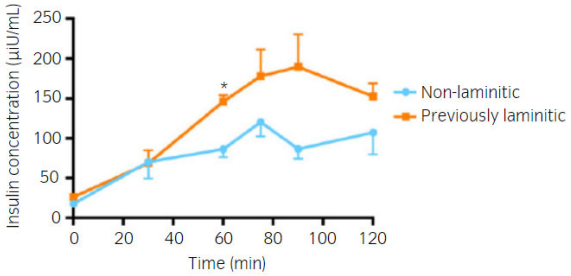

Fig 2: Estimated marginal mean (±1.96 s.e.) insulin concentration at single time points for NL (n = 3) and PL (n = 5) ponies when given a dose of 0.45 mL/kg bwt corn syrup (Karo Light Corn Syrup)[a]. *Values that are significantly different (P<0.05) between groups (NL and PL).

*Novel unexpected finding - Insulin was higher in the winter months in the Northern Hemisphere

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Seasonal Effects of Insulin and ACTH

Andy Durham, Liphook Equine Hospital, UK

5th Global Equine Endocrine Symposium
Bern, National Horse Center Switzerland
January 3rd – 5th 2023

- 14,737 submissions with baseline insulin and ACTH
- 1605 submissions with insulin following OST and baseline ACTH
- Seasonal variation of insulin occurred
  - Higher in winter, lowest in summer and autumn
- ACTH concentrations inversely correlated with insulin
- Why? Evolution?
  - Grazing season typified by relative insulin sensitivity, promoting energy stores
  - Winter season may have relative insulin resistance to facilitate mobilization of energy stores

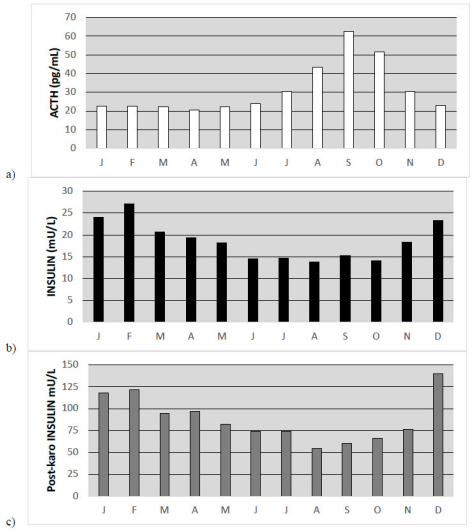

Figure 1. Median monthly values of a) ACTH, b) resting insulin, and c) post-Karo insulin including all breeds.

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OST is more sensitive for EMS diagnosis
Case example

Signalment: 10yo Morgan mare

History: Apparently healthy, BCS 7/9, pleasure horse in moderate work turned out on lush pasture

Plasma, Edta		
Oral Sugar Test: Insulin	Pre: 19.95 uIU/ml	0 - 20
	Post: 134.08 uIU/ml	0 - 45
	Post: 67.63 uIU/ml	0 - 45

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Coming soon? Glycemic pellets for OST

5th Global Equine Endocrine Symposium
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- New commercial product to replace karo syrup in OST - DysChEq™
- Standardized, *fairly* palatable glycemic pellet to stimulate insulin secretion
  - Horse is fed standard volume per BW
  - Given 10min to consume pellets
  - Blood sample collected 2hr later for glucose and insulin measurements

Received: 12 April 2022 | Accepted: 14 December 2022
DOI: 10.1111/jvim.16621
STANDARD ARTICLE
Journal of Veterinary Internal Medicine ACVIM
Carbohydrate pellets to assess insulin dysregulation in horses
Melody A. de Laat[1] | Tobias Warnken[2,3] | Julien Delarocque[3] | Dania B. Reiche[2] | Anne J. Grob[3] | Karsten Feige[3] | Harry B. Carslake[4] | Andy E. Durham[5] | Martin N. Sillence[1] | Kristen E. Thane[6] | Nicholas Frank[6] | Johan Brojer[7] | Sanna Lindase[7] | Johanna Sonntag[2]

Received: 2 March 2022 | Accepted: 8 December 2022
DOI: 10.1111/jvim.16614
STANDARD ARTICLE
Journal of Veterinary Internal Medicine ACVIM
Palatability, glycemic, and insulinemic responses to various carbohydrate formulations: Alternatives for the diagnosis of insulin dysregulation in horses?
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EMS Diagnostic Testing

Leptin

- Serum or EDTA plasma, fasting not required
- Function – 'the satiety hormone'
  - Inhibits hunger when the body does not need energy
  - Released from adipose cells, rises with increased body condition
- Objective measurement to correlate with increased adiposity, particularly *intra-abdominal* fat

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EMS Management

1. Low NSC diet of <10%

- Hay Analysis of hay core samples
- Restrict grass and grain
- Use ration balancer to supplement essential vitamins and minerals
- Slow feeder nibble nets to simulate grazing and small frequent meals

2. Exercise *if* not laminitic

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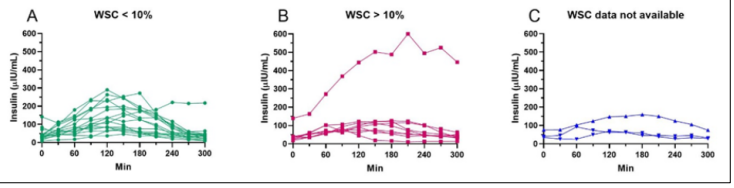
Svonni et al. Postprandial insulin responses to feeding forage with different carbohydrate content in horses with moderate to severe insulin dysregulation – preliminary results from ongoing study

5th Global Equine Endocrine Symposium
Bern, National Horse Center Switzerland
January 3rd–5th 2023

Figure 1. Insulin concentrations after feeding horses forage (0.4 kg dry matter/100 kg body weight) with a WSC content < 10% on a dry matter basis (A), > 10% (B) and with unknown WSC content (C).



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ORIGINAL ARTICLE

Equine Veterinary Journal WILEY

Postprandial insulin responses to various feedstuffs differ in insulin dysregulated horses compared with non-insulin dysregulated controls

Erica L. Macon[1] | Patricia Harris[2] | Simon Bailey[3] | Virginia D. Barker[1] | Amanda Adams[1]

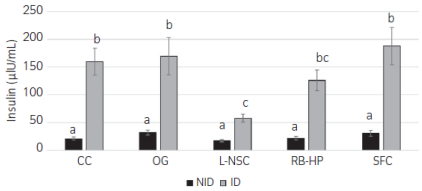

FIGURE 2 Postprandial insulin concentrations for non-insulin dysregulated (NID) and insulin dysregulated (ID) horses in Study A. Mean insulin concentrations ± SEM for postprandial insulin (T60) for five dietary treatments of cracked corn with molasses (CC), oat groats (OG), low NSC pelleted feed (L-NSC), ration balancer with high protein (RB-HP) and steam-flaked corn (SFC). All ID horses' T60 responses were different than NID horses ($P < .001$). Significance is denoted by difference of superscript

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EMS Management

Can some grazing/grain ever be re-introduced?

- ***Always remain cautious,*** but restricted access to grass may be considered if:
  1. Resolve obesity, return to ideal BCS of 5
  2. Demonstrate normal insulin regulation through OST results
  3. **Perform grazing trial – allow 1-2hr grazing, then measure insulin 1-2hrs later.**
     - **Unsafe if insulin >200 uIU/ml (this is not a precise test)**

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EMS Treatment When Diet and Exercise Fail

Levothyroxine sodium (Thyro-L)

- High Dose: 0.1mg/kg PO SID for ≤ 6 months
  - Side Effects – weight loss, tachycardia, hyperexcitability, arrhythmia, collapse
- Treat until reaching ideal body condition or when 6 month period ends
  - Gradually weaning off Thyro-L over 1 month period
- Long-term administration is not recommended

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EMS Treatment
Persistent Hyperinsulinemia Management

Metformin

- Mechanism: may decreases intestinal absorption of glucose
- Poor oral bioavailability in horses (7%)
- Dose range: 15-30 mg/kg PO BID to TID given 30-60min prior to feeding
  - Oral ulcers seen with high dose
  - Individual horse variability in bioavailability

Sodium-glucose co-transporter 2 inhibitors (SGLT2)

- Mechanism: Inhibit the reuptake of glucose from the renal glomerular filtrate. Glucose is lost in urine → decreases blood glucose and insulin concentrations
- Brand available for people in United States is Canagliflozin (Invokana)
- More research now available in safety and efficacy
- *Expensive and Novel*

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EMS Treatment
Persistent Hyperinsulinemia Management

Sodium-glucose co-transporter 2 inhibitors (SGLT2)

- Recommended use:
  - Short-term management of acute carbohydrate overload in EMS patient (escapes into grass paddock or grain bin)
- Contraindications – avoid in horses with liver disease
  - Side Effect – Stimulates lipid mobilization resulting in hypertriglyceridemia

RESEARCH ARTICLE

The sodium-glucose co-transporter 2 inhibitor velagliflozin reduces hyperinsulinemia and prevents laminitis in insulin-dysregulated ponies

Alexandra Meier[1], Dania Reiche[2], Melody de Laat[1], Christopher Pollitt[3], Donald Walsh[4], Martin Sillence[1]*

All ponies enrolled had insulin dysregulation (ID)

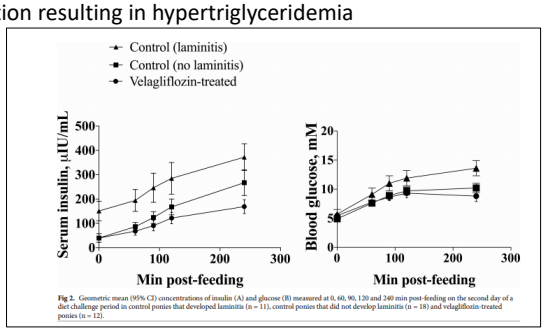

Fig 2. Geometric mean (95% CI) concentrations of insulin (A) and glucose (B) measured at 0, 60, 90, 120 and 240 min post-feeding on the second day of a diet challenge period in control ponies that developed laminitis (n = 11), control ponies that did not develop laminitis (n = 18) and velagliflozin-treated ponies (n = 12).

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The sodium-glucose cotransporter-2 inhibitor velagliflozin decreases basal plasma insulin concentrations in horses with moderate-severe insulin dysregulation

K. Thane[1], R. Voth[2], R. Klee[3], T. Warnken[3], N. Frank[1]

5th Global Equine Endocrine Symposium
Bern, National Horse Center Switzerland
January 3rd–5th 2023

- Investigate the ability of SGLT2 inhibitor velagliflozin to decrease insulin concentrations in horses with ID
- Privately owned horses with moderate to severe insulin dysregulation
  - OST insulin >75 uIU/mL
- Design:
  - n=19 placebo
  - n=18 active drug for first 20 weeks
  - Then all horses received active drug for 20 weeks
- Velagliflozen significantly decreased basal plasma insulin in ID horses
- All horses experienced increase in serum triglycerides with no apparent clinical abnormalities (lethargy, anorexia)

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Equine Veterinary Education BEVA AAEP

ORIGINAL ARTICLE

Preliminary observations on the use of ertugliflozin in the management of hyperinsulinaemia and laminitis in 51 horses: A case series

Tania Sundra[1] | Erin Kelty[2] | David Rendle[3]

Open Veterinary Journal, (2022), Vol. 12(4): 511–518
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Case Report
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Use of the SGLT2 inhibitor canagliflozin for control of refractory equine hyperinsulinemia and laminitis

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EQUINE ENDOCRINOLOGY GROUP 2022

Figure 4 – Algorithm for management of challenging cases (June 2022)

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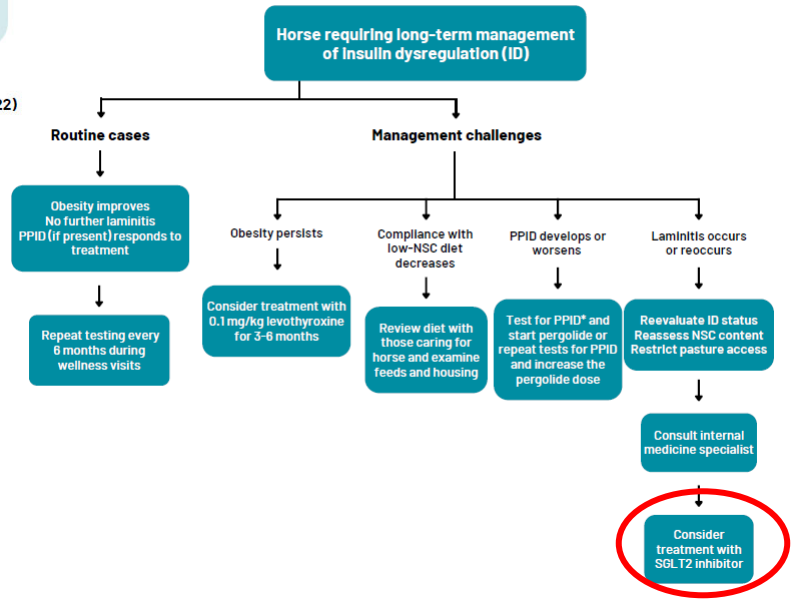

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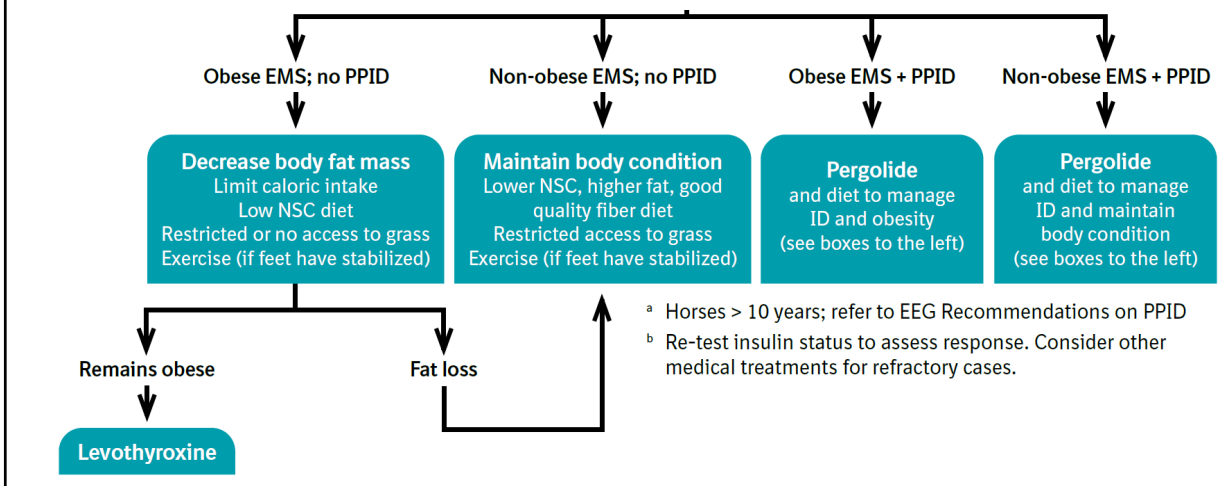
PPID vs EMS

2020 EQUINE ENDOCRINOLOGY GROUP



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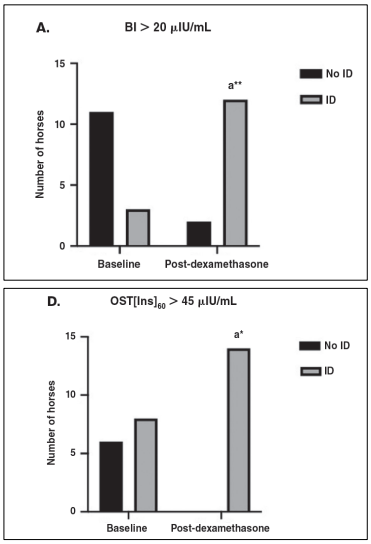
Diagnostic evaluation of insulin and glucose dynamics in light-breed horses receiving dexamethasone CVJ, June, 2022

Kathryn J. Timko, Laura D. Hostnik, Mauria R. Watts, Chiaming Chen, Adam Bercz, Ramiro E. Toribio, James K. Belknap, Teresa A. Burns

- Glucocorticoids can exacerbate insulin dysregulation
- 14 horses – administered dexamethasone 0.08 mg/kg PO SID for 7 days

- **Take caution using glucocorticoids in 'at-risk' horses:**
  - Obese
  - Subclinical laminitis or history of laminitis
  - PPID
  - Breed predisposition

- Sometimes the benefits outweigh the risks – requires careful client communication



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Questions?

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