

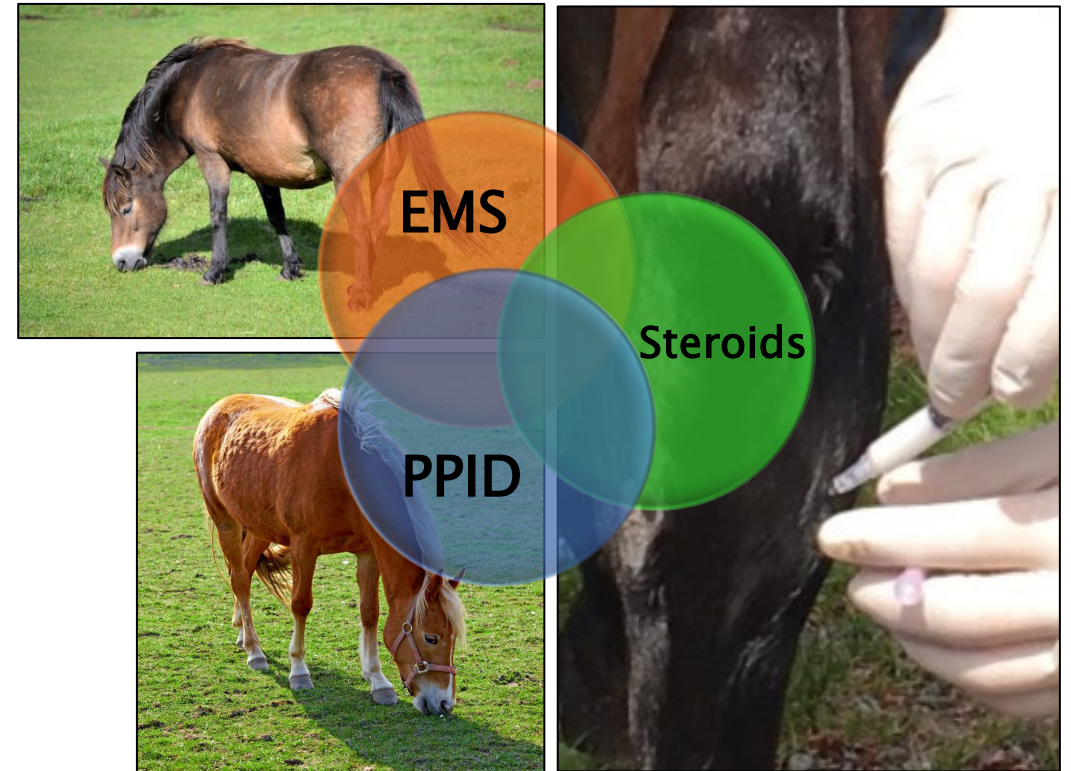


Use of diagnostic testing in diagnosis and management of equine endocrine disease

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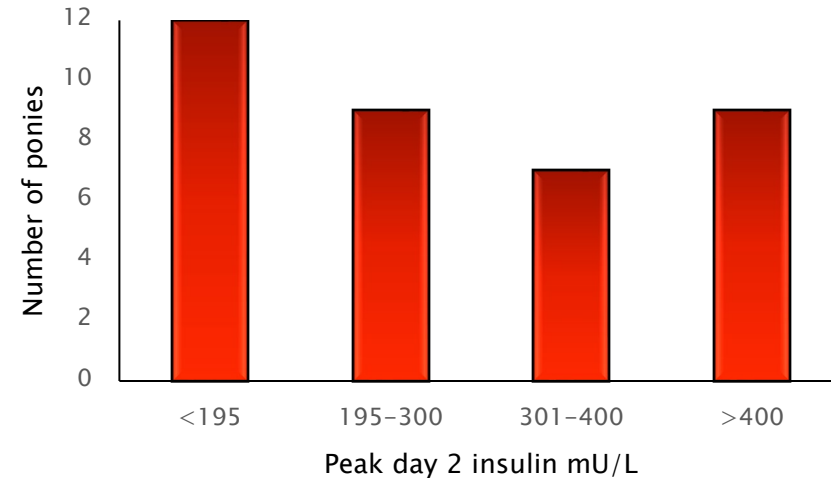
Endocrine Laminitis

- ▶ Represents the vast majority of laminitis cases seen in practice
- ▶ three distinct endocrine conditions associated with laminitis:
 - Equine Metabolic Syndrome
 - Pituitary *pars intermedia* dysfunction
 - Exogenous glucocorticoid administration
- ▶ May occur individually or in combination
- ▶ The final pathway for all is hyperinsulinaemia
 - Hyperinsulinaemia-Associated Laminitis (“HAL”)



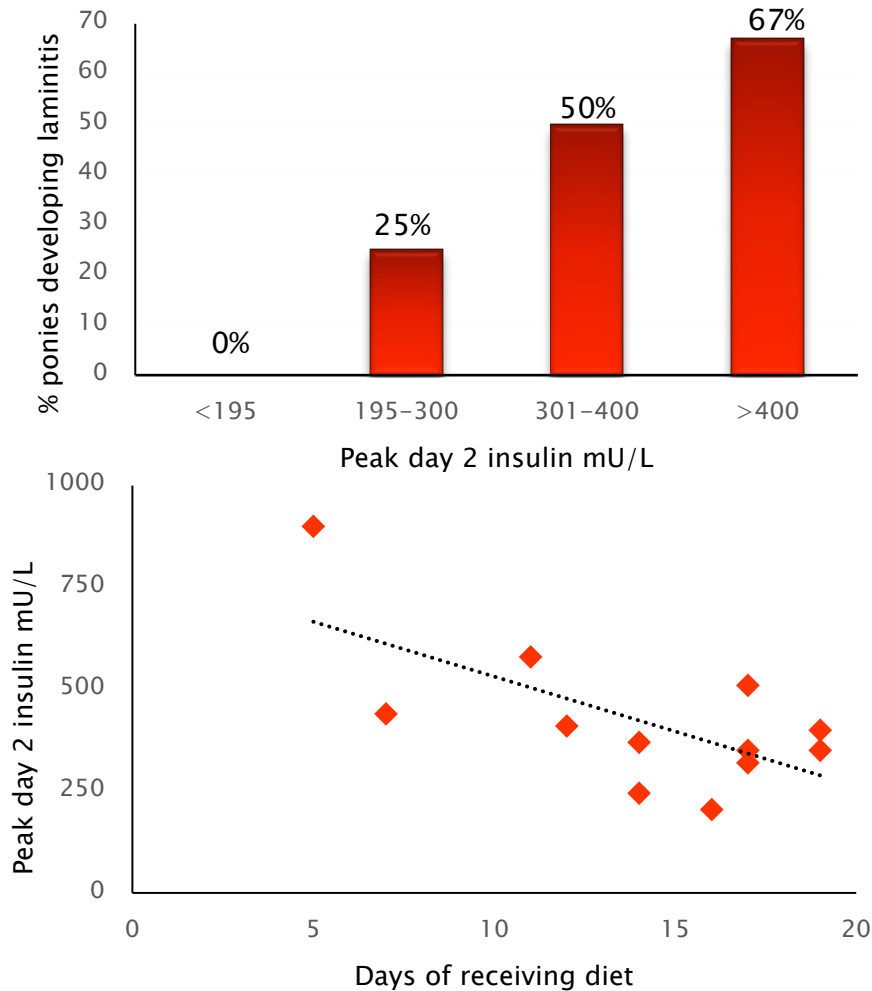
What actually causes laminitis?

- ▶ 37 ponies fed high starch diet (12.3 g/kg)
 - postprandial insulin response measured
 - responses very variable
 - 14/37 (38%) developed laminitis
 - **those with higher postprandial insulin:**



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 - 14/37 (38%) developed laminitis
 - **those with higher postprandial insulin:**
 - **were more likely to develop laminitis**
 - **developed laminitis soonest**



Meier *et al* 2018

Post-prandial hyperinsulinaemia is the final trigger

Courtesy of Kieran O'Brien



24 bites in 19 seconds!



What is the Plan ?

1. Weight loss

- 1.2-1.5% BWT daily feed allowance

2. Increased aerobic fitness

- Lots of exercise

3. Drugs?

- SGLT2 inhibitors?



Do you think this plan will work?!

What is the Plan ?

1. Weight loss

- 1 small meal daily



2. No treats



3. Increased aerobic fitness

- Lots of exercise



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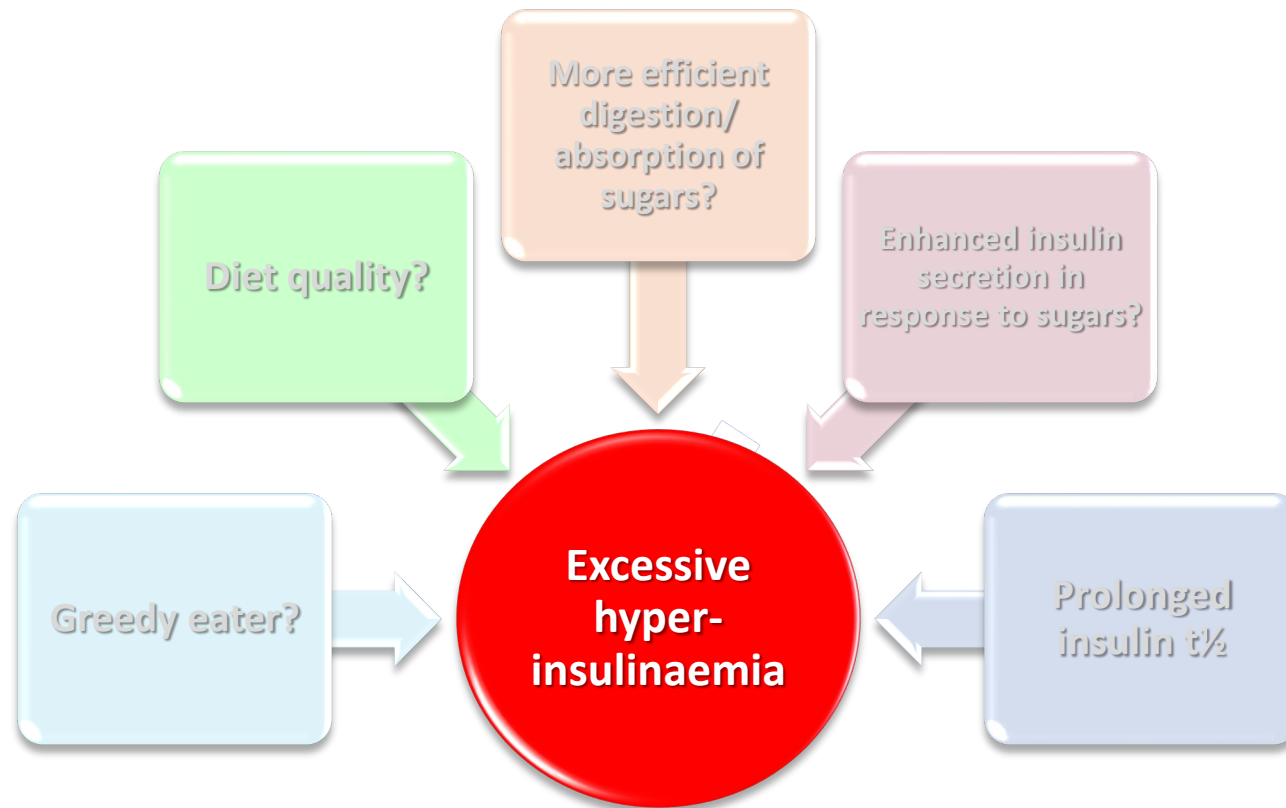
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LAMINITIS



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**None of these actions
directly target post-prandial
hyperinsulinaemia**

Do you think this plan will work?!



What actually causes laminitis?



There are 2 different questions/reasons for diagnostic testing:

1. Identify insulin dysregulation (ID)

- Post-sugar challenge tests are most sensitive to detect ID – e.g. check insulin after oral glucose
- A horse with ID is at higher risk of laminitis, butonly when fed inappropriately
- Having ID is not a problem if the diet is low in sugar/starch

=Potential risk

2. Assess the actual risk of the current diet

- The actual risk of laminitis depends on the actual post-prandial insulin
- check resting insulin after normal diet
 - a horse with high post-prandial insulin will get laminitis
 - a horse with low post-prandial insulin will not get laminitis

=Actual risk



What is the insulin response to their own diet?

► Dietary components?

◦ Hay

- Dry
- Soaked
- 50% straw

◦ Grass

- No Muzzle
- Muzzle

◦ Other feeds



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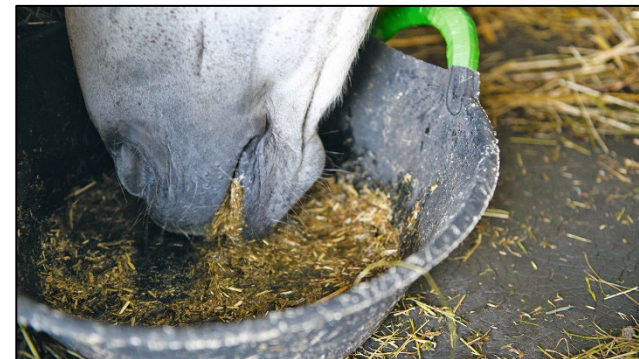
◦ Grass

- No Muzzle
- Muzzle

◦ Other feeds

Timing?

- Allow to eat for 3 hours and then collect blood sample
- Allow to graze for 1 hour, bring into stable, and then collect blood sample after a further 1 hour
- Allow to eat feed and then collect blood sample after 1-2 hours



What is the insulin response to their own diet?

► Example

◦ Hay

- Dry 86 mU/L
- Soaked 29 mU/L
- 50% straw 22 mU/L

◦ Grass

x1 hour

x3 hours

- No Muzzle 189 mU/L 465 mU/L
- Muzzle 66 mU/L 288 mU/L

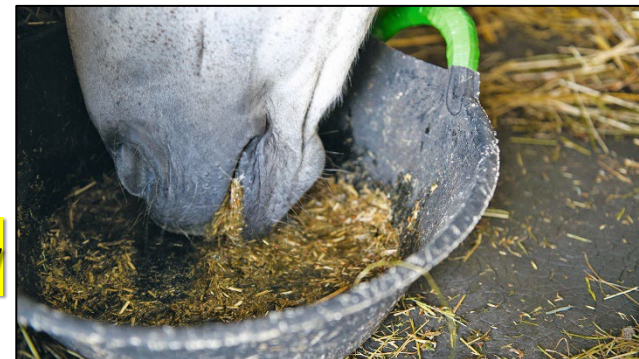
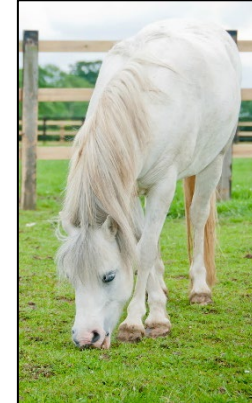
◦ Other feeds

1 big feed/day

3 small feeds/day

226 mU/L

46 mU/L



How high is “Excessive Insulin”?

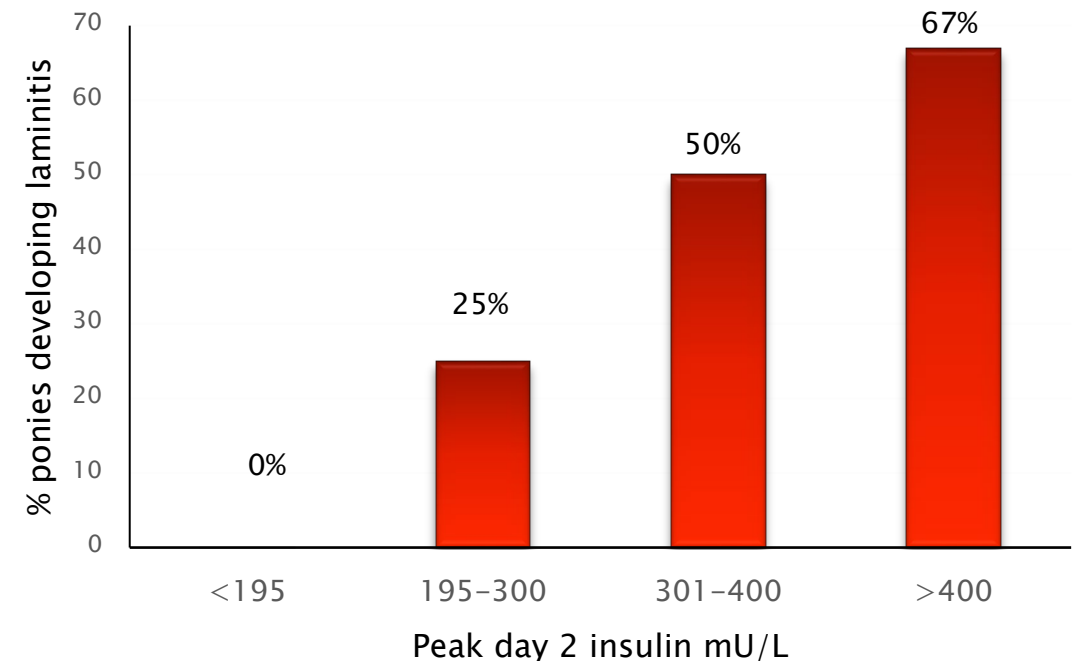
What is the insulin concentration threshold for causing laminitis?

- Insulin = 1500 mU/L for 48 h → clinical laminitis
- Insulin = 200 mU/L x 48 h → subclinical laminitis
- No pony with post prandial insulin <195 mU/L developed laminitis

(Asplin et al 2007)

(de Laat et al 2010)

(Meier et al 2018)



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Maybe aim to maintain peak insulin response <200 mU/L?

.....but unlikely to be as simple as a single insulin measurement threshold?

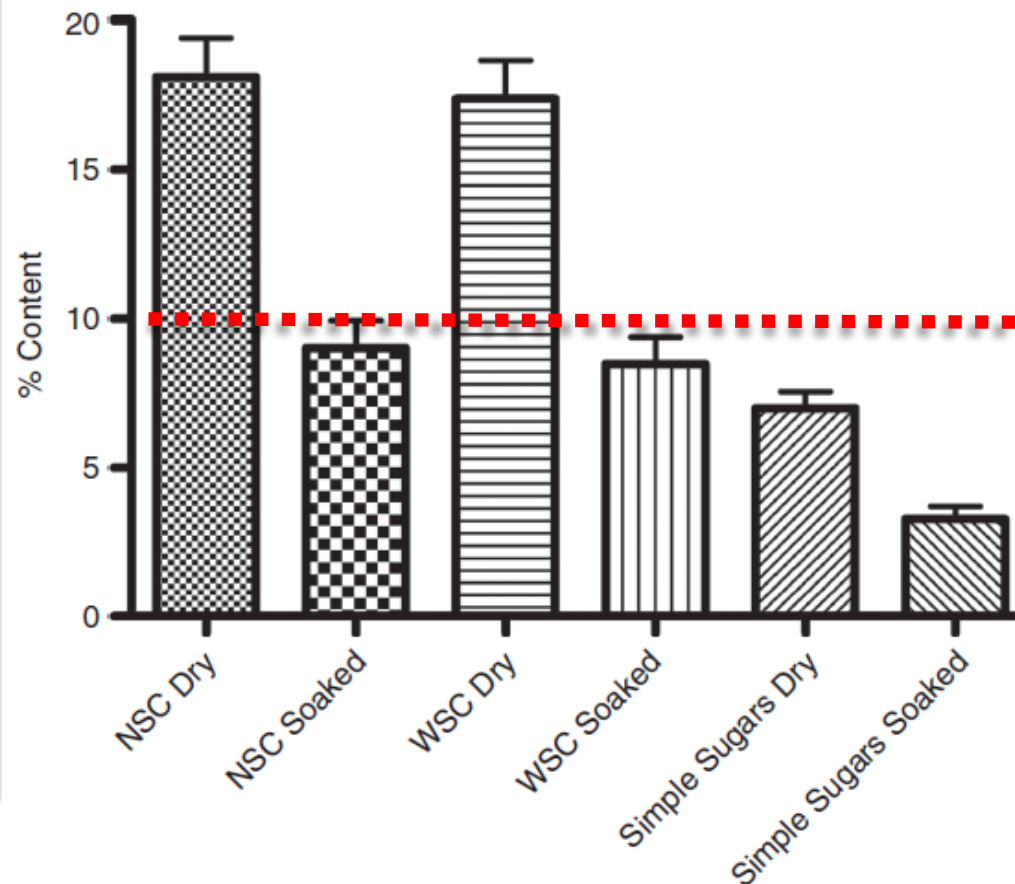
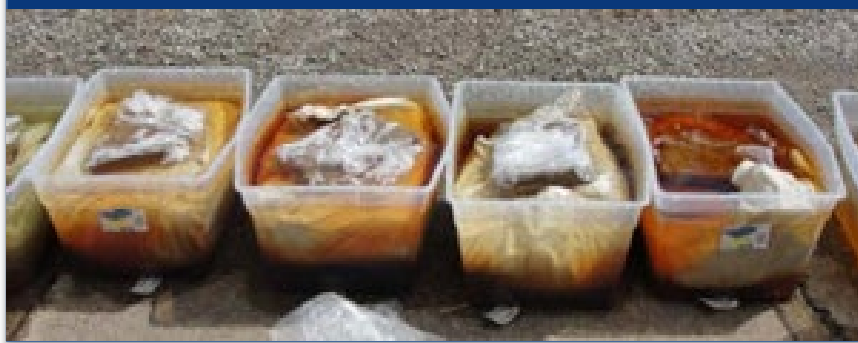
▶ maybe 100 mU/L is a problem if it persists for a longer period???

“The Lower the Better”!

Soaking hay?

Soaking hay

- ▶ Variable but generally good effect
- ▶ Sugars decreased by >50% after 8-16 hours soaking
- ▶ Minerals also decreased



Mack et al 2014



Mixing straw with hay?

- ▶ 30-50% of forage as straw is usually well tolerated
- ▶ significantly decreases insulinaemic effect of diet
- ▶ prolongs feeding times
- ▶ promotes weight loss
- ▶ NB. Impaction colic??
- ▶ Dentition must be good
- ▶ Ration balancer should be provided to ensure adequate protein/mins/vits



Grazing Muzzles

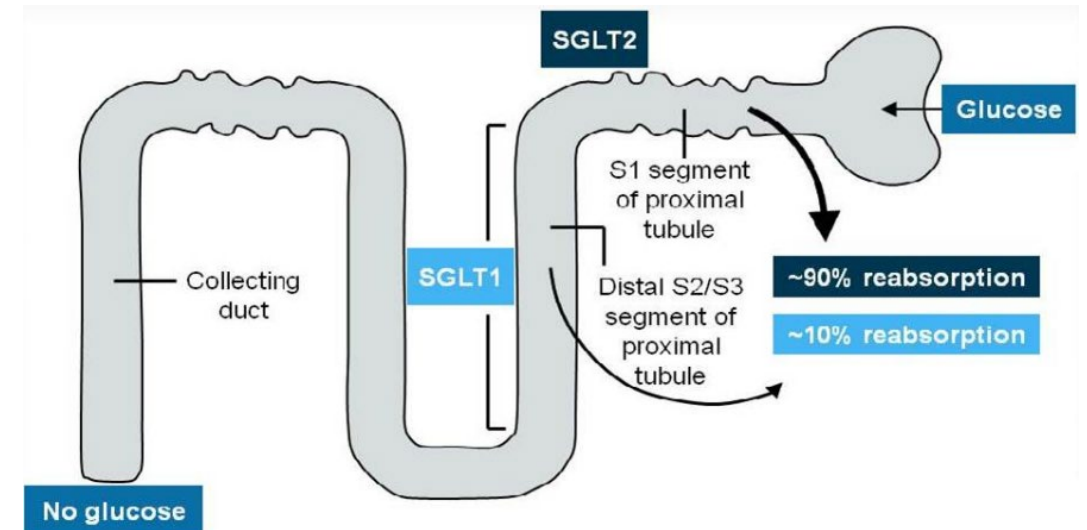
- ▶ Longland et al 2012
 - grazing muzzle decreased the amount of forage consumed by an average of **80%**
- ▶ Glunk et al 2014
 - grazing muzzle decreased the amount of forage consumed by an average of **30%**
- ▶ Some horses are better than others!



SGLT2 inhibitors

SGLT2 inhibitors

- Sodium Glucose cotransporter 2
 - the major transporter for glucose reabsorption in the kidney
 - inhibition leads to:
 - increased urinary glucose losses
 - decreased insulin
 - acute energy losses (NB. hyperlipaemia)
- Canagliflozin
 - Dapagliflozin
 - Empagliflozin
 - Ertugliflozin
 - Ipragliflozin
 - Velagliflozin (Meier *et al* 2018)



SGLT2 inhibitors

- ▶ 41 ponies fed high starch diet (12.3 g/kg)
 - postprandial insulin response measured

	29 untreated ponies		12 treated with Velagliflozin
	11 (38%) laminitis	18 (62%) no laminitis	12 (100%) no laminitis
Glucose	14.9 mmol/L	10.7 mmol/L	9.4 mmol/L
Insulin	396 mU/L	216 mU/L	149 mU/L



SGLT2 inhibitors

► Canagliflozin

- decreased insulin response to oral sugar test in 6 horses (Frank 2018)
- 0.5 mg/kg ($\frac{1}{2}$ x 300 mg tablet daily for a pony)

► Ertugliflozin

- no efficacy or safety data yet
- at least 1 case of hyperlipaemia post treatment
- 0.05 mg/kg (1 x 15 mg tablet daily for a pony)



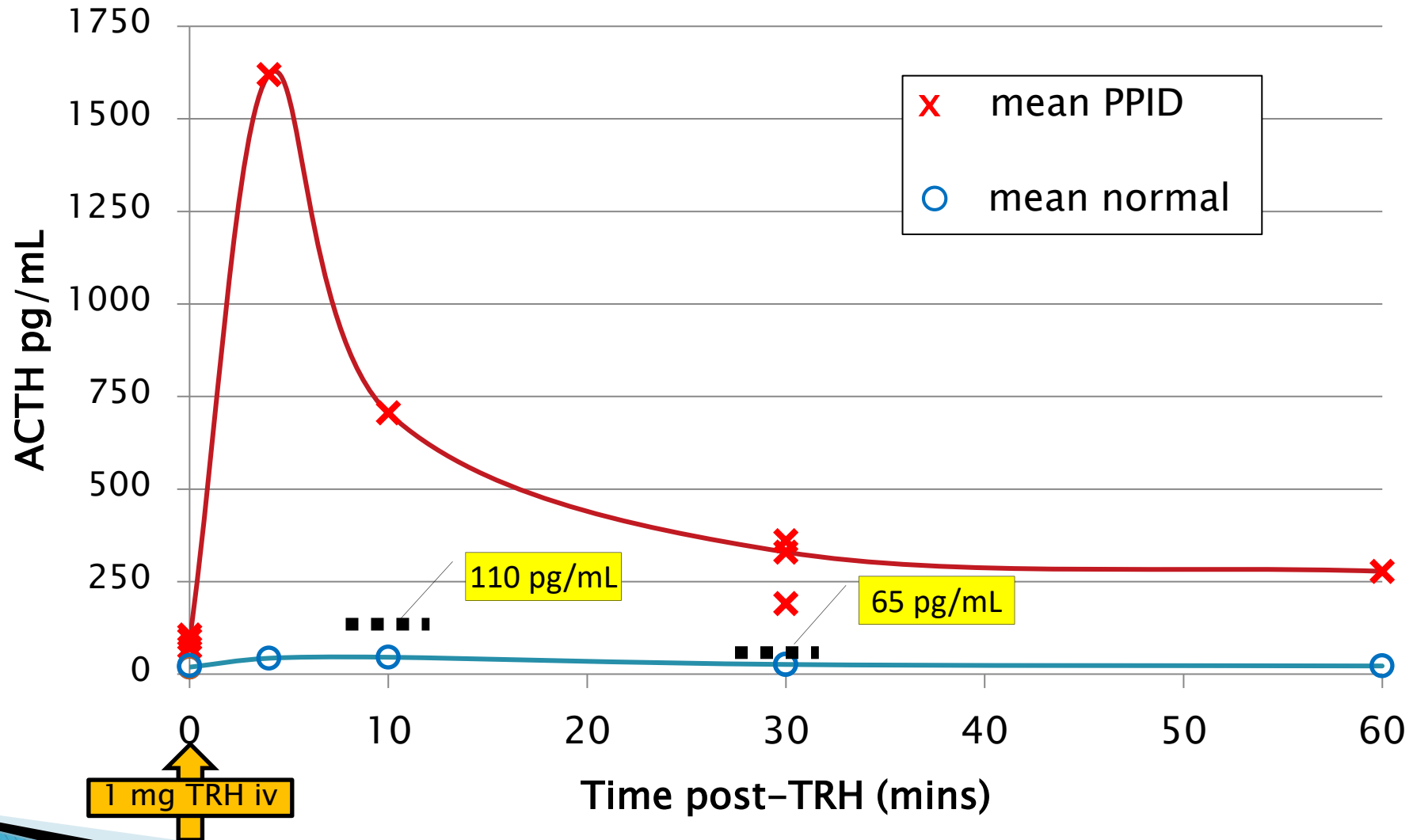
Testing for Pituitary pars intermedia dysfunction (PPID)

Basal plasma ACTH concentration

1. *Collect into EDTA tube*
2. *Chill sample within 3 hours of collection*
3. *Centrifuge as soon as possible*
(whole blood or gravity separated samples are fine as long as they do not freeze)
4. *Keep chilled during shipping to laboratory*

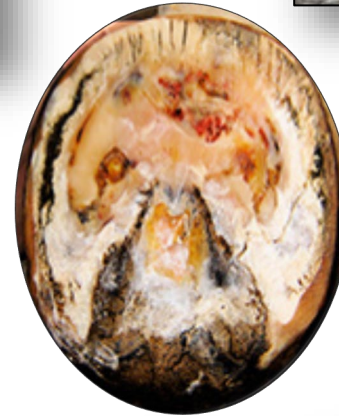


TRH stimulation test (of ACTH)



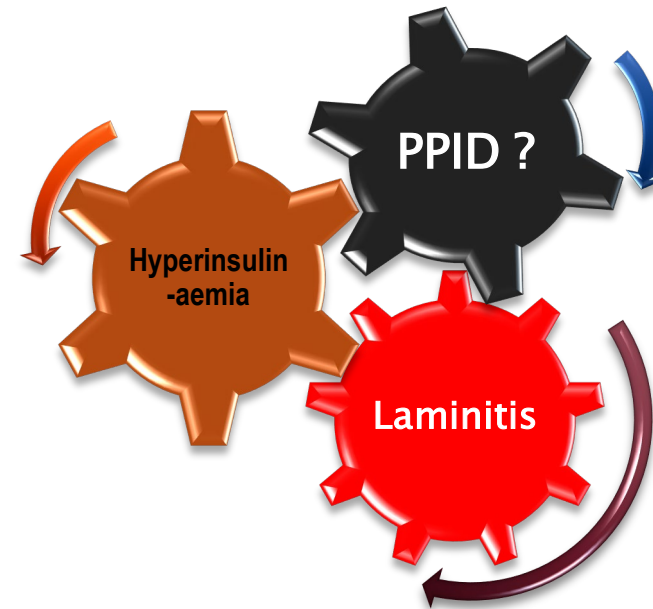
Why is PPID a problem?

- Subclinical
- Abnormal hair growth
- **Laminitis**
- Polydipsia/polyuria
- Lethargy
- Excessive sweating
- **Susceptibility to infections**
- Fat redistribution
- **Mild muscle loss**



Laminitis, insulin dysregulation and PPID

- PPID cases with insulin > 188 mU/L less likely to survive (McGowan *et al* 2004)
- Insulin concentration correlated with grade of laminitis (Walsh *et al* 2009)
- Insulin concentration higher with radiographically moderate to severe laminitis versus normal to mild (Tadros *et al* 2018)

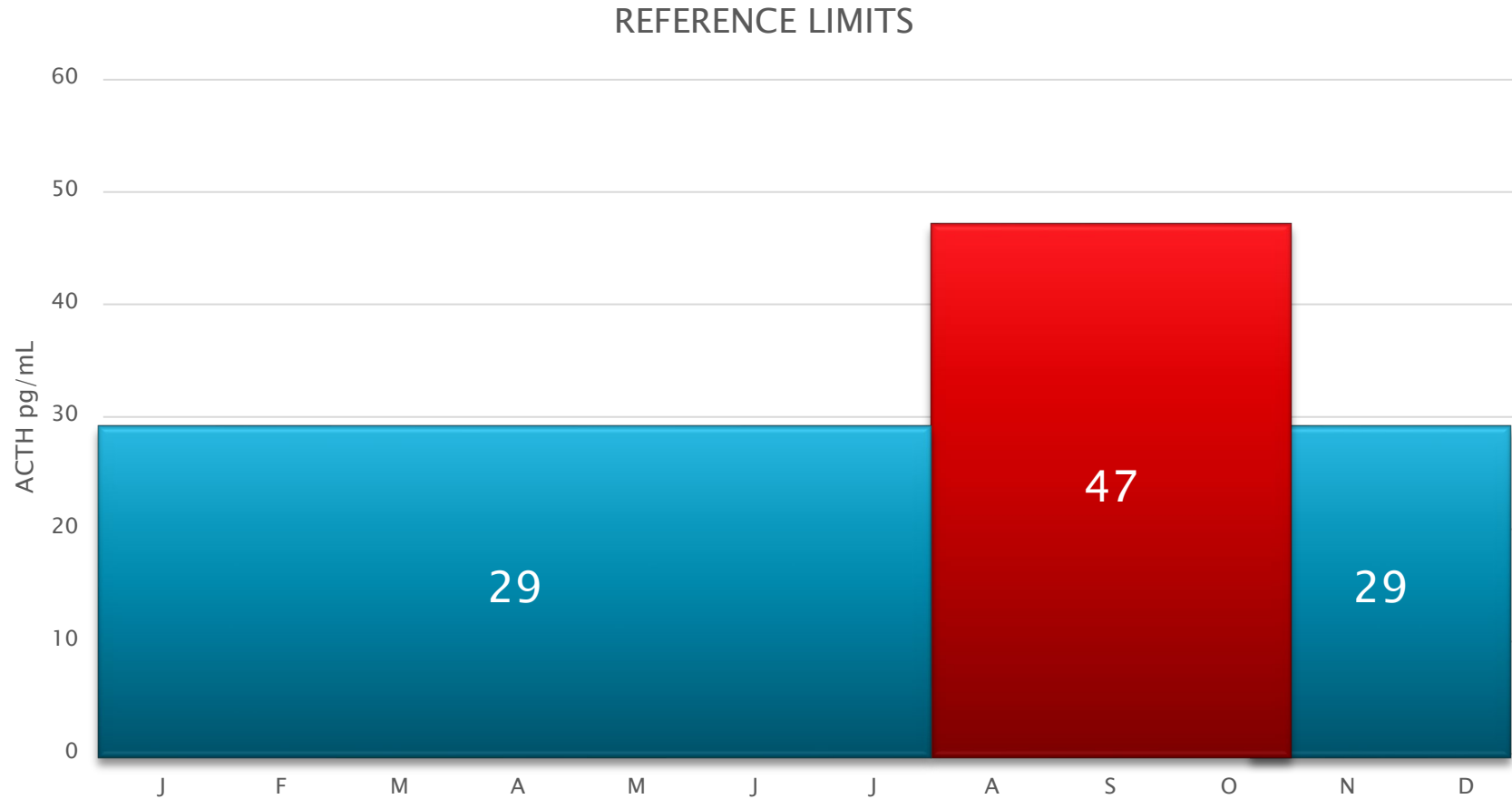


Laminitis, insulin dysregulation and PPID

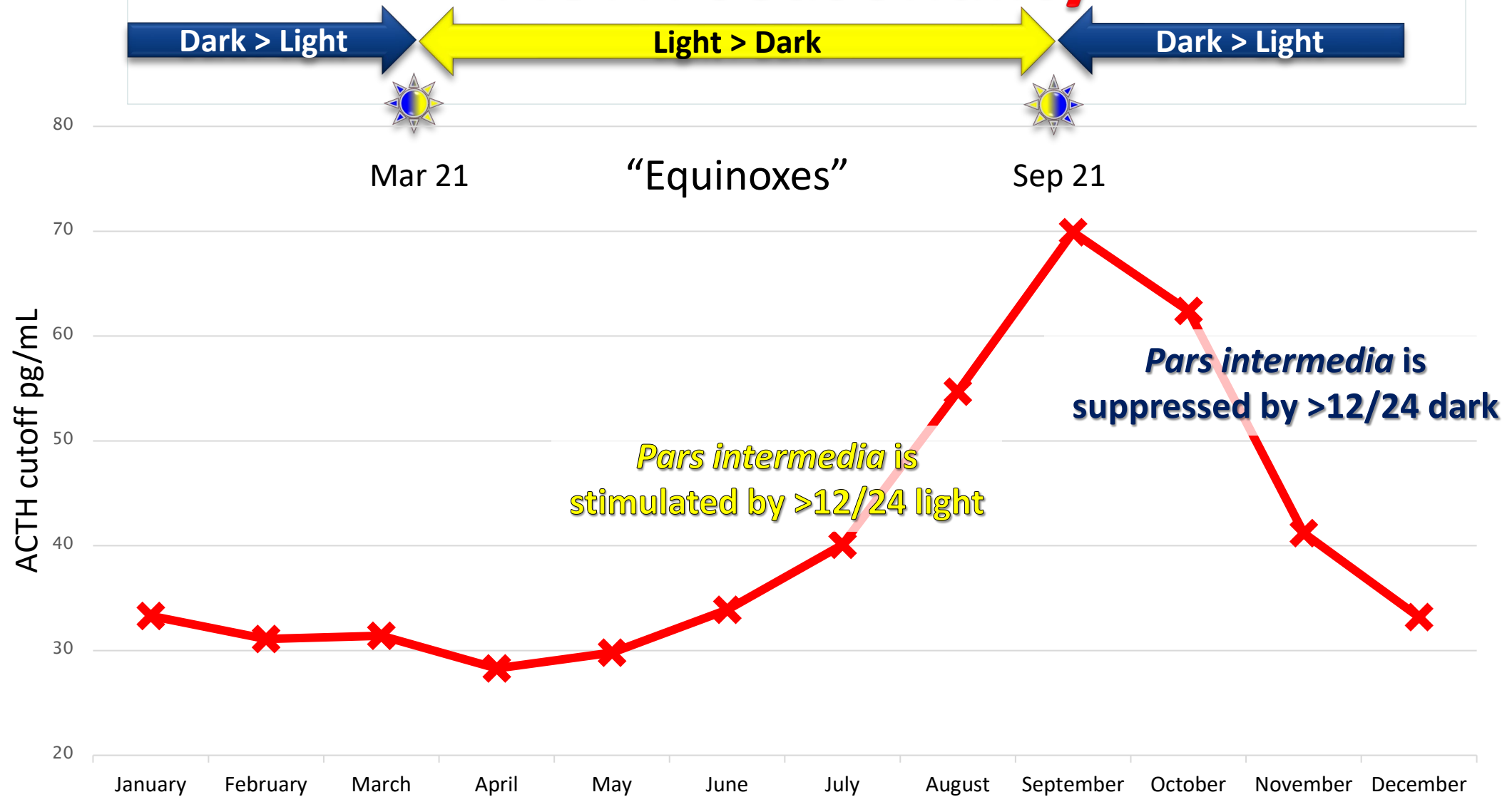
- ▶ 13,278 PPID cases where laminitis history was known
 - 11,807 (88.9%) laminitic PPID cases
 - 1,473 (11.1%) non-laminitic PPID cases
- ▶ Endocrine results compared between the 2 groups:

	Laminitis	No Laminitis	P
ACTH	126 pg/mL	117 pg/mL	0.059
Insulin	30.1 mU/L	13.1 mU/L	<0.001
Glucose	5.4 mmol/L	4.9 mmol/L	0.032
Triglycerides	0.54 mmol/L	0.36 mmol/L	0.001

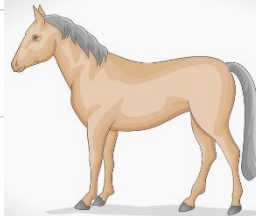
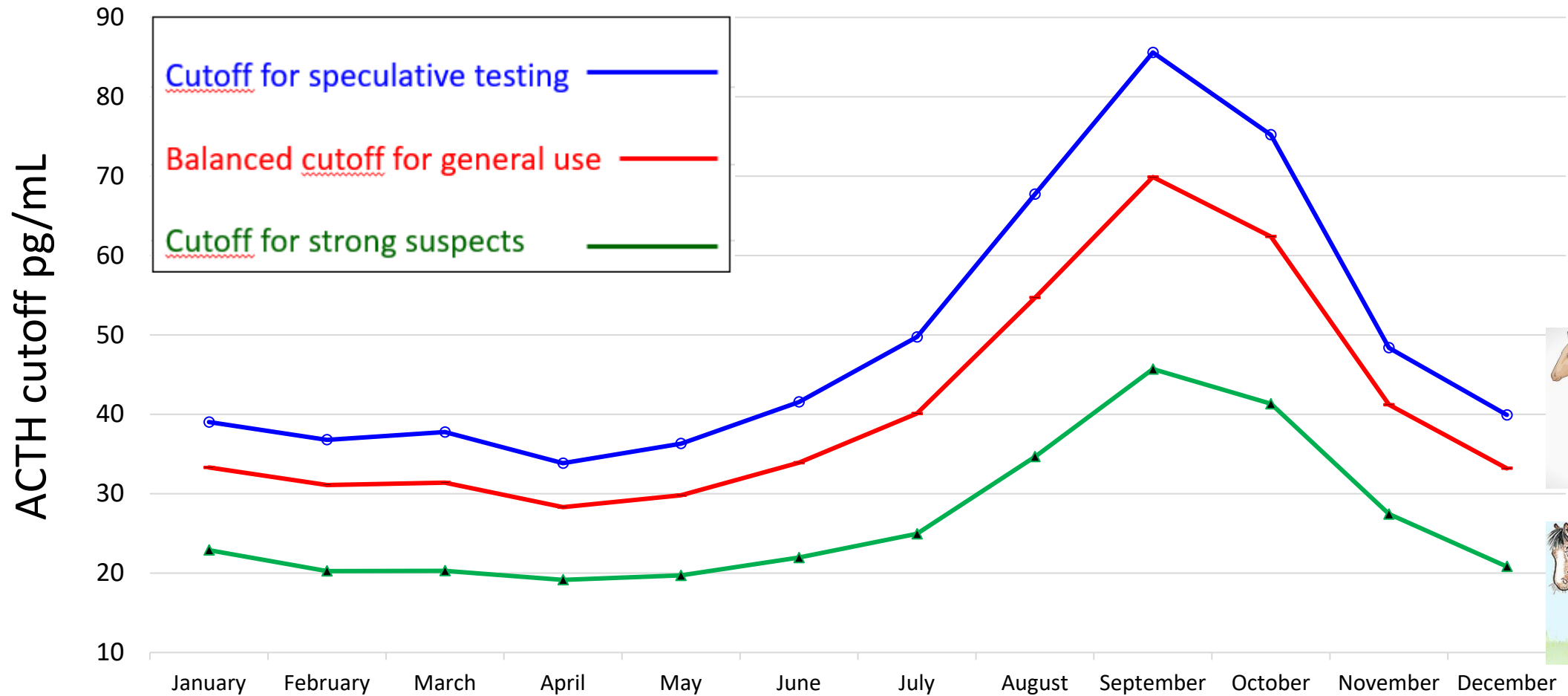
UK Reference Intervals



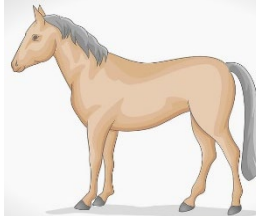
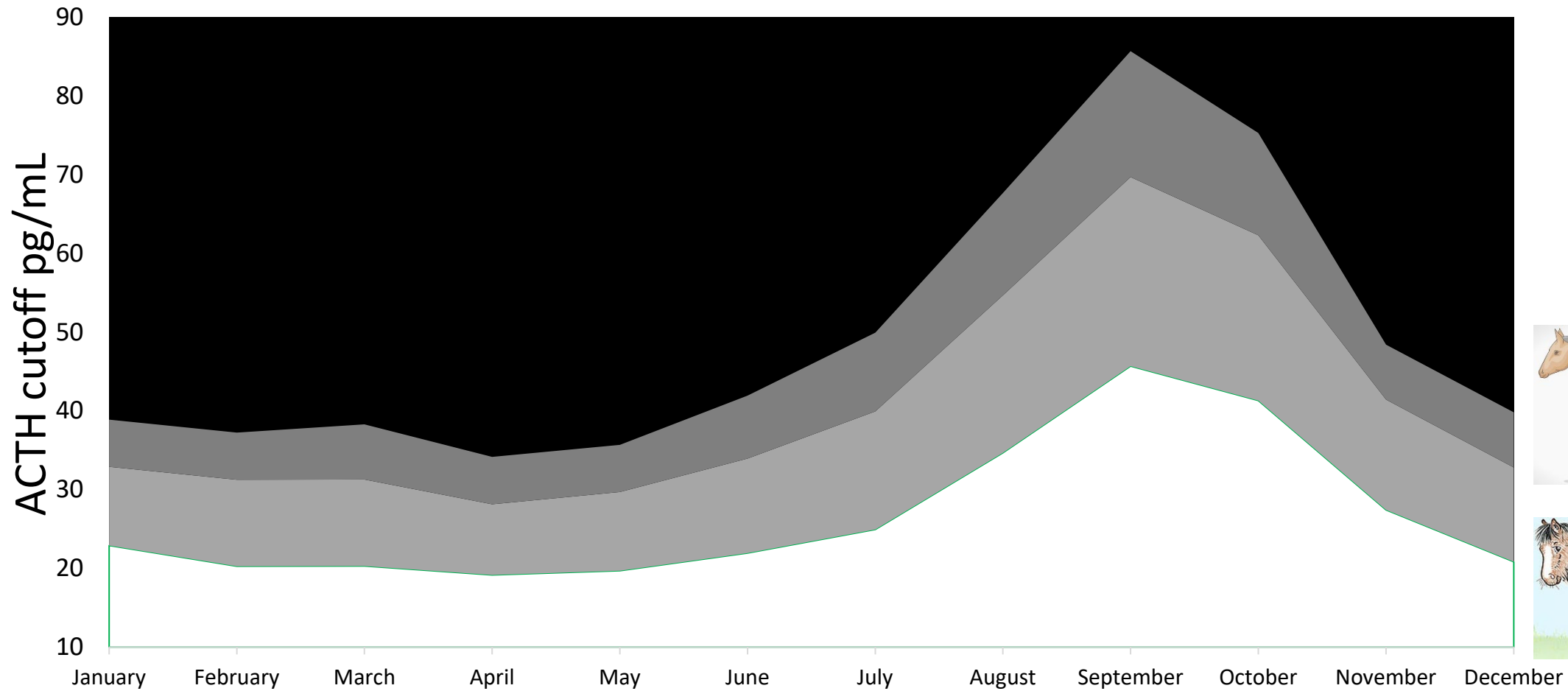
ACTH seasonality



The Importance of Pre-test Probability of Disease

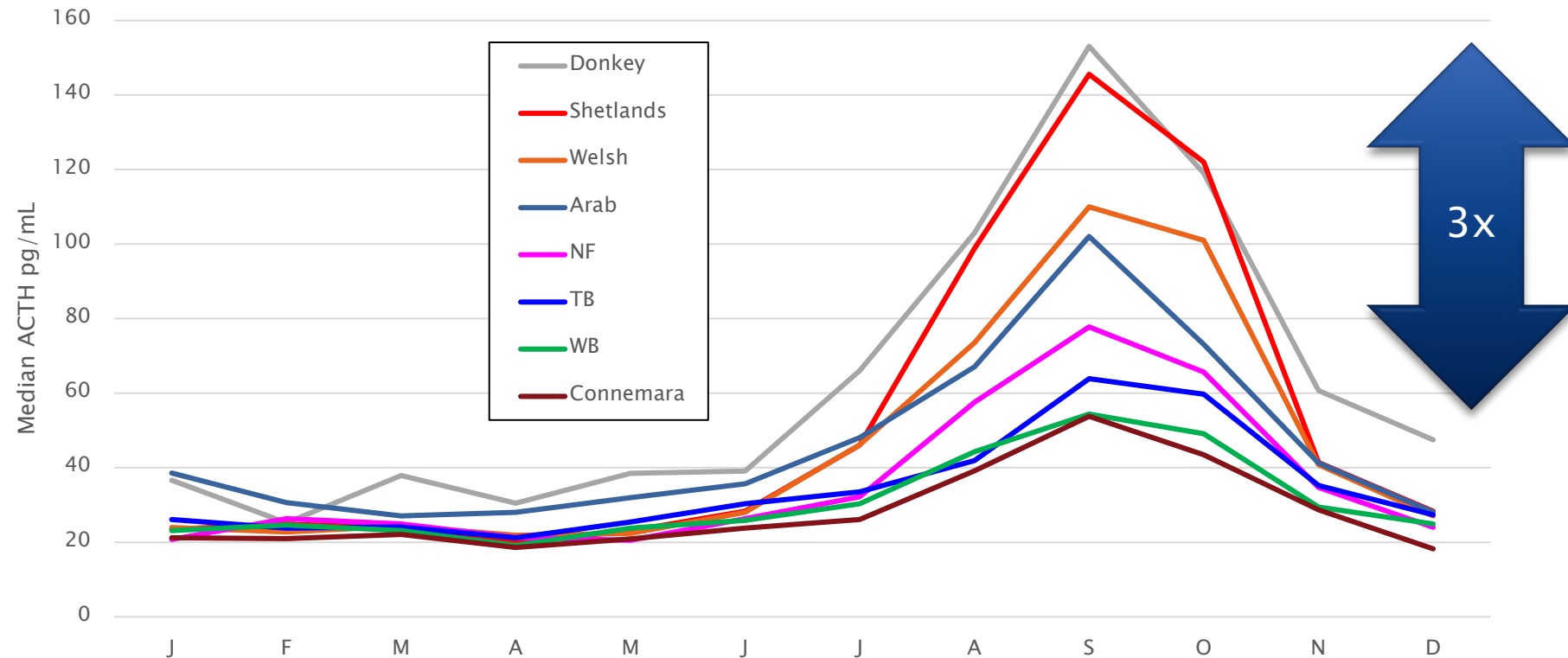


The Importance of Pre-test Probability of Disease



Effect of breed on ACTH values

- ▶ 43,092 samples from known breeds (incl. PPID and non-PPID)
- ▶ ACTH compared through the year



The Long Term Plan for Laminitis Cases

1. Define the endocrine status
2. Correct the foot shape so that newly growing hoof is properly aligned
3. Support the weakened lamellar attachment
4. Stop recurrent lamellar damage by constantly keeping insulin low

