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How to diagnose: Cushing's disease/metabolic syndrome

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Equine Cushing's disease

1. Resting plasma ACTH concentration

- Collect sample in an EDTA (purple) tube anytime of day (no need to fast).
- Chill sample within 3 h.
- Separate plasma prior to posting by centrifugation or by gravity (the timing of separation is unimportant as long as the sample is chilled within 3 h).
- Maintain chilling during postage using specialised chiller packs - (freezing is unnecessary although might help if the delivery is delayed).

Plasma ACTH is increased in Cushing's disease cases and also in normal horses and ponies in the autumn (August–October). Although considered a reason to avoid testing for Cushing's disease in the autumn, this potential problem is overcome by applying properly derived seasonally adjusted reference ranges. As can be seen from **Figure 1**, testing in the autumn may actually allow the greatest differentiation between Cushing's disease cases and normal horses and there is no reason to avoid testing in the autumn. ACTH might also be affected by pain and stress (e.g. from laminitis) although this does not appear to have a large effect in most horses.

2. Overnight dexamethasone suppression test (ODST)

- Collect serum sample for baseline cortisol at approximately 17.00 h.
- Administer 40 µg/kg bwt dexamethasone i.m. or i.v.
- Collect second serum sample 19 h later (11.00 h next day) for cortisol.

A normal horse has cortisol <27 nmol/l in the second sample whereas Cushing's disease cases have greater concencentrations.

The ODST may also be liable to false positive results in the autumn. Unfortunately as the ODST is a qualitative test it is not currently possible to reliably interpret results of this test in the autumn.

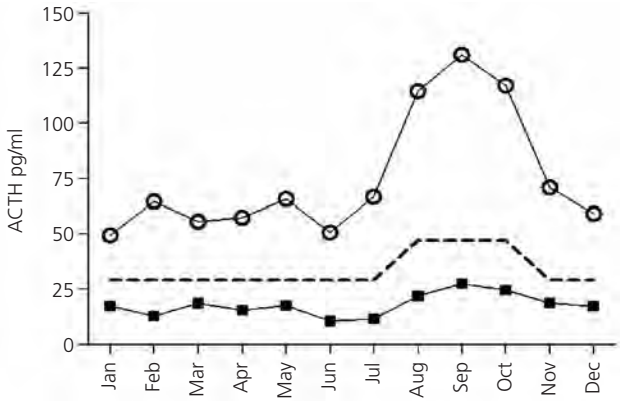

Fig 1: Median plasma ACTH in Cushing's disease cases (circles), normal horses (squares) and cutoff for normal plasma ACTH (dashed line) (data from Liphook Equine Hospital Laboratory).

3. TRH stimulation test

Measuring serum cortisol before and 15–60 min following a TRH bolus is an unreliable test for Cushing's disease. However, the test appears to be valid when comparing plasma ACTH (rather than cortisol) before and 30 min following a TRH bolus. As a single resting plasma ACTH concentration is well established as an excellent diagnostic test for PPID, the TRH stimulation test is only recommended where borderline resting ACTH results are found.

- Collect plasma sample for ACTH
- Inject 1 mg TRH i.v.
- Collect second sample 30 min later for plasma ACTH.

Cushing's disease is indicated by either a baseline plasma ACTH value greater than the seasonally adjusted reference range (typically >29 pg/ml) and/or a post stimulation plasma ACTH >100 pg/ml.

Equine metabolic syndrome

The only readily measurable components of EMS comprise obesity, IR and dyslipidaemia although other factors including blood pressure, uric acid or adipokines such as leptin may be considered in the future.

Estimates of obesity

The diagnosis of obesity is largely subjective (e.g. general visual assessment or use of body condition scoring) although might be defined more objectively with ultrasonographic measurement of fat deposits or morphometric measurements such as girth or rump width.

Estimates of insulin resistance (IR)

a) Resting hyperinsulinaemia

Hyperinsulinaemia in a single blood sample is strongly suggestive of IR as long as potential confounding factors such as pain, stress and recent feeding are controlled. The sampling protocol should be standardised by fasting for 6 h.

b) Resting hyperglycaemia

Hyperglycaemia is uncommonly encountered in insulin resistant equids but it is important to measure glucose so that occasional cases of *type 2* diabetes mellitus are detected (insulin may be high or low but glucose will be high).

c) Dynamic testing

Although resting hyperinsulinaemia suggests IR, a low (normal) resting insulin does not rule out IR. Many insulin resistant cases are only detectable by excessive endogenous insulin secretion in response to a glucose challenge (oral or i.v.) and/or delayed return to normoglycaemia following glucose challenge (= glucose intolerance).

i. the combined insulin-glucose tolerance test (CGIT)

- Overnight fast
- Measure basal glucose and insulin
- Give 150 mg/kg bwt 40–50% glucose solution i.v. (150 ml 50% per 500 kg bwt) followed by 0.1 iu/kg bwt soluble insulin (0.5 ml 100 iu/ml per 500 kg bwt) i.v.
- Collect further blood samples for plasma glucose at 1 min, 5 min, 15 min, then q. 10 min up to 45 min, then q. 15 min up to 2½ h
- Also test the 45 min sample for serum insulin.

The peak serum glucose occurs around 1–5 min and reaches 2–2½ x baseline. The serum glucose normally remains greater than baseline for between 30 and 45 min, followed by a negative phase for a further 1–2 h where the serum glucose is below the original baseline. Insulin resistant horses are expected to have a higher peak and a longer positive (>45 min) and shorter negative phase (and perhaps no negative phase at all). A 45 min insulin concentration >100 miu/l also implies IR.

Unfortunately this test is not popular due to the requirement for hospitalisation and frequent sampling.

ii. In-feed oral glucose challenge test

This test is simple to perform at home stables and is useful in suspected IR cases that are found to have normal fasted insulin concentrations.

- Fast horse/pony overnight (12 h)
- Ask owner to give a nonglycaemic feed (e.g. chaff) containing 1 g/kg bwt glucose or dextrose powder (wet the feed to facilitate mixing and ingestion)
- Take a blood sample to measure serum insulin 2 h after the feed is consumed.

Serum insulin >85 miu/l in the 2 h sample is indicative of insulin resistance.

Estimates of dyslipidaemia

Increased serum triglycerides are suggestive of both obesity and insulin resistance.

NOTES