DIAGNOSIS OF EQUINE METABOLIC SYNDROME

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A working definition of EMS was first offered by a study of a herd of in-bred ponies although the strong genetic influence on laminitis and IR suggests that this precise definition might not apply to all other populations [1] (Table 1).

Table 1: Diagnostic criteria indicating laminitis risk. Individuals with ≥3 of the listed variables were found to have a 10 times increased risk of laminitis [1] (see table 2 for calculation).*

1	Reverse Inverse SQuare of Insulin (RISQI*)	$< 0.32\ (mU/L)^{-0.5}$
2	Modified Insulin Response to Glucose (MIRG*)	$> 5.6\ mU^2_{ins}/10.L.mg_{Glu}$
3	Plasma triglyceride	> 0.64 mmol/L
4	Body condition score	> 6/9

Currently there is no universally accepted definition of EMS although it might be defined on the basis of establishing the presence of a combination of several laminitis-risk factors:

1. Estimates of obesity

Body condition scoring systems may not be applicable to all breeds and types of horse and are also subjective. Furthermore, measures of regional (rather than generalised) obesity might better reflect laminitis-susceptibility. One study found the ratio of mid-neck circumference to withers height reflected laminitis risk when >0.71 [2]. Interestingly, a study of diet-induced weight loss in ponies found objective measurements of neck circumference, girth and fat depth, but not body condition scoring, to be associated with decreasing body mass [3].

2.Estimates of IR

There is a wide choice of tests for IR although many are impractical for clinical use and/or have not been well investigated [4]. IR in an individual may be influenced by many factors including pain, stress, disease, age, diet, exercise and concurrent pituitary pars intermedia dysfunction and these must be considered when tests are performed.

a. Single blood samples

I. Fasting hyperinsulinaemia

Hyperinsulinaemia (>20 mU/L) in a single blood sample is suggestive of IR as long as potential confounding factors (above) are controlled. It is important to starve for 6 hours pre-sampling.

II. Fasting hyperglycaemia

Hyperglycaemia is only occasionally encountered in insulin resistant equids.

III. "Proxies"

Mathematically derived estimates of insulin-glucose dynamics may be calculated from fasting insulin and glucose concentrations [5,6] (table 2).

Table 2. Various "proxies", their acronyms and formulae for their calculation.

Proxy for	Test name	Acronym	Formula
Insulin resistance	fasting insulin concentration	-	-
	homeostasis model assessment for IR	HOMA-IR	[fasting ins x fasting gluc] ÷ 22.5
Insulin sensitivity	quantitative insulin sensitivity check index	QUICKI	1 ÷ [log fasting ins + log fasting gluc]
	fasting glucose to insulin ratio	FGIR	fasting gluc ÷ fasting ins
	reciprocal inverse square of insulin	RISQI	$1 \div \text{insulin}^{-0.5}$
Pancreatic beta cell function	homeostasis model assessment of percentage beta cell function	HOMA-B%	[20 x fasting ins] ÷ [fasting gluc – 3.5]
	modified insulin to glucose ratio	MIRG	$[800 - 0.3x(\text{ins} - 50)^2]$ ÷ [gluc – 30]
	fasting insulin to glucose ratio (insulinogenic index)	I:G ratio	fasting ins ÷ fasting gluc

b. Dynamic testing

Not all cases of IR will demonstrate fasting hyperinsulinaemia and several dynamic tests exist to investigate suspected IR in such cases. Abnormal insulin-glucose dynamics might be revealed by response to exogenous insulin and/or glucose challenge.

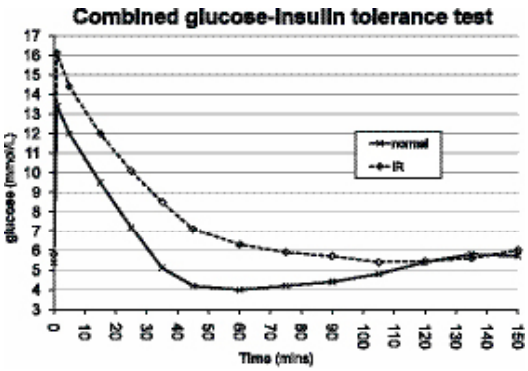
I. The combined glucose-insulin tolerance test (CGIT)

This test examines the glycaemic and insulinaemic response to a combination of exogenous glucose and insulin [7]:

- overnight fast
- samples collected for baseline glucose and insulin
- administer 150 mg/kg 50% glucose iv, followed by 0.1 U/kg soluble insulin iv
- collect further samples for plasma glucose at 1, 5, 15, 25, 35, 45 minutes, then q 15 minutes to 2½ hours
- measure insulin at 45 minutes

Normal horses show a "positive phase" (glucose above baseline) for 30 to 45 minutes, followed by a "negative phase" (glucose below baseline) for a further 1 to 2 hours. Insulin resistant horses have a longer positive phase (>45 mins) and shorter negative phase (perhaps no negative phase at all) (Figure 1). Insulin concentration at 45 minutes >100 mU/L also implies IR.

Figure 1: Examples of curves obtained from a normal horse and a horse with IR using the combined glucose insulin tolerance test



However, the CGIT is time-consuming and involves multiple blood samples making the test costly and frequently unattractive to owners. Additionally, the test is usually performed on hospitalised horses resulting in an additional stress factor that might influence test results.

II. Insulin response to oral glucose challenge

This test was developed to overcome the practical unattractiveness of intravenous tests:

- overnight fast
- (optional: samples collected for baseline glucose and insulin)
- 1 g/kg glucose or dextrose is fed with a non-glycaemic feed
- glucose and insulin measured at 2 hours post-feeding
  Insulin concentrations >20 mU/L at baseline and/or >85 mU/L at 2 hours post-feeding are considered indicative of IR (AE Durham, VN Copas 2010, unpublished data).

3. Estimates of dyslipidaemia

Valid inclusion of dyslipidaemia in EMS is likely but requires further investigation. One study found increased serum triglycerides to contribute to laminitis risk [1] although this might differ in other populations. A further study found dyslipidaemia to be associated with obesity and IR in horses, although the relationship with laminitis was not examined [8].

4. Blood pressure

Hypertension was demonstrated in laminitis-prone ponies during the summer in one study [9] and might be worthy of further investigation as a measurable component of EMS.

5. Other tests

Parameters including increased serum uric acid [9] and leptin [2] have been shown to be related to laminitis-susceptibility but are limited in their availability and require further investigation.

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