Study of EMS cases has revealed several measurable plasma analytes that serve as markers for dysregulation of glucose and lipid metabolism that culminates in increased laminitis susceptibility. Although the exact pathophysiologic pathways leading to laminitis have not been elucidated, it is likely that some of these analytes may have direct pathologic relevance whilst others simply act as indirect markers of abnormal metabolic responsiveness.

A common feature of the various definitions of metabolic syndrome in humans is one or more indices of insulin resistance (IR). Similarly, IR has become a prominent component of EMS and a number of studies have demonstrated a link between hyperinsulinaemia and laminitis. Plasma glucose concentration is normally tightly regulated within physiological limits and hyperglycaemia is minimised (primarily by increased insulin-dependent glucose uptake by insulin-sensitive tissues such as muscle and adipose tissue, and by inhibition of ongoing hepatic gluconeogenesis) even in severe EMS cases. However, increased insulin concentrations are commonly seen, presumably as a compensatory response to decreased insulin effectiveness although impaired insulin clearance may also be relevant.

Although many experimental studies aim to use specific and quantitative measures of IR such as the hyperinsulinaemic euglycaemic clamp or minimal model analysis of the frequently sampled intravenous glucose tolerance test, various simpler tests known or believed to correlate with insulin resistance or sensitivity are generally preferred in clinical practice. A number of tests have been used to investigate IR:

- combined insulin glucose test (CGIT)
- oral glucose tolerance test (OGTT)
- in-feed glucose test
- fasted basal insulin and glucose concentrations
- insulin to glucose ratio
- reverse inverse square of insulin (RISQI)

Hyperglycaemia, although relatively common in humans with metabolic syndrome, is relatively rare in EMS cases. Perhaps the simplest useful test is measurement of basal insulin concentrations although, as serum insulin concentrations are markedly affected by recent carbohydrate ingestion, use of basal insulin concentration should ideally follow withholding of feed for at least 6 hours. However, data from the LEH laboratory indicates that fasting insulin concentrations may be normal in up to 70% of subjects that prove to be insulin resistant when challenged with oral carbohydrates. Therefore, fasting insulin is associated with a low sensitivity, albeit with high specificity for IR (provided the sample was collected under appropriate i.e. starved and stress-free conditions). A further limitation of resting measurements (insulin, glucose, I:G ratio and RISQI) is their poor repeatability between measurements from the same horse on different days.

Hyperinsulinaemia, whether fasting or in response to exogenous glucose, is highly likely to reflect IR. In the light of evidence directly implicating hyperinsulinaemia per se, rather than hyperglycaemia or IR, in the pathogenesis of laminitis, attention has been drawn to the possible preferential use of more sensitive tests than fasting hyperinsulinaemia. An important defining feature of EMS is that certain individuals, and not others, are likely to suffer laminitis following pasture ingestion. Many important and interacting parameters may be influential in the mechanistic sequence of events occurring between grazing and laminitis.
These might include a greater appetite for grass resulting in a larger amount of ingested NSC, improved assimilation of simple sugars from the ingested grass due to digestive and/or fermentative differences, a greater pancreatic insulinaemic response to the assimilated sugars and perhaps a heightened pathologic effect of insulin at cellular receptor and/or post-receptor level. Several studies have indicated that laminitis-prone individuals characteristically demonstrate an excessive hyperinsulinaemic response to grazing or orally administered carbohydrates which may represent a fundamental metabolic/endocrine difference between normal horses and those endocrinopathically predisposed to laminitis. In this respect the use of tests that examine the insulinaemic response to oral carbohydrate ingestion might be more valuable than more sophisticated tests examining responses to intravenous glucose and/or insulin. In the USA, the “oral sugar test” (OST) has proved popular, whereas in the United Kingdom the “in-feed glucose test” is commonly used. These two similar tests challenge the horse with corn syrup and glucose respectively and compare the insulinaemic response of the tested individual to that expected in a normal animal. It is assumed that an excessive insulinaemic response to the ingested carbohydrate represents a risk factor for laminitis. Comparison of 21 normal and 199 laminitis-prone individuals at Liphook revealed significantly greater insulin concentrations in the latter group at 2 hours following in-feed glucose (Figure 1).

Healthy horses with no history of laminitis or clinical signs of EMS have an insulin concentration of < 57 mU/L 2 hours after oral administration of 0.5 g/kg glucose. A dose of 1.0 g/kg dose is preferable (as long as the horse will eat the whole meal) and should result in a 2 hour insulin of < 87 mU/L in a “normal” horse.

<table>
<thead>
<tr>
<th>How to perform an in-feed Glucose Tolerance Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Overnight fast (at least 6 hours)</td>
</tr>
<tr>
<td>• Give 0.5 or 1.0 g/kg BWT glucose or dextrose powder in a non-glycaemic feed (e.g. chaff)</td>
</tr>
<tr>
<td>• Measure serum insulin and plasma glucose after 2 hours</td>
</tr>
</tbody>
</table>

Figure 1. Serum insulin concentrations from 21 normal (N) and 199 laminitis-prone (L) horses and ponies subject to the in-feed glucose test 2 hours following administration of 1.0 g/kg dextrose. Grey line represents cutoff for normal response.

Further Reading: