## AN INTRODUCTION TO EQUINE METABOLIC SYNDROME

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### What is Equine Metabolic Syndrome?

Metabolic Syndrome is a common condition in humans characterised by a collection of risk factors for type 2 diabetes mellitus and cardiovascular disease [1]. The specific factors used to define the condition differ between various interest groups although all definitions essentially comprise presence of the following:

- Insulin resistance (IR)
- Abdominal obesity
- Hypertension
- Dyslipidaemia
- Pro-thrombotic status
- Inflammation

Laminitis-prone horses and ponies are frequently recognised to be obese and resistant to insulin. Recognising the analogy with Metabolic Syndrome in humans, Johnson [2] proposed the term "Equine Metabolic Syndrome" (EMS) to describe the clustering of laminitis risk-factors. There is no widely accepted definition of EMS although the syndrome may be regarded as "a collection of risk factors that are associated with an increased susceptibility to laminitis" and includes obesity and IR with further possible components including dyslipidaemia, hypertension, hyperleptinaemia and hyperuricaemia [3-7].

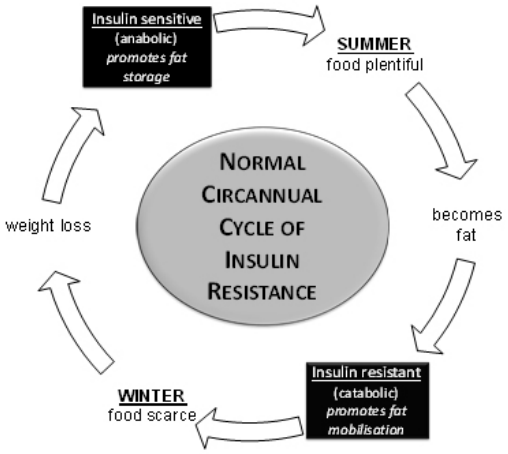
### Why do native types tend to be obese and insulin-resistant?

Metabolic syndrome in horses and humans is probably a consequence of chronic overprovision of food to metabolic systems adapted for efficient utilisation of a poor-quality and irregular nutrient supply [8]. Survival in nutritionally harsh environments is aided by several genetically determined traits including IR. Insulin is an anabolic hormone and the metabolic consequences of IR are:

a) to conserve and prioritise glucose for non-insulin-dependent tissues (e.g. kidneys, central nervous system, cardiovascular system) rather than muscle, fat and liver
b) to facilitate mobilisation of fat and glycogen when dietary intake is inadequate
c) to facilitate hepatic gluconeogenesis to bolster plasma glucose when required

Obesity is a further cause of IR that may relate to accumulation of fat within myocytes and the inhibitory effects of adipokines and fatty acids on insulin signalling [9]. A natural cycle may exist whereby ponies gain fat during the summer and autumn when food is plentiful so that they develop IR, thus preserving plasma glucose and facilitating gluconeogenesis and energy mobilisation as they enter times of food scarcity in the winter. Inevitable weight loss over the winter restores normal insulin sensitivity for the spring and summer to complete the cycle (Figure 1).

*Figure 1: Natural circannual cycle of weight loss, weight gain, insulin sensitivity and insulin resistance.*



Thus, wild ponies may have IR owing to a combination of genetics and seasonal adiposity as a beneficial, cyclical, metabolic adaptation that improves survival under conditions of irregular and sparse food supply. In contrast, many domestic ponies enter an uncontrolled spiral of pathologic and progressive IR with a genetic baseline upon which is superimposed continuous and often increasing obesity, possibly along with further causes of IR.

**How might IR lead to laminitis?**

Obesity, IR, hyperinsulinaemia and dyslipidaemia have been associated with both a history of laminitis and also prediction of further laminitis episodes [5]. Furthermore experimental maintenance of marked hyperinsulinaemia is an effective means of causing laminitis in normal ponies [10].

Although the precise links between IR, hyperinsulinaemia, obesity and laminitis are not yet explained, possible pathogenetic mechanisms include:

- thrombosis resulting from increased expression of endothelial adhesion factors
- hypertension triggering vasomotor reflexes
- catabolism of structural laminar proteins
- vasoconstriction resulting from decreased nitric oxide, increased endothelin and increased sympathetic drive
- dysregulation of laminar cellular growth, differentiation and mitosis

Interestingly, recent histopathologic studies of laminitis induced by hyperinsulinaemia demonstrate lamellar stretching, dyskeratosis and increased mitosis [11], in contrast to basement membrane destruction seen in starch-overload models [12].

**How might grazing cause laminitis?**

The most commonly recognised precipitating factor for laminitis is grazing (fructan-overload) rather than cereal consumption (starch-overload). As dietary fructans are indigestible it is plausible that excessive grass fructan ingestion might trigger laminitis via caecocolonic dysfermentation. However, it is unlikely that this mechanism will occur at realistically achievable rates of fructan consumption in grazing animals. An alternative explanation is that upper gastrointestinal bacterial hydrolysis of dietary fructans to glucose and fructose results in hyperglycaemia and hyperinsulinaemia that precipitates laminitis. Indeed, evidence suggests that laminitis-prone ponies experience a far greater insulinaemic response to ingestion of dietary fructan than do normal ponies [13].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