Laminitis and the Equine Metabolic Syndrome

Philip J. Johnson, BVSc(Hons), MS, MRCVS\textsuperscript{a,} *, Charles E. Wiedmeyer, DVM, PhD\textsuperscript{b}, Alison LaCarrubba, DVM\textsuperscript{a}, V.K. (Seshu) Ganjam, BVSc, MA (hc), PhD\textsuperscript{c}, Nat T. Messer IV, DVM\textsuperscript{a}

Although much has been written about laminitis in the context of its association with inflammatory processes, such as dietary carbohydrate overload and endotoxemia,\textsuperscript{1–5} recognition is growing that most cases of laminitis examined by veterinarians in private practice are those associated with pasture grazing, obesity, and insulin resistance (IR).\textsuperscript{6,7} The term endocrinopathic laminitis has been adopted to classify the instances of laminitis in which the origin seems to be more strongly associated with an underlying endocrinopathy, such as either IR or the influence of corticosteroids.\textsuperscript{8–11} Results of a recent study suggest that obesity and IR represent the most common metabolic and endocrinopathic predispositions for laminitis in horses.\textsuperscript{6,12} IR also plays an important role in the pathogenesis of laminitis that develops when some horses or ponies are allowed to graze pastures at certain times of the year (pasture-associated laminitis [PAL]).\textsuperscript{12–15} Moreover, IR is provoked by and contributes to pathophysiologic processes associated with endotoxemia and systemic inflammation under the more classic circumstances associated with risk for acute laminitis, such as grain overload, retention of fetal membranes, and gastroenteritis.\textsuperscript{16,17} However, a recent study using the oligofructose model showed that experimentally induced laminitis was not associated with a loss of insulin sensitivity.\textsuperscript{18}

The term equine metabolic syndrome (EMS) has been proposed as a label for horses whose clinical examination results (including both physical examination and laboratory

\* Corresponding author. Clydesdale Hall Veterinary Medical Teaching Hospital, 900 East Campus Drive, Columbia, MO 65211. 
E-mail address: JohnsonPJ@missouri.edu
testing) suggest heightened risk for developing laminitis as a result of underlying IR. EMS is not a disease per se, but rather is a clustering of clinical abnormalities that, when identified collectively in a given patient, indicates that the likelihood of developing laminitis is greater than in individuals lacking the EMS criteria. Use of the term EMS is especially practical for distinguishing affected horses from those affected with either Cushing’s (pituitary pars intermedia dysfunction [PPID]) or hypothyroidism, with which EMS is often confused.

The clinical importance of diagnosing EMS centers on the fact that recognized risk factors for laminitis can subsequently be avoided in the affected individual. Preventive measures aimed at reducing the risk for laminitis should be rigorously emphasized in EMS-affected horses and ponies.

Recently, the American College of Veterinary Internal Medicine (ACVIM) commissioned a panel of EMS-interested specialists to develop a consensus statement that would help define the syndrome based on current knowledge. During development of the consensus statement, contents of the working draft were presented and discussed at the ACVIM Annual Forum in Montreal, Canada and some of the following comments will be based on those discussions. Ongoing experimental and clinical studies will help better define EMS (which is distinctly different to the human metabolic syndrome) in the next few years.

DEFINING THE EQUINE METABOLIC SYNDROME: A WORK IN PROGRESS

IR represents the centerpiece of the pathophysiologic mechanisms that are at play in the equine metabolic syndrome. Most EMS-affected horses and ponies are characterized by the development of obesity (either generalized or regional obesity). Regional obesity includes thickening in the crest of the neck (referred to as a cresty neck) and a pattern of expanded subcutaneous adipose tissue at the base of the tail, in the prepuce (male horses), near the mammary gland (females), and near the shoulders. However, not all EMS-affected horses are obese and not all obese horses develop IR. Horse owners commonly refer to affected horses as easy keepers or good doers because they perceive that these horses tend to easily maintain their obese body condition when being fed minimal rations. IR represents a risk factor for laminitis, and consequently the development of laminitis is sometimes used to support a diagnosis of EMS. Although the physical or radiographic appearance of the hoof may indicate that laminitis had occurred in some EMS-affected equids, the owner may report that lameness (pain) per se has not been evident. Therefore, structural changes in the hoof–lamellar interface (HLI) may occur in the absence of laminitic pain in EMS-affected individuals. Moreover, EMS-affected equids seem to be especially prone to development of hoof pain after being allowed to graze pastures at certain times of the year.

Some have argued that the existence of laminitis should not contribute to the definition for EMS because diagnosis of EMS is intended to predict a risk for laminitis. As is the case for the definition of the human metabolic syndrome, evidence now exists that EMS-affected horses and ponies may be characterized by up-regulated markers of inflammation and a propensity to develop arterial hypertension. Other clinical and laboratory abnormalities that may be helpful for defining the syndrome include infertility in mares, hypertriglyceridemia, and hyperleptinemia.

HERITABILITY OF EQUINE METABOLIC SYNDROME

Some breeds seem to be at greater risk for the development of EMS, especially pony breeds (compared with horse breeds); Welsh, Shetland, and Dartmoor ponies are
especially considered in this respect. The fact that pony breeds tend to be relatively insulin resistant when compared with horses may help to explain why the incidence of laminitis is greater in ponies. Other breed predispositions that have been suggested include the Morgan breed, Miniature horses, Spanish Mustang, Saddlebred, Warmblood, Haflinger, Norwegian Fjord, Peruvian Paso, and Paso Fino breeds. EMS has also been recognized in some Quarter Horses and Tennessee Walking horses. However, Thoroughbreds and Standardbreds may be at less risk. Familial patterns are also recognized for EMS, and therefore specific genetic lines within any given breed might be at greater risk. With the exception of published data supporting a genetic predisposition in certain pony breeding lines, most information pertaining to the inheritability of EMS is anecdotal and will surely be supplemented by new genetic mapping studies in the near future.

RECOGNITION AND OBJECTIVE MEASUREMENT OF OBESITY IN HORSES

An ideal index of body weight, such as the body mass index (BMI) described for humans based on the individual’s height and sex, does not exist for horses. In fact, such an ideal standard would surely differ between different breeds. The body condition score (BCS; on a scale of 1–9, with 1 being emaciated and 9 being profoundly obese) is a commonly used visual estimate that serves to provide a subjective index of obesity in horses and ponies and does not require scales. The BCS is better suited for evaluating adiposity in horses than it is for ponies. More recently, experts have suggested that the circumference of the neck (compared with the horse’s height or girth) might be a practical index for suspicion of IR (similar to the use of waist circumference as an indicator of high BMI and IR in obese human patients). A cresty neck score (CNS) has been suggested as a method of assessing subcutaneous adipose tissue expansion in the neck region with scores between 0 and 5 (CNS >3 implies EMS). A CNS of 3 is specifically described as follows: “Crest is enlarged and thickened, so fat is deposited more heavily in middle of the neck than toward poll and withers, giving a mounded appearance. Crest fills cupped hand and begins losing side-to-side flexibility.”

To determine the neck circumference-to-height at withers ratio, the circumference of the neck should be measured at the mid-point between the poll and the withers with the neck in a normal elevated position. In one study, when the ratio (with respect to the patient’s height) exceeded 0.71, the affected pony was more likely to develop PAL.

PATHOPHYSIOLOGY

A satisfactory and unifying explanation for the development of laminitis as a result of potentially diverse endocrinologic and metabolic influences is still lacking. However, several plausible and, in some cases, supportable hypotheses have been proposed. Endocrinologic perturbations that have been linked to risk for laminitis include hypercortisolism (Cushing’s disease), pregnancy, obesity, and IR. Certainly, IR is a component of hypercortisolism, pregnancy, and obesity. For the purposes of this discussion, aspects of obesity and IR that might play a role in the pathogenesis of laminitis are reviewed (obesity and IR are recognized contributors in EMS). Because of the complexity and extent of the discussion pertaining to theories regarding the pathogenesis of laminitis in the context of EMS, readers are strongly encouraged to seek out excellent reviews of this topic elsewhere in the literature.

Glucose dysregulation is frequently cited as an explanation of the risk for laminitis associated with IR. This theory is derived from the observation that, using an in vitro explant model, hoof lamellar keratinocytes were shown to have a critical glucose
requirement and that keratinocyte separation from underlying basement membrane occurs when glucose is insufficient. More recently, insulin has been shown to not affect glucose uptake through HLI explants and the insulin-dependent glucose transporter (GLUT-4) is not present in hoof keratinocytes. Therefore, if glucose dysregulation is pivotal to the risk for laminitis associated with IR, it is not based on an insulin-dependent glucose uptake mechanism through hoof-lamellar keratinocytes. Glucose dysregulation may contribute to risk for laminitis in an insulin resistant state because hyperglycemia may directly influence vascular endothelial cells (glucotoxic endotheliopathy). Mild elevations in the plasma glucose concentration over time are sufficient to affect endothelial regulation of vasomotor tone (vasoconstrictive influence) and promote a prothrombotic endothelial phenotype.

Vascular endothelial cells are also directly influenced by insulin in such a manner that interference with the action of insulin (IR) would likely promote vasoconstriction and platelet/leukocyte adhesion to endothelial surfaces. Therefore, perturbations in the regulation and action of insulin and glucose could theoretically lead to a microvascular dysregulation basis for the risk of laminitis that attends IR. These increased vasoconstrictive influences likely contribute to hypertension that has been observed in both the human and equine forms of metabolic syndrome. Moreover, the increased platelet/leukocyte microvascular adhesiveness that is reported in insulin-resistant individuals likely augments the participating role of neutrophils in the development of laminitis resulting from endotoxemia, carbohydrate overload, systemic inflammation, and severe gastrointestinal disturbances.

Recent experimental work showed that acute laminitis could be directly induced by insulin through maintenance of a supraphysiologic plasma insulin concentration over the course of several days in a euglycemic clamp experiment. However, in these experiments, the plasma insulin concentrations that were associated with the development of laminitis significantly exceeded those that are reported for horses and ponies affected with EMS. The fact that insulin can act as an independent trigger factor is important because under certain conditions it might act alongside concurrent trigger factors to cause laminitis at lesser circulating concentrations. Several explanations for a mechanism through which insulin might directly cause laminitis have been suggested and include hoof–lamellar hypoxia associated with insulin-induced microcirculatory dysregulation and increased tissue protease activity (including matrix metalloproteinases), both of which could increase the likelihood of structural failure at the level of the HLI.

Although obesity is widely recognized as a risk factor for laminitis, a satisfactory mechanistic explanation is still lacking. Plausible theories include increased weight-bearing, obesity-dependent IR, and the secretion of proinflammatory cytokines by adipose tissue. Although small quantities of cytokines are normally produced by cells in adipose tissue to exert autocrine and paracrine functions, the presence of prodigious quantities of adipose tissue in obese states leads to the secretion of much higher levels of these same cytokines (adipokines) that circulate to exert pathologic influence beyond the tissue of origin (endocrine effect). Numerous different cytokines that are derived from adipose tissue have been identified. The adipokine repertoire produced by any single adipose repository is probably different depending on the location and many other factors. Certain repositories of adipose tissue (e.g., omental and mesenteric fat in obese human patients) are characterized by the acquisition of an activated macrophage population that secretes proinflammatory cytokines into the venous effluent. In obese individuals, these leukocyte-derived cytokines are released in substantial quantities and exert a systemic (endocrine) action. Elevated circulating levels of proinflammatory signaling
molecules have been suggested to contribute to the development of IR and the risk for laminitis in obese horses. Specifically, the circulating (blood) mRNA expression of both tumor necrosis factor-α (TNF-α) and interleukin-1β (IL-1β) are increased in obese horses. In another study, a group of laminitis-prone ponies were characterized by elevated plasma TNF-α levels. Elevated circulating TNF-α and IL-1β expression was identified as an independent risk factor for IR in one study.

Macrophages that are identified in mesenteric adipose tissue in human and laboratory animal species are also characterized by the presence of 11β-hydroxysteroid dehydrogenase-1, a steroid-converting enzyme that converts cortisone, the plentiful inactive metabolite of cortisol, to active cortisol. Therefore, the enhanced conversion of cortisol from cortisone in mesenteric adipose tissue leads to increased corticosteroid action in both the adipose tissue (where it stimulates activation of preadipocytes to adipocytes and promotes expansion of the adipose repository at this location) and the liver (downstream target organ, where it causes hepatic IR). In addition to cortisol and adipokines, mesenteric adipose tissue also releases free fatty acids (FFAs) into the circulation, and these FFAs contribute to the development of hepatic IR. Elevated FFAs also stimulate inflammatory processes through enhanced Toll-like receptor 4 expression in macrophages. Not all adipose tissue repositories are characterized by a population of leukocytes, and the circulating concentrations of other adipokines, such as leptin, resistin, and adiponectin, may be perturbed and contribute independently to the development of IR. Elevated levels of circulating adipokines, such as TNF-α, may contribute independently to the development of IR and microvascular dysregulation. For example, enhanced vasospasticity (stimulated endothelin-1 production and reduced nitric oxide production), up-regulated oxidative stress, increased vascular permeability, increased expression of endothelial adhesion molecules, and inhibition of insulin signaling may all be attributed to the action of TNF-α.

Different aspects of the metabolic syndrome (especially IR and obesity) may contribute diverse risk factors for laminitis, including increased weight-bearing of obesity, microvascular dysregulation in the HLI, hepatocellular dysfunction, enhanced inflammation, prothrombotic endothelial phenotype, increased endothelial adhesiveness, oxidative stress, and increased corticosteroid activity.

DIETARY FACTORS PRECIPITATE AND AGGRAVATE LAMINITIS IN EQUINE METABOLIC SYNDROME

A diagnosis of EMS implies that the individual is inherently at risk for laminitis when subjected to various and potentially diverse trigger factors. Horses and ponies that are affected with EMS seem to be especially sensitive to ingested nonstructural carbohydrate (NSC). One of the most commonly recognized trigger factors for laminitis in EMS patients is the ingestion of a ration that is characterized by a high NSC content. For example, grazing grass pastures is the most common cause for laminitis recognized by practicing veterinarians (PAL). The total carbohydrate content of pasture grass is characterized by the carbohydrates that constitute the cell wall structure of plant cells (structural carbohydrates or fiber, such as cellulose and hemicellulose) that are indigestible by mammalian enzymes, and by NSCs (starch, soluble sugar, and fructans). Modern pasture grassland species have been genetically selected for high NSC content as befits the needs of the food animal industry. Horses evolved to be nutritionally efficient on native grassland species that tend to have a lower NSC content.
A single and simple explanation does exist for why EMS horses tend to develop activated laminitis after ingestion of high NSC pasture grass. Several explanations are plausible: ingested NSC (starch and soluble sugars) cause both glycemic and insulimemic spiking that seems to be associated with aggravated laminitis; or certain types of fructan (not digested by the small intestine) may cause cecal/colonic floral perturbations leading to colonic acidulation, increased epithelial permeability, and the absorption of other laminitis triggers (bacterially derived exotoxins, endotoxins, and vasoactive amines).  

Studies have shown that the NSC content of common pasture grasses tends to increase at certain times of the year (eg, spring, fall) and that development of laminitis is more likely in EMS ponies at these times. IR and elevated systemic blood pressure (both components of EMS) are also more prominent when ponies graze high NSC-content pastures. The development of laminitis in equids during pasture grazing should alert veterinarians to the possibility of underlying EMS.

**Diagnosis of Equine Metabolic Syndrome**

Clinical suspicion of EMS is based on assessment of the patient’s medical history, results of the physical examination, evaluation of radiographs of the feet, and the results of laboratory tests. The best laboratory tests for IR include the frequently sampled intravenous glucose tolerance test (FSIGT) and the euglycemic hyperinsulimemic clamp technique. Unfortunately, these gold standard tests are impractical for practicing veterinarians and less-specific, alternative diagnostic approaches are generally recommended.

The easiest diagnostic test for IR is to simply determine the plasma insulin concentration. Compensatory hyperinsulinemia is a common finding in IR-affected equids. Nevertheless, veterinarians should be cautious when interpreting the results of single-sample insulin determinations without considering possible confounding factors. For example, serum insulin concentration can be influenced by many factors (in addition to the insulin sensitivity of the individual), including time since the animal was last fed; circulating cortisol concentration (diurnal variance, excitement, pain and stress, PPID); type of food on which the ration is based; reproductive status; and physiologic status (fitness/illness). However, fasting concentrations of both insulin and glucose tend to be relatively constant and may be used to provide insight into the patient’s insulin sensitivity.

For purposes of measuring the circulating glucose and insulin concentrations, it is important to fast the patient for 8 to 10 hours and to obtain the samples between 8:00 and 10:00 AM (standardization). It is also recommended that the patient should have been fed no more than one flake of low-NSC hay (per 500 kg horse) the previous evening (no later than 10:00 PM). Horses and ponies that are accommodated on pasture should be stalled or confined to a dry lot before the insulin and glucose concentrations are evaluated to determine insulin sensitivity.

Blood samples for insulin assay should be submitted to the same laboratory because different laboratories use different insulin assay procedures. Therefore, for purposes of comparing data, serum insulin assays should be performed consistently using a method validated (by a specific laboratory) for horses (with an equine-specific reference range).

Horses and ponies affected with EMS tend to be characterized by a high normal or slightly elevated plasma glucose concentration (reference range, 80–115 mg/dL) and hyperinsulinemia (reference range, <20 μU/mL [<144 pmol/L]). Because different laboratories use different assay methods, a universally accepted cutoff for significant hyperinsulinemia has not yet been determined. Furthermore, some EMS horses tend
to develop reduced glycemic control (hyperglycemia, >150 mg/dL) and may be characterized with type 2 diabetes mellitus. The extent to which type 2 diabetes mellitus develops in mature IR-affected horses is currently unknown (it may be more common than generally believed).

Testing for IR in horses that are experiencing pain (or excitement) is not practical because any activation of the sympathetic nervous system will cause a reduction in insulin sensitivity. Therefore, testing patients that are presently affected with laminitic pain is not recommended. Moreover, determination of the serum insulin concentration may yield false-negative results in EMS-affected horses and ponies that have been fed a low-NSC ration. Therefore, dynamic endocrine testing is recommended for the potential EMS candidates in which the resting serum insulin and glucose concentrations are within reference intervals.20

**Dynamic Testing for Insulin Resistance**

A better diagnostic test for IR in clinical patients is the combined intravenous glucose–insulin test (CGIT).66 Horses are tested through being administered both glucose and insulin (glucose, 150 mg/kg; insulin, 0.1 U/kg) and having the blood glucose concentration measured for 2 hours (12 blood glucose determinations at 0, +1, +5, +15, +25, +35, +45, +60, +75, +90, +105, and +120 minutes). Results of a CGIT are characterized by a two-phase curve with positive (hyperglycemic) and negative (hypoglycemic) portions. The test outcome is evaluated based on the time taken for the plasma glucose concentration to return to the (zero time) baseline level after administration of glucose and insulin. Normal insulin sensitivity is associated with a return to baseline within 45 minutes.66 The testing conditions for a CGIT are the same as those for evaluating the patient’s resting serum insulin and glucose concentrations.

Patients have a very small risk for development of signs of insulin-provoked hypoglycemia (weakness, trembling and sweating) during the test. If signs of hypoglycemia develop, patients should be treated using intravenous 50% glucose infusion.66 False-positive results (suggesting IR in a normal horse) may arise if any stressful or exciting event precedes or occurs during the test. Therefore, the test should always be performed in a quiet environment in patients that have been allowed to consume a simple grass hay–based ration. Intravenous catheters should be placed the day before the test. The CGIT represents a potentially practical clinical measurement of insulin sensitivity because it provides integrated information and more information than either the singular glucose tolerance test or an insulin sensitivity test.

**Use of Continuous Glucose Monitors**

Disadvantages of measuring the blood glucose and insulin concentrations in either a single sample or during dynamic testing include the possibility of the patient becoming excited (subsequently depressing insulin sensitivity) and the fact that the period of evaluation is short. Continuous glucose monitoring represents a technological innovation has been marketed in the human medical field for better studying glucose regulation in individuals with diabetes.67,68 Briefly, this method entails placing a tiny glucose sensor in a subcutaneous location to render a computerized digital recording (Fig. 1). Using this method, it is possible to unobtrusively record the concentration of glucose in the interstitial compartment (equivalent to the blood glucose concentration) every 5 minutes over the course of up to 7 days (288 data points per 24-hour period).67,68 A potential advantage of this method for equine practitioners includes the ability to monitor changes in interstitial tissue glucose concentration over time with minimal need for handling. Using this technique, the authors observed that the interstitial glucose concentration of lean, insulin-sensitive adult horses tends
to be maintained at the lower end of the reference range with minimal variance (horses being fed ad libitum low NSC grass hay) (Fig. 2A). In contrast, the interstitial glucose concentration of obese horses in which CGIT has shown IR tends to be more variable over time, runs relatively high within the reference range, and frequently exceeds the high end of the reference range (see Fig. 2B).

**Diagnostic Controversy**

Recently, it has become clear that PPID sometimes arises in teenage horses without the classic physical appearance (eg, inappropriate hirsutism, loss of musculature, polyuria/polydipsia). In fact, the clinical presentation of PPID in young horses may be very similar to that of EMS. The extent to which EMS and PPID may be related is the subject of considerable controversy. Nevertheless, before EMS can be diagnosed, diagnostic tests such as the low-dose dexamethasone suppression test and measurement of the plasma adrenocorticotropic hormone concentration may be undertaken to show that the patient’s clinical signs are not resulting from PPID. In one study, the prognosis was reportedly worse for PPID-affected horses in which IR could easily be shown.

**PREVENTION, MANAGEMENT, AND TREATMENT RECOMMENDATIONS FOR EQUINE METABOLIC SYNDROME**

The management and treatment options for EMS will be determined by a full evaluation of the individual patient’s specific clinical circumstances. Ideally, however, veterinary clinical recognition of EMS will primarily prevent laminitis in EMS-affected horses and ponies.

If EMS is diagnosed before painful laminitis has occurred, the following preventive strategies should be used:

- Reversal of obesity (when applicable), which entails both dietary change and physical activity.
- Dietary changes aimed at reducing the energy and NSC components of the ration.
- Increased level of physical activity.
- Avoidance of pasture grazing for susceptible individuals, especially at certain times of the year and day.
Fig. 2. (A) Graphic representation of interstitial glucose measurements obtained from a lean, healthy, 6-year-old physically active Arabian gelding fitted with a continuous glucose monitoring system (CGMS) for 24 hours of stall confinement. The arrow represents the beginning of the monitoring period and the asterisk indicates the point at which a combined intravenous glucose-insulin test (CGIT) was conducted. The gray zone represents the reference range for plasma glucose concentration in an adult horse (83–113 mg/dL). The interstitial glucose concentration tends to remain within the lower aspect of the reference range throughout the investigative period, and the outcome of the CGIT is consistent with normal insulin sensitivity (glucose concentration returns to baseline within 45 minutes). (B) Graphic representation of interstitial glucose measurements obtained from an obese, physically inactive, 14-year-old Quarter Horse gelding fitted with a CGMS for 24 hours of stall confinement. The arrow represents the beginning of the monitoring period and the asterisk indicates the point at which a CGIT was conducted. The gray zone represents the reference range for plasma glucose concentration in an adult horse (83–113 mg/dL). The interstitial glucose concentration tends to remain at the upper end of the reference range and drift into the hyperglycemic zone (poorly regulated glucose) throughout the investigative period, and the outcome of the CGIT is consistent with reduced insulin sensitivity (glucose concentration failed to return to baseline within 45 minutes).

Begin critical evaluations of the patient’s hoof (based on appearance and radiographic characteristics) with a view to promoting hoof care practices (farriery) that should reduce the risk for laminitis (maintain photographic records).

If EMS is diagnosed after painful laminitis has occurred, the following management/treatment strategies should be used:

Treatment of laminitis based on critical and objective evaluations of the patient’s hoof (based on appearance and radiographic characteristics; this topic is reviewed elsewhere in this issue).

Reversal of obesity (when applicable), which must be based on dietary change because physical activity can exacerbate the HLI during painful laminitis.

Dietary changes aimed at reducing the energy and sugar/starch components of the ration.
Avoidance of pasture grazing for susceptible individuals, especially at certain times of the year and day.62
Consider dietary supplementation using levothyroxine sodium (Thyro-L).72–74
Consider treatment using metformin (theoretically a good idea but poor bioavailability in adult horses at recommended/reported doses has been reported).75–77

**DIETARY STRATEGIES TO MINIMIZE THE RISK FOR LAMINITIS IN HORSES WITH EQUINE METABOLIC SYNDROME**

**Strategies for Reversal of Obesity**

Obesity has been associated with IR and risk for laminitis.20 Recognition of obesity (generalized or regional) is an important component of EMS.20 However, not all obese individuals are at risk for laminitis by virtue of the development of IR. Obesity is clearly a common finding in horses and ponies under modern management systems. Moreover, horse owners are often unaware of obesity when it is present in their horses. It is logical that the reversal of obesity should minimize the risk for laminitis and promote insulin sensitivity. Obese horses and ponies should not be starved for purposes of weight loss, because severe calorie restriction leads to the activation of physiologic mechanisms that worsen IR.78 Obese ponies, donkeys, and American Miniature Horses are especially predisposed to hyperlipemia and hepatic lipidosis (potentially fatal) when subjected to a calorie-restricted ration.79 Strategies intended to reverse obesity should include increased physical activity and a reasonable restriction of dietary energy intake. Adjustments to the horse’s ration should be instituted gradually, and progress with weight reduction should be evaluated objectively on a predetermined schedule.

Reduced dietary caloric intake coupled with increased physical activity represents the cornerstones of a successful weight-reduction program.80 Unfortunately, the development of painful laminitis in some EMS-affected equids precludes the enhancement of exercise for purposes of promoting weight reduction. In those patients, dietary adjustments and the specific management of laminitis must be undertaken to better address obesity and IR.

The recommended dietary strategy for obesity reversal in patients with EMS is the provision of energy from structural carbohydrates (such as cellulose) rather than from NSCs (starch, soluble sugars, and fructans). Energy-dense food items such as sweet feed and grain should not be used. Because the NSC content of a batch of hay cannot be visually assessed, a forage analysis should be obtained for any hay that is intended for feeding of EMS-affected equids.24,61,62 Ideally, the NSC content of hay used to both promote weight reduction and avoid glucose/insulin spiking should be less than 10% to 12%.20 For more detailed information pertaining to the analysis of forage and the differences in how the analysis is performed and reported between forage analysis laboratories, the reader is directed elsewhere.24,61,62 Weight reduction can generally be accomplished by providing 1.5% of the patient’s targeted body weight as low-NSC hay, daily (feeding 2% of the patient’s body weight failed to elicit weight reduction in one study). The daily forage intake should be provided as numerous small feedings throughout the day to minimize protracted periods of hunger and boredom. Recently, commercial horse feeding products (characterized by a certified low NSC content) have been marketed for EMS-affected equids and may be considered as a part of a weight-reduction program for obese or EMS-affected horses.

The nature of modern grassland species that are commonly found in horse pastures and paddocks have been genetically selected to support milk production and fattening of domesticated cattle, and are therefore characterized by a high NSC
content in distinct contrast to the native grassland species on which horses evolved. Therefore, discontinuation of pasture grazing should be emphasized for horses in which obesity reversal is important. If completely eliminating pasture grazing is not practical, the practice of restricted pasture grazing may be adopted. However, in one study, the authors showed that although time for grazing was reduced, significant weight loss did not occur because the consumption of grass increased in response to decreased time at pasture. Other management strategies that might promote weight loss under a restricted pasture grazing program include the use of a grazing muzzle (ensuring that the patient can drink water), strategic mowing of the pasture, strip grazing, and depositing wood chips across an area of pasture. That said, for purposes of weight reduction (and reduced NSC intake in general), strict avoidance of pasture grazing should be strongly recommended whenever possible for patients with EMS. Certainly, EMS-affected horses and ponies should never be grazed at the times of the year when pasture NSC levels are known to be elevated (spring bloom, early summer, and during the transition from fall to winter).

**Strategies for Minimizing Dietary Nonstructural Carbohydrate Intake**

In addition to addressing obesity, management of EMS-affected horses must also include a feeding regimen characterized by low NSC content and a low glycemic index. Some patients with EMS are relatively refractory to dietary strategies aimed at reversing IR and remain susceptible to laminitis, even when fed relatively low NSC rations. It is important to be exceptionally diligent with respect to lowered NSC intake in these individuals and to monitor the patient’s insulin sensitivity (serial serum insulin determinations on a regular basis) carefully over time. Other patients with EMS respond more favorably to less stringent dietary management strategies and may require a less rigorous and more practical approach. Practicing veterinarians should also consider consulting with specialist horse-oriented nutrition experts when formulating a suitable ration for EMS-affected horses and ponies.

For EMS-affected horses with relatively refractory IR, strict avoidance of pasture grazing must be considered and a forage-based diet characterized by a low (<10%–12%) NSC content should be provided. Limited (1–2 hours) pasture grazing may be allowed for horses with EMS and controlled IR at times of the day when the NSC content of grass is low (between 3:00 and 9:00 AM) but not at times of the year when seasonal and environmental conditions cause grass NSC to be relatively high (lush grass growth in spring and early summer; reactivated grass growth after rain in the summer; drought-affected pastures; and frost-affected pastures in the fall). The reader is directed to other literature sources for a more complete review of the seasonal and environmental factors that affect the NSC content of pasture grasses.

The basic recommendation is to feed EMS-affected horses hay that is characterized by a low NSC and high fiber (structural carbohydrate) content. Affected horses should not be fed alfalfa, grain, or sweet feed. Selection of a suitable source of hay should be based on results of a forage analysis, because the NSC content of hay cannot be speculated. Soaking hay under a large volume of water for 60 minutes can sometimes reduce its NSC content. Other potentially useful components of a suitable ration include (nonmolassed) sugar beet pulp and rice bran. If further dietary energy is required (for nonobese, athletic horses) at a level greater than that provided by forage, supplementing the ration with vegetable oil (typically corn or soy) should be considered. Additionally, various commercial horse food products have been marketed with a certified low NSC content that will likely be helpful in some cases.
Providing low-NSC forage will likely not provide sufficient protein, vitamins, and minerals in the ration, and therefore a low-NSC, protein-enriched mineral and vitamin balancer should be considered as a part of the dietary plan (after evaluating forage analysis results with a nutritionist). Although dietary supplementation using the

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<th>Box 1</th>
<th>Checklist for owners of horses with equine metabolic syndrome</th>
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<td>• EMS identification. EMS is initially identified based on results of physical examination (body condition and signs of laminitis). Recognition of the phenotype may be an incidental finding during veterinary consultation for other unrelated problems. The development of obesity is common in contemporary horse management systems.</td>
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<td>• Client education. Obesity and EMS represent important risk factors for laminitis. Discuss with client the health implications of obesity and feeding NSC-rich rations to physically inactive horses and ponies.</td>
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<td>• Investigation. Review the patient’s physical activity program and evaluate the feeding program based on the physical activity and nutritional requirements for the individual. Identify management and environmental factors that might increase risk for laminitis and counsel client regarding appropriate avoidance strategies.</td>
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<td>• Promote a heightened level of physical activity for the patient (assuming laminitis is not present) and encourage maintenance of an exercise record.</td>
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<td>• Help the owner obtain an accurate (calibrated scale at animal feed purveyor) or reasonably accurate (weight tape method) weight for the horse and determine an optimal weight to target after institution of both exercise and dietary strategies. Urge serial measurements of the patient’s weight to evaluate progress.</td>
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<td>• Record a primary evaluation of the patient’s body condition and adiposity. Assess the patient’s body condition score. Show the client how to measure the patient’s neck circumference, height, and girth. Encourage the client to record these measurements on a regular basis.</td>
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<td>• Undertake primary and follow-up endocrinologic evaluation of the patient to characterize insulin sensitivity (and to test for PPID, when appropriate). Serial endocrine testing might simply entail measurement of circulating insulin and glucose concentrations (using the same laboratory and ensuring that the samples are acquired as described earlier). Repeated testing will help to evaluate patient’s responsiveness to instituted management strategies and owner’s compliance.</td>
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<td>• Obtain primary objective evaluation of the patient’s feet (especially the forefeet). These objective evaluations may include photographs of the gross appearance of the hoof (including dorsal, lateral, and solar views) and radiographs (especially a carefully aligned lateromedial view).</td>
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<td>• Provide specific guidance regarding the need for obesity reversal and minimizing NSC intake. Discuss the avoidance of grain, sweet feed, sugary treats, alfalfa, and pasture grazing. Consider obtaining specialist veterinary nutrition input. Obtain objective data for (especially) the nutritional quality of forage (NSC content in hay). Urge objective approach to feeding EMS-affected horses, including actually weighing the food to be provided. As a general rule, small quantities should be fed frequently, and providing infrequent large meals should be avoided. Sensitize the client to times of the year when environmental circumstances are such that the NSC content of pasture grass may be dangerously high.</td>
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<td>• If avoiding pasture grazing is impossible, counsel the client regarding safer pasture management strategies that may help reduce the quantity of ingested grass or the NSC content of available grazing pastures (<a href="http://www.safergrass.com">http://www.safergrass.com</a>).</td>
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<td>• Help the client develop a program of ongoing vigilance and monitoring of patients to prevent obesity and maintain good glycemic and insulimemetic control.</td>
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micronutrients magnesium oxide and chromium picolinate has been recommended for promoting insulin sensitivity, evidence is not convincing that these products are helpful for managing EMS-affected equids.

**Pharmacologic Strategies for the Management of Refractory Equine Metabolic Syndrome**

Oral treatment using levothyroxine sodium seems to be helpful in managing refractory cases of obesity and EMS. A favorable response to this treatment approach should not be used to justify a diagnosis of hypothyroidism, and the client and horse should not be subjected to life-long dependence on this medication. Recently, interest has been shown in the use of the biguanide, metformin, for treatment of EMS. Although some preliminary studies have reported a positive response after administration of metformin to EMS horses, much remains to be learned of the drug’s pharmacokinetics and safety in the equine species. EMS occurs in some older horses that are also affected with PPID. If patients with EMS are concomitantly affected with PPID, treatment for PPID using low-dose pergolide (0.5–3.0 mg/d, orally, per 450 kg horse) should be instituted.

**WHAT CAN THE VETERINARIAN DO TO HELP OWNERS OF HORSES WITH EQUINE METABOLIC SYNDROME?**

Specific aspects of the veterinarian’s role in the management of EMS-affected horses and ponies are listed in Box 1.

**REFERENCES**


