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Nutrition of Horses with Muscle Problems

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The most basic aim of equine nutrition is to design diets that prevent diseases by meeting the minimum daily requirements for essential nutrients. Achieving these aims has drastically reduced the incidence of white muscle disease in foals caused by selenium deficiency (Roneus & Jonsson, 1984) and highlighted the role of vitamin E deficiency in Equine Motor Neuron Disease (Divers *et al*, 1994). A further aim of equine nutrition is to optimize nutrient content in order to maximize performance in specific equine disciplines. Research in this area with regard to muscle has focused on manipulating dietary vitamin, mineral, electrolyte, nonstructural carbohydrate (NSC) and fat content as one means to optimize performance and prevent muscle pain. Most recently, equine research has embraced nutrigenomics, in which a horse's nutritional requirements are tailored to its individual's genetic make-up. Equine nutrigenomics has been applied to the nutritional management of genetic disorders such as polysaccharide storage myopathy (PSSM), recurrent exertional rhabdomyolysis (RER) and hyperkalemic periodic paralysis (HYPP). This review will focus on dietary recommendations for horses with sporadic forms of tying up or exertional rhabdomyolysis (ER) as well as recommendations for specific genetic disorders.

Dietary Management of Sporadic Exertional Rhabdomyolysis

Sporadic ER is a term used to describe horses that have innately normal muscle function that sporadically is disrupted by dietary imbalances, trauma, change in exercise, or other management practices. Horses usually have a history of adequate performance prior to onset of muscle pain and successfully return to performance following a reasonable period of rest, provision of a balanced diet, and a gradual training program. Horses with these sporadic occurrences may be of any age, breed, or sex, and involved in a wide variety of athletic disciplines. Episodes of muscle pain may recur over a short period of time prior to resolving the external perturbations which affect muscle function. In many cases, horses are initially presumed to have sporadic ER; however, if over time episodes of muscle pain recur despite the best management, further investigation may lead to a diagnosis of a form of chronic ER.

Sporadic exertional myopathies may be the result of;

- 1) **Over-exertion.** A history of an increase in work intensity without a foundation of consistent training for this level of intensity is usually the basis for suspecting a training imbalance as a cause of ER.
- 2) **Heat and electrolyte exhaustion.** Prolonged exercise in hot, humid weather can lead to heat exhaustion (temp 105 - 108 F) and myoglobinuria especially during endurance competitions. Acute hyponatremia, hypokalemia, hypochloremia and hypocalcemia are apparent in blood samples and immediate intravenous fluid therapy treatment is required (Carlson, 1985). Commercial electrolyte mixtures containing a 2:1:4 ratio of Na:K:Cl are recommended prior to and during prolonged endurance rides to prevent depletion (Schott *et al*, 1997).

Chronic electrolyte imbalances. Chronic imbalances within the body are much more difficult to accurately assess than acute depletion. Work by Harris (Harris & Colles, 1988) established renal fractional excretions as a technique to evaluate electrolyte concentrations in horses. Blood and urine samples are obtained concurrently and creatinine and electrolyte concentrations measured in both. [Serum creatinine]/[urine creatinine] multiplied by the reciprocal for urine and serum electrolyte concentrations x 100 provides the fractional excretion of a particular electrolyte. This technique is complicated by marked electrolyte variations that occur because of diet, time of day, sampling technique and among individuals (McKenzie *et al*, 2003a). Furthermore, the high calcium crystal formation in equine urine makes acidification of samples necessary to accurately assess calcium and magnesium content. In the United Kingdom, a number of horses with ER had low fractional excretions of sodium and daily dietary supplementation of 60 g (2 oz) NaCl resulted in abatement of clinical signs. Other horses had high phosphorus excretion suggesting a dietary calcium:phosphorus imbalance and decreasing bran while providing a daily calcium supplement (60 g CaCO₃) was helpful in reducing clinical signs of ER (Harris & Snow, 1991). Hypokalemia has also been suggested to play a role in chronic ER, although it is not a common finding in horses consuming adequate quantities of forage. Supplementation with good quality forage or 30 g of KCl/day (lite salt) is recommended for horses with low renal fraction excretion of potassium.

- 3) **Selenium and vitamin E deficiency.** In some areas of the world soil selenium can be particularly low and factors in the soil may impair adequate selenium uptake from the diet. In addition, inadequate vitamin E intake can arise when horses receive restricted green pasture turn-out. While it is not readily documented that deficiencies of antioxidants vitamin E and selenium cause sporadic ER, it seems reasonable that

inadequate antioxidant levels may predispose horses to muscle soreness. Adequate values for blood selenium are usually considered to be >0.07 mcg/ml. Veterinarians in selenium deficient areas of the world often anecdotally report a higher degree of success in treating a variety of myopathies by providing selenium supplementation above that normally recommended for horses (0.2-0.3 mg/kg/diet dry matter of selenium) and report that higher doses of oral selenium are required in their area to maintain adequate blood levels. Adequate values for serum vitamin E are >2.0 mcg/ml. Adequate daily intake of vitamin E ranges from 1000 -4000 U per day depending on exercise intensity. In addition to vitamin E provided by green grasses and well-cured hay, supplemental vitamin E from commercially prepared diets and supplements may be necessary to achieve adequate antioxidant status. With extreme exertion such as endurance riding antioxidants such as vitamin E may have a key protective role in preventing muscle damage. A beneficial effect of supplementing beyond daily requirements, particularly for horses performing less intense exercise remains equivocal.

Dietary Management of Chronic Forms of Exertional Rhabdomyolysis

Horses that have repeated episodes of ER from a young age, or from the time of purchase, or when they are put back into training after a long period of rest may have an underlying intrinsic abnormality of muscle function. Chronic forms of ER are seen in many breeds of horses. Four specific intrinsic causes of exertional rhabdomyolysis have been identified to date; type 1 polysaccharide storage myopathy (PSSM),(Valberg et al, 1992) type 2 polysaccharide storage myopathy (McCue M.E. et al, 2009), recurrent exertional rhabdomyolysis (RER) (Lentz et al, 1999) and Malignant Hyperthermia (Aleman et al, 2004). It is likely that there are other specific causes that have yet to be identified (idiopathic chronic exertional rhabdomyolysis). In all of these intrinsic forms of chronic ER it appears that there are specific environmental stimuli that are necessary to trigger muscle necrosis in genetically susceptible animals. Animals cannot be cured of their susceptibility to these conditions, but if the specific disease is identified changes in management and diet can be implemented for PSSM and RER in order to minimize episodes of rhabdomyolysis.

Polysaccharide Storage Myopathy

PSSM occurs in at least two forms. Type 1 PSSM is due to an autosomal dominant point mutation in the glycogen synthase 1 gene (*GYS1*) which appears to cause unregulated synthesis of glycogen (McCue *et al*, 2008). The *GYS1* mutation, present in horses for over a 1000 years, is the same disorder described as “Monday Morning Disease or Azoturia” in draft horses in the early

20th century. This *GYS 1* mutation is present in over 20 breeds including Quarter Horses, Paint horses, Appaloosa horses, numerous Continental European Draft breeds, some Warmblood breeds, Haflinger, Morgan, Mustang, Rocky Mountain Horse, Tennessee Walking Horses, as well as mixed breed horses. Type 2 PSSM represents horses diagnosed with PSSM by muscle biopsy that do not have the *GYS1* mutation (McCue *et al*, 2006). Type 2 PSSM occurs in Warmblood breeds such as Dutch Warmbloods, Hannoverian, Westfalian, Canadian Warmblood, Irish Sport Horse, Geldlander, Hussien, and Rheinlander, about 28% of Quarter Horses with PSSM as well as other light breeds of horses.

Management recommendations for PSSM are based on research studies that retrospectively now appear to have largely included horses with type 1 PSSM. However, anecdotal and epidemiologic studies that include type 2 PSSM horses support a positive response of both forms of PSSM to a similar exercise and dietary regime.

Dietary recommendations for PSSM

Caloric balance: The first step in designing a diet for PSSM horses is to decide what the horse's caloric requirements are and what the horse's ideal body weight is or should be. Many horses with PSSM are easy keepers and may be overweight at the time of diagnosis. Adding excessive calories in the form of fat to an obese horse may produce metabolic syndrome and is contraindicated. If necessary, caloric intake should be reduced by using a grazing muzzle during turn-out, feeding hay with a low nonstructural carbohydrate content (NSC) at 1 to 1.5% of body weight, providing a low calorie ration balancer and gradually introducing daily exercise. Rather than provide dietary fat to an overweight horse, fasting for 6 h prior to exercise can be used to elevate plasma free fatty acids prior to exercise and alleviate any restrictions in energy metabolism in muscle.

Selection of forage: Quarter Horses have been shown to develop a significant increase in serum insulin concentrations in response to consuming hay with an NSC of 17% , whereas insulin concentrations are fairly stable when fed hay with 12% or 4 %NSC content (Borgia *et al*, 2011). Because insulin stimulates the already overactive enzyme glycogen synthase in the muscle of type 1 PSSM horses, selecting a hay with 12% or less NSC is advisable. The degree to which the NSC content of hay should be restricted below 12% NSC depends upon the caloric requirements of the horse. Feeding a low NSC hay of 4% provides room to add an adequate amount of fat to the diet of easy keepers without exceeding the daily caloric requirement and inducing excessive weight gain. For example, a 500-kg horse on a routine of light exercise generally requires 18 MCal/day of digestible energy (DE). Fed at 2% of body weight, a 12% NSC mixed grass hay almost meets their daily caloric requirement by providing 17.4 MCal/day. With a 12%NSC hay there is only room for 0.6 MCal of fat per day (72 ml of vegetable oil) in order to achieve 18 MCal of energy. In contrast, a 4% NSC

Blue Grama hay would provide 13.5 MCal/day which would allow a reasonable addition of 4.5 MCal of fat per day (538 ml of vegetable oil).

Selection of fat source: The major sources of dietary fat for horses are vegetable based including vegetable oils and rice bran or animal based fat (tallow, lard, fish oil). Vegetable oils are highly unsaturated, very digestible (90-100%) and very energy dense. Suitable forms include soybean, corn, safflower, canola, flaxseed, linseed, peanut and coconut. Controlled research studies in exercising PSSM horses have shown a decrease in muscle pain and serum indicators of muscle damage (CK) in response to the addition of corn oil (Borgia *et al*, 2010) and also soybean oil (in ReLeve) (Ribeiro *et al*, 2004). The amount of oil added in these trials constituted at least 13% of daily digestible energy. Some veterinarians have advocated as much as 25% of DE be fed in the form of fat to PSSM horses. As discussed above the principle consideration here should be whether this provides excessive calories and additional weight gain because feeding 13% DE as fat may well be effective in reducing muscle pain.

Limited research has been performed on the form of oil to feed PSSM horses. An odd carbon 7 chain fat (triheptanoin) fed to PSSM horses had a detrimental effect on muscle pain, exercise tolerance and serum CK activity whereas in the same study long chain fats fed in the form of corn oil or a ricebran/soy oil supplemented feed had a beneficial effect on lowering serum CK activity (Borgia *et al*, 2010). Whether there is any direct beneficial effect on skeletal muscle of providing energy in the form of Omega 3 versus Omega 6 fatty acids has yet to be determined. Corn oil, sunflower oil, and safflower oil are high in Omega-6, and lower in Omega-3, whereas soybean and canola oils are moderately high in omega-6 and Omega 3 and flax seed, linseed and fish oils contain more Omega-3 than Omega-6. It is usually cost-prohibitive to provide sufficient energy to a PSSM horse each day in the form of Omega 3 fats. Soybean and canola oils provide a relatively affordable alternative with moderately high Omega 6. Due to the potential additional oxidant stress of fats, vitamin E (1000 – 6000 U/day) should be fed to horses receiving high oil diets.

Low starch high fat concentrates: While oils are energy dense and inexpensive, they have the disadvantages of being messy, unpalatable to some horses, prone to rancidity in warm temperatures, and difficult to feed in large amounts. As such a number of concentrates have been developed that contain fats. The important principle to be met by such feeds is that the starch and sugar components are low enough and fat supplementation high enough to ensure that in the total diet, the calories supplied by NSC comprise no more than 10-15% of the daily DE and the calories supplied by fat comprise about 12-15% of daily DE. Common fat sources used in such concentrates include, in addition to the oils mentioned above, stabilized rice bran or animal fats. Rice bran and its products are palatable to most horses, have a moderate NSC content ~25% by weight, contain ~20% fat by weight as well as vitamin E and are naturally high in phosphorus. The NSC component of rice bran can vary if the manufacturing process is not careful to exclude the white rice grain. Commercial rice bran

products occur as powder or an extruded pellet, and are considerably more stable in warm temperatures compared to animal fat and vegetable oils.

The effect of low starch, high fat diets on exercise-induced muscle damage has only been demonstrated under controlled conditions in Quarter Horses (Ribeiro *et al*, 2004;Borgia *et al*, 2010). In PSSM Quarter Horses providing less than 10% of daily DE as dietary starch and 13% of daily DE as dietary fat (Re-Leve®)¹ resulted in normal serum CK activity four hours post exercise during a six week trial. Provision of higher starch content resulted in increased serum CK activity in the most severely clinically affected horses. There is a great deal of variation in individual tolerance to dietary starch however; horses with more severe clinical signs of PSSM appear to require the greatest restriction in starch intake. A number of well balanced low starch high fat commercial diets are suitable for horses with PSSM. Some commercial feeds meet the recommended nutritional needs of PSSM horses in one pelleted ration, These feeds typically contain at least 10-15% fat by weight and less than 20% NSC by weight. Some feed companies offer similar nutritional content by blending two or more manufactured feeds or by supplementing with oils or rice bran. At present, the NSC content of equine feed products is not consistently listed on the feed tag, and consultation with the feed manufacturer is necessary to obtain this information. Nutritional support is available through most feed manufacturers in designing an appropriate diet.

The beneficial effect of the low starch, high fat diet is believed to be the result of less glucose uptake into muscle cells and provision of more plasma free fatty acids for use in muscle fibers during aerobic exercise (Borgia *et al*, 2010). Quarter Horses naturally have very little lipid stored within muscle fibers and provision of free fatty acids may overcome the disruption in energy metabolism that appears to occur in PSSM Quarter Horses during aerobic exercise. This beneficial effect requires that horses are trained daily to enhance enzymes involved in fat and glucose metabolism. Exercise recommendations are provided in the proceedings from this meeting under PSSM.

Expectations: It is important to note that a horse diagnosed with PSSM will always have an underlying predilection for muscle soreness and the best that can be done is to manage horses to minimize clinical signs. With adherence to both the diet and exercise recommendations at least 80% of horses show notable improvement in clinical signs and many return to acceptable levels of performance (Firshman *et al*, 2003). There is, however, a wide range in the severity of clinical signs shown by horses with PSSM; those horses with severe or recurrent clinical signs will require more stringent adherence to diet and exercise recommendations in order to regain muscle function. PSSM horse that also have the mutation for Malignant Hyperthermia, do not respond as well to diet and exercise recommendations and may continue to develop ER with the possibility of a fatal episode (McCue M.E. *et al*, 2008).

¹ Re-Leve, Kentucky Equine Research, Versailles KY 40383

Recurrent Exertional Rhabdomyolysis

The term recurrent exertional rhabdomyolysis (RER) is used to designate one form of ER that appears to have a heritable basis in Thoroughbred horses (MacLeay *et al*, 1999c; Dranchak *et al*, 2005). The specific cause of RER has not been identified. Studies of muscle contraction suggest that it may be due to abnormal regulation of intracellular calcium in skeletal muscle which causes intermittent rhabdomyolysis in genetically susceptible horses (Lentz *et al*, 2002; Lentz *et al*, 1999). There are many clinical similarities with chronic forms of ER in some Warmbloods, Standardbred and Arabian horses however, much of the genetic and nutritional research into RER has been performed in Thoroughbreds. Horses with RER usually have a nervous temperament, are hard keepers and develop clinical signs when they are fit (MacLeay *et al*, 1999a; McGowan *et al*, 2002). Based on the known physiology of RER, the goal of nutritional research was to develop diets that would reduce nervousness and excitability in affected horses in hopes of decreasing the incidence of stress induced episodes of rhabdomyolysis. The results of a standardized nutrition trial with RER Thoroughbreds showed that provision of a diet with a reduced NSC content and higher fat content than conventional concentrates reduces serum CK activity and alters indices of nervousness (MacLeay *et al*, 1999b; MacLeay *et al*, 2000; McKenzie *et al*, 2003b). These dietary recommendations differ specifically from those described for PSSM in terms of caloric requirements and higher recommended starch and fat content as a % of daily DE.

Caloric balance: A nutritionally balanced diet with appropriate caloric intake and adequate vitamins and minerals are the core elements of treating RER. For RER Thoroughbreds and Standardbreds in training, the challenge is usually supplying enough calories in a highly palatable form to meet their daily energy demands. This is in part because they often require >30 MCal of DE a day and because with their nervous temperament they may be more discriminating in their eating habits.

Selection of forage: Thoroughbred horses do not appear to show the same significant increase in serum insulin concentrations in response to consuming hay with an NSC of 17% as seen in Quarter Horses (Borgia L. 2010 PhD thesis). This fact combined with the high caloric requirements of racehorses may mean that it is not as important to select hay with very low NSC content in RER Thoroughbreds as it is in PSSM horses. Anecdotally some trainers find horses with RER have more frequent episodes on alfalfa hay. The nervous disposition of some RER horses may predispose them to gastric ulcers and thus frequent provision of hay with a moderate NSC and alfalfa content may be indicated.

Low starch high fat concentrates: When RER Thoroughbreds are fed a moderate caloric intake (24 MCal/day in the form of high starch concentrates (2.5 kg of corn/oats/wheat middlings/molasses) they show very little elevation in

serum CK activity with exercise (MacLeay *et al*, 2000). Most Thoroughbred racehorses, however, are fed at least 5 kg of high starch concentrate/day at 30 MCal or more/horse/day and at this level of feeding, post-exercise serum CK activity, representing muscle damage, rises significantly (MacLeay *et al*, 1999a). The discovery that substitution of fat for starch in a high calorie ration significantly reduces muscle damage in exercising RER horses was a major advance in nutritional management of RER (McKenzie *et al*, 2003b). Practically, however, it was difficult to achieve the desired caloric intake of race horses because the maximum amount of fat that finicky Thoroughbreds will happily consume is limited often to 600 mls for vegetable oil or 5 lbs/day of balanced rice bran. Management of RER horses was significantly improved when a palatable means to provide the amount of fat required by fit finicky RER Thoroughbreds was developed. A controlled trial using the first specialized feed developed for RER (Re-Leve 13% fat by weight and 9% NSC), determined that NSC should be no greater than 20% of daily DE and 20-25% of daily DE should be provided by fat for optimal management of RER horses fed 30 MCal or more/day (McKenzie *et al*, 2003b). No beneficial effect on serum CK activity occurred when sodium bicarbonate (4.2% of the pellet) was added to the high starch pellet fed to RER horses (McKenzie *et al*, 2003b).

Pre and post-exercise muscle glycogen and lactate concentrations are the same in RER horses fed a low starch, high fat diet compared to a high starch (MacLeay *et al*, 1999b). Rather than altering muscle energy metabolism, low starch high fat diets in RER horses may decrease muscle damage by assuaging anxiety and excitability which are tightly linked to symptoms of RER. High fat low starch diets fed to fit RER horses produce lower glucose, insulin and cortisol responses and led to a calmer demeanor and lower pre-exercise heart rates (Finno *et al*, 2010). Neurohormonal changes may develop in response to high serum glucose, insulin and cortisol concentrations resulting in an anxious demeanor. While this calm demeanor is desired during training, some racehorse trainers prefer to supplement with a titrated amount of grain 3 days prior to a race if horses are on a low starch high fat feed, to increase a horse's energy during the race.

Expectations and other management changes: Studies in RER horses show that significant reductions or normalization of post-exercise serum CK activity occurs within a week of commencing a low starch high fat diet (McKenzie *et al*, 2003b). Days off training in a stall are discouraged because post-exercise CK activity is higher following two days of rest compared to values taken when performing consecutive days of the same amount of sub-maximal exercise. Failure to implement an appropriate exercise routine is very likely to lead to failure to control rhabdomyolysis in spite of dietary changes. Since RER appears to be a stress-related disorder, management strategies to reduce stress and excitability in these horses help reduce episodes of ER. These include turn-out, exercising or feeding these horses first before other horses, providing compatible equine company and the judicious use of low dose tranquilizers during training. Anecdotal reports of increased nervousness have been received when selenium is supplemented at higher than the recommended levels. Feeds designed for

RER should be evaluated for their selenium concentrations and should not be supplemented in addition if adequate levels are provided in the feed.

Hyperkalemic Periodic Paralysis

Hyperkalemic Periodic Paralysis is an autosomal dominant disorder in Quarter Horses descendant from the stallion Impressive (Spier *et al*, 1993). It arises from a mutation in the alpha subunit of the skeletal muscle sodium channel which is involved in initiating muscle contractions. The genetic defect affects horses at rest and causes intermittent muscle twitching which may progress to muscular weakness. It should be noted that many HYPP-positive horses show few or no signs of the disease in their lifetime. Trembling is triggered by a rise in potassium levels in the blood, as may occur with potassium rich meals. This induces the mutated muscle sodium channel to become stuck in the open position, producing cell membrane depolarization and uncontrolled muscle twitching. Affected horses may prolapse the third eyelid, sweat, show whole-body tremors and subsequently profound weakness, respiratory collapse and temporary paralysis. Signs may be induced by stress such as transport, showing, clipping, or veterinary procedures. For many HYPP-positive horses, however, the attacks come about without provocation.

Dietary management limiting potassium content is key to preventing attacks. Total potassium in the diet should not exceed 1% of the diet (Reynolds *et al*, 1998). Since forage is usually high in potassium choices narrow considerably for horses afflicted with HYPP. Legumes, particularly alfalfa, tend to be higher in potassium and should be used sparingly or not at all in the diets of HYPP-positive horses. Grass forages generally contain 1-2% potassium, however, it is often best to assay the potassium content of hay as it can vary between types and between cuttings. HYPP horses can be pastured on grass pastures with low legume content. Pasture/grass hay can be paired with a low-potassium cereal grain and an all-purpose vitamin and mineral supplement for HYPP horses. Oats are ideal whereas commercially prepared sweet feed and pelleted feeds that contain molasses or soybean meal should be avoided as they are higher in potassium. Even though mineral supplements likely contain potassium, when fed in recommended amounts they will not have a major impact on potassium in the total diet. In contrast, most commercial electrolytes are unsuitable for HYPP horses as they usually contain high levels of potassium. Exercise can increase potassium loss and is recommended for HYPP horses.

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Conflict of Interest Statement

Drs. Valberg, Mickelson and McCue own the license for PSSM testing and receive sales income from its use. Their financial and business interests have been reviewed and managed by the University in accordance with its conflict of interest policies. A portion of the profits from the sale of Re-Leve go to Dr. Valberg and her research.