Diagnosis and Treatment of Equine Polysaccharide Storage Myopathy

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Equine polysaccharide storage myopathy (EPSM) is a recently recognized metabolic condition with a high incidence in many breeds of horses and ponies. Clinical signs are extremely variable, but all can be related to underlying skeletal muscle dysfunction. Therapy employing a high-fat, high-fiber, low-starch, low-sugar diet and as much exercise as possible has proven to be extremely successful in control of this disorder. EPSM is progressive, and early detection and institution of therapy are vital.

Key words: *Horse; Myopathy; Polysaccharide*

INTRODUCTION

Equine polysaccharide storage myopathy is not a new disorder, but it has only recently been recognized. It is likely to have been present but undiagnosed for many years. This disorder has been found to be the cause of recurrent exertional rhabdomyolysis (tying up) in many breeds of horses.[1-3] Although exertional rhabdomyolysis is the most obvious sign of muscular dysfunction in affected horses, many other clinical signs related to skeletal muscle dysfunction are possible. The underlying cause of this metabolic disorder is not yet known but is thought to involve carbohydrate metabolism.[4] Therapy employing dietary change and regular exercise has proven to be successful in most horses. This review includes the author's experience and pertinent literature regarding diagnosis and successful treatment of this common disorder.

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SIGNALMENT AND HISTORY

The common clinical signs in various breeds are summarized in the Table. A study of 250 affected horses found that EPSM and many of its associated clinical manifestations occur with equal frequency in males and females. However, exertional rhabdomyolysis is more common in females with EPSM, whereas the abnormal hind limb action characteristic of "shivers" is more common in males.[4] Although considered an inherited disorder, clinical signs may not be apparent for many years. To date, age of onset of obvious clinical signs has ranged from 3 months[5] to 29 years of age. Quarter Horse, warmblood, Arabian, and draft-related breeds appear to have the highest incidence of this disorder; however, it is thought that any breed of horse, pony, or mule can be affected.

In addition to, or instead of, signs of recurrent exertional rhabdomyolysis, owners may report a lack of energy, poor performance, trembling after exercise, exercise intolerance, unwillingness to move in a forward manner, difficulty generating a smooth and balanced canter, difficulty backing or reluctance to back, behavior or attitude problems under saddle or in harness, back soreness, difficulty or unwillingness to lift feet for hoof care, weakness of the hind limbs, abnormal hind limb gait, loss of muscle or poor muscling (especially in the rear), and episodes of mild "spasmodic" colic. An overall stiff gait, sometimes described as a "pony gait," may or may not be recognized as abnormal. Similarly, a low energy level may or may not be recognized as abnormal in a draft-related horse. The most common presentation in miniature horses is poor muscling and low energy associated with persistent mild to moderate increases in serum muscle enzyme levels and occurs most often in young adults.

Sudden onset of weakness, muscle atrophy, exertional rhabdomyolysis, or mechanical lameness can occur without obvious previous problems. But careful questioning of the owner may reveal a history of subtle problems suggestive of muscle dysfunction. Onset of

Table Summary of clinical and clinicopathologic findings of equine polysaccharide storage myopathy in various breeds

Breed	Common clinical signs (in roughly decreasing order)	CK/AST
Draft related	Abnormal hind limb gait Poor muscling, either rump and topline or generalized Poor performance/lack of energy Exercise intolerance Severe rhabdomyolysis Spontaneous recumbency with inability to rise Episodic "colic"	Usually normal to slightly increased Markedly increased associated with severe rhabdomyolysis AST >500 U/L is suggestive of equine polysaccharide storage myopathy
Quarter Horse related	Exertional rhabdomyolysis Abnormal hind limb gait Attitude problems under saddle Poor performance/lack of energy Back soreness Episodic "colic" Generalized muscle atrophy	Can be very high in horses with exertional rhabdomyolysis, especially when obtained 4–6 hours after exercise Will be normal or only slightly increased in horses with other manifestions
Warmblood	Poor performance/lack of energy Attitude problems under saddle Back soreness Abnormal hind limb gait Exertional rhabdomyolysis Episodic "colic"	As for Quarter Horse related
Arabian	Exertional rhabdomyolysis Poor performance/lack of energy Abnormal hind limb gait	As for Quarter Horse related
Thoroughbred and Standardbred	Exertional rhabdomyolysis Poor muscling/generalized muscle atrophy Abnormal hind limb gait Attitude problems under saddle (Thoroughbred)	As for Quarter Horse related
American miniature (young adults)	Poor muscling Lack of energy	Persistent mild to moderate increase
Other breeds	Any or all of the above	Any or all of the above

CK, Creatine kinase; AST, aspartate amino transferase.

signs can also be associated with a change in feed or exercise intensity or can occur after an illness, injury, or other stress. In particular, exposure to *Streptococcus equi* or other respiratory pathogens can precipitate a severe bout of rhabdomyolysis in EPSM horses, often followed by rapid generalized muscle atrophy.

PHYSICAL EXAMINATION FINDINGS

Horses examined during episodes of exertional rhabdomyolysis will exhibit typical signs of reluctance to move, distress, and anxiety. Signs are often associated with tense to overtly swollen muscles, particularly of the rump and thigh.

Other, less obvious signs of myopathy include sensitivity to pressure applied to the region of the insertion of the semimembranosus and semitendinosus muscles or to the muscles of the back. The hind limb gait at the walk or trot may be slightly stiff or exhibit a mechanical lameness that can be asymmetric. Mechanical lamenesses associated with EPSM include shivers, a locking stifle, a mildly "stringy"-type gait, and a mild fibrotic myopathy–type gait.[6] The pelvic limb stride may be slightly short and "stabby," or it may be long but with little hock and stifle action, appearing as more of a swing from the hip joint. From behind, the gait may resemble a "goose waddle."

Neurologic examination can reveal evidence of hind limb weakness, including decreased resistance to a tail pull, especially while standing. Stumbling in the forelimbs or hind limbs, and pivoting on a hind limb during turns, can also be seen. But there is no evidence of pro-

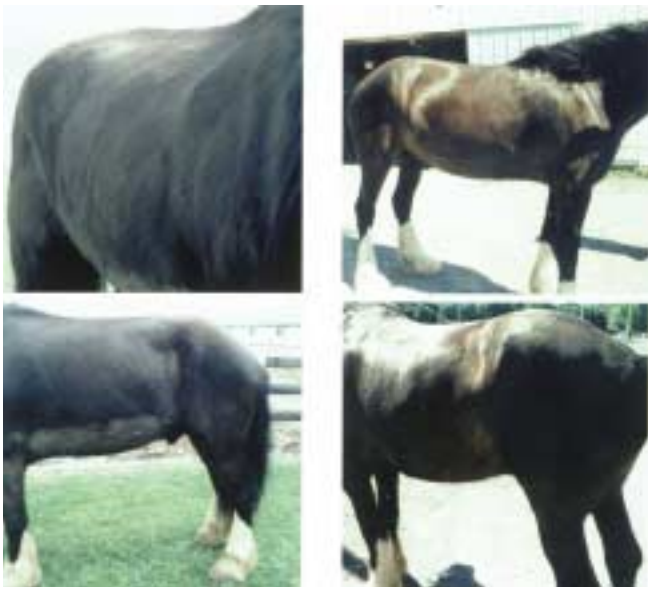

Figure 1. Muscle mass in a 7-year-old Shire gelding with EPSM before (*left*) and after (*right*) 4 months of dietary therapy.

prioceptive deficits or ataxia. Horses with weakness and/or mechanical lameness due to EPSM can be very difficult to distinguish from horses with neurologic deficits.

Body condition varies from overconditioned to wasted. Symmetrical muscle atrophy is often most obvious in the rump and topline (Fig 1). Muscle atrophy can also include the shoulder region or be generalized. Atrophy can be subtle to severe and is not a consistent feature. Post-anesthetic myopathy and post-anesthetic hyperthermia (hypermetabolic syndrome) have also been linked to underlying EPSM.[7]

LABORATORY FINDINGS

Clinical Pathology

Common clinicopathologic findings are summarized in the Table. Serum levels of creatine kinase (CK), aspartate amino transferase (AST), and lactate dehydrogenase (LDH) can be mildly to markedly increased, particularly in samples obtained after clinical exertional rhabdomyolysis or 4 to 6 hours after exercise. Post-exercise CK levels >1000 U/L are most common in EPSM horses that are prone to exertional rhabdomyolysis. Persistent high CK and AST levels can also occur. But muscle can be dysfunctional (ie, weak, painful, crampy, or stiff) without undergoing overt necrosis, and normal levels of these enzymes do not rule out EPSM. Laboratory normal ranges for equine muscle enzymes vary considerably, but the author considers the following to be acceptable high-normal values:

CK: 350 U/L
AST: 425 U/L
LDH: 450 U/L

Given the very short half-life of CK in serum, increased serum activity of AST and/or LDH may be the most prominent finding. Even a low-level increase in any of these enzymes can be significant, particularly in a draft-related breed. An AST >500 U/L in any draft-related horse is strongly suggestive of EPSM.[8]

Mild anemia is another common finding in EPSM horses and may be mistaken for the cause of poor performance or exercise intolerance. This finding may reflect anemia associated with chronic disease, as values generally return to normal with dietary therapy.

Selenium and Vitamin E

Levels of selenium and vitamin E are often evaluated in horses with exertional rhabdomyolysis, but deficiency of either of these antioxidants is not considered a primary cause. Horses with EPSM that are also selenium or vitamin E deficient may, however, exhibit more frequent and/or more severe signs of exertional rhabdomyolysis owing to oxidative injury incited by release of free radicals from damaged muscle cell membranes. Adequate levels of selenium and vitamin E are therefore considered an important part of therapy.

If testing is performed, whole blood selenium analysis is preferred over serum selenium analysis. Vitamin E analysis is performed on serum. Some horses with EPSM have had persistently low blood selenium values, even after high levels of selenium supplementation (up to 6 mg/day). After institution of dietary therapy for EPSM, blood selenium values in such horses have returned to normal with a minimal daily selenium supplementation of 1 mg per 454 kg (1000 lb). This suggests that low blood selenium concentration is a secondary phenomenon, possibly related to repeated or ongoing muscle necrosis.

Thyroid Function Testing

There is no evidence to suggest that thyroid dysfunction can lead to exertional rhabdomyolysis in horses. However, low serum levels of thyroid hormone can be seen in EPSM horses. In some cases, this may be due to previous therapy with nonsteroidal anti-inflammatory medication. There may also be concurrent pituitary dysfunction. In others, low thyroid hormone levels may re-

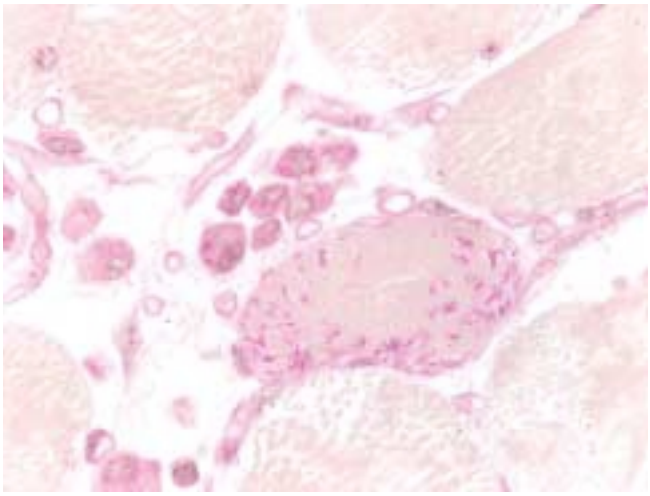

Figure 2. Multiple intracytoplasmic aggregates of complex polysaccharide in muscle from a 7-year-old Arabian broodmare with a history of "tying up" while on pasture. Adjacent macrophages containing similar material are indicative of prior myofiber breakdown. Periodic acid–Schiff stain for glycogen.

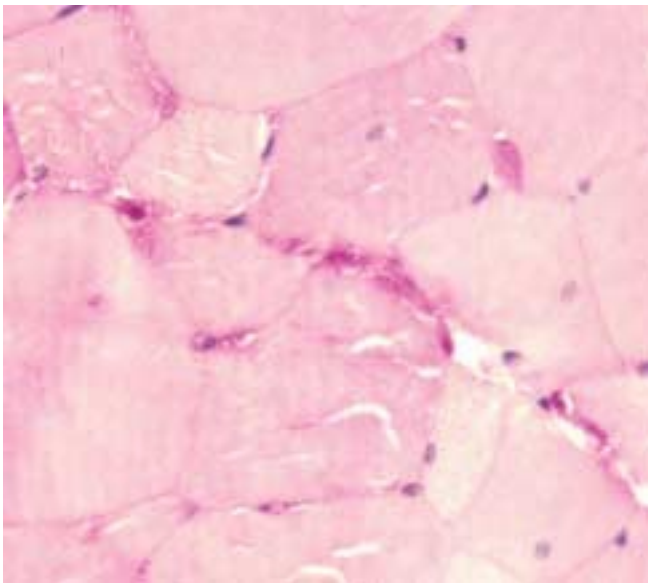

Figure 3. Peripheral aggregates of glycogen in muscle from an aged Clydesdale gelding with a history of "shivers." Abnormal variation in fiber size and increase in internal nuclei are also evident. Periodic acid–Schiff stain for glycogen.

flect underlying EPSM as a manifestation of "sick euthyroid" syndrome. In the author's experience, thyroid supplementation is rarely indicated in EPSM horses.

MUSCLE BIOPSY

Response to therapy can be considered a good indicator of EPSM, but evaluation of a muscle biopsy will most often provide a definitive diagnosis.[2] Abnormal subsarcolemmal to intracytoplasmic aggregates of amylase-resistant complex polysaccharide (Fig 2) and/or amylase-sensitive glycogen (Fig 3) are characteristic findings with periodic acid–Schiff stain. Determining the nature and degree of changes may have some predictive value regarding ease of control with diet change and exercise. But the degree of pathologic change does not always correlate with the severity of clinical signs.

Characteristic muscle biopsy changes are not present in young EPSM horses, despite clinicopathologic evidence of exercise-induced muscle injury.[9] Therefore, false negative results are possible in young horses. Pathologic changes in muscle are thought to increase with age. Abnormal polysaccharide storage is still evident years after complete recovery with diet change and exercise (BA Valentine, unpublished observation). These findings suggest that the polysaccharide storage is not the primary cause of the clinical signs, but rather reflects an underlying metabolic "difference." Although as yet unproven, therapy is thought to halt or slow the development of progressive muscle changes.

Although submission of an unfixed muscle sample for frozen section histochemistry is often preferred for muscle histopathology, the following procedure for formalin fixed muscle samples has proven to provide diagnostic samples when submitted to a veterinary pathologist with experience in interpretation of formalin fixed equine muscle. Handling and mailing of formalin fixed samples is less expensive and more convenient than submission of unfixed samples for frozen section.

Muscle biopsy is performed with the horse standing, using sedation and local anesthesia. Semitendinosus or semimembranosus are the preferred muscles to sample. The ideal site is between the base of the tail and the tuber ischium. A more medial site in the semimembranosus muscle may allow the scar to be obscured by tail hairs. Local anesthesia can be achieved with an inverted L block or a line block. If a line block is used, take care to place lidocaine only into the skin, subcutis, and fascia and not into the muscle itself. If additional anesthesia of the muscle itself is needed, drip a small amount of lidocaine onto the site. The skin, subcuticular, and fascial (epimysial) incision should be vertical, parallel to the muscle fiber orientation, and approximately 5 cm long. A

similar incision is made into the underlying muscle belly. Bleeding is usually minimal and is controlled with routine hemostasis. Using curved scissors or a hemostat, undermine the incision to create a strip of muscle approximately 3 to 4 cm long in which the dorsal and ventral ends are still attached. Handle the muscle gently, taking care to grasp only the ends of the strip with forceps. Cutting the muscle fibers transversely before undermining a strip will result in uneven contraction and difficulty in orientation for histopathology. Once the strip has been isolated, transection of the ends results in a strip of muscle with longitudinally arranged muscle fibers. This strip should be no more than 1 cm in diameter. If thicker, sagittally section the sample to obtain 2 smaller-diameter strips. Place the muscle sample or samples onto portions of a wooden tongue depressor and tie or pin the ends. Do not stretch the sample. This procedure minimizes contraction artifact and allows for proper orientation of sections for histopathology. Place the sample or samples into an adequate volume of formalin—a blood collection tube generally does not provide adequate fixation, nor do nonformalin fixatives. Closure includes the fascia (epimysium), subcutis, and skin. Placement of a gauze stent over the incision may aid in reduction of suture breakdown. Post-operative antibiotic therapy is generally not necessary, and stall confinement is contraindicated.

Formalin fixed samples are welcomed at the Oregon State University Veterinary Diagnostic Laboratory in Corvallis, Oregon, and will be interpreted by the author. Turnaround time is a week or less, and current cost is $58.

DIFFERENTIAL DIAGNOSES

Given the wide range of clinical signs of EPSM, other disorders with similar signs should also be considered.

Horses with muscle atrophy and abnormal hind limb gait due to EPSM are often misdiagnosed as having equine protozoal myeloencephalitis (EPM). At this time, the only reliable test for EPM is a careful neurologic evaluation for evidence of cranial nerve deficits and proprioceptive deficits resulting in ataxia. Hind limb weakness and awkward gait are not, in and of themselves, necessarily indicative of ataxia. In any case in which the neurologic evaluation results in a degree of uncertainty regarding evidence of ataxia, referral of the horse or of a videotape of the neurologic examination to an expert in equine clinical neurologic disease is advised. Severe asymmetric muscle atrophy is a hallmark of EPM, whereas the atrophy of EPSM is typically symmetric and varies from subtle to severe. A negative Western blot on serum or cerebrospinal fluid effectively rules out EPM; however, a positive Western blot, even on cerebrospinal fluid, may or may not indicate protozoal disease.

Equine motor neuron disease (EMND) will also result in overall muscle atrophy and weakness, with increased time spent in recumbency. Horses with EMND often have slightly increased serum levels of CK and/or AST. Similar to EPSM horses with generalized wasting and weakness, EMND horses typically have a normal appetite. Horses with EMND have very low serum levels of vitamin E, typically less than 1 μg/dL, owing to lack of grass pasture, alfalfa, or other legume products or vitamin E supplementation in the diet. Confirmation of EMND is best made by histopathologic evaluation of a biopsy of the sacrocaudalis dorsalis medialis muscle, which is present on either side of midline on the caudal rump just proximal to the base of the tail.[2]

Equine Cushing's disease typically occurs in older horses and can result in overall muscle atrophy and weakness. Affected horses may or may not have other signs such as laminitis, hirsutism, and polyuria/polydypsia. Appropriate testing for pituitary dysfunction is needed for diagnosis.

Episodic muscle pain due to EPSM can appear similar to episodic "spasmodic" colic. Episodes often occur after exercise or turnout. It is also possible that alteration in gastrointestinal motility can occur secondary to muscle pain in EPSM horses. Careful evaluation of gastrointestinal function, muscle palpation, and evaluation of serum levels of AST and CK will aid in the differentiation of true colic and episodic muscle pain. A horse with colic that is not down and thrashing sufficiently to cause muscle injury should have normal CK and AST values.

Horses with gastric ulcers can have a history of poor performance and/or attitude problems similar to horses with EPSM. Horses with gastric ulcers are often off feed, which is relatively uncommon in horses with EPSM. Gastric ulcers should be confirmed by endoscopic examination.

Hyperkalemic periodic paralysis (HYPP) occurs in horses of the Impressive Quarter Horse line. Episodic trembling, often followed by transient collapse, can mimic EPSM. Muscle enzyme levels are generally normal in HYPP horses, and DNA testing of mane or tail hairs provides a definitive diagnosis. Horses with HYPP can also have EPSM, making diagnosis particularly challenging.

Severe selenium deficiency (serum or whole blood selenium less than 10 mg/dL) can cause degenerative myopathy in horses. This is most often seen in foals ("white muscle disease"), but it can occur in adult horses of any age. Adults with selenium deficiency myopathy can present in recumbency due to severe diffuse acute myode-

generation, or with preferential involvement of masticatory muscles, causing bilateral swelling or atrophy and difficulty chewing and swallowing. Myotoxins in the feed (ionophores and toxic plants) can also cause severe acute degenerative myopathy.

The abnormal hind limb gait of shivers due to EPSM can be mistaken for stringhalt. True stringhalt is most often due to peripheral neuropathy. Horses with stringhalt have a characteristic mechanical lameness in which exaggerated upward flexion of one or both hind limbs occurs at every walk step, with the top of the fetlock almost hitting the ventral abdominal wall. The abnormal gait of shivers occurs sporadically, most often while backing, while turning in tight circles, in the first walk stride after standing, in the last walk stride before halting, and while standing still or having hind feet lifted. The action of shivers does not include the cranial motion and adduction of stringhalt.[6] A sudden onset of severe hyperflexion and "locking up" of both hind limbs can occur because of EPSM and can be mistaken for atypical stringhalt. This is especially true in the Pacific Northwest, where the plant *Hypochaeris radicata* (flatweed, false dandelion, hairy cat's ear) is associated with outbreaks of true stringhalt.

Depending on the clinical signs, intestinal malabsorption, laminitis, painful lameness, or renal, hepatic, or cardiac disease should also be ruled out by appropriate testing.

TREATMENT

Appropriate treatment can alleviate clinical signs and prevent recurrence. This disorder is progressive, and early diagnosis and institution of therapy are vital.

Exertional Rhabdomyolysis

Anti-inflammatory medication is indicated in most cases of exertional rhabdomyolysis, and acepromazine is also useful. Depending on the severity, intravenous fluid therapy may be indicated. Stall rest should be maintained only while the horse is uncomfortable and unwilling to move. Do not wait until muscle enzyme levels return to normal to resume turnout or mild exercise.

Acute Recumbency

In addition to supportive therapy, 480 mL (2 cups) of vegetable-based oil (soy, corn, canola, or other salad-type oil) per 454 kg (1000 lb) of horse per day can be administered through a nasogastric tube or by dose syringe. Sudden introduction of this amount of oil may cause diarrhea, but recumbency due to EPSM is a life-threatening situation. Intravenous lipid emulsions designed for use in total parenteral nutrition can be administered with no apparent side effects, at a rate of 0.2 g per kg slowly over 1 to 2 hours.[10] Intravenous lipid products are available at local hospitals, but they are expensive.

Long-Term Therapy

Diet change to one that is high in fat and fiber and low in starch and sugar is the mainstay of long-term therapy of EPSM. Nutritional analysis indicates that diets containing a minimum of 20% to 25% of total daily calories from fat, and no more than 15% of total daily calories from starch and sugar, are the most effective.[4] This is nutritionally sound advice but is difficult for the average horse owner or veterinarian to put into practice. The following are recommendations that this author has found to be effective: Aim for at least 0.45 kg (1 lb) of fat, which is about 480 mL (2 cups) of vegetable-based oil (any salad-type oil without added chemicals) per 454 kg (1000 lb) of horse per day. Gradually change to the lowest starch and sugar diet that the horse will eat with added fat. Gradually introduce fat into the horse's diet. Start with about 0.05 kg (0.125 lb, or 60 mL of oil) per day, and increase by the same amount every few days. Newer dry fat

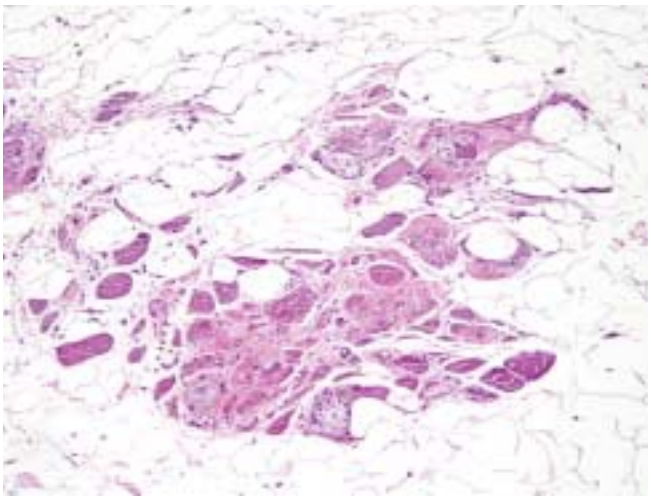

Figure 4. Muscle from an 18-year-old draft-cross mare with a history of sudden onset of recumbency and inability to rise. Severe chronic myopathy has resulted in massive replacement of muscle by adipocytes. Many remaining fibers are distorted by aggregates of pale stained stored glycogen and complex polysaccharide. Hematoxylin and eosin stain.

supplements are also effective, but these products weigh about half of their volume, so twice the volume per day will be required (ie, start with 0.5 cup per feeding and aim to feed at least 4 cups dry fat per 1000 lb of horse per day). A mixture of oil, dry fat, and higher-fat feeds can be used.

In the author's experience, a feed should be at least 10% fat and also formulated to be low in starch and sugar before the fat in the feed can be calculated into the total daily fat intake. For example, rice bran with 20% fat will provide $1 \times 0.20 = 0.2$ lb of fat per pound. Rice bran does contain some starch and sugar, though, so 5 lb of rice bran, which contains 1 lb of fat, is not equivalent to 2 cups of oil. Despite some manufacturers' advice to the contrary, rice bran products can be mixed with oils to achieve the proper fat intake. Many lower-starch, lower-sugar feeds are now available, varying from pure forage products such as alfalfa, other hay products, and beet pulp to complete feeds and specially formulated high-fiber, low-starch, low-sugar feeds. The owner should be advised to feed the horse whatever combination of feeds and fat supplements that he or she is happy to buy and that the horse is happy to eat. The amount of base feed should be the minimum that keeps the horse eating the right amount of fat and still maintaining good weight.

All horses should be fed an adequate amount of good-quality forage, but the type and amount of forage intake is not critical for most EPSM horses. Either alfalfa or grass hay can be fed, although alfalfa products should be avoided in cases of EPSM horses that also have HYPP. Do not feed oat or other grain hays that contain many seed heads.

There is no proof that horses on high-fat diets require additional dietary vitamin E, but it is this author's opinion that all horses should be supplemented with at least 1 IU vitamin E per pound of horse per day. In selenium-deficient areas, 1 to 2 mg selenium per 454 kg (1000 lb) of horse per day is also important.

Pure forage products are not often fortified with extra vitamins and minerals. Due to the high caloric density of fats (approximately 4 mcal = 4000 cal/lb), owners giving fortified feeds with added fat will likely be feeding less than the manufacturer's recommendations. Growing horses, hardworking horses, and breeding horses will likely need an additional vitamin and mineral supplement. If forage quality is good, this additional supplementation may not be necessary for adult horses on a moderate work schedule.

Exercise, even if it is just turnout, is the other important part of therapy. Once horses have started on diet change, this author has no specific exercise conditioning protocol. Owners are advised to let the horse be their guide as to how much exercise is too much. Many owners of EPSM horses are quite sensitive to subtle signs of a problem. If the horse exhibits discomfort or stiffness during or after exercise, the owner is advised to provide only turnout for 1 to 2 days and then resume exercise conditioning.

Horses that gain unwanted weight or that are overweight to start with should be fed the minimum amount of forage (but no less than 1% of total body weight in forage per day), and fat supplementation should consist of 100% fat sources such as oil or dry fat supplements added to a forage-based feed. Oil can also be poured onto hay, although it will be more difficult to monitor intake.

Confinement to a stall is not advised for EPSM horses. For horses confined owing to illness or injury, maintenance of as high a fat level in the diet as possible may provide some protection from the ill effects of lack of exercise.

Additional Therapy

It is possible that massage and physical therapy may benefit an EPSM horse, especially early on in dietary therapy. Some owners report improvement in horses with locking stifle problems after estrogen injection. If the veterinarian or owner feels strongly that other treatments, such as methylsulfonylmethane, baking soda, ginseng,

thyroid supplementation, or other therapy, have had some positive impact on the horse's condition, these do not interfere with diet therapy. Therefore, if veterinarians or owners are reluctant to stop such therapy, they may be continued. Ideally, if control of clinical signs is achieved after 4 or more months of diet change, these other treatments can be discontinued. However, horses should gradually be weaned off thyroid supplementation.

Response to Treatment

It will take approximately 4 months for full-fat adaptation in these horses.[4] Horses that show any signs of improvement during the first 4 months of diet change, even if episodes of muscle dysfunction still occur during this time, are likely to respond well to continued therapy. Response can occur within 1 to 2 months of dietary change. Positive signs include increased energy, better attitude, and improvement in gaits. Improved muscling is often seen within 2 to 4 months of diet change (Fig 1). Many horses with exertional rhabdomyolysis, exercise intolerance, or poor performance typically improve markedly after 4 or more months of diet change. For horses with exertional rhabdomyolysis that are responding well to dietary therapy, repeat analysis of serum CK and AST after 4 months of diet therapy should reveal significant reduction in exercise-induced muscle injury.[11] However, evaluation of post-exercise CK and AST in the first months of dietary therapy may reveal levels even higher than those obtained before diet change, even though the horse may appear to have improved. The exact cause of this observation is not known, although it may reflect the fact that horses are more active but are not yet fully fat adapted at this time.[12] This may be at least part of the explanation for the common observation of recurrence of clinical signs early on in diet therapy, especially at 2 to 4 months, in horses showing initial improvement.

A few horses will exhibit markedly increased energy levels in the first few months of diet change. These horses are often described by owners as "bouncing off the walls." As dietary fat has been shown to calm anxious horses,[13] it is thought that this high energy level reflects changes associated with fat use in horses previously "deprived of energy." Plenty of turnout and less demanding training during the first few months are advised for these horses. Such horses generally "settle down" with time, and only rare EPSM horses have been described as unmanageable after 4 months of diet change. For unmanageable horses, reduction in all feed, especially nonfat components, to decrease total daily calorie intake is often beneficial.

If clinical signs recur after apparent control, careful evaluation of husbandry for changes in diet that have resulted in decreased total daily fat intake is indicated. Decreased exercise can also result in recurrence of signs. Resumption of a higher level of dietary fat and exercise should result in regained control of clinical signs. Some horses are particularly sensitive to the increased sugar content of spring grass. For these horses, for "easy keeper" horses, and for horses prone to laminitis, a grazing muzzle to reduce grass intake but still allow pasture exercise can be useful.

PROGNOSIS

Improvement can continue for many months after the first 4 months of diet change. Back soreness due to EPSM may persist longer than other signs. Horses with shivers due to EPSM most often still show some signs of the problem, even after 6 months or more of diet change, and may require more aggressive dietary and exercise therapy than horses with other manifestations. Given that shivers is a progressive disorder, even if therapy only halts or slows progression, this is beneficial.

Therapy for horses with a large amount of amylase-resistant material should be aggressive, but therapy may not be able to restore muscle function sufficiently to allow for high-level performance. Some horses with severe muscle changes may still have occasional episodes of exertional rhabdomyolysis. For many horses, however, even those with severe muscle changes, complete control of exertional rhabdomyolysis and other clinical signs is possible.

Draft-related breeds with spontaneous recumbency and inability to rise are critically ill and require aggressive supportive, dietary, and exercise therapy. Affected drafts in which muscle biopsy reveals severe replacement of muscle by adipose tissue (Fig 4) have a poor prognosis. The first 4 months of diet change are the most critical. Some such horses have shown initial improvement, only to relapse into recumbency at 3 to 4 months after diet change. Approximately 50% of these horses survive the initial 4-month period. If the horse shows improvement and is continuing to improve after 4 months of therapy, the prognosis for recovery is good.

DISCUSSION

Findings in muscle from horses with EPSM suggest an abnormality in carbohydrate metabolism. Despite extensive study, however, no alterations in enzymatic pathways involved in glycolysis, glycogenolysis,[14,15] or glycogen synthesis have been detected. During exercise, EPSM horses do not develop lactic acidosis and there is no abnormality in glycogen use.[16] The failure to detect an enzyme defect in horses with EPSM makes this equine disorder unique, and the exact cause is still unknown.

Autosomal recessive inheritance has been suggested in Quarter Horses.[17] But the occurrence of EPSM in crossbreeds, including a draft mule,[8] suggests that a form of dominant inheritance is more likely. The incidence of EPSM varies among breeds. An astonishing incidence of 66% has been reported in draft-related breeds, based on postmortem evaluation of muscle.[8] A similar incidence has been detected in antemortem studies of groups of draft horses in the United States, Canada, and France (BA Valentine, unpublished observations). The incidence in light horse breeds is currently under study but appears to be approximately 33% in postmortem muscle samples.[18] Interestingly, EPSM often occurs in high-performance lines of many breeds of horses, and it is possible that we have actually selected for this type of metabolism as we selected for bigger horses with better muscling and improved performance. This author has come to consider EPSM horses to be "metabolically different" rather than metabolically impaired.

It has been suggested that recurrent exertional rhabdomyolysis in Thoroughbreds may occur because of a muscle calcium handling defect.[19] But pathognomonic findings of EPSM have also been detected in registered Thoroughbreds with recurrent exertional rhabdomyolysis (BA Valentine, unpublished observation), suggesting that more than 1 cause or factor may be involved in exertional rhabdomyolysis in this breed. Fortunately, regardless of the underlying cause, affected Thoroughbreds also respond to a high-fat, high-fiber, low-starch, low-sugar diet along with as much exercise as possible.[4,11,20]

It could be argued that the significance of abnormal glycogen and complex polysaccharide storage in horses examined at necropsy, in which myopathy is only occasionally related to death, is questionable. If so, it would mean rewriting pathology texts to describe such findings as abnormal in every species other than the horse. If indeed at least one-third of all horses are "metabolically different," attempting to breed away from this problem would be difficult. Alternatively, this type of metabolism in the horse may be more normal than not. The tradition of feeding starch-based concentrates to horses has been based on human convenience, not on equine muscle physiology. Particularly intriguing is the recent report of expression of membrane fatty acid transporters in all skeletal muscle fiber types of resting equine muscle.[21] Normal or not, as the effects of this type of metabolism can most often be controlled with relatively simple changes in husbandry, this seems the most prudent approach. Perhaps, like feline dilated cardiomyopathy, we might find a much lower incidence of a wide range of clinical disorders in horses if we just fed them right.

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