

Polysaccharide Storage Myopathy (PSSM) in horses

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1. What is polysaccharide storage myopathy (PSSM) in horses?

Several different acronyms have been used to describe this disorder including PSSM, EPSM and EPSSM. The variety of acronyms used are in part related to preferences of different laboratories, as well as to differences in the criteria used to diagnose polysaccharide storage myopathy. .

PSSM is a muscle disease in horses with Quarter Horse bloodlines such as Quarter Horses, American Paint Horses and Appaloosas. The American Quarter Horse Association (AQHA) has funded research into this disease since 1995 and has provided us with the opportunity to learn much about the diagnosis, cause and treatment for this disease.

Polysaccharide storage myopathy also occurs in many other breeds including Drafts, Draft crossbreeds, and warmbloods. Many of the clinical signs in these breeds differ from those found in Quarter Horses and related breeds. The signs found in Draft, Draft crossbreeds, and warmbloods include muscle soreness, reluctance to engage the hind quarters muscle atrophy, and weakness.

There are two different types of PSSM found in horses, Type 1 and Type 2. Type 1 is found in over 20 breeds and commonly affects Quarter Horses, Quarter Horse-related breeds, Morgans, some Draft breeds and some warmbloods. Type 2 PSSM is found in Quarter Horses, Arabians, Thoroughbreds and potentially other light breeds. The Draft breeds affected by Type 1 PSSM are Belgians, Percherons and many Continental European Draft breeds. A high percentage of Continental European Draft breeds (62%) were found to carry the mutation responsible for Type 1 PSSM. The mutation that causes Type 1 PSSM is found in very low prevalence in Shires and Clydesdales, which are of British and Scottish origin, possibly indicating a greater genetic difference between these breeds and mainland European breeds (and their descendants). However, Type 1 PSSM is not neatly geographically distributed in the United States or Europe.

The following table describes the number of randomly samples horses that tested positive for the PSSM1 mutation out of the total number of horses tested as well as the % of horses that were positive for the mutation (prevalence).

Number with PSSM1 Prevalence

QH	22/335	6.6
Paint	15/195	7.7
Appaloosa	9/152	5.9
Morgan	2/214	0.9
Percheron	93/149	62%
Belgian	58/149	39%
Shire	1/195	0.5%
Clydesdale	0/48	0
Belgian draught	34/37	92
Trekpaard	17/23	74
Comtois	70/88	80
Breton	32/51	63

The prevalence of PSSM1 1 in various Quarter Horse performance types

Quarter Horse type Percent positive for PSSM1
AQHA 11.3
Paint 4.5
Halter 28.2
Western Pleasure 8.6
Cutting 6.7
Reining 4.3
Western cow 5.7
Barrel racing 1.4
Racing 2.0

2. What are the signs of PSSM in horses?

Horses with both forms of PSSM have signs typically associated with tying-up. These signs are most commonly muscle stiffness, sweating, and reluctance to move. The signs are most often seen in horses when they are put into initial training or after a lay-up period when they receive little active turn-out. Episodes usually begin after very light exercise such as 10-20 minutes of walking and trotting. Horses with PSSM can exhibit symptoms without exercise.

During an episode, horses seem lazy, have a shifting lameness, tense up their abdomen, and develop tremors in their flank area. When horses stop moving they may stretch out as if to urinate. They are painful, stiff, sweat profusely, and have firm hard muscles, particularly over their hindquarters. Some horses will try pawing and rolling immediately after exercise. Most horses with PSSM have a history of numerous episodes of muscle stiffness at the commencement of training; however, mildly affected horses may have only one or two episodes/year.

Rarely, episodes of muscle pain and stiffness can be quite severe, resulting in a horse being unable to stand and being uncomfortable even when lying down. The urine in such horses is often coffee coloured, due to muscle proteins being released into the bloodstream and passed into the urine. This is a serious situation, as it can damage the horse's kidneys if they become dehydrated.

Very young foals with PSSM occasionally show signs of severe muscle pain and weakness. This occurs more often if they have a concurrent infection such as pneumonia or diarrhea. Some weanlings and yearlings, particularly those with type 2 PSSM can develop muscle stiffness with daily activities and difficulty rising.

3. What causes PSSM in horses?

Polysaccharide storage myopathy (PSSM) is characterized by the abnormal accumulation of the normal form of sugar stored in muscle (glycogen) as well as an abnormal form of sugar (polysaccharide) in muscle tissue. Thousands of horses have been identified with tying-up associated with polysaccharide accumulation in muscles. There are two forms Type 1 and Type 2 PSSM. We know that both are the result of the accumulation of muscle glycogen which is the storage form of glucose in muscles.

Type 1 PSSM is caused by a mutation in the GYS1 gene. The mutation causing PSSM is a point mutation on the GYS1 gene which codes for the skeletal muscle form of the glycogen synthase enzyme. The cause of Type 2 PSSM has yet to be identified. Both types have an abnormal type of glycogen staining in muscle biopsies, and the types can be distinguished by genetic testing. Horses with Type 2 PSSM lack the mutation that is specific for Type 1 PSSM. At

present there is not a specific genetic test for type 2 PSSM and we do not have conclusive evidence that it is inherited.

Carbohydrates that are high in starch, such as sweet feed, corn, wheat, oats, barley, and molasses, appear to exacerbate type 1 and type 2 PSSM. That is why they should be avoided and extra calories can be provided in the form of fat. An important part of the management of PSSM horses is daily exercise. This enhances glucose utilization, and improves energy metabolism in skeletal muscle. If only the diet is changed, we found that approximately 50% of horses improve. If both diet and exercise are altered, then 90% of horses have had no or few episodes of tying-up.

An old theory about tying-up is that it is due to too much lactic acid in the muscle. Many exercise studies have proven that this is absolutely not the case with PSSM. PSSM is actually a glycogen storage disease and there are several diseases in other species and in human beings that also result in the storage of too much glycogen in skeletal muscle. In these other diseases, glycogen accumulates because the muscle lacks an enzyme (protein) necessary to burn glycogen as an energy source. These similarities led us to test PSSM horses for the disorders in glycogen metabolism identified in human beings. We found that PSSM is a unique glycogen storage disease because the PSSM horses have all the necessary enzymes to burn glycogen as a fuel in their muscles. With exercise, PSSM horses show the expected decrease in muscle glycogen as it is burned as fuel.

The unique feature of PSSM is that the muscle cells in PSSM horses remove sugar from the blood stream and transported into their muscle at a faster rate, and make more glycogen than normal horses. Our recent research shows that the reason for this is that PSSM muscles are very sensitive to insulin beginning as early as 6 months of age. Insulin is a hormone released by the pancreas into the bloodstream in response to a carbohydrate meal. It stimulates the muscle to take up sugar from the bloodstream. Once inside the cell the muscle's of PSSM horses make much more glycogen than a normal horse due to an overactive enzyme called glycogen synthase in the case of type 1 PSSM.

4. What should I do if a horse is stiff and reluctant to move?

- Stop exercising the horse and move it to a box stall. Do not force the horse to walk.
- Call your veterinarian.
- Blanket the horse if weather is cool. Hose the horse to remove sweat if the weather is warm.
- Determine if the horse is dehydrated, due to excessive sweating. Pinched skin will normally spring back and saliva should be wet, not tacky.
- Provide fluids: small frequent sips of water. Electrolytes (potassium, sodium, and chlorine) may be added to drinking water, if palatable to the horse. Plain water should always be available as an alternative. If the horse is dehydrated, intravenous fluids may be needed. Once cool, the horse may have free access to water.
- Relieve anxiety and pain. Your veterinarian may administer drugs such as acepromazine and flunixin meglumine (Banamine).
- Remove grain. Feed only hay until symptoms subside.
- Provide small paddock turnout once the horse walks freely, usually in 12-24 hours.

5. Does PSSM differ from HYPP in horses?

Hyperkalemic periodic paralysis HYPP is a completely separate muscle disorder in Quarter Horses from PSSM. The two diseases have different clinical signs, different causes and different treatments.

6. How do I know if my horse is having an episode of tying-up? (not PSSM testing)

A blood sample can be used to determine what is happening inside your horse's muscles. Proteins measured in a blood sample can determine the extent of the muscle damage.

Two muscle proteins often used as a measure of muscle damage include creatine kinase (CK) and aspartate transaminase (AST). When muscle cells are damaged, they release these proteins into the bloodstream within hours. A blood sample taken to measure these proteins can determine how much muscle damage has occurred. This is not a specific test for PSSM as the presence of CK and AST in the blood occurs with any muscle damage. With many forms of tying-up, blood CK activity returns to normal within days if horses are rested. It is very common for horses with PSSM to have high CK activities even if they are rested for weeks after an episode of tying-up.

7. What if the episode occurred weeks ago and I want to know if my horse is susceptible to tying-up?

One way to see if tying-up occurs is to do an exercise test. This is useful if a horse shows no signs of muscle stiffness when a veterinarian performs a physical exam but still suspects the horse suffers from a form of tying-up. The horse should be worked in a round pen at a walk and trot for 15 minutes. If the horse shows any signs of persistent muscle stiffness, the test should stop. The idea here is not to produce signs of stiffness, but to see if this mild form of exercise causes slight muscle damage. In cooperation with your veterinarian, have a blood sample drawn 4-6 hours after the exercise test. A significant result indicating sub clinical muscle damage would be a serum CK activity greater than 800 U/L 4 hours after 15 minutes of exercise at a trot. The blood sample is not informative if taken right after exercise, as the CK protein has not had enough time to leak out of the muscle cells. **This test is not specific for PSSM, but does indicate muscle damage is occurring with exercise.**

8. Can my horse's muscles heal after an episode of tying-up?

Muscle has a remarkable ability to repair itself. After an episode of tying-up, the muscle cells usually heal completely within three to four weeks without any scarring. If the damage is severe, you may notice that the horse's muscle mass decreases in size as the body removes the damaged proteins. The muscle mass usually returns within two to four months.

9. How is a diagnosis of PSSM established?

Currently, PSSM type 1 can be diagnosed with a genetic test, however, at present PSSM type 2 must be diagnosed with a muscle biopsy. Which test is most appropriate depends on the breed of your horse.

Genetic Testing

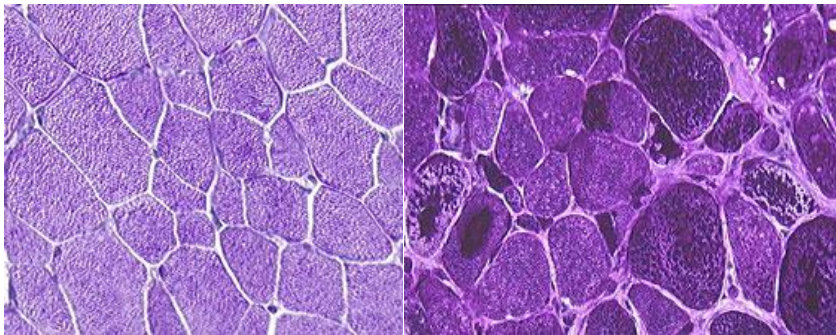
Submission information for genetic testing for PSSM type 1 is available. We strongly recommend your veterinarian be involved in genetic testing. We cannot make anything more than general recommendations about the disease as we have not evaluated your horse to know if there are any concurrent problems that would make our diet or exercise recommendations contraindicated.

Muscle Biopsy

Veterinarians can obtain instructions on how to perform a muscle biopsy by calling 1-800-605-8787. The sample must be specially prepared and shipped overnight to our laboratory. Results are usually available within 10 days.

The sample is taken from the semimembranosus muscle, which is part of the rear limb hamstring muscles. Sections of muscle are evaluated with a number of special stains. The periodic acid Schiff's (PAS) stain is used to look at the amount of sugar stored as glycogen in the muscle. With PSSM, the intensity of this stain is very dark indicating a large amount of glycogen is present in the horse's muscle. Measurements of glycogen are usually 1.5 to 4 X higher than normal horses. A large amount of glycogen, however, is not uncommon in trained horses, and not a basis for diagnosing PSSM. In addition to storing excessive normal glycogen, horses with PSSM have deep purple inclusions of an abnormal complex sugar stored in fibers. This is the classic diagnostic feature of PSSM muscle.

Biopsies are often graded as mild, moderate or severe based on the amount of abnormal polysaccharide. The abnormal polysaccharide always remains within the muscle tissues and does not decrease in amount over time.



A normal biopsy (left) and a biopsy from a horse with PSSM (right) stained with PAS. Note the lack of a uniform texture in the PSSM biopsy. The darker areas in the PSSM biopsy indicate the accumulation of excess glycogen and abnormal polysaccharide.

We have observed the accumulation of abnormal polysaccharide in the muscle of PSSM horses from a few months of age; however, establishing a diagnosis of PSSM in horses less than a year of age can be difficult because they not have developed abnormal polysaccharide yet. To be certain, a biopsy from a foal may have to be repeated at a later age.

Horses with unusually large accumulation of glycogen in muscle cells with a granular appearance are diagnosed with mild PSSM. In this case, the amount of abnormal polysaccharide is considered low, which may be associated with the horse being less than two years of age. In horses older than two, we advise veterinarians to ensure no other lameness issues may be contributing to signs of muscle pain.

Moderate to severe PSSM reflects the degree of accumulation of amylase resistant abnormal polysaccharide. The amount to abnormal polysaccharide does not always match the severity of clinical signs or prognosis.

10. Is PSSM in horses an inherited disease?

PSSM type 1 is inherited as a dominant trait and the mutation has been identified.

Pedigree analysis of PSSM type 2 suggests a familial basis but the genetic mutation for this disease has not yet been identified. .

Researchers at the University of Minnesota performed a small breeding trial to investigate the question of PSSM heritability. We bred mares with PSSM and followed their foals for five years. Many of their foals developed signs of muscle damage after a few months of age and signs of PSSM in muscle biopsies by age two. This research suggests there is strong evidence that PSSM in Quarter Horse-related breeds is inherited, likely as a dominant trait.

At present, evidence suggests that only one parent needs to pass the genetic mutation to its offspring for signs of tying-up to occur. Because this disease causes considerable pain, our laboratory does not recommend breeding horses that have been diagnosed with PSSM. No matter who is selected as the breeding partner there is a 50% chance or greater that a PSSM horse's offspring will develop the disease.

11. Is there a genetic test for PSSM in horses?

Yes there is a DNA test to determine if a horse has the genetic mutation that causes PSSM type 1. Until we know more about the basic cellular mechanism involved in PSSM type 2 we will have difficulty identifying the gene with its mutation. Genetic research into PSSM type 2 is on going.

12. How do I prevent another episode of tying-up in my horse?

Rest: For chronic cases, prolonged rest after an episode appears to be counterproductive and predisposes PSSM horses to further episodes of muscle pain. With PSSM it is NOT advisable to only resume exercise when serum CK activity is normal. Rather, horses should begin small paddock turn out as soon as reluctance to move has abated. Providing daily turn out with compatible companions can be very beneficial as it enhances energy metabolism in PSSM horses. Grazing muzzles may be of benefit to PSSM horses turned out on pastures for periods when grass is particularly lush. Most PSSM horses are calm and not easily stressed, however, if stress is a precipitating fact, stressful environmental elements should be minimized.

Reintroducing exercise: Re-introduction of exercise after an acute episode of ER in PSSM horses needs to be gradual. Important principles include 1) providing adequate time for adaptation to a new diet before commencing exercise (2 weeks), 2) recognizing that the duration of exercise is more important to restrict than the intensity of exercise (no more than 5 min walk/trot to start) 3) ensuring that exercise is gradually introduced and consistently performed and 4) minimizing any days without some form of exercise. Exercise should begin with light slow uncollected work on a longe-line or under saddle beginning with once a day for 3-5 minutes at a walk and trot. This initial work should be very mild and very short in duration. Work at a walk and trot can be gradually increased by two minutes each day. When the horse can exercise for 15 minutes, a five-minute break at a walk can be provided, and then a few intervals of walk and trot can gradually be increased. At least three weeks of walk and trot should precede work at a canter.

Exercise: Regular daily exercise is extremely important for managing horses with PSSM. Even 10 min of exercise has been shown to be extremely beneficial in reducing muscle damage with exercise. Once conditioned, some PSSM horses thrive with 4 days of exercise as long as they receive daily turn out. For riding horses with type 2 PSSM, a prolonged warm-up with adequate stretching is recommended. Rest periods that allow horses to relax and stretch their muscles between 2 – 5 min periods of collection under saddle may be of benefit.

Adherence to a strict diet will also help horses with PSSM.

When designing a diet for horses with PSSM there are several important considerations.

1) **Caloric balance:** Many horses with PSSM are easy keepers and may be overweight at the time of diagnosis. 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.=20

2) **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. This 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).=20

3) **Selection of fat source:** My initial approach would be to get the horse moving comfortably with a low starch/sugar diet and to get the horse into a suitable weight range before adding fat. The type and amount of fat to add depends on the individual horse and on the horse's weight and owner's budget. In an easy keeping horse, when you add fat the cheapest way to do so is to add oil or a solid fat supplement onto a pelleted ration balancer that provides enough energy. Check the caloric density of the ration balancer, you may want to use one for overweight horses. Suitable oils include soybean, corn, safflower, canola, flaxseed, linseed, fish, peanut and coconut. The amount of oil can be added gradually monitoring the horses exercise tolerance and weight. The amount added is usually between 1/2 and 2 cups. Horses with too little fat often have a cranky attitude toward exercise.

Low starch high fat concentrates: These feeds are only suitable if horses are going to consume enough to get a balance of vitamins and minerals as well as some fat. 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. If you feed a product like ReLeve or Ultium you usually need at least 4 lbs to achieve a balanced diet and this may be too many calories in lightly worked overweight horses.(products not available in New Zealand)

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.

Potential rations for a 500-kg horse with polysaccharide storage myopathy.

	Light Exercise	Moderate Exercise	Intense Exercise
FORAGE	7-9 kg quality grass hay or pasture	7-9 kg quality grass hay or pasture	7-9 kg quality grass hay or 20:80 mix alfalfa/grass
PLUS:			
DIET 1*	1.5 kg rice bran	2.25 kg rice bran	Cannot achieve required DE intake with rice bran alone
DIET 2	1.5 kg Re-Leve	2.5 kg Re-Leve	5 kg of Re-Leve
DIET 3*	1.8 kg alfalfa pellets + 475 ml oil	Combination cannot achieve required DE intake	Combination cannot achieve required DE intake

*Vitamin and mineral supplement required for nonfortified feeds. The mineral recommended for the specific rice bran product should be provided (not necessary for Re-Leve™).

Addition of 50-100 g of salt per day to all rations is recommended based on level of exertion.

13. Can my horse be cured?

When the described diet and exercise routines were followed we found that all horses improved, and >75% of horses stopped tying-up. PSSM horses, however, will always be susceptible to this condition and if their exercise schedule is disrupted. If they become ill from other causes, they may again develop clinical signs again. If this occurs, they should go back to the fitness program described above using longeing or round pen work. Many horses with this condition are happy trail horses, successful pleasure horses, and useful ranch horses. The greatest difficulty in owning a horse with PSSM is the time commitment to keep the horse fit and the moderate expense of special feeds.