# Paint Horse Journal

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## Horse & Farm Care Issue


# Untying THE KNOT

## Multiple equine muscle disorders, one name—get the scoop on PSSM: Polysaccharide Storage Myopathy.

By JESSICA HEIN

Though buying another horse was the furthest thing from her mind, Judi Rehm of Sultan, Washington, was smitten the moment she laid eyes on "Lahna," a 2013 buckskin tobiano mare registered as Fox Diamond Dee Bar.

"Something about her drew me in," Judi said. "She had the kindest eye. At 55 years old, I needed a coming-2-year-old like I needed a hole in my head, but off we went to look at her."

The match seemed kismet—Lahna reminded Judi of a mare she had recently lost, and she soon brought the buckskin home. After three months of professional training, Lahna and Judi hit the trails, and the young mare handled the new sights and sounds like a veteran.

A few months later, Judi received a seemingly innocuous Facebook message from an acquaintance who owned a horse related to Lahna. The friend alerted Judi that her horse had tested positive for the genetic disease PSSM1, and because their horses were related, she thought Judi would want to know.

"Things were going along great with my filly, so I just kept that information in the back of my mind," Judi said.

Things changed, however, in the fall of Lahna's 3-year-old year. After a few weeks off, the mare suddenly tied up while being longed, experiencing muscle cramping and soreness that made exercise excruciating. Thoughts of that casual Facebook exchange months earlier came rushing back, and Judi sent the mare's

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hairs for DNA testing. Sure enough, Lahna was diagnosed as n/PSSM1, meaning she carries one copy of the disease.

"The lab confirmed my suspicion. In hindsight, there were little things she would do on occasion, such as being cinchy, biting at me when I put the saddle on, and throwing her head when I asked her to go into a lope," Judi said. "From the point of diagnosis, we have worked to get a diet and exercise schedule that suits her.

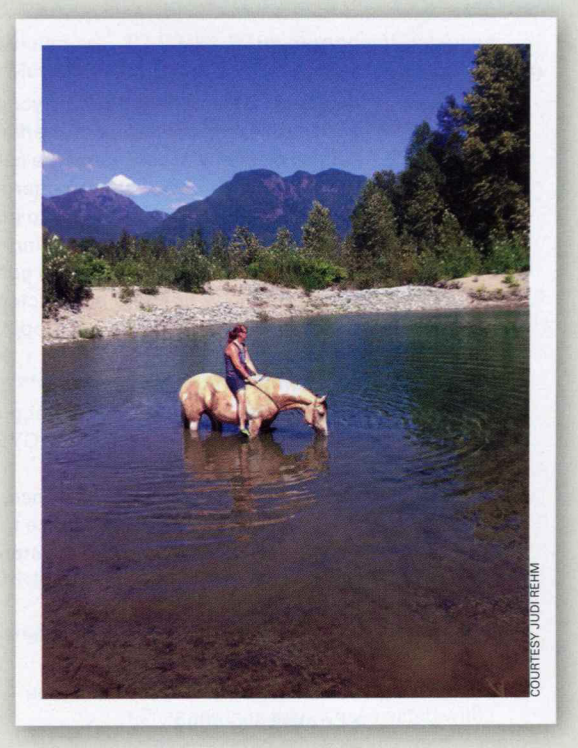
"One of the hardest lessons with this diagnosis is realizing that what works for one horse might or might not work for another—there is no easy fix. But I am 100 percent committed to getting Lahna to where she can lead a comfortable, productive life. This mare tries her heart out for me, and I owe her nothing less."

PSSM—Polysaccharide Storage Myopathy—is a hot topic in the horse world, but does all this talk about Type 1 and Type 2 leave you confused and uncertain if your horse might be at risk? Read on as we break down the details about the disorder collectively referred to as PSSM and what it means for affected horses, owners and the future of stock horse breeds.

## Two Types, Different Diseases

The general term "PSSM" is used as a catchall description that refers to several different equine muscle diseases, but they're not as familial as their names imply.

Research at the University of Minnesota examined Quarter Horses with a history of tying-up; abnormal muscle biopsies confirmed suspicion of a muscle disorder. That led to the discovery of a mutation in the GYS1 gene that explained most cases; this gene controls glycogen (sugar) storage and usage in skeletal muscle cells. Horses with the GYS1 mutation overproduce glycogen and store it abnormally, making it difficult for cells to use the glycogen for energy during exercise. Researchers



COURTESY JUDI REHM

*Fox Diamond Dee Bar is n/PSSM1; through diet management changes, owner Judi Rehm has been able to help "Lahna" lead a productive life in spite of the diagnosis.*

"I am 100 percent committed to getting Lahna to where she can lead a comfortable, productive life. This mare tries her heart out for me, and I owe her nothing less."

## PSSM Type 1

**Nickname:** PSSM1, P1
**Gene Mutation:** GYS1
**The Basics:** Affected horses overproduce glycogen and store excess amounts; this energy cannot be easily accessed by the cellular muscles, so it creates an energy deficit during exercise, leading to poor performance and episodes of tying-up.
**Inheritance:** Dominant—only one copy of the gene is required for a horse to be affected; homozygotes (those with two copies of the gene) are possible.
**Diagnosis:** Hair sample; muscle biopsy
**Symptom:** Development of symptoms is not guaranteed, even if horses carry the GYS1 mutation, but they can include:

- Exercise intolerance or resistance, such as reluctance or resistance to move forward, or poor/inconsistent performance
- Stiffness or muscle weakness
- Tense muscles, especially in the abdomen
- Muscle tremors in the flank area
- Profuse sweating
- Stretching out, as if to urinate
- Tying-up
- Muscle wasting (more common in draft breeds)
- Blood work often shows elevated muscle enzymes (CK and AST) at rest, and more so after exercise

**Severity:** Variable. Some heterozygous PSSM1 horses are asymptomatic, while others are affected; homozygotes seem to be more acutely affected with an earlier age of onset. Those who also carry Type 2 variants or the MH (malignant hyperthermia) mutation also seem to be more severely affected.
**Management:** Diet (low starch, supplemented with fat); consistent exercise, including access to movement in a pasture or dry-lot situation
**Takeaways:** With diet and exercise management, researchers estimate about 75 percent of PSSM1 carriers can be effectively managed and live normal lives. Knowledge is power, which makes genetic testing a valuable asset for horse owners. PSSM1 doesn't have to be a career-ending diagnosis, but it does require appropriate management strategies for success.


JESSICA HEIN

*PSSM Type 1 and Type 2 symptoms can resemble a number of other conditions and causes. Things like resistance or inconsistency in work could hint at a need to consider PSSM.*

called this Polysaccharide Storage Myopathy Type 1, or PSSM1.

But there were horses in the study with a history of tying-up and abnormal muscle biopsies that did not have the GYS1 mutation. While their glycogen totals were closer to normal, the cellular structure was different than that of Type 1 horses—though still disorganized compared to biopsies of normal horses. This indicated the disease might be caused by something else entirely, even though the outward symptoms were similar.

Molly McCue, D.V.M., Ph.D., one of the researchers who worked on the discovery, is an associate professor at the University of Minnesota's College of Veterinary Medicine and an expert on PSSM1.

"When we first started looking at this disease, we thought we might find one genetic disease in stock horses and find different glycogen storage diseases in other breeds; there are more than a dozen well-described glycogen storage diseases in people," she said. "When we did the original work and identified the PSSM1 mutation, it became clear that while it accounted for most of the PSSM in Quarter Horses and related breeds, it wasn't all of it; between 70–80 percent of those horses that were diagnosed by muscle biopsy had the Type 1 mutation. So we made a classification in the original paper when we talked about Type 1 vs. Type 2; in that, what we meant by Type 2 was anything without a glycogen synthase mutation."

Molly's research estimates about 11.3 percent of Quarter Horses and 4.5 percent of Paints are affected by PSSM1. The GYS1 mutation has been confirmed in more than 30 breeds.

One area of frustration is that symptoms associated with PSSM in general can resemble many different conditions, like EPM or Lyme disease.

The private New Mexico-based research group EquiSeq has taken a leading role in studying PSSM Type 2 and its contributing variants. Working with a subset of Type 2 PSSM-diagnosed horses, based on muscle biopsies, EquiSeq researchers sequenced the horses' genomes and compared them to that of non-affected horses.

"Previous researchers did a genome-wide association study for PSSM2, and they didn't find a variant—that tells us either the variants have incomplete penetrance, so not all horses who have the variant get the disease, or it's polygenic, where multiple different genes cause similar symptoms," EquiSeq's Chief Scientific Officer Paul Szauter said. "It turned out that it's both."

After wading through the data, EquiSeq found success: they nicknamed their discoveries P2, P3, P4 and Px; the specific names and mutation locations are classified pending publication in a peer-reviewed journal.

"Type 2 PSSM is a disorder of building muscle tissue," Paul said. "If a horse has one of these variants, he can't build muscle as well as a normal horse, and any situation that causes negative nitrogen balance—which is something the body normally uses in situations of stress to produce fuel—is catastrophic for these horses."

Nitrogen balance refers to the amount of nitrogen consumed and excreted by the body—nitrogen is the basis for amino acids, which are protein building blocks. In positive nitrogen balance, you're taking in more than you excrete; this results in growth or muscle building.

In negative nitrogen balance, your body is using and excreting more nitrogen than it's taking in; to make up for the lack of energy, your body robs amino acids from your muscles. This is the body's natural response when fighting an infection or recovering from surgery, Paul says—think of when you're recovering from the flu and feel weak. A horse with PSSM Type 2 variants is already behind the eight ball physiologically, so when he has even a minor illness, his body overreacts and depletes muscle for energy.

A key point is that a horse is diagnosed with either

## PSSM Type 2

**Nicknames:** P2, P3, P4, Px—independently inherited

**Gene Mutation:** Multiple, not specifically named yet (as of publication date)

**The Basics:** Affected horses don't overproduce glycogen, but they store it improperly in muscle cells and have trouble building muscle. Situations that cause negative nitrogen balance, such as injury or illness, significantly impact affected horses, causing muscle wasting/atrophy and other symptoms. Type 2 is used to describe horses with symptoms of PSSM without the GYS1 mutation.

**Inheritance:** Semi-dominant with incomplete penetrance. The degree to which a carrier is affected is variable, and only one copy of a particular variant can cause a horse to be affected, though some carriers will never show outward symptoms. Horses can have multiple variants, and homozygotes are possible.

**Diagnosis:** Muscle biopsy; blood test and hair samples to distinguish between specific variants

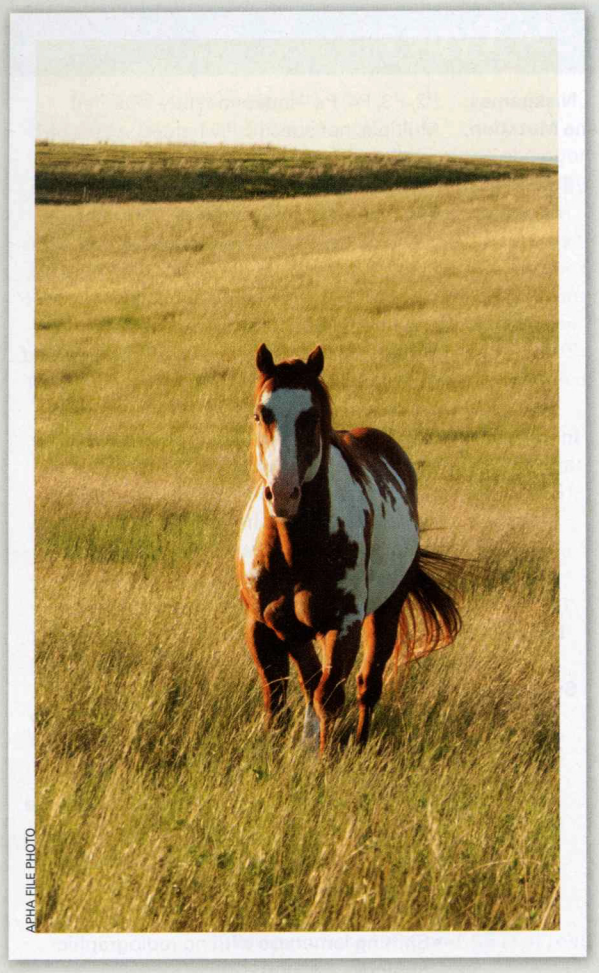
**Symptoms:** Development of symptoms is not guaranteed, even if horses carry a variant, but they can include:

- Changes in behavior associated with pain—difference in temperament, negative reactions to being ridden/saddled, biting at the flanks, bucking, rearing or other resistance
- Stifle problems
- Shifting lameness with no radiographic findings
- Changes in gait, including stiffness in the hindquarters, limited range of motion, cross-firing or bunny hopping at the canter, or ropewalking
- Heaviness on the forehand
- Tying-up
- Muscle wasting in the hindquarters and topline; rapid loss of muscle mass, especially following trigger events
- Muscle divots (focal muscle atrophy), often asymmetrical
- Respiratory difficulty
- Recumbency
- Blood work often shows muscle enzymes (CK and AST) in the normal range

**Severity:** Variable. Some carriers are asymptomatic. Homozygotes and those with multiple variants seem to be more acute with an earlier age of onset.

**Management:** Diet (high protein and low starch, supplemented with fat); consistent exercise

**Takeaways:** Some horses who test positive never develop issues related to Type 2 PSSM, and researchers are working to better understand how the variants interact with each other and conditions like PSSM1 and MH. There's no cure for Type 2 PSSM, but management adjustments and vigilant health monitoring can help prolong good quality of life.



APHA FILE PHOTO

*Anecdotally, limiting time confined to a stall and instead allowing the horse to move around at will in a paddock could help mitigate PSSM symptoms.*

JESSICA HEIN

*Near-daily exercise can also help manage PSSM-affected horses.*

Regardless if your horse has PSSM1 or Type 2 variants, management strategies can significantly benefit his quality of life.

PSSM Type 1 or Type 2, though it is certainly possible to test positive for PSSM1 and have underlying Type 2 variants.

One area of frustration is that symptoms associated with PSSM in general can resemble many different conditions, like EPM or Lyme disease, Paul says—that makes it difficult for horse owners and veterinarians alike to pinpoint the source of sometimes-ambiguous symptoms. Crowd-sourcing information through Facebook forums, where owners share their horses' test results, symptoms and photos, has proven invaluable in generating specifics about Type 2 variants, Paul says. To date, EquiSeq has tested about 500 horses, with plans to expand testing.

"People see this whole range of symptoms and they call it all PSSM, but until you're able to genotype the horses and sort them into groups, it's really hard to figure out what's going on," Paul said. "Horse owners have been very cooperative and they share detailed medical information, which has helped us put together a picture of what's going to trigger an episode. Now, it's turning into a story."

## A New Normal

Regardless if your horse has PSSM1 or Type 2 variants, management strategies can significantly benefit his quality of life.

"The good news for PSSM1 horses is that we know if we change their diet and exercise program—feeding them a diet that's low in starch, supplemented with fat if they need it, and exercise them everyday—about 75 percent of these horses can be managed pretty effectively and have limited episodes of tying-up," Molly said. "So if you know your horse has a mutation, you can proactively manage them before they tie-up."

Paul says horses afflicted with Type 2 PSSM also benefit from a protein-rich diet. Other anecdotal remedies include Vitamin E and magnesium supplementation, limiting access to sugary hay and pasture, and reducing stall confinement. Molly says many PSSM1-diagnosed horses' problems begin when they start training—that's when they typically move from a pasture setting to a stalled lifestyle and are introduced to high-starch grains.

For some affected horses, PSSM-linked symptoms like exercise intolerance and

resistance could be reactions to muscle pain, rather than obstinacy.

"I can't help but wonder how many horses have been labeled with having bad attitudes when in fact they were actually PSSM-positive," Judi reflected. "Looking back, things I attributed to my horse being grouchy were probably caused by PSSM1. A lot of horses act out way worse than Lahna did; they're telling us loud and clear that something is wrong."

Though research is still ongoing, both Molly and Paul hypothesize that PSSM-affected horses who are especially symptomatic likely have multiple variants at work; they also acknowledge there are confirmed Type 1 and Type 2 horses that are asymptomatic. EquiSeq has partnered with a number of other researchers to study a wider test population.

The culture of horse ownership has shifted, with more people owning their animals for longer periods of time. With a PSSM diagnosis in hand, owners might need to make some honest decisions about their horses, Paul says.

"Depending on the horse and its genotype, it might manifest symptoms and, eventually, might not be able to do the job you want," he said. "It comes down to what kind of horse owner they are and how willing they are to accept that answer and adjust. I hope people will learn that you can't take an animal that's in pain and push it through."

"I feel like a chemist out there mixing up Lahna's food," Judi said. "She still occasionally has episodes when we're trail riding and it gets strenuous. When she refuses to go, I know we need to stop and rest awhile. We still have a long way to go, but we're getting there."

## Much Ado About Breeding

A fissure of debate among horsemen revolves around breeding horses who test positive for a genetic disorder like PSSM. The answer, Molly says, is complicated and far from black and white.

"I'm not a supporter of limiting registration for animals that carry a disease gene," she said. "If we eliminated every single horse that is a carrier for a known mutation from the breeding population, we would severely limit the genetic pool in that breed. That would increase inbreeding, and we'd concentrate other genetic mutations that are, right now, very rare or unknown. That said, there is definitely a place for educated breeding."

Educated breeding, Molly says, involves using your horse's genetic test results as an asset—carefully select the horse to whom you breed so you can maximize positive traits and minimize negative ones, and look to a horse's offspring that test negative for genetic conditions as breeding-replacement candidates.

"You can choose an offspring that has all of the genetic traits of the parent that you like, but doesn't happen to have


APHA FILE PHOTO

*Culling horses with PSSM from the breeding pool might not be the answer and could have unintended consequences. Slower, but more strategic, breeding decisions—like searching for n/n replacements out of those bloodlines—might meet the same objective while maintaining genetic diversity in the breed.*

With a PSSM diagnosis in hand, owners might need to make some honest decisions about their horses.


*Research is ongoing into PSSM and related variants, with hope that future advances will yield even better management strategies and diagnostic tools.*

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"We supply the test and the science; people should do what they think is best with those results."

the mutation; that allows us, over time, to maintain diversity while decreasing the frequency of some of these diseases," Molly said. "Decisions have to be made carefully, and it has to be a slow process."

Paul agrees.

"The incidence of these conditions is high enough that it would be ill-advised to prohibit a horse with any of these variants from breeding," he said. "We probably should get to the point where breeders are testing for these conditions and avoid breeding homozygotes or horses that have multiple variants. But if you have a champion horse with P2, for instance, pick a broodmare that is negative so you have a 50/50 chance of getting a genetically clean horse that still has all of those other desirable characteristics.

"We supply the test and the science; people should do what they think is best with those results. As a scientist, I'm committed to the idea that good ideas will displace bad ideas over time. For the most part, breeders want good, healthy horses."

## Down the Road

Research into PSSM is far from over. Primary focus areas include developing better management strategies in diet, exercise and cellular energy conversion; gaining a better understanding of how variants interact with one another, and using that information to design a sliding scale of symptom severity; and even looking at possible drug therapy that could help affected horses perform more consistently.

Molly encourages horse owners to embrace genetic testing as a resource in helping improve their horses' quality of life.

"With five- and six-panel testing, we're seeing renewed focus on this disease, but there's no reason to throw the baby out with the bath water," Molly said. "Having information about your horse's genetics is empowering, both for the good of the horse in front of you and for making decisions about the future of a breed.

"PSSM is not necessarily a career-ending or life-ending diagnosis. There's still work to be done to better understand exactly what's happening so we can manage resources better. We don't have all the answers yet, but we're working on it."

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