When Two Worlds Merge

Kentucky Equine Research and Academia Join Forces to Benefit Stock Horses and Thoroughbreds

In the world of research, success is often the result of a team effort. Throughout its history, Kentucky Equine Research (KER) has collaborated with numerous researchers throughout the world to bring the horse industry the most progressive and scientifically substantiated feeds and services. But perhaps none of these relationships has been as longstanding and fertile as the one shared with Stephanie Valberg, D.V.M., Ph.D., of the University of Minnesota.

Photos by Z

Joe Pagan, Ph.D., founder and president of Kentucky Equine Research (KER), first met Valberg in Sweden in the mid-1980s.

Dr. Sune Persson and Arne Lindholm of the Swedish University of Agricultural Sciences invited to their Scandinavian laboratory a group of scientists interested in studying exercise physiology in Standardbred trotters. The single piece of equipment that most attracted Valberg and Pagan was, in fact, a high-speed treadmill, a monstrosity built by Saab, the Swedish airline company. "At that time, there were no high-speed treadmills for horses in the United States, so Sweden was the mecca for people interested in equine exercise physiology," explained Valberg.

Unlike the noisy treadmills of today, the motor for that piece of equipment was housed in a separate building. A mat of woven coconut hair lined the belt and softened the blows of hooves, so little noise was produced when it was being used. Construction expenses preclude the widespread duplication of this uber-treadmill, but researchers worldwide maximized its use for several years. During their time at the Swedish University of Agricultural Sciences, Valberg completed her Ph.D. studies and Pagan finished up postdoctoral research. Eventually, each returned to the United States with a different focus.

While Pagan was laying the groundwork for a fledgling company called Kentucky Equine Research in the late 1980s, Valberg continued exercise physiology research. She began working under Dr. George Cardinet, a specialist in neuromuscular diseases of animals at the University of California in Davis. Dr. Cardinet had invited Valberg to California with the expectation that she would develop an equine neuromuscular diagnostic laboratory, complete with biochemical analysis capabilities. She successfully accomplished that, and during her six years of study on the West Coast, Valberg identified two distinct muscle disorders, polysaccharide storage myopathy (PSSM) and recurrent exertional rhabdomyolysis (RER). Throughout those years, she became increasingly interested in the causes of the muscle disorders, specifically genetic and biochemical links.

Dr. Stephanie Valberg has been at the forefront of equine muscle research for nearly two decades. Much of her work has been accomplished with cooperation from KER.

Valberg was eventually lured to the University of Minnesota in 1994, due in part to the research work that was being done, oddly enough, on pigs. Some pigs are genetically predisposed to a condition known as malignant hyperthermia, which is not altogether dissimilar to RER. In addition, collaborations with biochemists and physiologists at the University of Minnesota allowed Valberg to delve deeper into PSSM. As her work at Minnesota progressed, Valberg was able to pinpoint that some horses, particularly those with Quarter Horse breeding, suffered from a condition characterized by excessive glycogen (sugar) storage and increased sensitivity to insulin within muscles.

If too much sugar was ending up in the muscle cells, Valberg figured that decreasing the starch content in the diet and substituting fat might help these horses. With this basic reasoning stirring in her mind, she reached out to Pagan, who by this time had solidified his reputation as a progressive equine nutritionist.

"I knew that Joe Pagan would design specific feeds for horses with specific problems, rather than simply using whatever was available," said Valberg. "Up to this point, we were decreasing the starch in the horses' diets, but we were doing it awkwardly. For owners of horses that needed more calories than roughage could provide, we'd advise them to pour corn oil over alfalfa cubes. Not only were the rations not properly balanced but they weren't particularly palatable or easy to feed."

When asked by owners how to manage their PSSM-affected horses, Valberg's answer was brief: feed a low-starch, high-fat diet and offer daily exercise, including as much turnout time as possible. Rice bran, such as Equi-Jewel, combined with a ration balancer proved to be a successful way to manage these horses. The advice was effective, but only if it was followed exactingly. All of the horses managed in a way faithful to Valberg's recommendations became free of tying-up episodes.

Taking the information she learned from her early work in Quarter Horses and other stock-type breeds, Valberg con-

A Closer Look at Polysaccharide Storage Myopathy


Mark Llewellyn

Exercise increases the risk of injury—there's no way around it. In Quarter Horse-related breeds, polysaccharide storage myopathy (PSSM) is a heritable muscle condition that strikes horses following light exercise.

Signs associated with PSSM include muscle twitching and cramping (including flank tremors), tucked-up abdomen, unusual sweating, a camped-out stance (posturing as if to urinate), gait asymmetry, hind limb stiffness, and reluctance to move. A horse may also exhibit signs typical of colic such as pawing or rolling after exercise. Frequency of episodes varies—one horse may have a few sporadic attacks over the course of a year, but another may be affected after each exercise session.

Definitive diagnosis of PSSM involves microscopic evaluation of the muscle. (See the sidebar titled "Mining for an Answer: Muscle Biopsies Help Researchers Discover Truth About Muscle Disorder" for a closer look at the biopsy procedure.) Researchers look for characteristic abnormalities in muscle cells including periodic acid Schiff's (PAS) staining for glycogen and polysaccharide, an abnormal sugar. The dark purple stains that indicate the presence of polysaccharide are the classic diagnostic feature of PSSM.

Based on the microscopic findings and pedigree research, a familial pattern for the presence of PSSM has been established in Quarter Horses, Paints, and Appaloosas.

PSSM resembles several syndromes in other species, including humans, that are characterized by excessive accumulation of glycogen in skeletal muscle. In these syndromes, glycogen collects because the muscles lack a specific enzyme that allows them to use glycogen as an energy source.

This did not hold true for horses, however. Horses were found to have all of the necessary enzymes to burn glycogen appropriately. The feature that sets apart PSSM from other syndromes is the unusually quick rate at which horses remove sugar from the bloodstream, create glycogen, and store it within muscle cells.

The prognosis for horses stricken with muscle problems caused by PSSM is promising. "Muscle has a remarkable ability to repair itself. After an episode of tying-up, the muscle cells usually heal completely in three to four weeks without scarring," explained Stephanie Valberg, D.V.M., Ph.D., an internationally recognized researcher who specializes in equine muscle disorders. "If the damage is severe, muscles may decrease slightly in size as the body filters out damaged proteins. Muscle mass usually returns in two to four months."

Management to prevent muscle pathology caused by PSSM involves adherence to a careful diet and exercise program. The first step is decreasing the amount of starch in the diet. This is most easily accomplished by eliminating all grains and sweet feed. In addition, horses benefit from a fat supplement. While a mixture of corn oil, alfalfa pellets, and a protein, vitamin, and mineral balancer may work for some horses, Re-Leve is the ideal choice for PSSM horses. Developed by Kentucky Equine Research (KER), Re-Leve is an incredibly palatable low-starch, high-fat feed that contains complete vitamin and mineral fortification. Most commercially available high-fat feeds contain too much starch and too little fat for PSSM horses.

The second step is implementation of a consistent exercise program that includes daily turnout and exercise under saddle or in a round pen. "In my experience, turnout is the single most important thing that can benefit horses with PSSM," said Valberg. "If PSSM horses are managed in a way that allows them to move about freely and graze for most of the day, it really decreases muscle soreness."

templated the mechanism involved in tying-up in Thoroughbreds. From a microscopic standpoint, she knew that the form of tying-up seen in racetrack Thorougbreds was unrelated to unusual glycogen accumulation in muscle. She believed instead that it was due to an irregularity in the way calcium is regulated in muscle cells. Though some researchers believed that a buildup of lactic acid was the culprit in these tying-up episodes, Valberg and coworkers decisively dismissed that notion following a trial in which horses afflicted with tying-up revealed no lactic acid accretion whatsoever.

One of the first trials conducted by Valberg and her coworkers involved six Thoroughbred fillies, each with a history of tying-up. Valberg removed the fillies from the racetrack and relocated them to the University of Minnesota's research farm. After a three-month letdown designed to acclimate the fillies to their new environment, they were introduced to the high-speed treadmill and training regimes.

An unsettling problem ensued. Despite intense exercise on the treadmill, the fillies did not any show signs of tying-up. Things did not look promising, according to Valberg. However, when more starch-laden sweet feeds were given to the fillies and exercise continued, the outlook shifted completely. The fillies began to show clinical signs of muscle pathology, and all eventually tied up.

"The question then became what can I feed these jazzed-up Thoroughbred fillies to keep calories up and starch down," observed Valberg. The fillies required significantly more calories than what could be provided by top-dressing low-starch feeds with corn oil or rice bran. "That's when I called Joe and cried, 'Help!'"

KER responded with Re-Leve, a high-fat, low-starch feed that contributes the necessary energy, protein, vitamins, and minerals to the racehorse without the excitability and muscle problems associated with starch. Longtime KER Team Member Hallway Feeds of Lexington, Kentucky jumped on board to help produce the special feed.

Mining for an Answer: Muscle Biopsies Help Researchers Discover Truth About Muscle Disorders

Shave, numb, snip, remove, and stitch. Wait a minute. What just happened? Simply put, a muscle biopsy.

"Horses are generous muscle donors. They don't mind sharing," quipped Stephanie Valberg, D.V.M., Ph.D., an equine researcher based at the University of Minnesota's College of Veterinary Medicine.

For years Valberg has been at the forefront of equine muscle disorder research. She and her coworkers have expanded knowledge of the crippling disease known broadly as tying-up. Specifically, her work has advanced the understanding of two distinct forms of tying up: polysaccharide storage myopathy (PSSM) and recurrent exertional rhabdomyolysis (RER).

Much of her research depends on the microscopic evaluation and biochemical analysis of muscle tissue. In order to test her hypotheses, Valberg must harvest the muscle tissue from horses diagnosed with the disease. Collecting the tissue samples is accomplished through a relatively painless procedure known as muscle biopsy.

"Horses don't have the type of sensors in their muscles that react to the biopsy procedure, so the greatest reaction usually occurs with the needle prick and local anesthetic that is necessary to desensitize the skin," explained Valberg.

President of Kentucky Equine Research (KER) Joe Pagan, Ph.D., concurs. "The horse doesn't feel any pain from muscle tissue recovery, only pressure. Making an incision in the skin is the only reason anesthetics are necessary."

Horses possess well-developed musculature, but not all muscle tissue is appropriate for diagnosis of muscle disorders. "The middle gluteal is the primary muscle examined in our studies. It's used extensively in locomotion and responds positively to training, which makes it ideal for studying exercise-related disorders," said Valberg. The middle gluteal muscle, which helps the horse propel its weight forward, lies over the croup and gives the rump much of its shape.

"Another option is the hamstring, or the semimembranosus muscle, which runs along the back of the hind leg," continued Valberg.

Interestingly, in human studies, exercise physiologists often sample from the quadriceps, the group of large muscles on the front of the thigh. "This doesn't work on a horse, though, as those muscles are used primarily to unlock the stifle, and they work little during exercise, especially when compared to the middle gluteal," explained Valberg. In the equine model, the quadriceps muscles are found directly above the stifle.

Once a standardized position in the middle gluteal has been identified, a small area, about two square inches, is shaved closely. The area is cleaned thoroughly with an

"Hallway Feeds is always willing to step up and try new things. They are extremely game, especially when it comes to advancing horse health," recalled Pagan.

To test the effectiveness of Re-Leve, Valberg designed a trial using six two- and three-year-old fillies, all with a predisposition to tying-up. Three diets were used in the trial: a typical sweet feed, the same sweet feed with added bicarbonate, and Re-Leve. The fillies were fed each diet for three weeks and exercised five times a week. Blood samples were taken following each exercise bout to measure the level of creatine kinase (CK). CK is a protein released into the bloodstream by damaged muscle tissue within hours of an attack, and its measurement is useful in determining the severity of the damage. Though all of the fillies repeatedly tied up on the two diets containing traditional sweet feed, none showed any signs of the disease when fed Re-Leve. When sweet feed was consumed, the fillies' CK levels were nearly ten times those when fed Re-Leve.

Further studies in Valberg's laboratory have reinforced Re-Leve's effectiveness in eradicating signs of tying-up.

The collaboration between KER and Valberg extends beyond the laboratories and to the classrooms of the College of Veterinary Medicine at the University of Minnesota. Third-year veterinary students are given the option to enroll in a series of lectures and labs geared specifically to equine medicine. Over the past five years, several KER nutritionists have traveled to St. Paul to teach students the finer points of horse feeding management. In reciprocation, Valberg has accepted numerous invitations to speak at KER's annual nutrition conference.

Finding answers to complex problems often requires the collective focus of several individuals. With an eye on discovering ways to nutritionally manage disorders like PSSM and RER, KER and Stephanie Valberg are making a difference in the lives of equine athletes.


Catherine Bishop

antiseptic such as Betadine, a povidone-iodine solution, and then anesthetized with lidocaine. A quarter-inch incision is then made in the skin. A biopsy needle is carefully passed through the opening and into the muscle. The needle is positioned in several areas during collection. Each time the position of the needle changes, a plunger is punched. With each punch, a small section of muscle is excised and tucked away into the needle's storage compartment.

Once it's released from the biopsy needle, a perfectly recovered muscle sample looks much like a two-inch earthworm. To minimize any changes in metabolism after they are taken, the samples are dipped quickly into liquid nitrogen. Within seconds the squishy muscle sample is hardened into a pellet and placed in a storage container. Kept at a temperature of -80° F, muscle samples can be preserved for years. For microscopic work, the sample is prepared in a special chemical to prevent ice crystals from forming as the tissue freezes in the liquid nitrogen.

Side effects of muscle harvesting are rare. "Needle biopsies are often taken before and after exercise in our work and the horses show no adverse effects. In the small area where the muscle is removed, regeneration is complete within a month," commented Valberg.

Valberg recently visited Kentucky on a training mission of sorts. KER is studying the effects of various antioxidant mixtures on the muscle tissue of performance horses. Blood is usually used as an indirect measure of muscle changes. In this series of trials, however, KER researchers have chosen to test the actual muscle tissue, which may yield more accurate results.

Because muscle biopsy in considered minimally invasive, a veterinarian is always present to help with the procedure. Jaye McCracken, D.V.M., with Hagyard Equine Medical Institute of Lexington, Kentucky, was on hand to learn the biopsy technique from Valberg. Prior to her introduction to KER several years ago, McCracken had little experience helping with equine exercise physiology research. Fine-tuning her muscle biopsy technique is just one added benefit of working with a team of researchers. McCracken will work with KER throughout the duration of this trial.