

CENTER FOR EQUINE HEALTH

HorseReport

SCHOOL OF VETERINARY MEDICINE • UNIVERSITY OF CALIFORNIA, DAVIS

FALL 2018



**Vitamin E: Key to
Equine Health**

– Page 4



UCDAVIS

VETERINARY MEDICINE

Center for Equine Health

Director's Message



At the [Center for Equine Health \(CEH\)](#), we continually strive to bring you the latest in equine health through this award-winning publication.

This particular issue of *Horse Report* is near and dear to my own research program. My research team studies the consequences of [vitamin E deficiency](#) in the horse. In this *Horse Report* issue, we focus on the importance of vitamin E as part of a well-rounded nutritional regimen. For horses in areas with lush green pastures, vitamin E is abundant, as the grass consumed in a normal grazing routine provides a sufficient amount. But most of us in California know that lush green pastures are an extreme luxury due to recent drought conditions. As a result, many of our horses require vitamin E supplementation. This powerful antioxidant protects against cell damage from free radicals.

You may be familiar with the importance of vitamin E in human diets. Its advantages include an increased immune system response, balanced cholesterol levels, lower inflammation, natural repair to damaged skin, and balanced hormones. Most importantly, however, is its ability to prevent debilitating neuromuscular disease. This also holds true for horses. In this issue, we will discuss these diseases and give you information on how to properly supplement your horse's diet.

With your help, CEH continues to advance the well-being of horses and educate horse owners on the latest discoveries in horse health. At UC Davis, we are at the forefront of research into the importance of vitamin E in the equine diet. What an exciting time to be part of our journey!

Thank you for your continued support,

Carrie J. Finno, DVM, Ph.D.
CEH Director

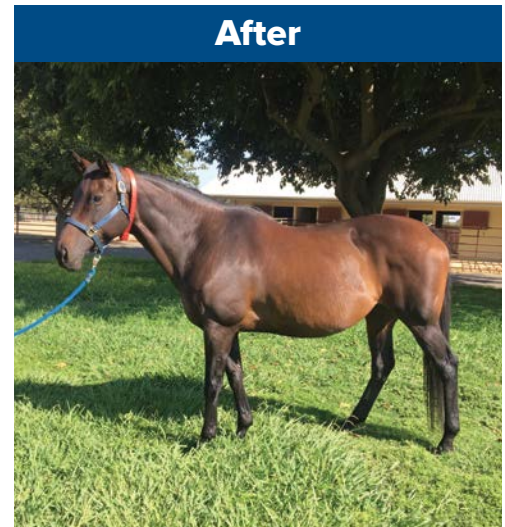
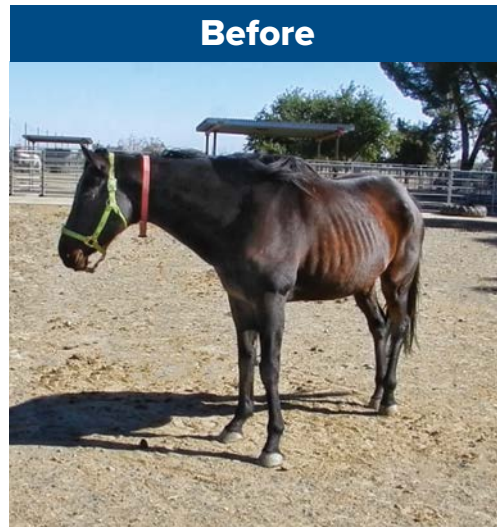
Due to the importance of vitamin E in every horse's diet, the Center for Equine Health has invested in irrigating its pastures for the teaching herd. Since the best source of vitamin E is fresh green grass, these lush pastures at UC Davis provide an ideal environment for the teaching herd to graze.



Recovery from Vitamin E Deficiency

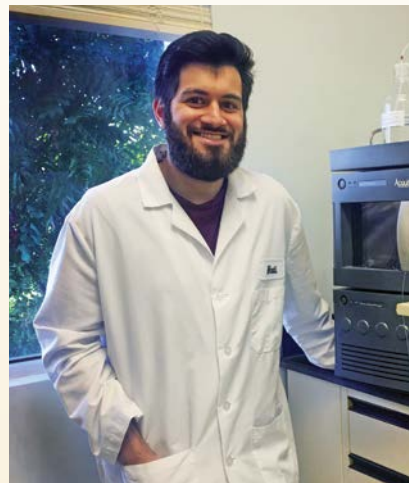
Tarnisha, a 10-year-old Thoroughbred, came to live at the CEH in 2012 after her owners donated her following an injury that forced her retirement from racing. Three years later, she began showing clinical signs of muscle wasting and weakness. The [Finno Laboratory](#) at the CEH diagnosed her with vitamin E deficient myopathy, confirmed via muscle biopsy. She was started on a treatment plan consisting of oral vitamin E supplementation and showed improved clinical signs within two weeks. She continued to make steady improvements and

has never looked back. To maintain her health, she will need to remain on oral supplementation for the rest of her life or live on green pasture. “Tarnisha is a perfect example of how quickly some horses can improve from vitamin E deficient myopathy simply with the proper supplementation,” said CEH Director Carrie Finno. “This is the one disease that horses can completely recover from with appropriate treatment.”



Meet the Scientists Behind the Discoveries

Hadi Habib recently graduated from UC Davis with a bachelor's degree in [Chemistry](#) and a master's degree in [Forensic Science](#) with an analytical chemistry focus. Hadi's research quantified vitamin E and vitamin E metabolite levels in horse blood, particularly in serum and plasma. Vitamin E actually consists of eight compounds that can be measured individually. To investigate how fast a horse “uses” vitamin E and each of these eight compounds, vitamin E metabolites are measured. Under the mentorship of Drs. Birgit Puschner and Ingrid Gennity, Hadi developed a method to measure levels of all of the components of vitamin E and its metabolites in equine plasma and serum. Quantification was achieved using analytical instrumentation (UHPLC-MS/MS). The validated method determined concentrations of these analytes in plasma and serum of horses. Assessment of vitamin E and metabolites is a critical component of diagnostic investigation in horses with neuromuscular



Hadi Habib

diseases. Alpha-tocopherol (isoform of vitamin E) levels were found to range from 3-6 $\mu\text{g/mL}$, while the metabolites were found at much lower levels, ranging from .0002 – .0010 $\mu\text{g/mL}$ in healthy horses. This work has been pivotal in investigating the rate at which certain horses “use,” or metabolize, vitamin E. The team is discovering that some horses may require higher doses of vitamin E than others, based on a more rapid metabolism of the vitamin.

Hadi performed his training through the [Bioanalytical Research Core](#), a unique interdisciplinary analytical core that provides method development and validation for therapeutics and toxicants in support of the [School of Veterinary Medicine's](#) drug discovery efforts. Core members have advanced training and experience both in the pharmaceutical industry (preclinical drug development) and academia as well as extensive experience with pharmacokinetic modeling of drug and metabolite concentration data in a variety of biological matrices (blood, urine, milk, synovial fluid, tissue).

Cut grass is not a good source of vitamin E since nutrient levels start to diminish at harvest.



Vitamin E: Key to Equine Health

Proper nutrition—particularly appropriate levels of vitamin E—is critical to equine health. This biological antioxidant helps maintain normal neurological function by limiting the damage caused by oxidative stress and free radicals. The best source of this nutrient is fresh green grass. As soon as the grass is dried for hay, the potency of vitamin E in the forage declines dramatically.

Many research studies, including some conducted at the Center for Equine Health (CEH), have shown that horses without access to grazing on green grass are often deficient in this essential mineral, which leaves them vulnerable to three different types of neuromuscular diseases associated with vitamin E deficiency: equine neuroaxonal dystrophy/equine degenerative myeloencephalopathy (eNAD/EDM), equine motor neuron disease (EMND) and vitamin E deficient myopathy (VEM). These diseases are typically diagnosed based on the clinical signs, exclusion of other disorders and a low blood vitamin E concentration.

While not all animals deficient in vitamin E exhibit clinical signs, individual genetic factors, the age of the horse during deficiency (such as early growth phases), and the duration of deficiency all play a part in determining whether insufficient levels of vitamin E in a horse's diet will impact their health.

Equine neuroaxonal dystrophy occurs in young animals and has a genetic predilection. Affected horses appear

uncoordinated. They may stand with forelimbs too far apart (or too close), have difficulty navigating curbs or hills, or lack coordination while walking and making tight turns. Manifestations of the disease can vary among horses with some showing mild performance issues, while others are severely debilitated. Although there is no cure yet for eNAD, one of most common equine neurological diseases, researchers are closing in on how to prevent the onset of symptoms—and early intervention is key.

Dr. Carrie Finno, director of the CEH, said studies show that vitamin E is necessary to prevent degeneration of the neurons and axons throughout the brain and spinal cord during early life in many species. Axons are the part of nerve cells that transmit impulses, so when those cells are damaged, communication breaks down between the brain and the rest of the body, leading to a lack of coordination.

“We still don't understand the cause of the degeneration, but we do know there is an interaction between genetics and nutrition for this disease to manifest,” Finno said. “You need the perfect storm of genetic susceptibility and a deficiency of vitamin E during the first few years of life.”

Researchers in the Finno Laboratory are working hard to develop a genetic test for eNAD, but until one is available, she advises horse owners to supplement their horses, especially pregnant mares and newborn foals. The supplement may

not entirely eliminate the disease, but it does appear to result in less severe neurological signs if the foal receives supplementation during the early stages of life.

Equine motor neuron disease occurs in older horses that have been vitamin E deficient for more than 18 months. It affects lower motor neurons, nerves that supply the direct neurological input into all muscles. Without these, the associated muscles atrophy, resulting in the clinical signs of weakness and weight loss characteristic of this disease. Affected horses may carry their heads lower and lie down for longer periods of time. With treatment, approximately 40 percent of horses affected by EMND improve; 40 percent stabilize but remain disfigured; and 20 percent progress in severity of disease.

Vitamin E deficient myopathy is typically found in horses with a shorter duration of vitamin E deficiency and exhibit muscle weakness, low muscle alpha-tocopherol concentration and mitochondrial alterations (i.e. changes to the “power house” energy storage unit of the cell) in skeletal muscle but no evidence of neurogenic atrophy. These animals are generally able to recover within three months with proper supplementation.

These three diseases are the only conditions definitively associated with vitamin E deficiency. Despite this, many horses with neurologic disease caused by other diseases (i.e. equine protozoal myeloencephalitis, or EPM, and cervical compressive vertebral myelopathy, or “Wobblers”) are placed on vitamin E supplementation.

“At this time, we know nothing about vitamin E metabolism in horses, the appropriate dosage or its actual efficacy in preventing or treating neurological conditions other than eNAD, EMND and VEM,” said Finno, who was appointed as the inaugural holder of the Dr. Gregory L. Ferraro Endowed Directorship this spring. “Supplementation with vitamin E may alter drug metabolism and disposition, since, in humans, the same cytochrome isoforms that metabolize vitamin E metabolize approximately 50 percent of therapeutic drugs.”

Therefore, while vitamin E supplementation may not necessarily be harmful for these other neurologic diseases, it is unlikely to be beneficial. Baseline blood vitamin E concentrations should always be assessed before initiating any vitamin E supplementation.

Finno notes that recent droughts in California may also contribute to the decline in forage with sufficient vitamin E levels. Her laboratory is currently conducting research into how both healthy horses and horses with neuromuscular disease metabolize

Mares and foals are especially ►
susceptible to vitamin E deficiency.



Dr. Carrie Finno examines a case of equine motor neuron disease displaying the abnormal stance with all four feet placed close together underneath the horse.

vitamin E. There may be an underlying genetic variation in certain horses that results in them having a higher requirement of vitamin E. When these horses are then placed in a vitamin E deficient environment, such as a dry lot in California, neuromuscular disease may develop. If the Finno Laboratory can identify which horses require more vitamin E than others, supplementation could be individualized to prevent disease in those individuals.

“Continued research into this vital nutrient is critical to promoting equine health,” Finno said. “Especially for those horses that live in areas where access to green pasture is limited, like many areas in this state.”

For more information on vitamin E deficiency and suggested supplementation, please see the accompanying article in this issue of the *Horse Report*.



Importance of Vitamin E

When it comes to horse health and nutrition, geography can play more of a part than most would think. With horses achieving a significant portion of their diet through grazing, where they graze can make a big difference. And most California horses are at a distinct disadvantage when it comes to the nutrients—especially vitamin E—they could be getting from grazing.

Vitamin E is an essential nutrient for horses and one that can easily be provided with access to a lush green pasture in which to graze. Grass is an abundant source of vitamin E, but most California horses don't have this luxury. Vitamin E from grass can only be found in fresh grass. The nutrient levels decrease, and eventually are lost, as soon as the grass is harvested and stored, so cut hay is not an option.

Much of California has a hot, dry climate with little rain. Some desert areas of the state see less than five inches of rain per year, and the more populated centers—the Southern California coastal areas and the Central Valley—receive less than 20 inches—well below the national average. With this lack of rain comes lack of green pastures for horses to graze. Therefore, these horses are not getting the proper amount of vitamin E naturally, and if not supplemented, that deficiency could have dire consequences.

Consequences of Deficiency

In short, vitamin E helps a horse's muscles and nerves function properly. The biological antioxidant helps maintain normal neuromuscular function, and a lack of it can lead to diseases such as nutritional myodegeneration in conjunction with selenium deficiency, equine neuroaxonal



A case of eNAD/EDM displaying an abnormal stance due to damage of the proprioceptive tracts.

dystrophy/equine degenerative myeloencephalopathy (eNAD/EDM), vitamin E deficient myopathy (VEM) and equine motor neuron disease (EMND).

These diseases can be extremely debilitating to horses, if not fatal. EMND manifests in horses similar to amyotrophic lateral sclerosis (aka Lou Gehrig's disease) in humans, ultimately wasting away the muscles due to lack of nourishment. Horses with eNAD can have gait abnormalities and lose all limb control, while EDM escalates those conditions, resulting in a more severe incoordination.

The Center for Equine Health (CEH) is studying vitamin E deficiency—not only the effects it has on horses, but also potential correlations it may have with humans. Research reveals a number of similarities in how vitamin E deficient neurodegeneration takes place in the equine and human systems. CEH Director Dr. Carrie Finno hopes further funding will allow her team to expand on how vitamin E deficiency contributes to neurodegenerative diseases across species.

Supplementation

Since there is no effective treatment for most of the diseases vitamin E deficiency can cause, it is imperative that they be prevented from happening in the first place. If horses are not able to access fresh pastures to graze in, vitamin E must be supplemented in their diet. All vitamin E supplements

Vitamin E, an essential nutrient for horses, can be acquired by grazing in lush green pastures.



consist of alpha-tocopherol because alpha-tocopherol is the most biologically available and well researched isoform of vitamin E.

The National Research Council (NRC) recommends a daily vitamin E supplement to be 1-2 international units (IU)/kilogram of the horse's body weight. So for a 1,000-pound horse, 450-900 IU of supplement would be necessary daily.

"It's important to remember that not all horses with vitamin E deficiencies will exhibit clinical signs," said Finno. "And we want to prevent those clinical signs from happening anyway, so we don't want to wait around until we are certain of a vitamin E deficiency before supplementing their diets. Unless your horse is on a year-round green pasture, he or she requires supplementation."

However, Finno stresses the importance of testing blood vitamin E levels before initiating a supplementation program.

"Some horses may require higher doses of supplementation than others, and it is difficult to tailor their dosing without a baseline vitamin E level," said Finno. "Healthy grazing horses maintain a blood vitamin E level between 3-4 $\mu\text{g/mL}$, so that should be our target."

Historically, there was little concern associated with giving too much vitamin E. This was mainly due to the fact that most vitamin E supplements were not very well absorbed in the horse and the NRC levels were based on these synthetic vitamin E supplements. With newer formulations, however, excessive supplementation can occur.

"Previous studies have shown that detrimental effects may not occur until supplementation reaches 10-20 times the

recommended amount," Finno said. "However, these studies were performed using less bioavailable vitamin E supplements (see below). High dosages can lead to bleeding disorders. With the newer supplement formulations, it is critical to repeatedly check blood vitamin E levels so as to not exceed the recommended range."

Not all vitamin E supplements are created equally. The first generation of supplements were termed synthetic vitamin E, in that they contained alpha-tocopherol, the main antioxidant component of vitamin E, in all of its different chemical configurations. Later research demonstrated that only the "natural" form of vitamin E, or the one containing only one particular highly bioavailable configuration, was highly effective at increasing vitamin E levels in the blood of horses. Since then, additional alcohol-based vitamin E supplements, termed "water-dispersible," have been developed for use in horses. These are the most effective of all supplements in that the water-dispersible formulation is readily absorbed and the natural vitamin E quickly increases blood and tissue levels in most horses.



Horses in dry pastures, especially mares and foals, need vitamin E supplementation.

Horses in different conditions and different stages of life may require varying levels of supplementation. Additionally, dosing is based on the type of vitamin E formula used (synthetic powder/pellet, "natural" powder/pellet or "natural" water-dispersible). After assessing baseline blood concentrations and identifying deficiencies, pregnant mares should be given 5,000 IU/day of the natural water-dispersible vitamin E and foals should receive 500 IU/day (i.e. 10 IU/kg as the foal grows) of the same product as soon as the foal is born to decrease the risk of eNAD. Blood levels should be checked frequently to ensure that they remain in the normal range.

Finno encourages all horse owners to discuss with their veterinarian what level would be best for their horse before implementing any supplements into their horse's diet.




www.vetmed.ucdavis.edu/ceh

Mail ID 1415
Center for Equine Health
School of Veterinary Medicine
University of California
One Shields Avenue
Davis, CA 95616-8589

The *Horse Report* is published by the University of California, Davis, School of Veterinary Medicine: Michael D. Lairmore, dean; Carrie Finno, CEH director; Tom Hinds, director strategic planning and communications; Rob Warren, editor; Katie Blakewell, Don Preisler, Carolyn Sawai, Trina Wood, contributors. The Center for Equine Health is supported with funds provided by the State of California Pari-Mutuel Fund and contributions from private donors.

The University of California does not discriminate in any of its policies, procedures or practices. The university is an affirmative action/equal opportunity employer.

 **Help us go green!** E-versions of the CEH *Horse Report* are now available twice a year – to start receiving your copies via e-mail (and other SVM electronic publications), visit www.vetmed.ucdavis.edu/go/subscribe

Join Us in Improving Equine Health

We are grateful to equine enthusiasts like you who share our commitment to the well-being of horses. Thanks to generous support, we continue to make great strides in advancing equine health to help horses like Tarnisha, highlighted in this issue of *Horse Report*. Please consider joining us in our mission by becoming a partner today. The welfare of horses depends on the improvement and advancement of equine medicine. To make a gift to the Center for Equine Health, call our Advancement team at 530-752-7024 or visit give.ucdavis.edu/Go/CEH.



CEH-Funded Research Published in *Journal of Veterinary Internal Medicine*

A recent study, funded by the UC Davis Center for Equine Health, aimed to identify biomarkers for equine neuroaxonal dystrophy/degenerative myeloencephalopathy (eNAD/EDM). Biomarkers are measures of a substance, ideally in the blood, that would support a diagnosis of eNAD/EDM in suspect cases. Researchers specifically evaluated whether or not biomarkers of oxidative stress as a vitamin E deficiency are present in horses with eNAD/EDM. Although an accurate biomarker was not identified in the blood or spinal fluid of affected horses, insight was gained into the possible mechanism by which eNAD/EDM leads to disease in the spinal cord of affected horses by disrupting processing of cholesterol. These findings will serve as the basis for future studies aimed at developing more accurate diagnostic tests and potential treatments for eNAD/EDM.



www.vetmed.ucdavis.edu