ACVIM Wrap Up

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The researchers supplemented eight stalled horses for 42 days.

Say your horse has a fever of unknown origin and your veterinarian has exhausted his resources trying to pinpoint the cause. Or, maybe your horse is exhibiting neurologic signs and your vet is looking for a peer's input to aid in diagnosis and treatment.

At that point, your general equine practitioner might contact or refer to a veterinarian certified with the American College of Veterinary Internal Medicine (ACVIM). These specialists focus on internal systems and, quite literally, know animals inside as well as out. And, veterinary internal medicine specialists working with a variety of species gather at the ACVIM Forum each year to present research results, share successes and challenges, and learn from each other.

This year's forum, aptly titled "Elevate Your Knowledge," held in Seattle, Wash., offered a robust selection of equine-related internal medicine topics, ranging from respiratory problems to endocrine disorders. We at *The Horse* attended those lectures and sifted through research to bring you this year's ACVIM Forum highlights. Here's what you need to know.

Supplement Reduces Gastric Ulcer Reoccurrence

Owners who've had horses with gastric ulcers know firsthand how frustrating—and expensive—it is to manage this often chronic condition. And with an estimated 75% of horses suffering from gastric ulcers, it's no surprise that treatment and prevention of the condition—which is common enough to have its own acronym, EGUS (equine gastric ulcer syndrome)—has become big business.

The array of products, supplements, ingredients, and botanicals touted as the next "big thing" in EGUS management, as well as anecdotal success stories found online, left Frank Andrews, DVM, MS, Dipl. ACVIM, and his research team at Louisiana State University's (LSU) School of Veterinary Medicine wondering about the validity of company and consumer claims.

"Many supplements are marketed on the Internet (for treatment and prevention of gastric ulcers in horses), including one I call 'faith,' but little is known about their effectiveness," Andrews said. "When horse owners feed these advertised antiulcer supplements they're literally 'going on faith,' because there's very little scientific information available on the efficacy of these products in horses."

The clinical success of the drug omeprazole (marketed as GastroGard) to treat gastric ulcers is well-documented in the equine veterinary world. Long-term EGUS management is a bit trickier, and gastric ulcer reoccurrence is common, Andrews noted.

The LSU study researchers examined the use of SmartGut Ultra in horses after the animals received omeprazole to treat nonglandular ulcers (the most common equine gastric ulcers, occurring in the upper part of the stomach). SmartGut Ultra, a supplement marketed by SmartPak Equine, contains sea buckthorn, pectin and lectin, glutamine, and aloe vera.

Andrews and his team performed a masked crossover study of two 42-day period on eight mature Thoroughbreds. The team divided the horses into two groups and sorted the animals by nonglandular ulcer lesion score and then by sex. One

group of horses underwent SmartGut Ultra treatment during the first study period while the other group served as controls (no treatment); during the second study period the groups switched treatment protocols. All horses were stall-confined and subjected to alternating periods of feed-deprivation, both factors known to contribute to gastric ulcer development.

The researchers performed gastroscopy on the day before the study began and again on Days 14, 28, 35, and 42, and a blinded clinician scored each horse based on nonglandular lesion number (NGN, meaning quantity) and severity (NGS). They also measured gastric juice pH (low stomach pH is normal for horses but can be associated with ulcers, Andrews said).

Not surprisingly, he noted, average NGN and NGS scores decreased significantly in all horses after two weeks of omeprazole treatment.

Two weeks after the team discontinued omeprazole administration, average NGN scores did not increase significantly in the treated horses, whereas NGN scores increased significantly in untreated control horses, Andrews said.

By Day 35, after feed-deprivation, NGN scores increased in both groups, but NGN scores were significantly lower in the SmartGut Ultra-treated horses than in the untreated controls on the same day. However, SmartGut Ultra did not alter the normal acid pH of the stomach significantly.

Overall, SmartGut Ultra treatment resulted in fewer ulcers two weeks after discontinuing omeprazole treatment and resulted in lower gastric ulcer numbers after feed deprivation than in the untreated group, without altering gastric juice pH, Andrews explained.

The research team concluded that SmartGut Ultra supplementation might be an affordable alternative to help protect the nonglandular stomach from the rebound acid effects once omeprazole treatment is discontinued and for stall-confined horses undergoing intermittent or scheduled feedings.

Andrews also noted that this product isn't a substitute for omeprazole paste treatment for gastric ulcers but, rather, an aid in maintaining stomach health.

Inhaled Corticosteroids, Management Changes for Heavey Horses

Imagine horses with recurrent airway obstruction (RAO, or heaves) wearing Darth Vader-like masks and breathing in corticosteroids every day. That was essentially the scene at the Université de Montréal in Quebec, Canada, during a yearlong study in which Mathilde Leclere, DVM, PhD, Dipl. ACVIM, and colleagues investigated the effect of inhaled corticosteroids (ICS) and limiting exposure to allergens in horses with RAO.

> **"Avoiding hay and barn dust leads to a better control of lung inflammation."**
>
> DR. MATHILDE LECLERE

Recurrent airway obstruction is a chronic and debilitating equine condition formerly known as chronic obstructive pulmonary disease. It describes a condition similar to asthma in humans in which the horse seemingly cannot "catch its breath."

For the study, the researchers employed 11 heaves-afflicted horses stabled and exposed to hay to induce RAO clinical signs, including coughing, increased respiratory effort, nasal discharge, and abdominal lift at the end of exhalation. They established baseline lung function and inflammation values in these animals using bronchoalveolar lavage (BAL, a procedure in which the veterinarian passes a bronchoscope through the nose into the lungs to flush fluid into a small part of the lung, recollecting the fluid for examination), blood samples, and lung biopsies. Next, researchers assigned five of the horses to the antigen-avoidance group, meaning they lived in 24-hour turnout without stabling. These horses ate a grass and pellet-only diet to limit dust and mold exposure but received no other treatment.

The second group of six horses had

VITAMIN E FOR NEUROLOGIC DISORDERS

Carrie Finno, DVM, PhD, Dipl. ACVIM, a researcher in the University of Minnesota Equine Neuromuscular Diagnostic Laboratory, presented a review of vitamin E supplementation in horses with neurologic disorders.

Vitamin E is a biologic antioxidant believed to help horses maintain normal neuromuscular function, Finno explained. "Vitamin E ... is a complex nutrient consisting of eight closely related, fat-souble, naturally occurring compounds that form two groups: tocopherols (saturated) and tocotrienols (unsaturated)," she said. "There are four individual isoforms—α, β, γ, and δ—within each group. The majority of the commercially available vitamin E supplements for horses contain natural or synthetic α-tocopherol, the most biologically active (or available) and researched isoform."

Many horses with vitamin E deficiencies show no outward ill effects, Finno said. A select few, however, develop signs of neuromuscular disease. Some of the disorders linked to vitamin E deficiencies include neuroaxonal dystrophy and equine degenerative myeloencephalopathy, vitamin E deficient myopathy, and equine motor neuron disease. While vitamin E deficiencies play a role in these issues, she said veterinarians must consider other factors during diagnosis: "The diagnosis of (these) neuromuscular disorders ... requires not only determination of vitamin E status, but also the appropriate clinical signs, supporting clinical pathology and/or muscle biopsy results, and elimination of other possible diseases."

Determining vitamin E status involves measuring serum α-tocopherol concentrations in order to confirm any underlying deficiency and monitor supplementation's efficacy, Finno said. Monitoring levels is important because although vitamin E doesn't accumulate in horses' bodies to the point of toxicity, some disorders—including coagulopathy (impaired blood clotting) and impaired bone mineralization and beta-carotene absorption—have been reported in horses with very high dietary vitamin E concentrations, Finno said. The current vitamin E recommendation for mature horses is 1 to 2 IU/kg (international units per kilogram) body weight per day, she said.

Owners supplementing their horses with vitamin E should select natural-source, water-dispersible forms because they are "five to six times more bioavailable (a greater amount is absorbed by and made available in the horse's body) than synthetic vitamin E," she said.

—Erica Larson, TheHorse.com/32115

no housing or feed changes, remaining stabled with a hay-based diet. However, this group received daily ICS treatments of fluticasone propionate through a respirator mask covering both nostrils. Physicians commonly prescribe this drug to treat asthma, hay fever, sinusitis (sinus swelling), and rhinitis (nasal swelling) in humans.

The researchers administered a one-month weight-based loading dose consistent for all Group 2 horses. After the first month, they customized each horse's dosage to control that individual's clinical signs.

Researchers repeated lung function and inflammation measurements using BAL and blood samples after one, six, seven, and 12 months of treatment. They also took lung biopsies from all horses again at six and 12 months to record changes in inflammation based on smooth-muscle thickening measurements as well as other inflammatory markers and airway remodeling (or a structural change to the airway associated with chronic inflammation), Leclere explained.

COURTESY DR. MATHILDE LECLERE

Researchers administered inhaled corticosteroids using respirator masks.

Clinical signs of RAO improved in horses treated with ICS but still eating hay, though lung inflammation persisted in these animals. Once moved outside, the horses' lung function continued to improve and the inflammation resolved.

The biopsy results also indicated that the thickening of the smooth muscle around the airways is partially reversible, even in animals that have been affected for many years, Leclere said.

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"However, avoiding hay and barn dust leads to a better control of lung inflammation and has additional beneficial effects on pulmonary function, even when clinical signs are apparently controlled by medication," Leclere said.

In other words, ICS treatment improved the clinical signs of RAO, much like it does with human asthma, even in the face of persistent exposure to hay dust. Antigen avoidance alone also helped reduce clinical signs, but horses received the most relief when medicated and avoiding environmental antigens.

CT for Diagnosing Lung Disease in Foals

Veterinarians are taking a page from human medicine books as they examine applications for computed tomography (CT) in evaluating pulmonary disease in foals. Kara M. Lascola, DVM, MS, Dipl. ACVIM, an assistant professor at the University of Illinois at Urbana-Champaign College of Veterinary Medicine, described related research and potential challenges.

Computed tomography is an imaging method that creates a detailed cross-sectional picture of structures inside the body using a series of radiographs (X rays). Lascola explained that CT is the preferred imaging modality for numerous human pulmonary problems, including emphysema, acute respiratory distress syndrome, and other airway diseases. Veterinarians typically use radiography to evaluate equine neonate lungs for disease, though CT images' higher resolution can make it easier to identify pathologic (disease) processes.

Generally speaking, "current CT imaging technology allows for whole lung imaging within seconds and provides very high-quality resolution, allowing for more accurate anatomic and morphologic (structural) characterization of all components of the lung," she explained.

Pulmonary disease is a significant cause of illness and death in young foals, she said, which highlights the need for veterinarians to be able to recognize normal lung structure on CT in different species and ages. And although CT use has been widely described in dogs and cats, there's just one published report describing the use of it in horses—in an older foal.

Lascola and colleagues recently completed a pilot study, funded by the Morris Animal Foundation, using CT images to characterize lungs in healthy, sedated equine neonates breathing without assistance from a ventilator. The team found that veterinarians can perform CT imaging rapidly when foals are sedated, and the foals tolerate the procedure well. Morphologic findings included:

- All foals showed atelectasis (failure of a lung to expand properly—essentially, lung collapse).
- Foals younger than seven days old had lower volumes of normally aerated lung compared to older foals.
- The atelectasis in younger foals was considered more severe than in older foals.

EQUINE EMERGING DISEASE LUNCHEON

Tracking emerging and re-emerging equine diseases helps the horse world attempt to stay a step ahead of economically devastating and deadly outbreaks. For that reason, equine veterinarians and industry members gathered on Thursday, June 14, for Merck Animal Health's Equine Emerging and Re-Emerging Disease Luncheon at the 2013 ACVIM Forum to discuss which infectious diseases concern leading veterinarians and researchers the most.

Wendy Vaala, DVM, Dipl. ACVIM, senior equine technical veterinarian with Merck Animal Health, moderated the presentation and subsequent discussions, which covered equine coronavirus, equine protozoal myeloencephalitis, Lyme disease, equine influenza virus, and *Corynebacterium pseudotuberculosis* (the bacterium that causes pigeon fever, also known as dryland distemper).

In addition to Vaala, presenters included Nicola Pusterla, DVM, PhD, Dipl. ACVIM, of the University of California, Davis, School of Veterinary Medicine, and Amy Johnson, DVM, Dipl. ACVIM, of the University of Pennsylvania's New Bolton Center.

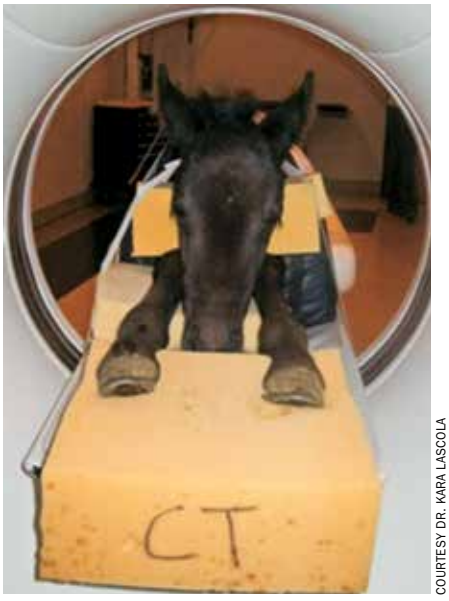
To read about the meeting in its entirety, see TheHorse.com/32296.—*Michelle N. Anderson*

While CT appears to be a useful tool for imaging equine neonates' lungs, Lascola noted that the team identified two potential limitations this modality poses in foals breathing on their own: the risk of developing atelectasis and the inability to control at which phase of breathing the image is taken.

Veterinarians have options for combating the latter issue, including controlling the foal's breathing with a manual or mechanical ventilator or opening collapsed portions of the lungs with recruitment maneuvers (sustained increases in airway pressure).

Lascola's team continues to study CT use for evaluating neonatal foals' lungs.

"We are completing a study using recruitment maneuvers and positioning the foals on their back versus on their chest to minimize atelectasis," she said. "The most important things are to find a technique that is fast, safe, and clinically applicable for our patients; provides the best image quality for diagnosis; and provides other (veterinarians) who may use CT with information regarding potential limitations … that may need to be accounted for when interpreting the images."



COURTESY DR. KARA LASCOLA

CT has proven to be a useful tool for evaluating neonatal foals' lungs.

Equine Collapse Causes Reviewed

Unraveling the reason behind an equine collapse often presents veterinarians with a diagnostic challenge.

Neil P.H. Hudson, MA, VetMB, PhD, DEIM, DipVetClinStud, MRCVS, a senior lecturer at the University of Edinburgh's Royal (Dick) School of Veterinary Studies, reviewed with veterinarians how to evaluate a collapsed horse and listed some common diagnoses.

Usually, a veterinarian makes two types of calls to examine collapse cases: emergency visits immediately following collapse, or nonemergency visits to horses with histories of episodic collapse.

"Frustratingly, in many cases of collapse a definitive diagnosis is not reached," Hudson said.

He cited one recent study in which researchers evaluated 44 horses presented for cardiac evaluation after collapse; veterinarians weren't able to determine the cause of collapse in 18% of those horses. In another recent study of 25 horses, veterinarians determined a definitive cause of collapse in 11 cases, a presumptive diagnosis in eight cases, and no cause in

the remaining six cases. And finally, in a postmortem study of 268 racehorses that collapsed and died either during work or within an hour of working, veterinarians weren't able to determine what caused collapse in 22% of cases.

When the veterinarians did find causes, they described the following:

Syncope Veterinarians use this term to describe fainting caused by a drop in arterial blood pressure leading to insufficient blood flow to the brain. The disorder remains poorly understood in horses, but its root is generally in a cardiovascular system malfunction, Hudson said, noting, "Syncope in the absence of cardiac failure is rare."

Hudson said in a recent study researchers found that syncope was either the definitive or presumed cause of 12 of 25 equine collapse cases.

He cautioned that differentiating syncope from either seizures or sleep disorders can be difficult.

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Collapse can be due to seizures, loss of motor function, and sleep disorders, among others.

Seizures Hudson said equine seizures can manifest as partial (focused in a localized area) or generalized (all-over) events and can be status epilepticus (in a state of persistent seizure, which is life-threatening). He said repeated seizures are most commonly seen in foals with an underlying disease process (acquired, such as sepsis—infection of the bloodstream) but, in some cases, can have a genetic basis. Seizures in adult horses also are largely considered acquired and generally are associated with an underlying disease process.

Hudson cited one recent study in which researchers evaluated 104 horses with histories of seizures and improved the classification system for equine seizures. Of the 73 horses described as epileptic (having two or more recurrent seizures) in the study, Hudson said, "35.6% were classified as symptomatic (with underlying brain pathology), 54.8% were classified as cryptogenic (unknown cause), and 2.7% as idiopathic (unknown cause but with suspected genetic predisposition)."

Sleep Disorders Equine sleep disorders can also cause horses to collapse, although they're slightly different than what most people are familiar with in humans.

"In humans, narcolepsy is characterized by chronic sleepiness, a marked disorganization of sleep/wake behavior, and pathological manifestations of rapid eye movement (REM) sleep," Hudson said, noting that narcolepsy is sometimes, but not always, associated with cataplexy (a sudden but usually brief loss of muscle tone, which causes horses to fall).

Hudson said that while narcolepsy with

cataplexy can occur in foals and some pony breeds, sleep attacks (called idiopathic hypersomnia and characterized by excessive drowsiness, buckling at the knees, stumbling, and even total collapse) in adult horses are less likely to represent true narcolepsy.

"There is a certain degree of debate regarding nomenclature, but it is possible that some sleep attacks seen in adult horses may be a form of idiopathic hypersomnia associated with chronic sleep deprivation," Hudson said.

Finally, he touched briefly on three other potential causes of collapse:

- ***Coma*** can be caused by trauma or by ailments including central nervous system disorders, bacterial infection, parasite infection, or liver disease.
- ***Loss of motor function*** can have its source in trauma, botulism, myasthenic syndromes (abnormal muscle weakness), and hyperkalemic periodic paralysis (commonly known as HYPP).
- ***Generalized or metabolic causes*** of collapse include shock, hypoglycemia, electrolyte abnormalities, endotoxemia, and anaphalaxis.

Hudson said in the cases practitioners can pinpoint the definitive cause, they can often treat the horse successfully.

Postoperative Ileus Insights

When an owner sends a horse to go under the knife for colic surgery, first and foremost he or she is hoping the horse survives the operation. But just because the animal makes it through the procedure doesn't mean he's out of the woods: Many horses develop a dangerous complication called postoperative ileus—a lack of gut motility after surgery.

Hudson provided insight on what we know, what we're still trying to learn, and what controversies surround postoperative ileus.

Study results indicate four to 10 out of every 100 horses colic each year. And while not all of those colics are surgical cases—meaning veterinarians can successfully manage some cases medically—Hudson noted that all horses undergoing laparotomies (i.e., exploratory colic surgery) for acute abdominal crises are at risk of developing postoperative ileus.

"Postoperative ileus has been described as being responsible for between around 9% and 40% of postoperative deaths," he explained. "Indeed, the fatality rate of postoperative ileus cases sadly can be high—ranges of 13-86% are described (in the literature)."

Researchers still aren't sure exactly what causes the condition in horses; however, they have estimated that it occurs in 10-50% of surgical colic cases, Hudson said. Scientists are exploring the disorder in a variety of species, trying to understand its pathophysiology better.

Traditionally, Hudson said, researchers believed ileus resulted from inhibited intestinal motor activity. More recently, scientists have suggested there is a significant inflammatory component, possibly triggered by the surgeon's manual manipulation of the horse's intestines. And researchers have also learned that intestinal macrophages (specialized white blood cells that kill and "clean up" damaged tissue and cells) likely play a role in developing and maintaining ileus, he said.

Postoperative ileus treatment generally involves one or more mainstays, including nasogastric decompression (removing the horse's stomach contents via a nasogastric tube), fluid and electrolyte therapy, endotoxemia control (eliminating toxins in the bloodstream), infection control, pain management, prokinetic therapy (administering drugs that make the bowel move contents faster), and inflammation reduction. Hudson said individual clinicians have their go-to treatments and preferred order of application, but treatment methods most practitioners agree upon include:

- ***Fluid therapy*** Hudson said fluid therapy is largely administered postoperatively, but is initiated on the operating table or even before the operation if the horse is cardiovascularly compromised.

> **"Postoperative ileus has been described as being responsible for between around 9% and 40% of postoperative deaths."**
>
> DR. NEIL P.H. HUDSON

- ***Anti-inflammatory therapy*** Hudson said researchers are continuing to examine inflammation's role in postoperative ileus development and maintenance; preliminary and anecdotal results have led many veterinarians to administer non-steroidal anti-inflammatory drugs (NSAIDs) in these cases.
- ***Early feeding and movement*** Hudson said that in humans with postoperative ileus, doctors often recommend eating to encourage intestinal motility. Likewise, some veterinarians use feeding as early as clinically possible after surgery as an attempt to counteract the effects of postoperative ileus. He said hand walking horses after colic surgery, if possible, might also help.
- ***Carboxymethylcellulose administration*** Researchers have found that when surgery is performed on the small intestine, administering carboxymethylcellulose—an intestinal lubricant—during the operation could help "improve survival, potentially by reducing adhesion formation (or, adhering of the resected intestine to nearby tissues)," Hudson said. However, he cautioned, another research group found that intraoperative carboxymethylcellulose administration was associated with a higher adhesion rate.
- ***Second surgery*** Hudson said there is controversy surrounding whether and when taking the horse to a second surgery (called a relaparotomy) is beneficial. "On one side, there is the argument that an early decision to go back in and … potentially correct a mechanical obstruction or a surgical complication may be warranted," he said. "Counterbalancing that is the evidence that the survival rate for horses requiring relaparotomy is reduced and the complication rate is high."
- ***Prokinetic therapy*** Veterinarians' therapeutic drug of choice is most commonly lidocaine (sometimes referred to as lignocaine). Other prokinetic drugs practitioners can use include metoclopramide, erythromycin, and bethanecol, Hudson said.

Although veterinarians have made strides in understanding and managing postoperative ileus, Hudson said there is much left to learn. Questions remain about the differences between healthy and diseased tissue behavior, inflammation's role, and lidocaine's effects.

View "Comparing Human and Equine Neonates" at TheHorse.com/32064

Fetal Consciousness' Impact on Equine Neonatal Health

Sometime between when the birthing process begins and when the long-legged foal takes his first wobbly steps, he transitions from an unconscious fetus to a conscious horse. Researchers believe the nature of this transition could have a significant impact on neonatal health.

John Madigan, DVM, MS, Dipl. ACVIM, ACAW, professor in the Department of Medicine and Epidemiology at the University of California, Davis, School of Veterinary Medicine, said that for many years veterinarians and researchers believed neonatal maladjustment syndrome (NMS, also known as dummy foal syndrome) was caused by pre-, intra-, or postnatal hypoxia (lack of oxygen). Oxygen deprivation can result in neurologic deficits, behavioral abnormalities, and, sometimes, death.

"Histopathologic (microscopic) evidence of cerebral hemorrhage and hypoxia

has been detected in (samples from) some severely affected foals in the mid-1970s," Madigan said. "However, many foals in recent studies do not have histological evidence of hypoxia, edema (fluid swelling), or hemorrhage." Additionally, he noted, about 80% of foals with NMS fully recover, unlike hypoxic human infants, who retain neurologic deficits.

These disparities prompted Madigan to take a closer look at what causes NMS.

He and colleagues began by looking at steroids with important neuromodulatory roles, called 5alpha-reduced pregnanes (such as progestogens), which are often referred to as neurosteroids. He explained that foals are subjected to high levels of progestogens while in the dam's uterus; these steroids essentially keep the foal in a quiet state to prevent damage to the mare.

"Neonatal foals have high concentrations of pregnanes at birth, which begin to decrease rapidly within an hour of birth and continue to decline over the first 24-48 hours of life," Madigan said. "Compared to healthy age-matched neonatal foals, NMS foals show significant ongoing elevation of plasma pregnane concentrations."

Madigan and colleagues administered a pregnane called allopregnanolone to healthy equine neonates in an experimental setting to produce clinical signs consistent with NMS. These effects were short-lasting, and foals returned to normal after administration ceased, he said.

Madigan said that while the team administered allopregnanolone, they used an electroencephalogram (EEG) to evaluate electrical impulses in the foals' brains. He said the foals' readings as they were standing were consistent with slow wave sleep.

"These data suggest that these steroids can cross the blood-brain barrier and exert neuromodulatory effects, which at high concentrations may have a dampening effect in the central nervous system with resulting alterations in states of consciousness, altered behavior, and responsiveness to stimuli, such as observed in NMS cases," Madigan said.

> **"There must be a clear and reliable signal that it is safe for the foal to wake up, to transition the consciousness."**
>
> DR. JOHN MADIGAN

He hypothesized that a possible reason neurosteroids might persist and prompt NMS-like signs in some foals is that normal signaling events during the birthing process don't take place properly. For instance, he said, if a foal passes rapidly through the birth canal or is delivered via cesarean section, normal transition signals prompting reduced fetal pregnane levels might not take place, leaving the foal with elevated neurosteroid levels.

"There must be a clear and reliable signal that it is safe for the foal to wake up, to transition the consciousness," he said.

Another theory, he said, is that some neonates revert to fetal-like brain status in response to adverse effects after birth.

"Based on these findings, the concept of reducing post-birth circulating plasma

pregnanes would seem to offer a potential new therapeutic option for NMS foals and perhaps other ill foals which appear weak and are not nursing," Madigan said.

His team is also evaluating the possible use of a technique he and his colleagues developed called squeeze-induced somnolence, which is believed to mimic passage through the birth canal. Madigan said this method might signal to the foal that he is outside the uterus and that it's time for pregnane production to decrease, allowing him to stand, nurse, and run. Squeeze-induced somnolence involves applying pressure to the thoracic (chest) area in healthy foals to induce recumbency, non-rapid eye movement sleep, muscle relaxation, and increased beta-endorphin levels.

During their studies the team noted a unique hormone surge after 20 minutes of squeezing, which is about the amount of time a foal is squeezed in the birth canal during a normal delivery, Madigan said. The internal signal for the foal to "wake up" involves the hypothalamic pituitary adrenal axis, which the team believes downregulates the pregnane secretion so the foal can transition to birth consciousness.

Madigan and colleagues are continuing research on the mechanisms behind NMS and possible treatments. A better understanding of this phenomenon could lead to rapid management in the field and less need for intensive care of dummy or ill foals.

Box Elder Tree Seeds Linked to Seasonal Pasture Myopathy

A horse starts showing stiffness and a reluctance to move. His muscles suddenly become weak to the point he can no longer remain standing. Then, as quickly as clinical signs set in, the horse dies.

Just 48 hours earlier the horse grazed happily in his pasture—an overgrazed field full of seed heads and dead leaves.

This story is typical of suspected cases of seasonal pasture myopathy (SPM), a highly fatal muscle disease described in the Midwestern United States and Eastern Canada, and atypical myopathy (AM) in the United Kingdom and the rest of Europe. For decades the disease had baffled veterinarians on both continents, who struggled to pinpoint and agree on a cause.

That changed in 2011 when Stephanie Valberg, DVM, Dipl. ACVIM, and a team of researchers from University of Minnesota

ANNE M. EBERHARDT

The neonate's transition from an unconscious fetus to a conscious foal is a critical step.

(UM) and Iowa State University (ISU) started investigating SPM cases and found a link to box elder trees.

Valberg said SPM and AM outbreaks vary year to year and usually occur in the fall. "Horses that develop SPM and AM are usually kept on sparse pastures with an accumulation of dead leaves, dead wood, and trees in or around the pastures," she explained.

In their study, Valberg and her team looked at 12 SPM cases that occurred at 11 Midwestern farms. Of the 12 cases, the team defined two as suspect and 10 as confirmed.

The team visited the farms located in Iowa and Minnesota, taking photos of pastures, plants, and trees. Team members also noted information about pasture topography, any overgrazing, and whether the pastures contained dead wood or standing water. They obtained photos from farms included in the study located outside of those two states, Valberg said.

A control group for the study included 23 Minnesota farms with no history of SPM in resident horses.

The farms with SPM cases all had one thing in common: the presence of box elder trees (belonging to the *Acer* family) "laden with seeds," Valberg said. Horses with SPM at all the affected farms also were on 24-hour turnout, "which was significantly longer than horses on the control farms," and all SPM pastures were overgrazed.

Researchers found that control farms were less likely to have box elders (61%

compared to 100%). Additionally, they were less likely to have overgrazed pastures (44% compared to 100%). Horses at SPM farms were less likely to receive supplemental hay or concentrate than those at the control farms, Valberg said.

"Thus, the common features for SPM horses were little supplemental feeding and prolonged grazing of sparse pastures that were in close proximity to seed-laden box elder trees," she said.

The research team collected box elder seed samples randomly from seven of the 11 SPM farms during fall 2011, as well as a control sample of ash tree seeds. Testing found that one nonproteogenic amino acid, hypoglycin A, was "highly abundant" in the box elder seeds but not in ash seeds. This amino acid is known to block the same enzyme in fat metabolism in humans as was detected in SPM-afflicted horses.

Recently, scientists have found a related tree, the European sycamore maple tree (*Acer pseudoplatanus*), in northern European pastures where horses have died from AM, Valberg said. European sycamore maple seeds also contain hypoglycin A.

"Hypoglycin A is a common cause of both SPM and AM," Valberg concluded. "This is supported by common epidemiology of SPM and AM, a common block on fat metabolism, the presence of hypoglycin-A-containing *Acer* species in affected pastures, and the presence of the toxic principle of hypoglycin A in the bloodstream of afflicted horses."

Young horses and those new to an affected pasture appear to be at great risk if:

- Pastures are overgrazed in the fall and early spring;
- Turnout time is greater than 12 hours per day; and
- No supplemental hay is provided on pasture.

Valberg noted that some horses do not develop SPM even after years of living on affected pastures.

To address owners' concerns of SPM developing in their horses, Valberg suggested removing box elder or European sycamore trees from affected pastures, although "this might not always be feasible."

In cases where the trees can't be removed, Valberg recommended decreasing turnout time on affected pastures from October through mid-December and in the early spring.

"Other important preventive measures could include providing additional forage

COURTESY DR. STEPHANIE VALBERG

Farms with SPM-affected horses all contained box elder trees laden with seeds.

if pastures are overgrazed, preventing overgrazing of pastures through rotational grazing, and limiting turnout to less than 12 hours per day during fall and early spring," she said.

More research is necessary to determine if seasonal and annual fluctuations occur in box elder and sycamore maple trees' hypoglycin A content, she said.

Botulism in Horses: An Update

Rising hay prices and the financial crunch caused by 2009's recession drove many horse owners to seek less expensive forage sources, including large round bales, haylage, and silage. But according to Amy Johnson, DVM, Dipl. ACVIM, compromising on hay quality and feeding from half-ton bales led to a larger problem: an uptick in reported botulism cases.

Johnson, who studies the disease at the University of Pennsylvania's National Botulism Reference Laboratory, described advances in diagnosing botulism in horses.

Botulism is a highly fatal multispecies neurologic disease cause by the bacterium *Clostridium botulinum* and the toxin it produces. The Centers for Disease Control and Prevention classifies it as a Category A (highest priority/highest risk) agent because it's a food-safety concern for humans and poses a real risk as a bioterrorism weapon for use against human and animal populations.

Despite their large size, horses are the most susceptible species to botulism toxicity, making them an important piece in understanding the botulism puzzle.

There are seven known strains of *C. botulinum*, described as Types A through G. Types A and B are most common in horses and are usually acquired through forage sources, Johnson said, adding that Type C is caused by carrion exposure (i.e., a decaying dead animal in feed). Type B is the only strain for which a vaccine is marketed for use in horses. Types D through G have never been reported in U.S. horses.

Johnson reviewed the three ways horses can contract botulism:

- Ingesting the botulinum toxin produced by *C. botulinum*;
- Foals—which have immature digestive tracts unable to protect them from the bacteria—ingesting *C. botulinum* spores that grow and subsequently elaborate toxin, leading to "shaker" syndrome; and
- Wound contamination.

A mouse bioassay is the species-wide "gold standard" for diagnosing botulism. In the simplest terms, this test exposes mice to samples from patients showing signs of botulism. If the sample contains botulism neurotoxin, and the mouse dies as a result, the horse likely has botulism. However, the mouse bioassay test takes time (anywhere from five days to two to three weeks, depending on the sample), and time is something a horse with botulism doesn't have, Johnson said.

"Laboratory confirmation with the mouse bioassay can be difficult," she said. False negative results are common because it takes very little toxin to cause botulism in a horse, and what little toxin there is does not remain in the gastrointestinal tract or bloodstream for long.

Experienced practitioners often base diagnosis on a horse's clinical signs and case history. Pertinent case history information includes whether the horse lives in an endemic area and the animal's current vaccination status against botulism Type B. Evaluation of feeding practices is also important because horses fed from large bales or with haylage or silage are more likely to contract botulism. Carrion exposure is also an important factor.

Johnson described the following two tests for botulism:

- ***Tongue tone or tongue stress test.*** For this test, the veterinarian gently pulls the horse's tongue from its mouth. The examiner then holds the horse's jaw shut and assesses the animal's ability to retract his tongue into his mouth.
- ***Grain test.*** In this test the horse is fed about eight ounces of sweet feed in a pan. "A normal horse can eat that amount of grain in less than two minutes, some faster," Johnson said. "Horses with botulism can take 15 minutes, with feed falling from mouth and nose, and even then might not finish it."

Botulism treatment includes a combination of antitoxin administration and supportive care. Veterinarians should give the horse antitoxin as soon as clinical signs and case history point toward botulism. "Every hour of delay reduces chances of survival," she stressed.

At this time horses can also receive the botulism Type B vaccine, Johnson said. Unlike with some diseases, natural exposure to *C. botulinum* toxin does not reliably stimulate the horse's immune system to produce protective antibodies. Vaccinating the horse with the Type B *C. botulinum*

ANIMAL SURVIVOR Q

Trainer Julie Blacklow thought Q's quiet demeanor and willing attitude had to do with her team's excellent training skills at Rosebud River Ranch in Snoqualmie, Wash. In reality, the yearling Rocky Mountain Saddle Horse gelding was critically sick with proliferative enteropathy, a diseased caused by the bacterium *Lawsonia intracellularis* and something Blacklow, a veteran horsewoman, had never heard of. She's not alone.

The American College of Veterinary Internal Medicine (ACVIM) is trying to change that by making owners more aware of *L. intracellularis* in horses. At the 2013 ACVIM Forum, the organization introduced Q as part of its "Animal Survivor" program, which highlights animals that—thanks to advances in veterinary internal medicine—have lived through severe disease.

COURTESY ACVIM

Q survived a severe case of proliferative enteropath.

Q's survival story started when he spiked a temperature of 104°F (99-101°F is normal). He also became lethargic and stopped eating, a sign to Blacklow that something was very wrong with the young horse. After an inconclusive initial exam by a general practitioner, Blacklow sought a specialist's second opinion. She contacted Chantal Rothschild, DVM, Dipl. ACVIM, of Northwest Equine Veterinary Associates, in Maple Valley, Wash.

Rothschild performed ultrasounds of Q's chest and abdomen looking for the source of the infection causing his fever. Then the gelding's blood work came back with extremely low protein levels. This is a telltale clinical sign of proliferative enteropathy, a spreading infection of the intestine most common in foals two to seven months old that renders the animal unable to absorb protein from his diet. Edema (swelling) had also developed around the horse's jaw and down into his chest.

L. intracellularis is common in pigs, and certain wild animals are thought to carry it, Rothschild said, adding that the disease is believed to be contracted when horses ingest bacteria from infected animal feces. Rothschild had treated equine cases during her time practicing in Texas and at Washington State University on the eastern edge of the state. "But I'd never seen a case in the Seattle area," she said.

After examining Q, Rothschild recommended treating him for proliferative enteropathy immediately rather than waiting for test results confirming *L. intracellularis* infection. "It would take too long to get a positive test back, so I asked the owners to trust me," Rothschild said. "If we'd waited we might not have been able to save him."

Q responded within three days and started acting less like the calm horse Blacklow knew and more like an energetic youngster.

Q's intensive treatment continued for six weeks, multiple times per day, and required dedication from the farm's workers and the horse's patience. Q was an excellent patient, Blacklow reported, and has since made what she considers a full recovery.—*Michelle N. Anderson*

toxoid vaccine reliably induces a protective immune response and prevents future susceptibility to botulism, she said. "Unfortunately, there is no cross-protection between types, so the Type B vaccine will only protect against Type B botulism and not against Types A or C," she said.

Antitoxin prevents additional botulism toxins from binding to their target, halting progression of the disease, but it does not reverse the disease or treat clinical signs. "So you should expect the horse to get a little bit worse before getting better," Johnson said.

Supportive care includes management of the down horse, hydration, and nutrition, Johnson said. She described recumbent horses with botulism as "Swiffers," because they are very susceptible to "picking up" environmental contamination and as such become very susceptible to nosocomial (hospital-acquired) infections. She said they are also susceptible to developing pressure sores and secondary infection, even when receiving high-quality care.

Practitioners and nursing staff should not force horses to rise frequently or stand for prolonged periods, Johnson said, because doing so can weaken the horse and cause clinical signs to worsen.

She also doesn't recommend sling support in the first one to three days of treatment. "However, after antitoxin treatment and stabilization of signs some severely affected horses will benefit from use of a sling to assist them to rise," she said.

In addition to pressure sores, complications in severely affected horses can include cellulitis (a diffuse inflammation resulting from infection of deep connective tissue), myositis (muscle inflammation), colic, cystitis (inflammation of the bladder), pneumonia, and salmonellosis.

A New Bolton study cites a 96% survival rate in a group of 30 shaker foals treated in the hospital and receiving antitoxin. Among the foals requiring ventilation support, 88% survived. In comparison, Johnson said in an older study researchers reported that 98% of foals not treated with antitoxin die.

Researchers haven't completed any papers on survival rates in a large group of adult horses with botulism. Based on a handful of published case reports, adult survival has been markedly lower than foal survival (90% mortality rate from Type A, 70% from Type B, and 80% from Type C), Johnson pointed out. Horses managed intensively in hospital settings have a higher survival rate, but probably not more than 50% of adult horses survive the disease.

"It's much harder to manage an adult horse with botulism," Johnson explained.

She and the other members of the National Botulism Reference Laboratory have optimized and validated polymerase chain reaction (PCR) techniques to detect the neurotoxin gene of *C. botulinum* in samples from equine cases of botulism.

The PCR assays identify the three clinically relevant types (Types A, B, and C) and offer several benefits over the mouse bioassay. "Results are available more quickly, the false negative rate is lower, and no lab animals are used," she said.

Additional objectives include finding, optimizing, and validating a test that detects the *C. botulinum* neurotoxin itself in equine samples, Johnson said, adding that "if such a test exists, it will eliminate the need for the mouse bioassay.

ABOUT THE AUTHORS

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