

Top Equine Medicine Studies of 2018

Dr. Rob MacKay shared presented research on ice boots and cryotherapy for laminitic horses, *R. equi* and insect bite hypersensitivity vaccines, EPM, and more.

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Researchers tested a new vaccine to help protect horses against insect bite hypersensitivity. Current management techniques include applying insecticides and repellents, stabling horses when insects are active, feeding omega-3 fatty acids to boost the horse's immune system, and using protective barriers such as fly sheets and masks. | Photo: iStock

The 2018 Kester News Hour medicine topics featured promising new innovations that will benefit horses in the future and practical clinical advice veterinarians can use today. The studies ranged from immunity and vaccination to equine protozoal myeloencephalitis (EPM) investigation and laminitis treatment.

Held annually at the American Association of Equine Practitioners' (AAEP) Convention, "Kester" is a rapid-fire roundup of the leading equine veterinary research studies published that year. For the 2018 AAEP Convention, held Dec. 1-5, in San Francisco, California, Rob MacKay, BVSc, PhD, Dipl. ACVIM, a professor of large animal internal medicine at the University of Florida's College of Veterinary Medicine,

in Gainesville, selected and presented medicine-related studies for the third consecutive year.

Here's a look at the papers he highlighted.

PNAG Vaccine for Pregnant Mares Protects Foals From *R. Equi* After Birth

The bacterium *Rhodococcus equi* is one of the leading causes of pneumonia in foals one to six months of age. The disease creates significant economic losses on equine breeding farms because it can affect many foals in a herd, is expensive and difficult to treat, and is often deadly. In seeking a vaccination option to protect foals from *R. equi*, a research team from Texas A&M University, in College Station, and Harvard Medical School, in Boston, Massachusetts, found that **vaccinating mares against a specific and common surface antigen**, poly-N-acetyl glucosamine (PNAG), prior to foaling offered protection to their foals. Why Harvard Medical School? Targeting PNAG with a vaccine could have human applications, as well.

Mackay explained that PNAG is a polysaccharide (large molecule made up of many simple sugars) that envelops the *R. equi* cell wall, as well as those of other important intracellular microbes (i.e., bacteria, fungi, protozoans) affecting many species—including humans.

Unlike humans, horses don't transfer immunity from mother to offspring via the placenta prior to birth. Instead, foals are born naive to disease and gain protection only via passive transfer of immunity by drinking their dam's colostrum (the antibody-rich first milk) in the initial hours of life. Therefore, vaccinating mares against specific pathogens is an important part of gestational care to protect their foals.

The study started with researchers administering a PNAG vaccine to 12 pregnant mares six and three weeks prior to their expected foaling dates. A seven-mare control group did not receive the PNAG vaccine. Researchers then exposed all their foals to *R. equi* at 28 weeks of age. Of the 12 foals born to vaccinated mares, only one developed pneumonia from *R. equi*, while six out of seven foals in the control group contracted the disease.

The results show that PNAG vaccination protects against the disease, Mackay said.

"A 28-day challenge is different than natural disease exposure," Mackay said, adding that the results are, however, promising for preventing *R. equi*, as well as other diseases, in horses, humans, and other species.

Cywes-Bentley C, Rocha JN, Bordin AI, Vinacur M, Rehman S, Zaidi TS, et al. **Antibody to Poly-N-acetyl glucosamine provides protection against intracellular pathogens: Mechanism of action and validation in horse foals challenged with *Rhodococcus equi*.** *PLoS Pathog* 2018;14(7): e1007160.

Ice Boot Therapy Helps, but Method Matters

Cryotherapy (cold therapy) is a proven preventive and treatment for laminitis. But getting a horse to stand in an ice bucket can prove challenging for even the most seasoned horse handlers and veterinary technicians. Commercially available cryotherapy sleeves can be applied to the limb above the hoof and potentially offer a problem-specific solution, while maintaining effective cooling of the hoof. In two studies, overlapping investigators from veterinary schools at the University of Pennsylvania (Penn Vet), in Kennett Square; Cornell University, in Ithaca, New York; and North Carolina State University (NC State), in Raleigh, looked more closely at how these commercial cryotherapy sleeves are used and whether their application could cause issues by overcooling

In Study 1 Penn Vet, Cornell, and NC State investigators included eight horses and used a thermocouple (temperature gauge) inserted into the foot to evaluate laminar tissue cooling when using an ice sleeve. Laminae are the tissues that suspend the coffin bone within the hoof capsule; they suffer injury during laminitic episodes, and cooling them can reduce inflammation with the hope of taking the “-itis” out of laminitis.

The researchers found the temperature dropped to 10 degrees Celsius (14 degrees Fahrenheit) in about 45 minutes using the sleeves, which MacKay said is comparable to results from similar techniques. He said this confirmed the usefulness of ice sleeves as an alternative to less-specialized solutions.

In Study 2 Penn Vet and Cornell investigators found soft tissue injury from overcooling in 7% (20/285) of horses treated with cryotherapy using an ice boot; seven of these were serious. Overcooling results from leaving the boot on for too long, MacKay said.

Additionally, he said, researchers used two different sleeve application techniques. With the first, they placed the sleeve above the hoof, as directed by the manufacturer, and with the second, they placed the boot lower on the leg to partially cover the coronary band. Importantly, researchers only used the modified technique of sleeve placement in Study 1, so no conclusion about effectiveness of conventional sleeve placement can be .

MacKay said the studies show that ice therapy sleeves, when modified to partially cover the coronary band, are effective for cooling the laminae. However, careful observation is important to prevent side effects caused by making the horse’s tissue too cold for too long, MacKay said.

Burke MJ, Tomlinson JE, Blikslager AT, Johnson AL, Dallap-Schaer BL. Evaluation of digital cryotherapy using a commercially available sleeve style ice boot in healthy horses and horses receiving i.v. endotoxin. *Equine Vet J.* 2018 Nov;50(6):848-853.

Proctor-Brown L, Hicks R, Colmer S, Guilfoyle D, Dallap-Schaer B, Johnson AL, Tomlinson J. Distal limb pathologic conditions in horses treated with sleeve-style digital cryotherapy (285 cases). *Res Vet Sci.* 2018 Dec;121:12-17.

Vaccine for IBH

A Swiss research group **tested an immunotherapy vaccine** for insect bite hypersensitivity (IBH, aka “sweet itch”) that resulted in reduced clinical signs of the condition in horses.

Approximately 10% of horses suffer from IBH, which is an allergic reaction to the saliva of biting insects (usually *Culicoides* midges). It’s common among Icelandic horses, which are genetically predisposed to the condition. Clinical signs can include intense itching, inflamed skin, scabbing, and hair loss from rubbing. Owners can manage the disease by applying insecticides and repellents, stabling horses when insects are active, feeding omega-3 fatty acids to boost the horse’s immune system, and using protective barriers such as fly sheets and masks. But, even when combining these various methods, keeping an IBH horse comfortable can prove challenging, MacKay said.

Interleukin-5 (IL-5) is a cytokine (a protein secreted by certain immune system cells that affect other cells) responsible for the maturation and release of eosinophils, which are white blood cells designed to fight invading antigens. In the case of IBH, the horse’s body responds to midge saliva by releasing excessive eosinophils, leading to inflammation and itchy skin. Thus, the itch-scratch cycle begins: The horse itches, so he scratches, which creates more itching, which results in more scratching. As the skin sustains damage, it also becomes vulnerable to secondary infection, making the itching and scratching worse.

Because of IL-5’s involvement in releasing and activating eosinophils, the research team hypothesized that inhibiting it would also limit IBH clinical signs in affected horses.

For this two-year study MacKay said 19 Icelandic horses received the IL-5 vaccine and 15 received a placebo. In Year 1, researchers vaccinated the horses on Days 0, 28, 56, 84, and 140. They vaccinated the horses again in Year 2 on Day 420 of the study.

Researchers monitored IBH clinical signs in the horses using a skin lesion scoring system developed for humans with eczema. Results showed 47% and 21% of vaccinated horses improved by at least 50% and 75%, respectively, and the second year of vaccination offered even better protection, said MacKay. Horses in the placebo-treated group showed markedly less improvement, with no horses getting more than 50% better during the study.

Additionally, the researchers tracked anti-IL-5 blood titer levels, which rose significantly after initial inoculation and stayed high throughout the warmer months, when IBH is most severe.

MacKay noted that this vaccination could offer an inexpensive and easy way to make IBH horses more comfortable; however, further investigation might be necessary. “It needs to be evaluated in other breeds,” he said.

Fettelschoss-Gabriel A, Fettelschoss V, Thoms F, Giese C, Daniel M, Olomski F, et al. **Treating insect-bite hypersensitivity in horses with active vaccination against IL-5.** *J Allergy Clin Immunol.* 2018 Oct;142(4):1194-1205.

Previously Undescribed Parvovirus Found in Vaccine Serum

A Cornell-led research team identified a new liver-disease-causing virus after a Nebraska horse died 65 days after routine vaccination. The team found equine parvovirus-hepatitis (EqPV-H) in both the deceased horse's liver and the tetanus antitoxin he had received.

Veterinarians around the world have recognized hepatitis (liver disease) in horses caused by vaccination for the past century, said MacKay. In 1919 Sir Arnold Theiler first described equine-serum hepatitis (liver disease) in South African horses during experimental vaccination against African horse sickness. So-named "Theiler's disease," serum hepatitis has been associated with administration of several equine serums, antitoxins, and plasma,

After identifying EqPV-H, the research team tested serum samples of 100 horses submitted to the New York State Animal Health Diagnostic Center at Cornell for nonclinical reasons. Thirteen tested positive for the presence of the virus. That means these apparently healthy horses had contracted the virus at some point and "subclinical (without clinical signs) cases are common," MacKay said.

EqPV-H is the most recent addition to the albeit short list of viruses found to cause Theiler's. Notably, parvoviruses such as EqPV-H are relatively resistant to heat treatment, said MacKay, which might explain how they occasionally survive in commercial tetanus antitoxin.

Divers TJ, Tennant BC, Kumar A, McDonough S, Cullen J, et al. **New Parvovirus Associated with Serum Hepatitis in Horses after Inoculation of Common Biological Product.** *Emerg Infect Dis.* 2018 Feb;24(2):303-310.

Can SAA, CRP Testing Identify EPM?

Equine protozoal myeloencephalitis (EPM) causes neurologic clinical signs, including (but not limited to) incoordination, weakness, and muscle atrophy, and is notoriously difficult for veterinarians to diagnose. Options for diagnosis include cerebrospinal fluid (CSF) and blood testing, as well as observing whether the horse responds to treatment based on clinical signs and case history. Could additional blood testing looking at **inflammatory markers such as serum amyloid A (SAA) and C-reactive protein (CRP)** offer another avenue to help identify EPM cases? A Penn Vet research team investigated.

MacKay said both SAA and CRP are acute phase proteins, which increase or decrease in response to inflammation in the body. Several studies in recent years have confirmed SAA testing on blood and serum can offer early detection of certain infections in horses. It can also help differentiate between infectious and noninfectious causes of certain diseases. For example, a veterinarian can use SAA to confirm a horse has allergy-induced asthma rather than an infectious respiratory disease such as equine herpesvirus or equine influenza. Like SAA, high CRP is associated with infectious diseases such as enteritis (intestinal inflammation) and pneumonia.

The researchers on the study included plasma and CSF samples from horses with confirmed cases of a variety of either infectious or noninfectious neurologic diseases but focused on EPM and cervical vertebral stenotic myelopathy (CVSM, or wobbler syndrome) cases. The researchers compared SAA and CRP levels in EPM and CVSM horses and found no differences.

“So far, acute phase proteins have no value in differentiating among equine central nervous system diseases,” MacKay said.

Mittelman NS, Stefanovski D, Johnson AL. **Utility of C-reactive protein and serum amyloid A in the diagnosis of equine protozoal myeloencephalitis.** *J Vet Intern Med.* 2018 Sep;32(5):1726-1730.

EPM and Protozoal Coinfection in Eastern U.S.

Coinfection by multiple protozoa is unlikely the cause of EPM cases in the Eastern United States, reported an Oregon State University researcher who looked at EPM cases originating from this area and diagnosed and treated by Penn Vet practitioners.

Both *Sarcocystis neurona* and *Neospora hughesi* are known to cause EPM. However, not all horses exposed to these parasites develop EPM. Researchers theorized that another protozoon, *Toxoplasma gondii*, might also play a role in EPM by increasing the of *S. neurona* and *N. hughesi*.

Researchers had previously shown that coinfection of sea mammals by *S. neurona* and *T. gondii* causes more significant neurologic signs than does single infection with either protozoon. Based on that knowledge, the research team wanted to find out if polyparasitism (infection with multiple parasites) increased the likelihood of horses developing the neurologic signs associated with EPM.

Investigators on the study reviewed lab results on 101 cases of horses diagnosed with EPM or CVSM. As expected, the researchers found that a significantly increased proportion of the EPM cases were positive for *S. neurona* compared to the CVSM cases. However, instances of *N. hughesi* and *T. gondii* were not significantly higher in EPM cases compared to CVSM cases. The results “do not support a role for polyparasitism in EPM,” MacKay said.

Schale S, Howe D, Yeargan M, Morrow JK, Graves A, Johnson AL. **Protozoal coinfection in horses with equine protozoal myeloencephalitis in the eastern United States.** *J Vet Intern Med.* 2018 May;32(3):1210-1214.