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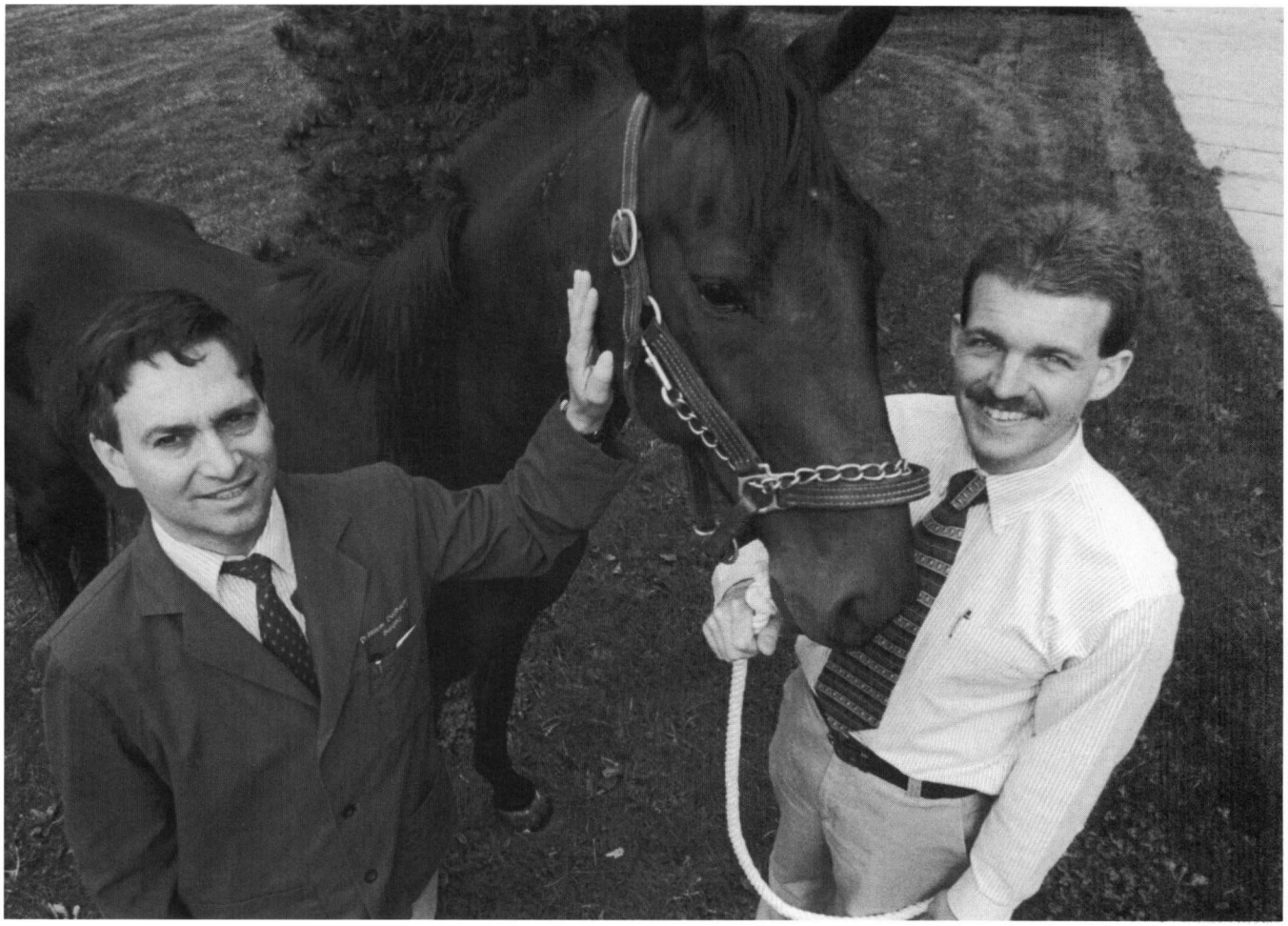
A report from the Harry M. Zweig Memorial Fund for Equine Research at the College of Veterinary Medicine at Cornell University



NICOLA KOUNTOUPES/UNIVERSITY PHOTOGRAPHY

Norm Ducharme and Brett Woodie are finalizing their design for the Cornell DDSP collar, which holds the hyoid bone and larynx in place when horses run.

INSIDE

New Cornell Collar Prevents Dorsal Displacement of the Soft Palate

Dorsal displacement of the soft palate (choking down), known as DDSP, is a common cause of respiratory noise and performance impairment among racehorses. When some horses—Thoroughbreds and Standardbreds, especially—race at high speeds and breathe heavily, their soft palate (the rear roof of the mouth) moves up and over the epiglottis and partially blocks the airway. ▶

Dorsal Displacement

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Without understanding why DDSP occurs, veterinarians haven't been able to find a reliable treatment that works more than 60 percent of the time. Recently, however, Norm G. Ducharme, DVM, MSc, Dipl ACVS and his colleagues at Cornell have made an interesting series of discoveries: First, they have isolated a muscle (the thyrohyoid) that is responsible for causing DDSP and can now reliably reproduce and surgically repair palate displacement by cutting and repairing the thyrohyoid muscle. What's more, they can *prevent* palate displacement by manually holding a horse's voice box while it exercises on the high-speed treadmill.

"We have designed what we are calling a 'Cornell DDSP collar,' which should be able to perform the same function as our hands during exercise," explains Ducharme, who has just received a grant from the Harry M. Zweig Memorial Fund to test and redesign the collar with colleagues Brett Woodie, DVM, MS, Richard P. Hackett, DVM, MS, Dipl ACVS, and Hollis N. Erb, DVM, MS, PhD.

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>
> Norm Ducharme

"Hopefully, the external collar will reposition and hold the larynx and hyoid bone (which connects the muscles of the tongue to the muscles of the throat) to prevent the palate from moving over the airway. This repositioning will hopefully prevent exercise-induced DDSP and reduce the need for surgery."

The road to the collar's development, however, has been a rocky and long one. Over the past 50 years, veterinarians have held various theories as to the causes of DDSP and have tried different treatments, accordingly.

"Originally, veterinarians thought the palate itself was abnormal, either weak or elongated," says Ducharme, explaining that the soft palate is the structure that separates the food pathway from the airway. As air pumps in and out of the lungs through the voice box (larynx) above the soft palate, the airflow can catch and lift the palate on exhales so that half or more of the airway is blocked.

Surgery to remove a small section of the tongue (staphylectomy) seems to help about 60 percent of the time; cutting the strap muscles on the lower side of the neck (sternothyroid muscle resection) to prevent the voice box from slipping back and away from the palate also helps about 60 percent of the time. Ironically, performing both procedures, which has became fashionable in the past decade, also only helps about 60 percent of cases. Trainers also use tongue ties on exercising horses in an attempt to prevent palate displacement but this doesn't always work either.

Recent research has confirmed that inflammation of the airway (pharyngitis) can trigger some DDSP cases by damaging the nerve going to the soft palate. This can paralyze the palate and render it no longer able to effectively resist pressure changes in the airway and thereby get moved out of its normal position.

"We now know to look for and treat any inflammation with anti-inflammatory agents first before considering surgery," says Ducharme.

Most horses that develop DDSP, however, do not experience inflammation near the palate nerve. Thus it was a major step forward when Ducharme and his colleagues found that the thyrohyoid muscle (one of the four muscles in the throatlatch area) was critical in controlling the tension and position between the palate and voice box.

With the Zweig grant, the researchers are perfecting the collar's design to be sure it prevents airway obstruction, fits well, is well tolerated, and is easy to use. First they will test the collar on normal horses, then on horses in which the researchers have induced DDSP (by cutting the thyrohyoid muscle) to evaluate whether the collar prevents DDSP in these cases. Last they will test it on horses with naturally occurring DDSP.

The collar could have widespread application for the racing industry for use in training and racing to prevent DDSP.

"Conceivably the collar could be used to 'teach' horses where to place their voice box during exercise training," says Ducharme. "The collar also could play an important role in identifying horses that are the best candidates for surgery, whether the collar is accepted for use during racing or not. We think we are very close to offering a relatively simple, low-cost tack-change design that could have a major impact on the industry." ■

Glaser Develops Improved Test for West Nile Virus

The West Nile Virus (WNV) was eventually identified as the culprit when, back in 1999, 25 horses on Long Island and in New York City were stricken with encephalitis. Nine of the horses eventually died or were euthanized. After this epizootic event, predictions were made that the virus would not overwinter and that WNV would disappear.

The next year, however, 61 equine cases were confirmed in a broader geographic area and 23 died or were euthanized. Numbers of cases and range of distribution increased further in 2001, when 738 cases of WNV-associated encephalitis were confirmed in horses from 20 states. Twenty-two cases were found in New York State. Clinical outcome was reported for 470 of the confirmed cases; 33 percent of these were fatal or required euthanasia.

By early April of this year, clinical WNV-associated encephalitis cases in horses had been reported in Florida. More are expected.

The disease is difficult to diagnose. Signs of infection include the sudden onset of ataxia (lack of coordination, loss of balance), depression (listlessness), weakness, and muscle tremors. These signs, however, are not specific to WNV but also symptomatic of other diseases such as rabies, equine herpes myelitis, equine protozoal myelitis, eastern equine encephalitis, spinal chord compression caused by malformation or trauma, and lead poisoning.

"Since the clinical signs are nonspecific, veterinarians must use laboratory tests to determine whether the cause of the horse's illness is WNV or another disease," says Amy Glaser, MS, PhD a senior research associate in the Department of Population Medicine and Diagnostic Sciences. "And the only specific test for WNV is a serum neutralization test." However, this test requires specialized laboratory facilities, which are not commonly available.

NICOLA KOUNTOUPES/UNIVERSITY PHOTOGRAPHY

Amy Glaser is searching for proteins present in the serum of horses after natural infection with West Nile Virus that are not present in horses vaccinated against the disease.

On the prevention side, an inactivated whole virus vaccine is available from Fort Dodge Animal Health Laboratories. This vaccine is being widely used in regions of the country where WNV has been identified. Horses produce antibodies in response to vaccination, which neutralize WNV in cell culture.

To better diagnose WNV, Glaser has received a grant from the Harry M. Zweig Memorial Fund to develop a new ELISA screening test for WNV. ELISAs (enzyme-linked immunoassays) are widely used laboratory techniques because they can rapidly detect whether certain substances are present in the serum (the fluid from blood samples after red blood cells have been removed).

When a horse is infected with WNV, for example, the immune system launches an attack on the virus by producing antibodies against the virus. The current ELISA test for WNV detects antibodies to the envelope protein of the virus. If the enzymes used in the ELISA test bind to the envelope protein, they know that the horse has been exposed to the virus and has produced antibodies against

> "Once we have defined the proteins that are recognized by antibodies in the serum of horses that have been naturally infected, we will test the suitability of these proteins for use in an ELISA test that can differentiate between vaccinated and naturally infected horses."
>
> Amy Glaser

West Nile Virus

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it. The problem, however, is that these antibodies are produced by both naturally infected horses and horses vaccinated for WNV.

Glaser's goal is to find proteins other than the viral envelope protein that would be present in the serum of horses after natural infection but not present in horses vaccinated for WNV. In humans, for example, the current vaccine used induces antibody to the envelope protein, as in horses, but not to a protein referred to as NS1. Thus, Glaser plans to focus on NS1 initially in equine serum samples after natural infection as a potential protein to test for in the ELISA. She also will investigate the antibody response to other proteins if necessary.

"Once we have defined the proteins that are recognized by antibodies in the serum of horses that have been naturally infected, we will test the suitability of these proteins for use in an ELISA test that can differentiate between vaccinated and naturally infected horses," she says. ■

Endometrial Cups Appear to Play a Role in Mare Reproductive Loss Syndrome

For an unknown reason, hundreds of mares in central Kentucky have lost their pregnancies. The syndrome, named the Mare Reproductive Loss Syndrome (MRLS), is costing the thoroughbred breeding industry hundreds of millions of dollars.

To determine how to best help out in the crisis, Dietrich H. Volkmann, BVSC, MMed Vet visited Kentucky in May 2001.

"I became aware of the lack of specific investigations aimed at characterizing the hormonal profiles of mares that had lost their fetuses during early pregnancy," says Volkmann.

He learned that mares that had begun forming their placentas, which occurs at about 35 days after ovulation, were at much higher risk of losing their pregnancy than mares that had not progressed to that stage in their pregnancies. Of particular interest was that although mares were losing their fetuses, most were retaining their endometrial cups.

Endometrial cups are unique glands that develop only in equine pregnancies and, although they are formed by fetal tissue, their survival is independent of the fetus's survival. Several weeks after conception, as the placenta develops, the cups begin to form and produce the hormone equine chorionic gonadotropin (eCG), which can be detected in high concentrations in the mare's blood.

One function of eCG is to stimulate the ovaries to produce additional (accessory) corpus luteums. If a pregnancy is lost during the stage when the cups are present, this stimulatory effect on the ovaries continues with unabated force, preventing the mare from returning to regular heat cycles.

"The result is that the mare can't be rebred again that season," Volkmann points out. "Not only is this a major problem with MRLS, but it also occurs on a regular basis in smaller numbers when mares suffer fetal losses during the endometrial cup phase and cannot be rebred."

In normal pregnancies the endometrial cups are destroyed by an as yet ill-defined mechanism once the mare is between 70 and 80 days pregnant and her eCG concentrations fall to basal levels. This allows the mare that has lost her pregnancy to return to regular cycles only about 120 days after the original conception.

With a new grant from the Harry M. Zweig Memorial Fund, Volkmann is setting out to characterize the hormonal patterns associated with these early pregnancy losses. He hopes to confirm or reject assumptions now held about the behavior of endometrial cups after pregnancy loss, as well as glean crucial information regarding the mechanisms that lead up to pregnancy losses in mares.

"For example, by using hormone production as an indicator of fetal and placental well-being or disease, we may be able to predict whether mares that show some abnormalities in their

ARIEL BULLION/UNIVERSITY PHOTOGRAPHY

Harry M. Zweig Memorial Fund for Equine Research—2002 Awards

The following research awards were made by the Zweig Committee at its annual meeting in November.

New

$54,000 to Dorothy Ainsworth for "Influence of an Underlying Immune Environment on the Subsequent IgG Isotype Response to a Foreign Antigen"

$40,542 to Norm Ducharme and Brett Woodie for "Design of a Training and Therapeutic 'DDSP Collar' to Prevent Dorsal Displacement of the Soft Palate"

$18,640 to Robert Gilmour and Brett Woodie for "Are ERG K+ Channels in Equine GI Smooth Muscle Molecular Targets for Prokinetic Drugs?"

$22,154 to Katherine Houpt for "Effects of Iso-Caloric Diets Differing in Sweetness or Lactic Acid Production on Cribbing"

$77,748 to Alan Nixon for "Growth Factor Gene Enhanced Chondrocyte Function Using Adeno-Associated Viral Vectors"

$29,525 to Dietrich Volkmann for "Hormonal Function in Mares Suffering from Mare Reproductive Loss Syndrome (MRLS)"

$24,558 to Amy Glaser for "Detection of WNV Antibodies and Discrimination Between Vaccinated and Infected Horses"

Renewal

$52,013 to Douglas Antczak for "Horse Genome Project"

By examining hormonal patterns, Dietrich Volkmann hopes to determine whether it is the corpus luteum, the endometrium, or the placenta that initially malfunctions in early pregnancy loss.

placental function will return to normal or continue to be high risk," Volkmann points out. "We also may be able to predict whether the fetuses that survive MRLS-related abnormalities will be normal or abnormal at birth."

He will compare hormone levels in blood from normal pregnant mares and affected mares at similar stages of pregnancy. Such an endocrine analysis hopefully will determine whether the corpus luteum, the endometrium, or the placenta initially malfunctioned and caused the demise of the pregnancy.

The grant also will allow Volkmann to examine in detail why some mares that had lost pregnancies as a result of MRLS, and presumably retained their endometrial cups, were still able to ovulate and conceive while most cannot. To do so, he will compare the hormonal patterns of successfully rebred mares with those unsuccessfully rebred. He also hopes to identify some hormones that could be used to treat mares to return them to a breedable status.

"In an attempt to return these mares to a fertile status, we also plan to test a novel approach that manipulates the effect of eCG on the ovaries by injecting mares that have lost their pregnancies but retained their endometrial cups with a highly specific monoclonal antibody against eCG, which is available for use in cattle," Volkmann says.

Although some veterinarians now try to surgically obliterate the endometrial cups in an attempt to destroy the source of eCG so that the mares can be rebred, the injections may neutralize the circulating eCG sufficiently so that the mares can ovulate. Volkmann hopes to determine whether the injections will affect the health of the mares and whether subsequent pregnancies will be normal, considering that the mare still has active endometrial cups from the very beginning of her first pregnancy.

Studying mares that are successfully rebred also will help determine whether MRLS has any long-term deleterious effects on placental function or fetal well-being in mares whose pregnancies were abnormal, and yet the fetus still survived. ■

Check Out the Zweig Memorial Fund Web Site

Where can you read all about current and past research sponsored by the Harry M. Zweig Memorial Fund for Equine Research? Or relive the history of the memorial fund, scan information about the 13 members of the Zweig Committee, review all the Zweig newsletters since 1997, and explore numerous equine-related links?

All of this and more is available through the new home page of the Zweig Memorial Fund.

In addition, the new web site has links to more than three dozen articles describing, in lay language, the equine research conducted in the past five years at Cornell. Among them are articles on ovary stimulation, immunotherapy for treating COPD, and gene therapy techniques for repairing equine cartilage damage, as well as those about equine leptospirosis, equine protozoal myeloencephalitis (EPM), and cardiac arrhythmia.

The site also offers quick access to equine organizations and societies and to numerous other equine resources, such as Equine Info (a gateway to numerous horse-related links), Equine Online, the Horse Interactive (an online guide to equine health care), and Horse Net (an internet community for horse people).

So, check it out:

www.vet.cornell.edu/public/research/zweig/

The Harry M. Zweig Memorial Fund for Equine Research honors the late Dr. Harry M. Zweig, a distinguished veterinarian, and his numerous contributions to the state's equine industry. In 1979, by amendment to the pari-mutuel revenue laws, the New York State legislature created the Harry M. Zweig Memorial Fund to promote equine research at the College of Veterinary Medicine, Cornell University. The Harry M. Zweig Committee is established for the purpose of administering the fund and is composed of individuals in specified state agencies and equine industry positions and others who represent equine breeders, owners, trainers, and veterinarians.

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