Zweig

Memorial Fund News Capsule

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

No. 30 November 2000

NICOLA KOUNTOUPES

Robert Gilmour explains the laboratory technique he's developed for recording the electrical activity of a single living Purkinje fiber cell—the type of cell suspected to cause cardiac arrhythmia.

INSIDE

Unraveling the Cause of Cardiac Arrhythmias

Horses have a wide range of normal heart rates and rhythms that vary widely depending on the animals' activity. Compared with other companion and performance animals, however, horses show more variety in their heart rates and rhythms than many other species. And one of those rhythms is an abnormal heartbeat called an arrhythmia, which horses experience more frequently than most other domestic species. Arrhythmias often occur during intense exercise and endurance training but are also caused by certain drugs, such as cisapride, which is used for noncardiac purposes. And while some arrhythmias are benign, some compromise athletic performance and some are even life threatening. ▶

Cardiac arrhythmias

continued from page 1

As in many species, the equine heartbeat is regulated by electrical impulses. Protein structures in heart cells, called ion channels, control the flow of ions (charged atoms or groups of atoms) such as potassium, sodium, and calcium ions. The flow of these ions in and out of the cells produces the electrical activity of the heart, explains Robert F. Gilmour, Jr., Ph.D., a professor of physiology, who has a grant from the Zweig Memorial Fund to study the cardiac electrophysiology of the equine heart.

When the heart activates contractions in a normal orderly sequence, cardiac output is optimal and plenty of oxygenated blood flows to the body's muscles, brain, and other tissues. When the sequence is disrupted, however, as during an arrhythmia, the contractions are compromised and the body's tissues and brain may not get enough oxygen and blood. The result can be fatigue, severe disorientation, and even death.

One of the most common causes of life-threatening arrhythmias in humans is medication that is also commonly used in equine practices, such as erythromycin, cisapride, and trimethoprim-sulfa combinations. These drugs can block potassium channels that are responsible for the heart's repolarization, that is, the recharging of the electrical system after each heartbeat. Evidence suggests that horses might be at risk for these kinds of problems as well.

"The outward potassium current is thought to play a particularly important role in sustaining the complex patterns of electrical activity that exist in different regions of the heart," says Gilmour. The potassium movement from the inside of the cardiac cells to the outside via specific potassium channels is largely responsible for how long the cellular electrical response is and the subsequent heart contraction.

Although the molecular nature of these potassium channels in different regions of the heart is very well understood in humans, dogs, cats, rats, and other animals, very little is known about it in horses.

"A major lesson learned from a decade of intense research, however, is that you can't generalize from one species to another with respect to these potassium channels and repolarizing cardiac currents because a tremendous amount of species variation has been observed," Gilmour adds.

> **"These very preliminary results indicate that the spectrum of potassium channels in the horse heart may differ significantly from those in the human heart."**
>
> Robert F. Gilmour, Jr.

Gilmour's Zweig grant focuses on the potassium channel function in the horse. His study is designed to identify the potassium channels in the equine heart and to characterize their biophysical properties and their response to various potassium channel-blocking agents to determine which may promote or suppress cardiac arrhythmias. In addition, Gilmour and his colleagues, which include Dr. Thomas Divers at Cornell University and Drs. Lisa Freeman and James Lillich at Kansas State University, are correlating the effects of various drugs on individual currents with changes in the electrical response of isolated cardiac cells in the lab as well as cardiac electrical activity in live horses.

"So far we've shown in isolated horse ventricular tissue that cisapride and several other drugs that are known to block the potassium current called IKr prolong the duration of the cardiac action potential and, in high doses, induce cellular rhythm disturbances (known as early afterdepolarizations)," says Gilmour. "The latter would be manifest in the intact horse as a potentially lethal cardiac arrhythmia.

"We also have demonstrated, using confocal microscopy and immunoblotting (or Western blotting), that several potassium channels that we expected to be present in the horse ventricle, including the rapid delayed rectifier (Ikr), are there, as is the ultra-rapid /potassium current (Ikur), which we hadn't expected to find. In addition, a channel that we expected to be present, the transcient outward potassium current (Ito), apparently is not. These very preliminary results indicate that the spectrum of potassium channels in the horse heart may differ significantly from those in the human heart. Consequently, different types of drugs may be required to control equine cardiac arrhythmias than are used to control human arrhythmias."

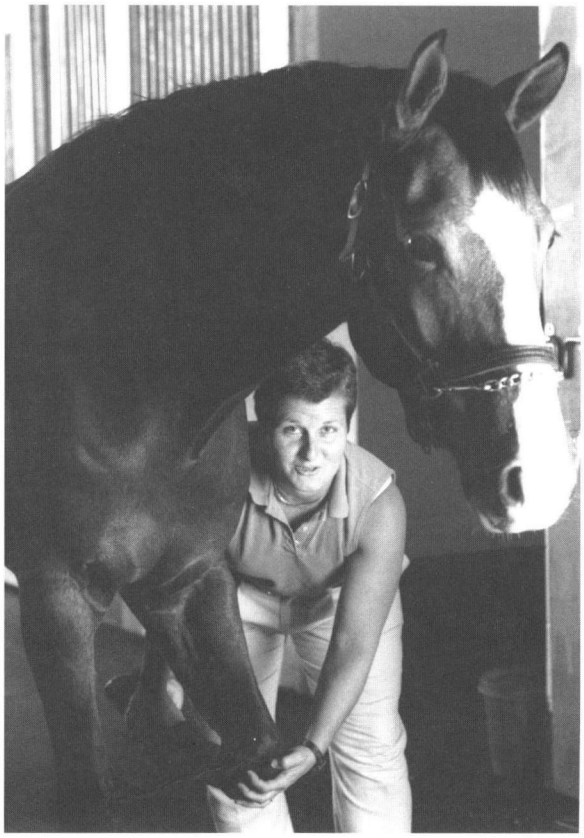
Gilmour's research is important not only for understanding the normal function of equine cardiac electrical activity but also for identifying the mechanisms and potential therapy for cardiac arrhythmias in the horse. Many drugs now used have undesirable side effects or only limited abilities in treating chronic or recurrent problems. His work also should help veterinarians develop protocols to treat heart arrhythmias with fewer side effects and allow clinicians to anticipate and avoid toxicities and potential life-threatening reactions associated with non-cardiac drugs that block cardiac potassium channels. It should also confirm whether medications such as cisapride put horses at risk for cardiac arrhythmias. ■

Study Points to Prognosis for Lame Racehorses

Joint problems are very common in performance horses. When joint injury is serious, horses are often sent to a referral center such as the Equine Hospital at Cornell University. Ideally, the hospital could give owners an informed, objective prognosis on the survival and future performance of the horse. Although lameness is the most significant factor responsible for a Thoroughbred's failure to race, veterinarians have few reports to rely on when they determine the short- and long-term prognosis for a horse affected with joint disease.

To determine which indicators are most significant for horses that are lame owing to joint disease, a group of veterinarians evaluated the risk factors of 507 horses with joint disease that came to the Cornell Equine Hospital between 1983 and 1990. Supported by the Harry M. Zweig Memorial Fund, the study used logistic multiple regression analyses to simultaneously examine more than one predictor variable for successful outcomes.

"Simultaneous examination of variables is important because it 'corrects' for relationships among the predicator variables," explains Susan L. Fubini D.V.M., Dipl ACVS, professor of surgery. The study, published in a recent issue of the *Canadian Journal of Veterinary Research* (1999, Vol. 63, pp. 253–260), was co-authored by Rory J. Todhunter BVSc, M.S., Ph.D., Dipl ACVS, associate professor of surgery; Hollis N. Erb D.V.M., M.S., PhD., professor of population medicine and diagnostic sciences; and Kathleen P. Freeman, now at the Animal Health Trust in Suffolk, England.



ROBERT BARKER

Susan Fubini checks the corpus of a show horse for swelling and pain.

> "For racing horses the risk factors linked to better odds of survival were osteoarthritis, higher hospitalization costs, hospitalization longer than a day, and having had arthroscopic surgery."
>
> Susan L. Fubini

The researchers looked at breed, gender, how the owner used the horse, diagnosis, joint(s) involved, and the procedure used on the horse at the clinic. They divided the horses by age. There were 53 foals four months old or younger, and 87 yearlings between four months and two years of age. There were 367 adult horses, of which 141 were non-racers and 226 were racers.

"Interestingly, we found that some of the risk factors that predicted whether racehorses would be alive at follow-up were different from those that predicted whether non-racehorses would be alive," says Fubini. For the non-racing horses, the following risk factors were associated with higher odds of being alive three months after admission to the hospital: lameness associated with the corpus, having had arthroscopic surgery, a prognosis other than "poor" given, having become sound, above-average hospitalization costs, and duration of follow-up. For racing horses, however, the risk factors linked to better odds of survival were osteoarthritis, higher hospitalization costs, hospitalization longer than a day, and having had arthroscopic surgery.

Surprisingly, the researchers found that within age and use class, the horse's age, breed, gender, intended use of the particular joint, or number of joints involved made little difference in whether the horse was discharged from the hospital, became sound, or was alive at a three-month follow-up.

What did matter was that foals with infectious arthritis had good odds of surviving, at least in the short term.

"Our interpretation of this finding is that when foals with septic joints are given appropriate therapy, they respond well, at least in the short term," adds Fubini.

Moreover, the researchers found that multiple joint involvement was not a poor prognostic sign. Further, yearlings with osteochondrosis dissecans (OCD) did very well, although this finding also implied that all the other diagnoses associated with joint lameness among yearlings had less favorable outcomes. ■

How Does High-Intensity Exercise Affect the Immune System?

Equine athletes get lung infections, such as pneumonia, infectious bronchitis, and lung abscesses, significantly more often than other horses do. These diseases not only compromise racehorses' performance but also often force horses into lengthy and costly convalescent periods. In fact, respiratory diseases are the second most common cause of lost training or performance days among racehorses.

"And one of the greatest risk factors for developing pneumonia, pleuritis, or lung abscesses in athletic horses is the racing itself or strenuous exercise," says Dorothy Ainsworth D.V.M., M.S., Ph.D., Dipl ACVIM, an associate professor of medicine in the department of clinical sciences and section chief of large-animal medicine in the Equine and Farm Animal Hospital.

Racing is one of the greatest risk factors for developing pneumonia, pleuritis, and lung abscesses.

"We need to better understand how the naturally occurring stress of exercise adversely affects the immune response and contributes to vaccine failures and respiratory disease development in racehorses. This is critical considering the growing body of literature showing vaccine failures for the common equine respiratory pathogens."

Dorothy Ainsworth

Evidently, the strenuous exercise temporarily compromises racehorses' immune systems, which makes the animals much more susceptible to developing lung conditions.

"Because of the immunosuppression, aspirated bacteria, which normally reside in the pharyngeal cavity, can take advantage of the depressed respiratory tract defense mechanisms, rapidly proliferate, and develop into infections," explains Ainsworth, a large-animal pulmonologist with a special interest in pulmonary immunology. In addition, the immune suppression that's triggered by intense exercise also can allow viruses to establish themselves more easily in the respiratory tract, which, in turn, can predispose the horse to secondary bacterial infections.

"We need to improve the pulmonary defense mechanisms so that viruses and bacteria can be effectively cleared before they are able to proliferate and cause illness," Ainsworth points out. "It is especially critical that pulmonary infections and abscesses be prevented since the window of opportunity available for a racehorse to establish itself is only about two years, which is relatively small. Infections with a prolonged convalescent period would, therefore, lesson the chances that the horse would return to racing."

Although many medications are available and commonly used on the racetrack and show circuit to boost the immune system, says Ainsworth, no objective studies have shown how effective these medications actually are in enhancing the immune response of the athletic horse or in protecting these horses from respiratory tract infections.

To that end, the Zweig Memorial Fund has awarded Ainsworth a new grant to characterize the specific effects of high-intensity exercise on the immune system. Specifically, Ainsworth is running about six horses on the high-speed treadmill to simulate race conditions so she can measure how much the high-intensity exercise affects immune cells in the lungs and blood of exercising horses. She will measure how the exercised horses respond to a sprayed vaccine compared with age-matched sedentary horses. Ainsworth and her colleagues will use molecular biology techniques to measure the horses' antibody and cytokine response to the vaccine. Cytokines are proteins

produced by immune cells that are crucial for directing the magnitude and nature of the immune response. How well the cells can generate certain cytokines or cytokine combinations, for example, in response to an infection can determine the course of the infection. Ainsworth wants to know how exercise affects cytokine production and how that influence may boost the risk of pulmonary infections.

In the second phase of the research (a grant application to the 2001 Zweig competition), Ainsworth plans to pretreat the horses in the high-intensity exercise regimen with a medication that boosts the equine immune response; she will use the immunomodulator EqStim or *Proprionobacterium acnes* and then compare the response of the pretreated, exercising group with both the sedentary horses and a group of exercising horses that did not receive the pretreatment.

"Infectious lung diseases negatively affect the athletic capability of the racehorse, impose a significant economic burden to horse owners and trainers, and most importantly, contribute to horse wastage," says Ainsworth. "We want to thoroughly understand the immune cell function and interactions in the equine athlete and determine ways to enhance these interactions. We need to better understand how the naturally occurring stress of exercise adversely affects the immune response and contributes to vaccine failures and respiratory disease development in racehorses. This is critical considering the growing body of literature showing vaccine failures for the common equine respiratory pathogens. Ultimately, our findings can help lead to more effective vaccination programs for young horses in race training, improve the overall health of the equine athlete, and reduce horse wastage." ■

Cornell Offers Horse Lovers the Latest on Equine Health Care

Equine experts from Cornell's College of Veterinary Medicine partnered with the New York Thoroughbred Breeders, Inc., to present a three-day symposium, "Cornell at Saratoga: A Symposium on Equine Health Care for the 21st Century," July 31 to August 2, 2000, in Saratoga Springs.

Thanks to an overwhelmingly positive response by the several hundred attendees, exhibitors, and sponsors from the equine industry, the event is now planned to be repeated annually. The symposium offered horse owners, breeders, trainers, and other horse lovers access to the latest knowledge and technologies in equine health care. Format included presentations by leading veterinary clinicians, researchers, and nationally renowned equine experts from various sectors of the Thoroughbred industry, interactive panel discussions, and exhibits by vendors.

The first day's kickoff session took participants from the inception of a breeding plan to Thoroughbred performance on the track. Leading owners, trainers, veterinarians, bloodstock agents, and pedigree consultants offered special insights on creating, managing, buying, and selling the racehorse.

On day two of the symposium, Cornell research veterinarians presented programs on topics ranging from understanding angular limb deformities, use of drugs in horses, nutrition, prevention of osteochondritis dessicans (OCD), and gastric ulcers, to the latest information on Lyme disease, equine protozoal myelitis, equine motor neuron disease, and West Nile virus.

On the final day, Cornell equine experts discussed health issues related to foals, such as diarrhea and Rhodococcus pneumonia, health maintenance, pasture management, infertility, and modern techniques for diagnosing and treating OCD.

Those interested in sponoring or participating in next year's Cornell at Saratoga should contact the college's Office of Continuing Education at 607-253-3200. ■

THE NEW YORK THOROUGHBRED BREEDERS, INC.'S

CORNELL AT SARATOGA

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.

2000 Harry M. Zweig Memorial Fund Committee

Jean Brown
Blue Chip Farms, Inc., Wallkill, NY

Bruce Hamilton
Executive Secretary, Harness Horse Breeders of New York State Albany, NY

John L. Hardy
Featherstone, Haut, Conway, Wiley & Cline, LLP, Albany, NY

Mike Hoblock
Chairman, NYS Racing and Wagering Board, Albany, NY

John E. Jagar, DVM
Millbrook, New York

Philip Trowbridge
NYS Thoroughbred Breeding & Development Fund Corp., Ghent, NY

Charles Knauss
Executive Director, Agriculture and NYS Horse Breeding Development Fund

Paul C. Mountan, DVM
Rhinebeck, NY

Donald F. Smith, DVM, Dipl ACVS
Dean, NYS College of Veterinary Medicine at Cornell University Ithaca, NY

Harry D. Snyder
Saratoga Springs, NY

Patricia Wehle
Wehle Stock Farm, Scottsville, NY

William Wilmot, DVM
Saratoga Springs, NY

Anna Zweig
Middlebrook Farm, Nassau, NY

Zweig News Capsule
College of Veterinary Medicine
Cornell University
S3020 Schurman Hall
Ithaca, NY 14853-6401

The Zweig News Capsule is produced periodically throughout the year to report on research at the College of Veterinary Medicine, Cornell University, funded by the Harry M. Zweig Memorial Fund for Equine Research.

Writer: Susan S. Lang
Editor: Metta Winter
Designer: Barbara Drogo
Photography: Cornell University Photography

11/00 GPP 3.5M MTS00049

Printed on recycled paper

Cornell University is an equal opportunity, affirmative action educator and employer.

Produced by Media and Technology Services at Cornell University

www.mediasrv.cornell.edu

CORNELL
UNIVERSITY