Zweig Memorial Fund News Capsule

A Report on Equine Research at the College of Veterinary Medicine at Cornell Sponsored by the Harry M. Zweig Memorial Fund

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Does Giving Lasix Stress A Race Horse?

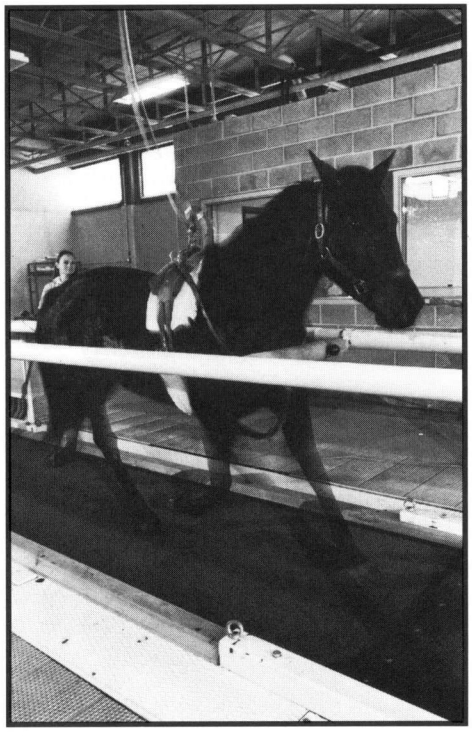
Although administering the diuretic furosemide (Lasix) to a horse before a race is illegal in New York State it is a common, although controversial, practice elsewhere in the U.S. The drug is used medically in treating "bleeders"—horses suffering from exercise-induced pulmonary hemorrhage.

Although the cause of pulmonary hemorrhage isn't well understood, it may be partly due to the very high blood pressure horses show when racing. And it has been found that some horses don't bleed when given the diuretic.

But there is another reason the use of Lasix is so widespread. "It's been statistically shown that those horses given Lasix run faster," says Dr. Katherine Houpt, professor of veterinary physiology.

Dr. Houpt suspects this is because when they're given Lasix, horses lose weight. What happens is that the drug causes the fluid part of the blood (plasma) to be filtered by the kidneys and not reabsorbed, resulting in the output of much more urine, hence, reduced blood volume. "Horses are lighter by the pounds of urine they have lost," explains Dr. Houpt. "Trainers may or may not be conscious of how the drug works; however, they do know the horse does better when it's on Lasix."

But how does the combination of a diuretic drug and exercise, as in racing, affect the horse? Dr. Houpt, a specialist in animal behavior, set out to find the answer with a grant from the Harry M. Zweig Memorial Fund for Equine Research.



The exercise routine was run on the Equine Performance Testing Clinic's treadmill

Exercise alone causes decreased blood volume in a horse; the addition of the drug causes them to lose even more. "We wanted to determine whether the horse can compensate for both the losses incurred in exercise and those caused by the drug," Dr. Houpt explains. This compensation can occur one of two ways: either the horse conserves water later, that is, it puts out less urine after the Lasix is given, or he can drink more. In her study Dr. Houpt measured the urine output and the water intake of Standardbreds at rest and after exercise.

The exercise routine involved trotting for 20 minutes. Although not comparable to racing, it was comparable to training. Dr. Houpt also measured fluid and salt loss due to sweating to see if the horse compensated for the loss of salt.

"We found that, with the combination of Lasix and moderate exercise, the horses lost between 15 and 20 pounds of urine plus several pounds of sweat," Dr. Houpt says. "Given as much salt and water as the horses wanted, within 24 hours their blood volume, as well as its content of potassium and sodium [salt], was back to normal."

This represented little change from the behavior of horses who were given Lasix but not exercised. Dr. Houpt was surprised. "I expected more changes when we added exercise," she says. "Although the horses were not conditioned, they were good enough athletes to compensate for the combination of the drug and exercise."

Just how did this compensation happen? For one thing those horses who were exercised after being given Lasix drank more water than horses on the drug alone. Dr. Houpt thinks that this extra intake of water helped replace the fluids lost by sweating. During the first eight hours after exercise, the amount of water the animals consumed was less than the amount that they lost. But during the next 16 hours the horses did drink enough fluid to compensate. The horses given Lasix and exercised did not eat enough salt to compensate for their

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How Much A Race Horse is Fed Makes A Difference

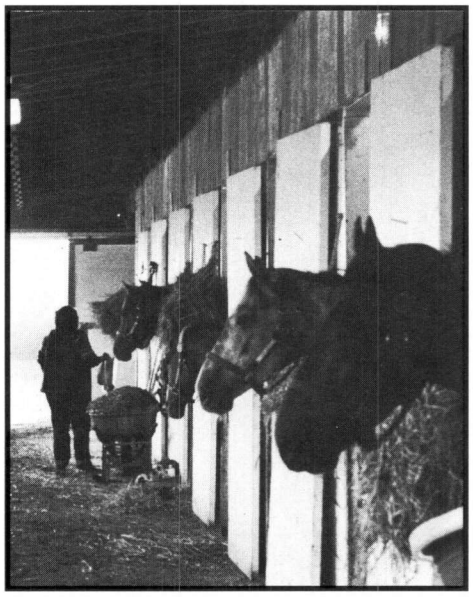
How much should a horse be fed on the day of a race? That's one of a series of questions that must be answered in order to feed horses properly to prevent fatigue. With less fatigue come fewer injuries which, in turn, leads to better performance.

Successful trainers use a variety of different feeding practices. Some restrict hay, others, grain; some don't feed the horse at all the night before a race, thus running it in a fasted state. Just what effect does fasting or being fed different amounts of grain have on the horse's metabolism?

That's the question Dr. Harold Hintz, a professor of animal nutrition in the College of Agriculture and Life Sciences and the College of Veterinary Medicine, and Dr. Laurie Lawrence, a visiting professor from the University of Illinois, set out to answer with support from the Harry M. Zweig Memorial Fund for Equine Research.

Four Standardbred horses were used in the six-week study. The horses were variously fed no grain for 16 hours before exercising, or one, two, and three kilograms of whole corn about two and a half to three hours before exercising. The exercise, consisting of a warm-up, walk, and a fast mile (phases similar to an exercise routine for Standardbreds), was conducted on a treadmill in the Equine Performance Testing Clinic.

"The theory behind the test was that if you give too much carbohydrate before an exercise event, it causes blood glucose to go up, thereby triggering the production of insulin. The insulin then



"Metabolism can be changed by dietary management. Further study is needed to determine the effect on performance."

results in a drop in blood glucose level," Dr. Hintz explains. "We think that an animal might fatigue quicker, particularly in a long event, if he has a low blood glucose level. So that if you don't have the feeding volume just right, the blood glucose value is going to be low when the horse is actually working."

Dr. Hintz found this indeed to be the case. The horses which were fed the most grain before exercising showed the greatest initial increase in blood glucose (about 20 percent) and a 3- to 4-fold increase in insulin; this insulin response then caused the blood glucose level to drop markedly. The blood glucose level in those horses who received no corn remained much the same during the exercise period. The amount of insulin in these fasted animals gradually decreased as the exercise progressed.

"By the time the horses went the full 2400 meters, the animals that were fed the most corn were actually lower in glucose than the animals that didn't get any corn at all because of the insulin effect," Dr. Hintz points out.

Another observation Dr. Hintz made concerned free fatty acids in the blood. The horses not fed carbohydrates had higher levels of free fatty acids, indicating the animals were using free fatty acids as a metabolic energy source. Free fatty acids are normally released from fat in the body.

"We don't know which—glucose or fat—is a better metabolic energy source for various activities," says Dr. Hintz. "The study demonstrates that metabolism can be changed by dietary management. Further study is needed to determine the effect on performance."

The measure of performance used during the study was the amount of lactic acid produced during exercise. "When an animal is working hard, the level of lactic acid can be used to evaluate metabolism and degree of conditioning," explains Dr. Hintz. "We didn't find any big differences in lactic acid concentrations between the fasted and fed horses, or those fed different amounts of corn."

Although the treadmill test cannot show the fine discriminations in performance that make all the difference between winning and losing at a racetrack, Dr. Hintz's work clearly shows that there are major metabolic effects as a result of feeding different amounts of grain to a horse before it works.

Now that the volume of feed is known to influence metabolism, the next step is to look at timing: how long before the race should the horse be fed? Is one hour best? Three, five, or eight hours? After that, Dr. Hintz plans to investigate the effect of different types of feed: protein, carbohydrates and fats. Eventually the answers to all of these questions will add up to determining the best feeding management for the working horse.

Test Tube Development of Embryos:

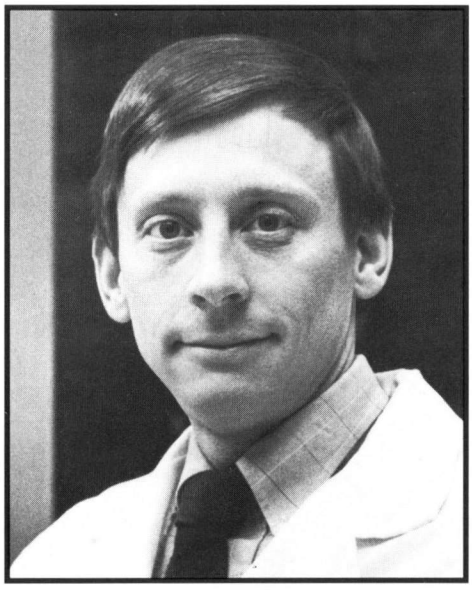
A Critical StepToward Understanding Early Pregnancy Failure

The horse is reputed to be the least fertile of all domestic animals. Among older mares, those often of most value to the breeding industry, 60 to 70 percent of pregnancies fail within the first two weeks. Even as early as the fourth day, certain factors seem to impede the embryo's ability to develop normally.

Until now, the only way to approach this daunting problem was to remove embryos surgically at various stages to see what might be amiss. Not only was it an expensive and laborious process, but this, so-called "snap shot" method resulted in limited information about the state of the embryos since they were seen only at single points in time. What's more, because of the expense involved in surgically removing individual fertilized eggs, only a small number of embryos could be examined.

To make timely progress in learning why so many early pregnancies fail, a method was needed for looking at the entire process of embryonic development through the highest risk period, from the second to the seventh day of pregnancy. Researchers, somehow, needed literally to watch the embryo grow, but outside of the mare.

With support from the Harry M. Zweig Memorial Fund for Equine Research, Dr. Barry Ball and his co-workers in the section of theriogenology have succeeded in creating a tool for doing just that. "We are very excited; it's the breakthrough that will allow us to study the critical period in embryonic development," says Dr. Ball, an assistant professor of theriogenology, who has been investigating the problem of early pregnancy failure since 1984.



Dr. Barry Ball

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What Dr. Ball and his colleagues did was to create an environment in the laboratory, referred to as the co-culture system, in which an embryo consisting of only four to eight cells could live and grow in its normal fashion for five days, just as it would inside the mare's oviduct. At the end of five days, the embryo had reached what is called the blastocyst stage, a hollow ball of cells that would typically be ready to enter the mare's uterus.

To be sure that the co-culture system did not impede the embryo's development in any way, nine of the cultured embryos were placed back into the uteri of nine mares. Five of the nine embryos established pregnancies—a survival rate comparable to that of embryos that had not been cultured.

"This is a significant achievement," explains Dr. Ball. "While microscopic examinations can be made of the cultured embryo to determine if it appears to be normal, the true test is its ability to establish a pregnancy after embryo transfer back into the mare. The 55-percent survival rate showed that we had achieved a first. No one has ever cultured equine embryos during the five days when pregnancies are most likely to fail, then reintroduced them to the uterus where they continued to develop normally."

The team continued to monitor the pregnancies using ultrasound techniques through the 30th day. Once a pregnancy gets this far, most embryonic development is complete, and the rest of gestation is primarily a matter of growth. "Based on what we saw at the end of 30 days there is every reason to believe the foals would have been healthy," Dr. Ball concludes.

Having perfected the co-culture technique, Dr. Ball and his team can now begin to examine the embryos as they develop over time to look for metabolic changes, genetic abnormalities, and a host of other factors that might be the cause of pregnancy failure.

In addition to examining embryos, the team will also study the function of the mare's oviduct. In previous research leading to the development of the co-culture technique, Dr. Ball found that in order for the embryos to survive, tissue from the mare's oviduct had to be included in the culture medium. Further experiments are planned which will ex-

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Embryo *(continued from page 3)*

amine the role this tissue plays—the growth factors, proteins, and other substances it contributes to embryonic development.

When Dr. Ball began his work back in 1984 with a grant from the Zweig Fund, he started with embryos collected from the mare's uterus. He then moved back to the previous stage of pregnancy, that is the time the embryo is in the oviduct. The next step is to move the final step back to fertilization.

This coming year, Dr. Ball and his team will begin work on in vitro (test-tube) fertilization. "At present equine in vitro techniques are not very reliable," Dr. Ball explains. Yet once this additional technique is perfected, any point from conception through the establishing of a pregnancy in the uterus will be observable in the laboratory. Dr. Ball and his team will then be in an ideal position to determine the cause of early pregnancy loss.

Lasix *(continued from page 1)*

needs, yet their blood levels of salt were restored to normal within 24 hours. This lead Dr. Houpt to conclude that the horses conserved salt though physiological means.

To the horse this means stress. "By exercising a horse that's been given Lasix, you are adding an extra stress—you're expecting a thirsty animal to perform," she says. Remember too, Dr. Houpt cautions, "that the drug seems to prevent bleeding only in some horses and does not treat the underlying cause of the problem." Lasix serves only to lower a horse's high blood pressure, one of the contributing factors to pulmonary hemorrhage. "If the animal has extra friable blood vessels, you're not treating that with Lasix," explains Dr. Houpt. "You're just exercising the horse with less than the amount of plasma it would normally have."

The Harry M. Zweig Memorial Fund honors the late Dr. Harry M. Zweig, a distinguished veterinarian, and his numerous contributions to the state's equine industry. In 1979, by an amendment to the pari-mutuel revenue laws, the New York State legislature created the Harry M. Zweig Memorial Fund for the promotion of equine research at the College of Veterinary Medicine, Cornell University. The Harry M. Zweig committee is established for the purpose of administering the funds and is composed of individuals in specified state agencies and equine industry positions and others who represent equine breeders, owners, trainers and veterinarians. Current committee members are Daniel J. Burke, Longford Farm; Donald G. Butcher, former Commissioner of the New York State Department of Agriculture and Markets; Richard Corbisiero, Jr., Chairman, New York State Racing and Wagering Board; Mr. Bruce Hamilton, Executive Secretary, Harness Horse Breeders of New York State; John L. Hardy, Tucker and Hardy Associates; Charles Knauss, Jr., Executive Director, Agriculture and New York State Horse Breeding Development Fund; Albert W. Miller, DVM; Everett Schoenborn, Climax, New York; Patricia Wehle, Scottsville, New York; William H. Welch, Executive Administrator, New York State Thoroughbred Breeding and Development Fund; Theodore J. Zornow, Avon Farms; Anna Zweig, widow of Dr. Zweig; and Robert D. Phemister, Dean of the College of Veterinary Medicine, Cornell University, who serves as chairman of the Committee. The Zweig Fund receives two percent of all monies accruing to the Agriculture and New York State Horse Breeding Development Fund and the New York State Thoroughbred Breeding and Development Fund from the state's tracks and off-track

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