ZMF

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

Number 6, 1990

Artificial Cartilage Transplants to Ward Off Arthritis

For years researchers have been looking for a way to stimulate the repair of damaged cartilage before the onset of crippling arthritis. One approach has been to take young, cartilage-producing cells from another source and put them in the damaged joint area in such a way that they grow and produce new cartilage.

Until now the problem with that method has been how to hold the cells, called chondrocytes, in place. Experiments conducted in the sixties and seventies in which the chondrocytes alone were injected into the spaces left by the eroded cartilage, failed because the cells were washed away in the joint fluid as soon as the animals moved about.

What's needed is something that a horse's body would not reject and that would firmly attach the chondrocytes to the exposed bone. According to Dr. Alan Nixon, assistant professor of clinical veterinary sciences at the College of Veterinary Medicine at Cornell University, the answer may well be found in imitating nature more completely.

"In normal cartilage, the chondrocytes are supported by collagen fibers in what's called a matrix," explains Dr. Nixon. "We're looking now at how to create such a matrix—an artificial cartilage if you will—that can be put as a whole into the damaged area."

With support from the Harry M. Zweig Memorial Fund for Equine Research, Nixon is collaborating with Dr. George Lust, a cartilage biochemist at the James A. Baker Institute for Animal Health at Cornell, and cell biologists at the Hospital for Joint Diseases in New York City on techniques for producing such an artificial cartilage. Their first challenge was to successfully harvest immature chondrocytes, grow them in the laboratory to increase their numbers, size, and robust quality, and then to preserve them, alive, until needed. The next was to imbed two to three million of these cells in one-inch disks of collagen, which are commercially manufactured from bovine tendons.

▲ The photo shows cartilage cells growing in new tissue grafted into a horse's knee.

Now Nixon is in the process of determining how well the cells survive and reproduce in the collagen disks. "The results seem very positive," he says. "Working with the cells in this way is very new, but it has been done successfully with rabbits. This technique holds great promise as the means of repairing not only equine cartilage but human cartilage, as well."

Cornell's Equine Research Receives $432,500 from Racing Industry

Through the Harry M. Zweig Memorial Fund, the racing industry will support equine research at Cornell's College of Veterinary Medicine in 1990. 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 betting. In 1990 sixteen projects have been selected to receive a total of $432,500. The following are the funded areas of study and researchers:

Immunogenetic studies of the horse will continue under the direction of Dr. Douglas Antczak. In the area of equine infectious diseases, Dr. Judith Appleton will analyze the equine immune response to the influenza virus and Dr. John Timoney will work on the synthesis of an artificial peptide vaccine against strangles that could be used as an intranasal spray.

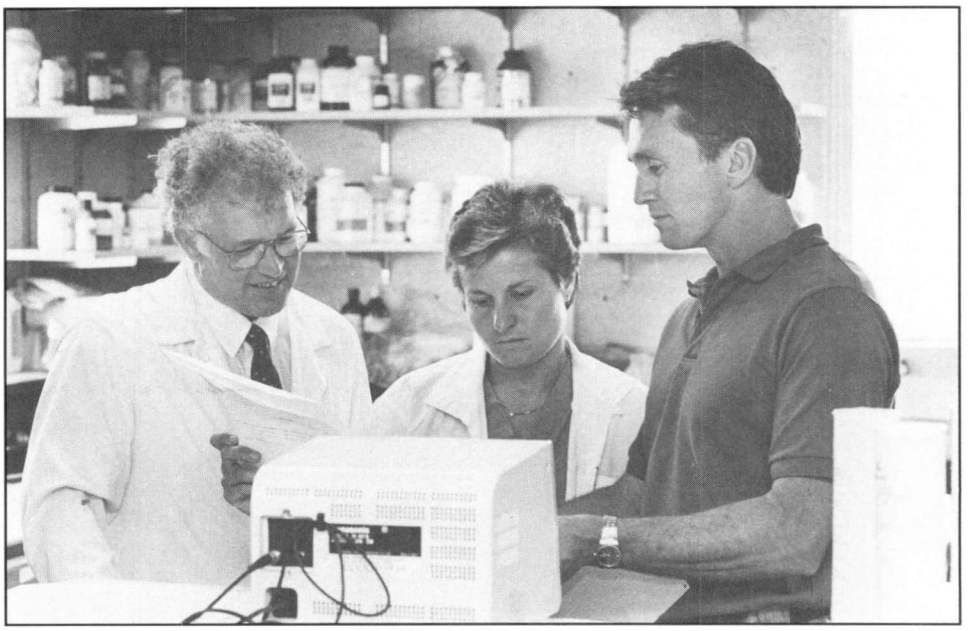
(continued on page 4)

Early Detection — A Key to Preventing Lameness

Veterinarians in the Large Animal Clinic at the College of Veterinary Medicine at Cornell University see more horses for lameness than for any other single disease. And nearly half of those horses suffer from joint diseases, primarily osteoarthritis.

This painful disease is characterized by destruction of the articular cartilage. This cartilage, which transmits load to the bones, covers the opposing bones of joints and facilitates nearly frictionless movement. Yet X-ray pictures, which are the currently available diagnostic tool, can only reveal osteoarthritis long after the cartilage is severely damaged, often beyond all hope of recovery. With no effective drugs to help severely damaged cartilage repair itself, preventing osteoarthritis becomes very important.

"Once diagnosed, osteoarthritis is considered an irreversible disease," says Rory Todhunter, a veterinary surgeon who is a Ph.D. candidate under the direction of Dr. George Lust at the James A. Baker Institute for Animal Health. "Although the damaged cartilage attempts to heal itself, it is mostly unsuccessful. If we could detect the disease process early, before additional physical or mechanical trauma to the tissue aggravates its progress, the disease process could be arrested through a combination of rest, physical therapy, and drug intervention. At present all we can do is treat the symptoms, the most common of which is pain."

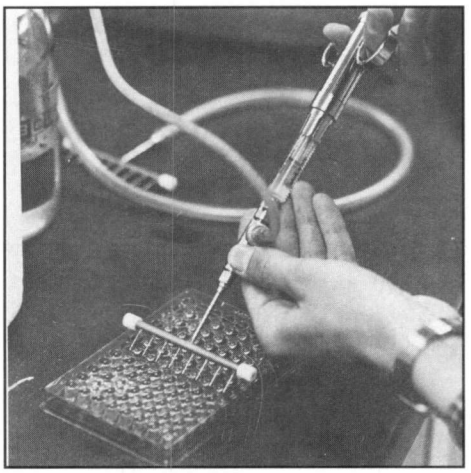


▲ **Dr. George Lust, professor of physiological chemistry, Dr. Susan Fubini, a surgeon in the Veterinary Medical Teaching hospital, and Dr. Rory Todhunter are studying the pathogenesis of osteoarthritis in horses.**

With a grant from the Harry M. Zweig Memorial Fund for Equine Research, Todhunter is attempting to develop an enzyme-linked immunosorbent assay (ELISA) test. If he is successful, this convenient, efficient, and inexpensive test which could be done on blood samples within a matter of hours could detect the early stages of osteoarthritis.

The test is based on the observation that at the onset of osteoarthritis the cartilage in the synovial joint produces an increased amount of the glycoprotein fibronectin. Todhunter is developing a monoclonal antibody used in the ELISA to measure the amount of cartilage-fibronectin present in synovial fluid and in blood. Such an antibody is not commercially available in the United States.

"A cartilage-fibronectin ELISA could not only detect the presence of the disease but it could be used prognostically as well—to predict the likelihood that the cartilage will recover from various types of treatment, to give an idea of how the horse might perform down the road," notes Todhunter. In addition, because fibronectin seems to be an important component of equine cartilage, monoclonal antibody against cartilage fibronectin could give us further insight into the cause of this disease that is so costly to the racing industry.



▲ **The enzyme-linked immunosorbent assay (ELISA) test is a sensitive immunologic method to measure protein. Dr. Todhunter's test on blood samples could detect the early stages of osteoarthritis within a matter of hours.**

ZMF 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.
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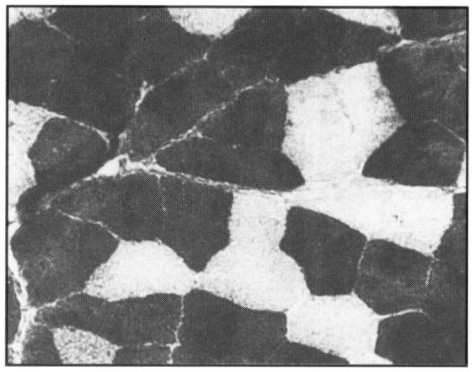
Muscle Structure Gives Clues to Cause of Lameness

Shoulder lamenesses are notoriously difficult to diagnose, in part because so little is known about the form and structure of the muscles in the equine forelimb. Some types of forelimb lameness, for example, appear to be caused by an excess of fibrocartilage in the tendinous region where the biceps brachii muscle comes up over the shoulder joint. To discover why such an excess would occur, researchers must answer a very basic question that's never been tackled before: What happens to this large and complex muscle when a horse is in motion?

For the past three years, Dr. John W. Hermanson, assistant professor of anatomy at the College of Veterinary Medicine at Cornell University, has been pursuing the answer. With support from the Harry M. Zweig Memorial Fund for Equine Research, the work of this zoologist and expert in locomotion is producing some startling preliminary results.

"What we know so far is that although the biceps brachii is considered one muscle, it actually performs two quite different functions when the animal is moving and when it's at rest," says Hermanson. He examined eight different sections of this muscle, which weighs about as much as the average house cat. What intrigued him was that, unlike most muscles, which are attached to bones by short tendons at either end, the biceps brachii is divided in half lengthwise by one continuous spiraling tendon.

"Surprisingly, each half of this muscle, which bears 65 percent of the horses weight in locomotion, is as different from the other as night is from day," Hermanson says. "For example, on one side, referred to as the medial region, the muscle fibers are five times longer than those on the opposite side and are adapted to fast actions, enabling that side to contract with far more speed and power than the other side can. In contrast, the lateral region is adapted only for slow, postural actions."



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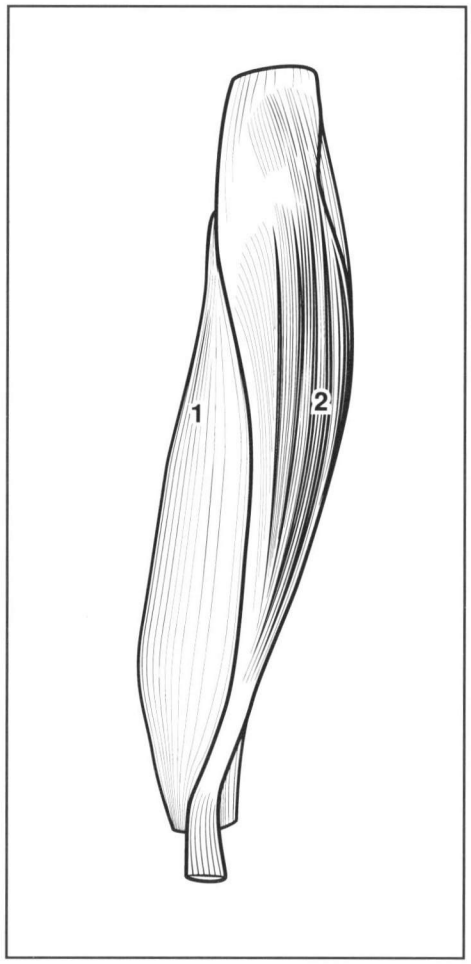

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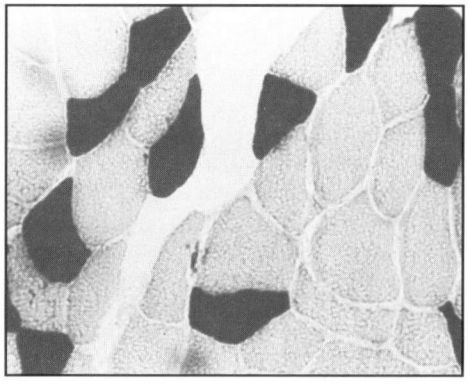

"This means that each side of the muscle, while not operating independently from the other, is nevertheless geared up to perform quite a different function," Hermanson explains. "As our work proceeds, we expect to find that when a hunter and jumper goes over the fence and comes down, it is the medial side that's primarily at work in producing the motion. When the horse is still, the opposite, or lateral, side takes over, allowing it to stand for long periods of time while expending little energy."

An understanding of the biceps brachii's complex muscular structure and operation will enable Hermanson to design treadmill tests that could show whether particular training practices might contribute to the excess accumulation of fibrocartilage leading to lameness. Such tests could also be used to devise more effective exercise programs for healthy horses and improved physical therapy treatments for those already lame.

▲ Cranial view of the left biceps brachii muscle (center) from a 10-year old Bay gelding. The top photo shows a cross section of the numerous darkly stained fibers (fast-twitch fibers) found in the medial head of this muscle, labelled (1) in the illustration. In contrast, the bottom photo is a sample from the adjacent lateral head, labelled (2) in the illustration, containing mostly unstained slow twitch fibers and fewer dark fibers.

Cornell's Equine Research

(continued from cover)

In reproductive studies, Dr. Barry Ball continues his investigations of equine embryonic loss; Dr. Joanne Fortune is studying the regulation of ovarian follicular development and function in mares; and Dr. Robert Hillman and Dr. Claire Card are examining the control of the transition from pregnancy to labor in the mare and delivery of the foal.

In other studies related to the health and performance of the horse, Dr. John Cummings and Dr. Susan Hackett are investigating "roaring"; Dr. JohnHermanson is conducting an in depth anatomical analysis of the shoulder and arm muscles and soft tissues of the muscle morphology & motor control of the normal equine forelimb; Dr. George Lust is developing a diagnostic test for osteoarthritis in horses to aid diagnosis and improve prognosis; Dr. Alan Nixon is looking at the use of artificial cartilage to repair damaged cartilage in horses.

Dr. Katherine Houpt will determine the effect furosemide may have on salt intake in horses; Dr. Dwight Bowman has undertaken to isolate and identify the cause of Equine Protozoal Myeloencephalitis; Dr. Harold Hintz and Dr. Laurie Lawrence are studying the effect of carbohydrate feeding prior to exercise on metabolism and athlete performance; Dr. David Slauson and Dr. P. Bochsler will seek to define the mechanisms of neutrophil-mediated microvascular injury and its modulation by endotoxin and anti-inflammatory drugs. In addition Zweig Fund monies will help support a symposium on the control of animal pain under the direction of Dr. Charles Short, and funds will provide for the addition of a research associate in equine sports medicine.

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; Dr. Wendell Cooper, Lana Lobell Farms, Inc.; Richard Corbisiero, Jr., Chairman, New York State Racing and Wagering Board; 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 betting.

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