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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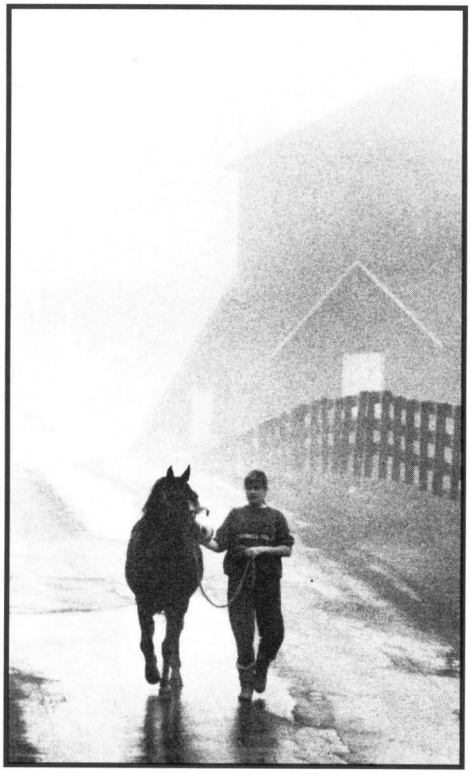
Interdisciplinary Team Seeks Parasite That Causes EPM

EPM (Equine Protozoal Myeloencephalitis) is the most common cause of neural disease in American horses. Usually affecting young adult Standardbreds, its course is particularly cruel: progressing from weakness, incoordination, and sometimes the loss of balance, to the inability to stand, paralysis of the hind or all four limbs and, eventually, death. At present, there is no effective treatment.

It's a disease that's particularly difficult to diagnose. There is no definitive serologic test because the parasitic protozoan that causes EPM is unknown. Before a clinical diagnosis can be attempted the disease must be in its advanced stages, when much brain or spinal cord tissue damage has already been done by the parasite as it spreads from cell to cell. Even then it's tough to be sure because EPM looks very much like three other major spinal cord disorders; usually only an equine clinician experienced with neurologic diseases is equipped to recognize it.

"The fact that EPM is so difficult to diagnose means that the actual number of cases is probably much higher than just those we know about," says Dr. Dwight D. Bowman, an assistant professor of parasitology, who with support from the Zweig Memorial Fund, heads a team of researchers investigating the cause of EPM.

"The horses we see here already have lesions in the spinal cord or the brainstem, but these horses may only be the tip of the iceberg," he explains. "There may be a lot of horses out there that harbor the organism, but don't show any signs, just as there are many people who have antibodies to *Toxoplasmosis*, a similar disease affecting people, yet very few have the disease.



▲ **EPM usually affects young adultStandardbreds. at present, there is no effective treatment for the neural disease.**

"On the other hand, it could be that as soon as the horse becomes infected with the organism, the symptoms appear. We just don't know because there is no serologic test. And because we don't know how horses are becoming infected we can't come up with any scheme to break the cycle, to prevent their exposure to the parasite."

The key lies in identifying the infectious parasite. Then veterinarians can make a definitive diagnosis, which could later lead to discovering both how the disease is transmitted and how it could be treated.

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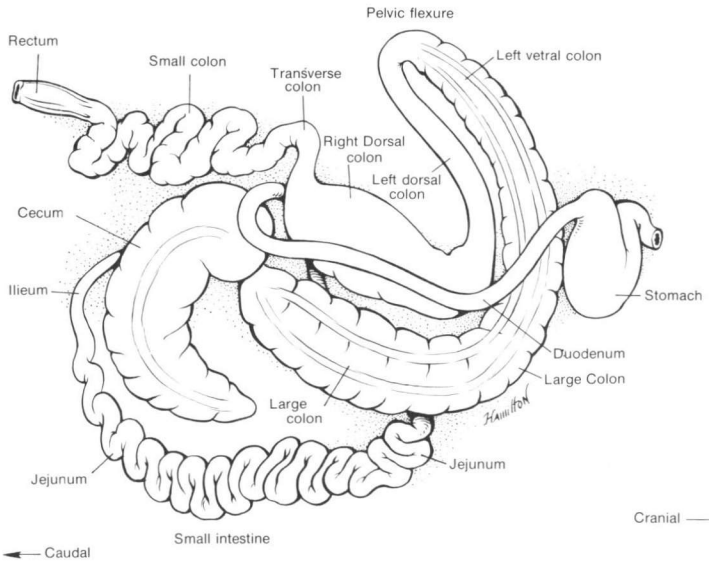
To find the parasite, Bowman and is working with a neurologist; an anatomist/organismal morphologist; a pathologist/immunohisto-chemist; and a scientist from the United States Department of Agriculture who is an expert in the group of suspected organisms. He and his team have narrowed the field to those parasites that are morphologically related, that is similar, to *Toxoplasma* and to the newly discovered dog parasite *Neospora*.

"Based on our knowledge of these two organisms there is no reason to believe that EPM is infectious from horse to horse. Rather there is probably another host animal in whose intestines the parasite reproduces and then is expelled in its feces," says Bowman. "Horses then come in contact with the parasite by eating contaminated foodstuffs."

In order to isolate the organism, infected brain or spinal cord tissue must be removed from a horse with EPM. The

(continued on page 4

Intestinal Nerve Damage May Cause Colic



Schematic Diagram of the Gastrointestinal Tract of the Horse

Colic—which can result from a variety of intestinal disorders—is the leading cause of death in horses. One insurance company reports an annual loss to the horse industry of $100,000,000 due to colic.

Most cases of colic are caused by poor management practices, according to Dr. Gil Burns, a doctoral candidate in the Department of Anatomy. "Inappropriate parasite prevention programs, abrupt changes in nutrition or low quality nutrition, an insufficient water supply, poor trailering techniques, and pasturing in sandy paddocks can all lead to the abdominal pain known as colic," Burns says.

But what about those horses who are well cared for yet, nevertheless, experience chronic colic? Through a grant from the Zweig Memorial Fund, Burns is investigating whether damage to the nerves in the gastrointestinal tract might be the answer.

The equine intestinal nervous system consists of two large groups of nerve cells called plexuses. One plexus coordinates the absorbing and secreting activities that occur during digestion and the other causes the smooth muscles of the intestinal wall to contract, moving food through the system. It is in this latter plexus, called the myenteric plexus, that Burns suspects the trouble may lie. "Any disturbance in the function of these nerves would cause abnormal movement in the gut which the horse would then experience as colic," he explains.

A site along the intestine that is of particular interest to Burns is a portion of the large colon called the pelvic flexure. It is in this area that horses regulate the flow of digesta through the large colon. "Horses are hindgut fermenters, that is they digest cellulose and complex carbohydrates in the large colon as opposed to cows which digest these substances in a series of fore-stomachs," Burns explains. "The plant materials are kept in the initial portion of the colon, which acts like a holding vat, for about 72 hours by waves of muscle contractions that sweep large food particles backward into this region until they are fully digested. Then they proceed down the intestinal tract."

Previous research conducted at Cornell's College of Veterinary Medicine would indicate that these coordinated waves of contractions that move food back up into the initial portion of the colon and then eventually through the pelvic flexure seem to be controlled by a pacemaker mechanism. Such a mechanism would require a larger number of nerve endings in this location than elsewhere in the large colon. And that is just what Burns discovered.

In his research Burns examined samples of the myenteric plexus at 10 different sites along the gastrointestinal tract. His study results indicate that there is increased nerve density at the pelvic flexure, corroborating the presence of the pacemaker mechanism. This is the first detailed account of the structure and numbers of these nerves in the healthy horse. As such they provide an essential baseline against which to judge damage to the intestinal nervous system. What's more, to coordinate such complex muscle function these nerve endings secrete perhaps as many as 17 different kinds of neurotransmitters, some of which induce the muscles to contract, others to inhibit contraction, and yet others to regulate the two actions.

Burns next step is to delve into the complexities of how each of the different types of neurotransmitters function. In the end, what he learns about the structure and the function of the nerves in the equine intestine will enable researchers to confirm whether their damage is, indeed, a cause of colic.

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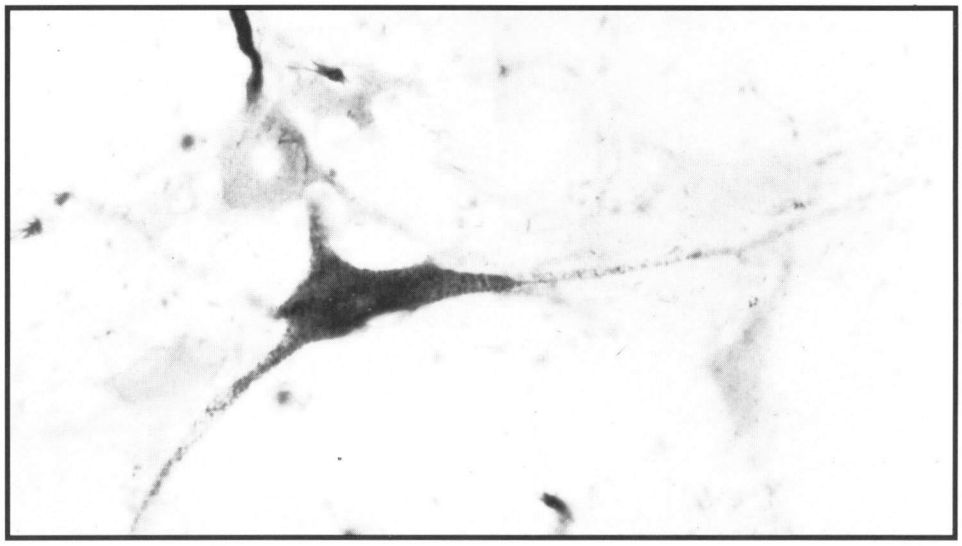
Brain Cell Studies Seek Cause of Roaring



▲ **Labeled neuron in left nucleus ambiguus following injection of the left vagal nerve with horseradish peroxidase**

Imagine a cluster of cells the size of a grain of rice. It's one such tiny group of neurons, imbedded deep in the brainstem of a horse, that is responsible for opening its larynx at each breath. An abnormality in these few cells might well be the cause of roaring. Dr. Susan Hackett, a doctoral candidate in the Department of Anatomy, wants to find out.

Roaring (idiopathic laryngeal hemiplegia) is the most common upper respiratory obstructive disease in horses, affecting at least 5 percent of the Thoroughbred population. Typically the larynx of a roarer is paralyzed on the left side, so that the horse has use of only half of its airway. Unable to breath fully while running, the horse quits.

Although roaring has been recognized as a disease for many years its cause is still unknown. The symptoms can be treated through surgery but this is effective in only about half the cases. Hackett, supported by a grant from the Zweig Memorial Fund, aims to pinpoint the cause.

"Early research into roaring showed that the muscles activating the larynx were smaller than they should be," Hackett explains. "Then in the '40s and '50s it was found that the muscles were atrophied because the nerve that activates them was damaged: it became clear that roaring was primarily a disease of the nerves, not of the muscles."

The nerve in question ends at the larynx after traveling about 7 1/2 feet in a tall horse. The nerve runs down the neck from the larynx, loops around the aorta in the chest, and then goes back up to the brainstem where it began as a tiny group of neurons (or nerve cell bodies) known as the nucleus ambiguus. From this one spot, signals are sent along the nerve (via axons, which compose the nerve and which are extensions of the nerve cell bodies) telling the muscles to contract, opening the larynx. An abnormality here, Hackett believes, would cause the whole system to falter.

Her first problem was to find that grain of rice, because the nucleus ambiguus is aptly named. "It's only a small number of neurons loosely grouped together," Hackett explains. "At it's thickest point it only contains about 30 neurons. The area where it's located has been examined before but with only a light microscope and there was no way for researchers to be certain they were even looking at the correct neurons. What I needed first was a road map to find the exact location."

Hackett created this map by using a retrograde tracing technique whereby she injected the nerve with horseradish peroxidase (HRP). The HRP was transported along the axons back to the nucleus ambiguus, marking each neuron.

In the second phase of the project, just now underway, Hackett will use the map to remove the ambiguus neurons from two healthy horses and two that roar. She'll then examine these under an electron microscope, looking at what's never been seen before.

"I will be looking for two things," Hackett says. "First I want to see if there's a difference between the cells from the horses that roar and those that don't. Then secondly I want to identify what kind of difference it is, whether the difference suggests there's something basically wrong with the nerve cell body so that the axon can't function properly or whether a problem located in the axon is affecting the nerve cell body."

Observable differences could lead to an understanding of cause, hence both to prevention and to treatments that are less invasive and expensive than surgery, the only treatment available today. "If we saw differences that suggest there is a dietary deficiency or found evidence of hypothyroidism or an environmental toxin then we could supplement the diet, chemically treat the hypothyroidism, or remove the toxin," she explains. "Although we know there is a genetic component to roaring, it's clear that other factors are involved in developing the disease."

Hackett's work is a major stepping-stone to a fundamental understanding of the form and function of nerve cells that have never been described before. And from it could come the key to preventing one of the racing industry's most pervasive problems.

EPM *(continued from page 1)*

organisms present in that tissue will then be grown in the laboratory using two different procedures: in laboratory animals by the team here at Cornell's College of Veterinary Medicine and in tissue at the Zoonotic Disease Laboratory of the United States Department of Agriculture in Beltsville, Maryland.

"Having isolated the organism we can identify what it is," says Bowman. "Once we get it to multiply then it's possible to do two things: begin drug trials to find an effective treatment and develop an immunodiagnostic test. When this is accomplished early cases of EPM could be diagnosed and treatment commenced before this devastating disease cripples the animal."

Preventive work could also progress more rapidly. With a serologic test in hand, field studies could be done in locales where there have been outbreaks of EPM to find out how many horses have been exposed to the organism. Then epidemiologists could identify the definitive and, possibly, intermediate hosts—those animals in whose bodies the organism breeds. "This is the ultimate goal of a parasitologist," says Bowman. "To break the cycle by limiting contact between the host animal transmitting the disease and horse."

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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