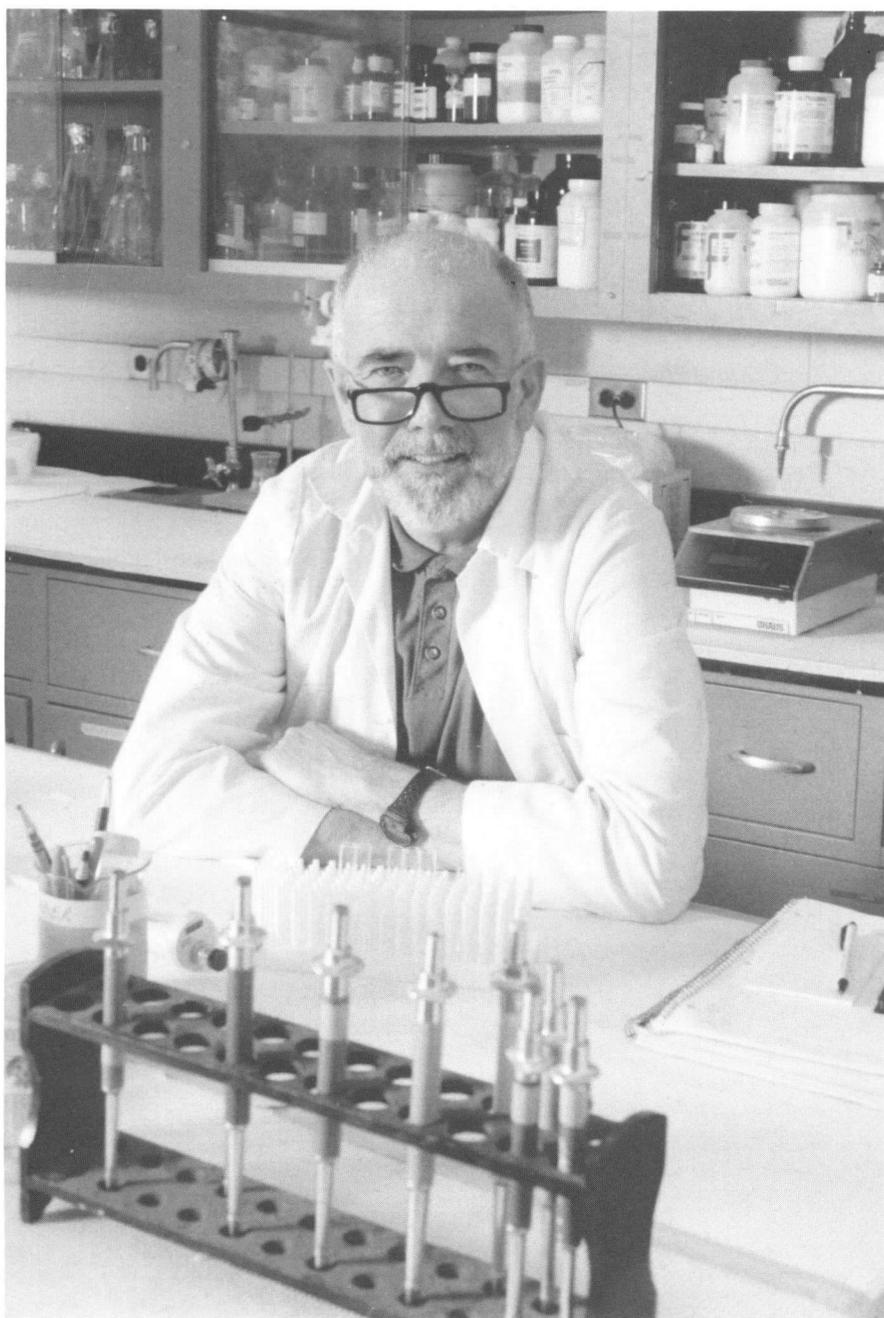


# Zweig

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

Memorial Fund News Capsule

No. 24 November 1997



ADRIANNA ROVERS

Patrick W. Concannon

## Inexpensive Medication Stimulates Early Ovulation in Mares

For years, horse breeders have been trying to gain more control over the onset of their mares' breeding seasons. Although simulating increased day length with artificial lighting is a proven method for advancing the breeding season in winter-anestrous mares, it is expensive, time-consuming, and downright impractical for most breeders.

To perfect a new and simpler method that can advance reproductive function of mares by up to two months, Patrick W. Concannon, Ph.D., an endocrinologist, reproductive biologist, and expert on the effects of photoperiods in animals, is using Zweig funds to fine-tune the protocol for the use of the drug sulpiride. He is working in collaboration with Cornell equine reproductive specialist Peter F. Daels, D.V.M., Ph.D.

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Currently, breeders use two methods to advance ovulation: artificial photoperiods or the experimental injection or implantation of a drug that costs up to \$20 a day to administer. Sulpiride, however, costs only 75 cents per injection or \$2.25 per oral dose.

Sulpiride inhibits the release of dopamine, a neurotransmitter hormone in the brain. Previously, Concannon and Daels had shown that, as in sheep, dopamine inhibits reproductive function and controls the non-breeding period in horses. By blocking the activity of dopamine with sulpiride, a so-called dopamine antagonist that has been widely used in humans to treat psychosis and in horses to treat fescue toxicity in pregnant mares, reproductive function was no longer inhibited and the mares' breeding cycles began early.

Initially, in 1994, they found that mares maintained outside and treated daily with sulpiride beginning in early February ovulated about 40 days earlier than untreated mares (on March 12 instead of April 20, on average).

"That was only 10 days later than mares kept indoors under artificial lighting for almost three months," Concannon says. In 1995, they repeated the experiment and found that treated mares ovulated about 20 days earlier than the controls. Concannon suggests that these poorer results were probably because of the exceptionally cold and wet winter that year.

Last year, Concannon switched to twice-daily doses of sulpiride with mares kept indoors under artificial lights beginning on January 18. These mares started ovulating on February 3, on average, while untreated mares maintained outside did not start to ovulate until two months later, about April 1, on average.

With Zweig funding this year, Concannon is doing a much more comprehensive analysis by maintaining both treated and untreated mares indoors and outdoors. So far, the results have been dramatic. Mares

maintained inside under an artificial photoperiod began ovulating within 14 to 24 days of starting sulpiride treatment on January 18. They began ovulating on average on February 5. The untreated animals kept indoors ovulated, on average, a month later, and much less synchronously. The treated mares had their first ovulations of the year within a 10-day period, while in the group of untreated mares, first ovulations occurred not only later but over a 40-day period.

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"This Zweig-funded study will allow us to not only make informed recommendations but also determine the role of dopamine in the regulation of seasonal reproduction in mares and the mechanism by which dopamine exerts its inhibitory effect."

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With the animals maintained outside, sulpiride treatment beginning in mid-February appears to have had little or no effect this year, as they, like the untreated animals outside, had not ovulated by mid-April.

"Unfortunately, these outside animals were mares recently purchased at auction, and for which we have no breeding history," Concannon says. "Now we know that just being inside and given sulpiride has a clear advantage to being outside and treated with sulpiride. Mares that were treated with sulpiride and maintained inside under artificial photoperiods for only 12 to 22 days ovulated at the exact time when horse breeders would like to have their mares bred.

"Whether the greater effect of the sulpiride in animals kept indoors is

due to warmer conditions or to the indoor lighting needs to be examined further," Concannon adds. The study also is allowing the researchers to characterize the hormone activity in the mares as a way to show the specific effects of treatment. They are looking, for example, to see if the hormone prolactin is also involved in this aspect of the reproductive cycle.

"Strangely, prolactin can stimulate the ovaries in some species while it inhibits them in most others," Concannon says. "In previous studies, we've found that inhibiting prolactin secretion did not seem to affect the timing of ovulation in horses so we suspect that prolactin is not a mechanism at play here in horses. In contrast, we have shown in dogs that if we suppress prolactin secretion, we stimulate ovulation. In the mares, the hormone assays we do this spring, however, will determine if changes in another important hormone, follicle-stimulated hormone, play an important role."

The research will also lead to more practical and specific protocols, including one using the oral administration of either sulpiride or perhaps a different dopamine antagonist.

"Since our preliminary results, we have received many inquiries from the veterinary community on the correct use of the dopamine antagonist for inducing reproductive function in mares," Concannon says. "This Zweig-funded study will allow us to not only make informed recommendations but also determine the role of dopamine in the regulation of seasonal reproduction in mares and the mechanism by which dopamine exerts its inhibitory effect.

"In the future, we should also be able to determine the relative roles of stimulatory photoperiod and increased temperature in the response to treatment and identify the most effective treatment protocol for advancing the breeding season in winter-anestrous mares." ■

## Zweig Supports Students in Summer Leadership Program

Some veterinary students stand out as having the potential to be veterinary decision makers and leaders in their profession. Not only are they at the top of their classes, they also demonstrate other exceptional qualities that set them apart, such as being an Olympic-caliber athlete, a female Navy pilot with a third degree black belt in the martial arts who served in the Gulf War, a published author of numerous scientific papers, or a Ph.D. in molecular biology.

These characteristics describe some of the students who recently participated in the Leadership Program for Veterinary Students in the College of Veterinary Medicine. After a highly competitive selection process, some two dozen veterinary students from around the globe come to Ithaca for ten weeks each summer where they are groomed as potential academic or research leaders in veterinary science. Four of these students have been supported by the Zweig Fund.

"The leadership program targets students who are the best of the best—they have superb academic records but also have achieved things in their lives that suggest they could be future veterinary medicine faculty members or leading research scientists in government or industry," says program director Dr. Douglas D. McGregor, associate dean for research and graduate education and professor of immunology in the College of Veterinary Medicine.

The four students supported by the Zweig Fund participated in Career Development Training for Equine Research. They were interested in pursuing careers in equine research rather than clinical practice after veterinary school.

Working with a faculty mentor, each student participated in a research project that gave them the opportunity to apply investigative strategies and glean an insight into how a re-

search laboratory uses its professional and material resources.

Melinda Story, 26, from Colorado State University, spent the summer working with Dr. Douglas Antczak on linkage mapping for the equine genome project.

"With so many questions out there, I would like to use my mind to delve into them on a broader spectrum," she says. "By being an equine re-

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"The leadership program targets students who are the best of the best—they have superb academic records but also have achieved things in their lives that suggest they could be future veterinary medicine faculty members or leading research scientists in government or industry."

—Dr. Douglas D. McGregor

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search scientist, I hope to help a lot of horses rather than just one horse at a time in private practice."

Tanya LeRoith, 25, from the Virginia-Maryland Regional College of Veterinary Medicine, worked with Dr. Alan Nixon in characterizing the alternate splicing pattern of a particular gene important in normal and osteoarthritic equine cartilage. "I'm interested in an academic future because I think it would be so much more dynamic and interesting than private practice. I'm especially interested in equine internal medicine or equine infectious diseases."

In addition to the research projects, the students participated in a wide range of activities geared to developing leadership potential, such as technical, communication, and critical thinking skills and exploring ethical and professional issues. They had training in chemical and radiation safety, examined biomedical ethics, discussed the scientific method and leadership responsibilities, participated in a creativity workshop, and listened to presentations on how to judge a good residency and research program and how to critically review scientific manuscripts.

To think more about the future, the students participated in a "career day" during which various research scientists talked about their careers. The students had the opportunity to speak privately with prominent veterinary leaders, such as deans and faculty members of other veterinary colleges, and industry and government research scientists.

The students also spent three days in Washington, D.C. touring research facilities and meeting with senior scientists and administrators at the National Institutes of Health and the U.S. Department of Agriculture.

A final objective of the program is to allow students to participate in interactive projects with one another. "The idea is get the students working together now so that in the future, when they are in leadership positions, they will form a professional network and continue to interact to work on solving problems on a global basis," says McGregor.

In addition to the Zweig Fund, the program is supported by the National Institutes of Health, the U.S. Department of Agriculture, the Fundación Purina, the Merck Foundation, the Richard King Mellon Foundation, the Wellcome Trust, the Florence Gould Foundation, the Marilyn Simpson Trust, and the Robert W. Woodruff Foundation. ■

## A Look Back at 18 Years of Zweig-Funded Research

Since the Zweig Fund was established in 1978, many equine researchers at the New York State College of Veterinary Medicine have received support for studies that benefit both equine health and New York State's racing industry. This is the third of a series of articles that look back at some of their accomplishments.

### Zweig-Funded Accomplishments in Cardiopulmonary Research

What limits the athletic performance in racehorses? Why do some fail to perform up to their potential? Equine researchers tend to agree that the limitation lies within the cardiopulmonary system. Thanks to Zweig funding, researchers at Cornell have made great strides in better understanding exercise intolerance, roaring, bleeding, hypoxia, and edema in exercising horses.

#### Evaluating Diaphragm Function and Fatigue

Dorothy Ainsworth, D.V.M., Ph.D., a large-animal pulmonologist and an expert in equine respiratory physiology, studies the diaphragm, the major inspiratory muscle of breathing.

With Zweig funding, Ainsworth has developed new techniques to evaluate diaphragm function and fatigue in horses. She has shown that the equine diaphragm is an active muscle in the generation of air flow patterns in horses and was one of the first researchers to successfully record its electrical activity during intense exercise. She has found that as the exercise of healthy horses intensifies, the electrical activity of the diaphragm and the amount of pressure it generates to bring air into the horse's lungs both increase.

"In healthy horses, the diaphragm probably does not normally fatigue, despite the development of severe arterial hypoxemia and hypercapnia," says Ainsworth. She suspects that as bronchioconstriction and airway exudate make breathing more difficult, the electrical activity of the horse's diaphragm continues to increase but becomes ineffective in generating increased pressure. The result: diaphragm fatigue.



Dorothy Ainsworth

Ainsworth has been measuring changes in diaphragm length and contractions using specialized ultrasonic crystals, defining the relationship between exercise-induced increases in the electromyographic activity of the diaphragm and the diaphragmatic muscle shortening that occurs with each breath. She has also discovered that published reports that advocate the use of a diagnostic technique called flow:volume loop analysis erroneously assume that so-called end-expiratory lung volume (EELV) remains constant during exercise. Her work has shown that, in fact, EELV actually decreases as exercise becomes more intensive.

"This actually invalidates how the flow:volume technique is currently being utilized," she says.

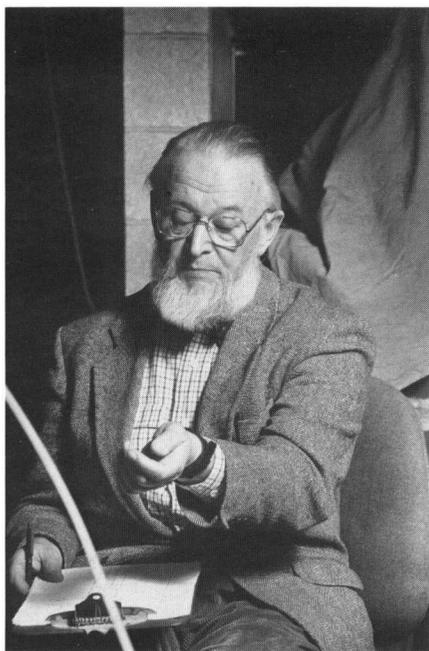
In addition, Ainsworth's work has shown that passive diaphragmatic shortening only occurs when the esophageal pressure is becoming

more positive, during expiration. Although it was widely known that such length changes do occur when horses exercise, she has shown that the abdominal contents are unlikely to contribute significantly to inspiratory airflow generation.

#### Studying the Causes and Effects of Lung Edema

Dr. Alan Dobson, a physiologist, and Dr. Robin Gleed, a veterinary anesthesiologist, have used Zweig funding to study lung edema, the buildup of fluid in the lungs of exercising horses. With previous Zweig support, they had shown that blood pressure in the lung capillaries increased in the horse during exercise. This is unlike other species, in which the pressure remains fairly constant.

The team extended a technique developed in Russia for humans to successfully measure lung water



Alan Dobson

before and during exercise and during recovery. This approach also yields much additional cardiovascular information, including stroke volume, central blood volume, and the state of the lung capillaries.

"The magnitude of water accumulation in the lungs with exercise is sufficient to thicken the tissue separating the gas and blood in the lung, increasing the barrier to gaseous diffusion, contributing to hypoxemia, and thereby, compromising performance," Dobson explains. The researchers also have found that the edema from the raised pressure does not dissipate during a 30-minute recovery in spite of the rapid normalization of the pressure. This raises interesting questions about the lymphatic drainage.

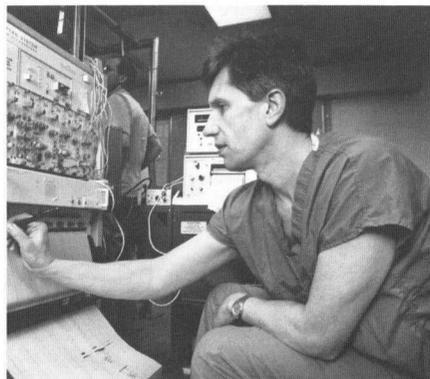
Comparable data collected from horses that have been given Lasix is still being evaluated.

### Defining the Etiology of Exercise-Induced Pulmonary Hemorrhage

Prior to his work on hypoxia and edema, Gleed, along with Dobson and Dr. Richard Hackett, used Zweig funding to study the bronchial artery and exercise-induced pulmonary hemorrhage, also known as EIPH or

bleeding. They developed new techniques using a flow probe to understand exactly what happens to bronchial artery blood flow in both standing and exercising horses, developing what they believed to be the first measurements of bronchial-artery blood flow in the horse as well as in any exercising species.

Gleed and his colleagues have also developed techniques that allow them to simultaneously record systemic (body) blood pressure and bronchial-artery blood flow in both standing and exercising horses. Their work has helped to better define the etiology of EIPH and made great strides in developing a rational approach to methods of preventing or curing the condition.



Robin Gleed

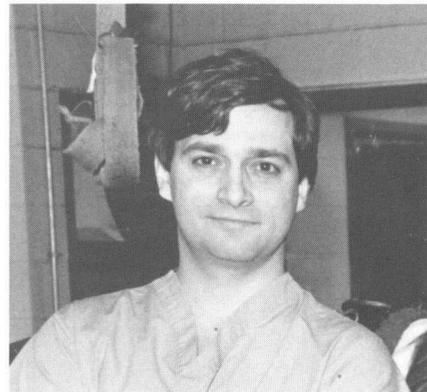
### Understanding the Mechanics of Respiration

Hackett and Dr. Normand Ducharme have also used Zweig funding to study the mechanics of respiration, including laryngeal function and the use of endoscopy.

Specifically, they have developed protocols for testing respiratory function in horses exercising at their maximum on the college's high-speed treadmill. The protocols have produced reliable, repeatable results that take into account the effects of speed, slope, and duration of exercise on measured respiratory parameters.

The protocols result in the greatest peak airflows (the maximum amount of air passing through the airway) and greatest negative airway pressures. By

using this method, the equine surgeons have determined measurements in normal horses and now understand how variations are related to particular respiratory problems such as roaring during exercise and exercise intolerance.



Norm Ducharme

As a result of their Zweig research, Hackett, Ducharme, and their colleagues now routinely use video endoscopy to visually evaluate the upper airway function with pressure measurements taken by small pressure transducers in the airway of the horse. To noninvasively measure volumes of incoming and outgoing air, they designed a face mask that has an ultrasonic flowmeter lined up with each nostril.

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Richard Hackett

## Cardiopulmonary Research

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By correlating their data, the researchers have developed a range of values for inspiration and expiration during high speed exercise. They also can determine where pressure drops occur and identify the specific site of a problem in the horse's respiratory tract.

This kind of information allows them to assess far more accurately the upper airway of the horse and how the appearance of the larynx during a resting examination is associated with its ability to transmit adequate airflow during intense exercise. With their new information, they have developed a grading system for categorizing laryngeal function, which has been adopted nationally, and determined which characteristics of the horse's larynx are reliable predictors for problems during exercise horse and which are not.

Their work now allows them to assess whether a horse has a problem, where the problem is, when it occurs (either during inspiration, respiration, or swallowing), how it interferes with performance, and how the various problems respond to particular treatments.

More recently, the researchers have been concentrating on the effects of these upper airway obstructions on the lower airway, collecting measurements of blood flow through the lungs. They have compared the respiratory functions of normal horses against those of horses that suffer various upper airway obstructions such as laryngeal hemiplegia (roaring), dorsal displacement of the soft palate, nasal obstruction, and tracheostomy. The correlation of their affect on EIPH is being elucidated and contributes to the understanding of bleeding in horses. ■

## Donald F. Smith Named Dean of Vet College

Donald F. Smith, professor of surgery and former associate dean for academic programs, was named the College of Veterinary Medicine's ninth dean in July. He had been acting dean since January, when former dean Franklin M. Loew resigned to pursue other interests. A member of the Cornell faculty from 1977 to 1982 and again since 1987, Smith is an elected member of the National Academy of Practices and a diplomate of the American College of Veterinary Surgeons. As dean, Smith will chair the Zweig Memorial Fund Committee.

Smith was born on November 25, 1949, in Picton, Ontario. He earned the doctor of veterinary medicine degree, with distinction, from the University of Guelph in 1974. After serving a residency in large animal surgery under Drs. Charles Raker and William Donawick at the University of Pennsylvania's New Bolton Center, he was named assistant professor of surgery at Cornell in 1977. From 1982 to 1987, Smith taught and did research at the University of Wisconsin-Madison School of Veterinary Medicine, where he was named chair of the Department of Surgical Services in 1986. He returned to Cornell in 1987 as professor and chair of the Department of Clinical Services.

Smith is a general large-animal surgeon with research interests in metabolic abnormalities associated with gastrointestinal obstruction. He is credited with developing a unique model for representing gastrointestinal obstructions in ruminants.

As associate dean for academic programs beginning in 1990, Smith provided administrative support to faculty members involved in the development and implementation of the academic program for the veterinary college.

Smith stood at the helm of the college as acting dean this past May when the D.V.M. Class of '97 received

their diplomas, the first class to be educated for all four years under the "new curriculum." The college now uses an interdisciplinary tutorial approach to learning that includes case-based exercises as well as laboratory sessions, lectures, interactive computer courseware, and independent study.

"The new curriculum is the result of a partnership between faculty with innovative ideas and an administration that facilitated their implementation," says Smith. "I think that's why we continue to have such a high level of commitment from the faculty as well as the continual opportunity for fine-tuning at the suggestion of both students and faculty."

One recent change allows first-year students more opportunity to practice clinical skills early in their education, including techniques for the physical examination of animals. Smith points to the study of new topics such as equine neonatal intensive care as an example of the expanded offerings for students.

Now turning his attention to an ever-growing list of challenges, Smith is working on building or rebuilding Cornell's strengths in clinical oncology, theriogenology—the clinical arm of reproductive biology, infectious disease, and medical genetics, all areas that have tremendous potential for the equine industry.

"Cornell has been extraordinarily blessed with a superb clinical and research infrastructure for its equine programs," says Smith. "With our talented and energetic faculty and staff and gifted students in both our professional and postgraduate programs, we have a unique opportunity to serve the equine industry. I am committed to supporting efforts that will promote clinical service, research, and education and ensure that we remain at the forefront of equine work in the nation." ■

Unlike most members of the Harry M. Zweig Memorial Fund committee, Harry Snyder has never owned a horse. In fact, he's not even that interested in riding. But that doesn't mean he isn't knowledgeable about the horse racing industry. Born and raised in Saratoga Springs, Snyder practically grew up on the track where his father was a full-time pari-mutuel clerk selling tickets at the betting windows around the state.

"I hung around the racetrack a lot and worked there in high school and during summers in college, watering and raking the track, white washing, and doing general maintenance for 75 cents an hour. That was a lot of money then," says the 66-year-old Snyder of the wages of the late 1940s and early 1950s.

Snyder left Saratoga to go to Notre Dame University, graduating in 1953 and earning a law degree in 1955. He promptly returned to his hometown to practice law, which he has been doing ever since.

Always a racing fan, Snyder has represented many clients in the horse industry over the years, including the New York State Racing Association and the Fasig-Tipton Company, a horse auction firm.

"I suppose Governor Hugh Carey knew of my expertise in the horse industry when he asked me in 1980 to become one of the three commissioners for the New York State Racing Commission," says Snyder, who was later reappointed by Governors Cuomo and Pataki and has served in the unpaid position ever since.

As a commissioner, Snyder says he doesn't use his legal expertise as much as he relies on basic horse sense. He serves as an advisor on issues relating to thoroughbred horses and thoroughbred racing with the Racing and Wagering Board. He also is a member of the New York State Thoroughbred Breeding and Development Fund, the major supporter of the Zweig fund. Obtaining its money from racetrack betting, the Breeding and Development Fund gives two percent of its revenues—a value of about a quarter of a million dollars—to the Zweig fund each year.

After about ten years as a racing commissioner and member of the Breeding and Development Fund, Snyder joined the Zweig committee in the early 1990s.

"Upon joining, I recognized that I had to do a lot of homework on the technical aspects of veterinary medicine," he says. "My focus has been to try to support projects that deal with veterinary problems that we see often on the track. My philosophy is that since the money that supports Zweig comes from



BARRY DELIBERCO

race tracks and racing, no matter how worthy some projects might be, I prefer to support projects that have to do with matters that affect the breeding shed or race track, specifically race horse reproduction or performance."

Snyder and his wife Helen are the parents of seven grown children and have seven grandchildren. Although no one else in his family is professionally involved with horses or racing, he says they are all keenly interested in the sport and have a long history of going together to the thoroughbred racing track at Saratoga each summer season.

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**T**he 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 parimutuel 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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