

WINTER 1999-2000

Scientists Uncover Structure of Essential Protein Complex A Key Step Toward Cancer-Fighting Drugs

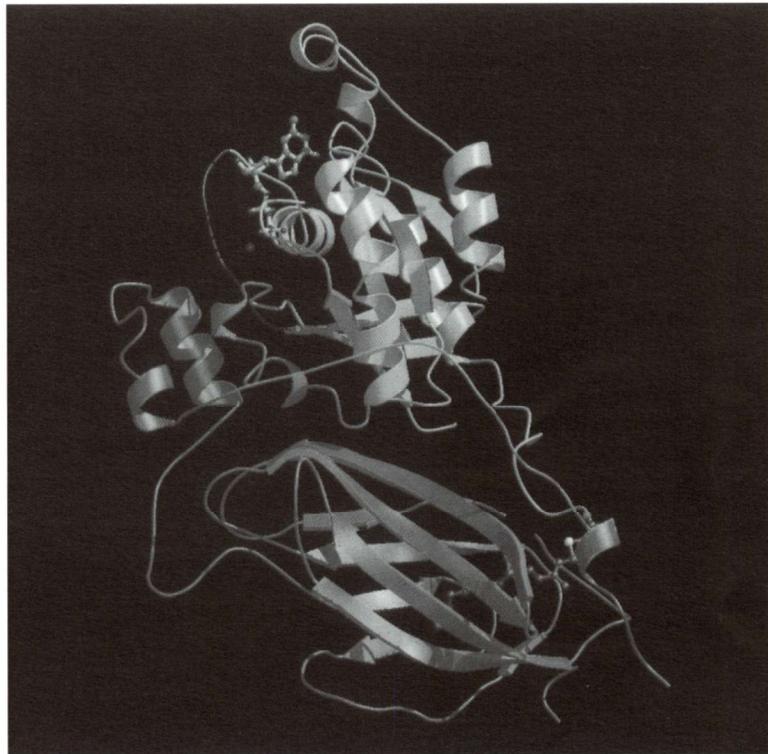
by Roger Segelken
Cornell News Service

Cancer researchers at Cornell's College of Veterinary Medicine have revealed the molecular structure of a protein complex believed to influence the malignant transformation of cells, thus setting the stage for development of unique tumor-blocking drugs.

The structure of Cdc42, a molecular switch that turns on essential pathways in both normal and cancerous cells, and GDI (guanine nucleotide-dissociation inhibitor), a key

The researchers believe it should be possible to block signals that lead to cancer by modulating Cdc42 activity.

regulator of the Cdc42 switch, is reported in the February 4 issue of the journal *Cell* (vol. 100, pp. 345-356) in a paper by Richard A. Cerione, professor of molecular medicine in the College of Veterinary Medicine and professor of chemical biology in the College of Arts and Sciences at Cornell. Co-authors of the report are Gregory R. Hoffman, BS, a Cornell graduate student in biophysics, and Nicolas Nassar, PhD, a



COURTESY GREGORY HOFFMAN, NICOLAS NASSAR, RICHARD CERIONE

The three-dimensional structure for the complex that includes Cdc42 — a key player in cell growth, and GDI — a protein important in the regulatory process.

research associate in the College of Veterinary Medicine's department of molecular medicine.

"Knowing the precise, atom-by-atom structure and shape of this molecular switch [Cdc42] and the structure of other cellular proteins that regulate its activity," explains Cerione, "should eventually allow us to identify and even design small molecules that alter Cdc42 function and thereby prevent the Ras oncogene from inducing the malignant state." [The Ras oncogene is a gene that can

Cornell University is one of the few institutions in the world with the scientific capability to move a discovery from the basic-biology stage, to the determination of molecular structure, to the design of drugs, and finally to clinical trials.

cause cancer when it is altered.]

The structure of the protein complex was mapped at MacCHESS, Cornell's high-energy synchrotron source, where the scientific technique

Cornell's Veterinary Legacy

James Law, our college's founding dean, was veterinary medicine's quintessential scientist-educator. He came to America in 1868 at a time when a veterinary license could be obtained following a brief sojourn at one of several private, for-profit establishments known more for farriery than medicine.

In 1908, when Law retired from Cornell's deanship, he had fulfilled 40 extraordinary years in laying the foundation for modern veterinary medicine through an unwavering commitment to ensuring that scientific principles govern both research and clinical practice. He also was a much-loved educator and influenced the most inspired veterinary minds of the day, including Daniel Salmon, the chief of the Bureau of Animal Industry and discoverer of *Salmonella*; future Cornell faculty members Theobald Smith, Simon Henry Gage, and Denny Udall, among others; and future deans Veranus Moore and Pierre Fish

(Cornell), and Leonard Pearson (Pennsylvania).

Dr. Law established an enviable record in science with his work on hog cholera, contagious pleuro-pneumonia in cattle, foot-and-mouth disease, and rabies. His research into these infectious diseases was largely influenced by his desire to impact the health of production animals and, through that, to be able to improve human health and food safety. Remarkably, towards the end of his deanship, he also was a leader in the development of the small-animal clinical sphere.

Law had an unyielding commitment to establishing comparative medicine as the foundation for the veterinary profession. This resolve was displayed with great power to the Cornell Board of Trustees, in response to an attempted coup by Liberty Hyde Bailey (then dean of the College of Agriculture) to merge the Veterinary College with the larger College of Agriculture. Bailey's argument to merge the colleges in the name of expediency and fiscal responsibility, was thwarted by James Law who gave an eloquent rebuttal to this hostile takeover bid. Law's central thesis was that "Veterinary Medicine is closely allied to Medicine of man; not to agriculture." Incredibly, he used the descriptor *veterinary medicine*, though the name of our college would not bear this designation for many decades. To the great credit of President Schurman and the Cornell Trustees, the wisdom of Law's arguments prevailed, and the veterinary college main-

tained its independence within the university.

Throughout his distinguished career in both Europe and America, Law demanded that veterinary education and clinical practice be based upon sound scientific principles with a keen appreciation of comparative medicine...*Science must inform practice*. However, he recognized equally that the focus of scientific inquiry needed to be influenced by practical societal needs...*Practice must influence the direction of science*.

This translation of science to practice — and of practice to science — defined Cornell's veterinary medical legacy then and also governs the decisions that we make today.

The recent establishment of our Comparative Cancer Program and hiring of Dr. Rodney Page to serve as its director is one example of our continuing commitment to fulfill the James Law legacy. The goal of the cancer program is to unite discovery and application and thereby improve the health of animals (and, by extension, people). As well, the remarkable discovery by Dr. Richard Cerione and colleagues, featured in this newsletter issue, bears testament to the wisdom of making strategic investments in the highest quality of science and in building meaningful bridges to unite the research laboratory with the clinical domain.



Donald F. Smith, dean



CORNELL
Veterinary Medicine

Cornell Veterinary Medicine is published quarterly for friends and alumni of the college. Visit our World Wide Web site at: <http://www.vet.cornell.edu>

Office of Public Affairs — Box 39
College of Veterinary Medicine
Cornell University, Ithaca, NY 14853-6401
Email: cvmopa@cornell.edu

Managing Editor: Jeri Wall

©1999, College of Veterinary Medicine,
Cornell University. All rights reserved.

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

Robert H. Udall, AB '38, DVM '41, PhD '51, with his wife Mary, in 1997 at Cornell's Wall of Benefactors on the terrace of Uris Library.



© JON REIS/PHOTOLINK

Recent Gifts

Gifts to Baker Institute and Cancer Program

Sylvia and Neil Van Sloun recently made a contribution of \$75,000 to support the James A. Baker Institute for Animal Health building campaign. They also contributed \$25,000 to support the college's Comparative Cancer Program.

Canine Genetics

The Van Sloun Foundation added \$25,000 to the Van Sloun Fund for Canine Genetics Research to support Gustavo Aguirre's research in the genetic basis of canine inherited blindness. The Foundation also contributed \$10,000 to help fund Rory Todhunter's studies of the genetic basis of canine hip dysplasia.

Endowed Scholarship in Feline Medicine

Patricia Cope '50, through her affinity for cats and her desire to help current veterinary students, recently established the Jessie D. & Denny W. Speidel Scholarship, in memory of her parents.

Recipients will be veterinary students who have demonstrated financial need as well as shown an interest in pursuing a career in feline medicine.

Greenwich Kennel Club Scholarship

The college has received a \$4,000 gift from the Greenwich Kennel Club of Connecticut. This is the first time that the club has sponsored a scholarship at Cornell. Preference will be given to one deserving veterinary student from Fairfield County, Connecticut.

In Honor of His Father:

Foremost Benefactor Gift

This past summer, Robert H. Udall, AB '38, DVM '41, PhD '51, a Cornell foremost benefactor, made a significant additional contribution to the university in the form of a charitable gift annuity, thus enlarging his original bequest. Udall was formally recognized in 1997 as a foremost benefactor for a generous bequest to the College of Veterinary Medicine.

Udall's bequest, based on his residuary estate, was intended for an endowment fund to honor his father, Denny Hammond Udall, Cornell DVM 1901, a world-renowned Cornell faculty member and large-animal clinician at the College of Veterinary Medicine from 1908 until he retired in 1942.

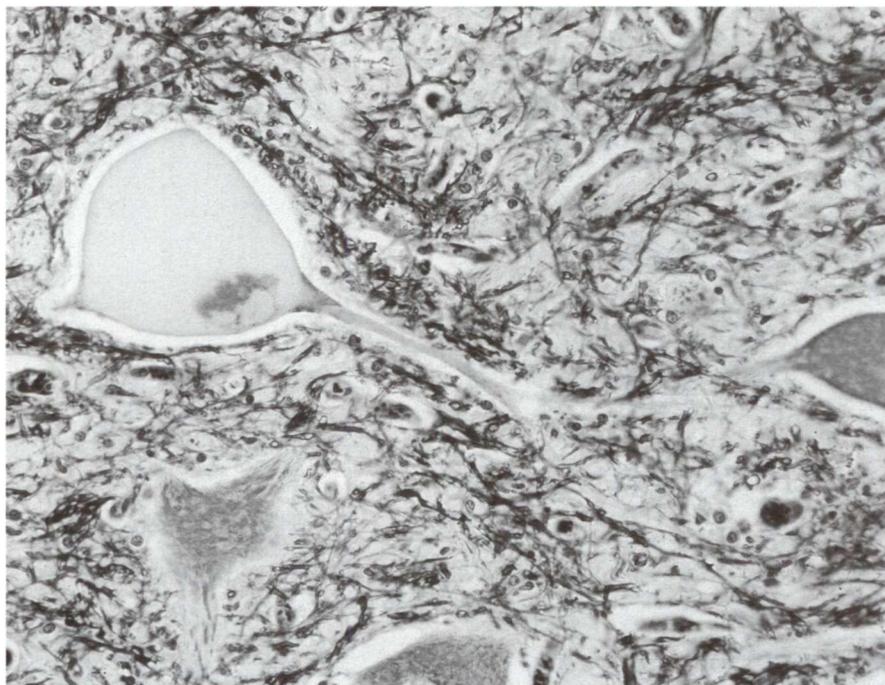
Robert Udall followed his father into a career in veterinary medicine. After earning his PhD at Cornell in 1951, Udall worked his entire career at

Colorado State University, where he was a faculty member in the department of pathology at the College of Veterinary Medicine. His expertise is in the biochemical aspects of animal pathology, particularly sheep metabolic diseases.

His gifts to Cornell, Udall explains, are heartfelt decisions made to honor the life and professional contributions of his father.

With gifts of securities totaling \$1.4 million to the Denny Hammond Udall Endowment Fund and the charitable gift annuity that will ultimately be added to the endowment fund, Dr. Udall and his family are assured to see the tangible benefits of his generosity to the College of Veterinary Medicine in the years ahead.

The endowment fund is unrestricted, to be used at the discretion of the college dean. ■



COURTESY ALEXANDER DELAHUNTA

A swollen, degenerating neuron (pale-staining) contrasts with the smaller, darker normal neurons (with the dark bodies in their cytoplasm). This is the early stage of degeneration of the neuron, when abnormal neuro-filaments accumulate in the cytoplasm.

Nutritional Deficiencies Cited as Risks in Equine Motor Neuron Disease

Since November 7, 1999, a nonfiction book called *Tuesdays with Morrie* has been on the *New York Times* best-seller list.

As writer Mitch Albom recounts his weekly visits with his dying professor, he leads thousands of readers on an excruciatingly intimate encounter with the slow, insidious decay of amyotrophic lateral sclerosis (ALS), commonly known as Lou Gehrig's disease. For Morrie, readers learn early on, suffocation is the inevitable end of the road.

Veterinary epidemiologist Hussni O. Mohammed, BVSc, DPVM, MPVM, PhD, professor in the college's department of population medicine and diagnostic sciences, knows ALS from the inside out. He's one of the world's foremost experts in equine motor neuron disease (EMND), a disease in which changes in the spinal motor

by Metta Winter
Cornell Media & Technology Services

"No one has ever before been able to reproduce the motor neuron disease in a natural model."

neurons are remarkably similar to those in people with ALS.

For the past decade Mohammed has methodically narrowed the field in his search for the cause of EMND, which, although not necessarily fatal, saps the strength and vigor of horses world-wide.

The breakthrough came when, in two different studies, Mohammed and his colleagues — Alexander deLahunta, DVM PhD; Thomas J. Divers, DVM; and Brian A. Summers, BVSc, MSc, PhD — succeeded in reproducing EMND.

"No one has ever before been able to reproduce the

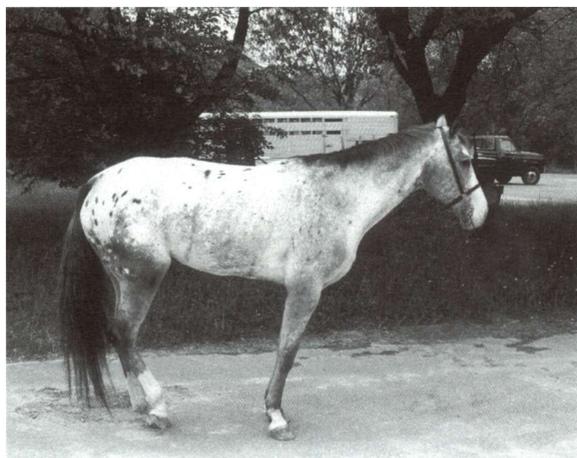
motor neuron disease in a natural model," Mohammed says. "Now, we'll be able to observe it under controlled conditions that we can manipulate."

Being able to do so is a researcher's dream.

Mohammed began to track the cause of EMND by investigating the association between 120 putative risk factors and the likelihood of developing the disease. Among them, a deficiency in vitamin E stood out. Field trials confirmed that horses with EMND did have low levels of vitamin E. Mohammed then set out to establish whether a deficiency in this nutrient could be a major risk factor.

Results of the study showed that a low level of vitamin E is conclusively a strong risk factor for the disease.

Additionally, Mohammed explains, during the study the researchers also found that



COURTESY HUSSNI MOHAMMED

A horse with equine motor neuron disease.

oxidative stress was involved in EMND. [Vitamin E typically protects against oxidative stress.] However, Mohammed believes that oxidative stress, although it is a predisposing factor in EMND, is not the only cause.

From the original 120 potential risk factors, a number showed a significant association with EMND. These results have led Mohammed to conclude the disease is caused by several factors that interact either additively or synergistically.

Now that he can reproduce EMND under highly controlled conditions, he's in a position to

"We are at a critical point in our research now, where we are poised to complete our understanding of the risk model."

design studies that can take each of the prime candidate factors and examine their role, one by one.

"We are at a critical point in our research now, where we are poised to complete our understanding of the risk model," Mohammed says of the large and highly demanding effort that's currently in the final planning stages. Moving forward depends on continued

financial support for the work, much of which in the past has come from foundation and government grants.

It is at this time of such outstanding progress, Mohammed says, that he and his collaborators are most keenly aware of the loss of their former colleague, John Cummings, who died suddenly in 1996. Cummings, DVM '62, MS '63, PhD '66, former James Law Professor of Anatomy at the college, had a distinguished career in comparative neurology and neuropathology. He was the founding member of the research group, having first identified EMND in horses in 1990. Cummings focused on identifying neurological disorders in domestic animals that were natural disease models for similar human disorders. During his career, he recognized and described a variety of these models, including EMND.

"Dr. Cummings stood for the best in veterinary medicine," Mohammed says in remembering his friend and colleague, "and we have continued the work with great respect to him." ■

Simple Tests Promote Reporting of EMND

Reported cases of EMND have increased dramatically since Mohammed and his team perfected two simple tests that can be conducted on live horses.

In one test, veterinarians take a biopsy from a peripheral nerve in the neck. An even easier test uses tissue from the muscle of the tail.

These procedures have resulted in much wider geographic reporting of EMND, so that now Mohammed's studies include confirmed cases from Japan, Europe, South American, and the United States.

"The hope is that these tests, performed without charge, will continue to help us identify cases and encourage owners and practitioners to contact us for diagnostic assistance," Mohammed says.

Collaboration on Brazilian Epidemic

In December 1993, Mohammed was contacted by Brazilian veterinarians at the Policia Militar do Estado de Sao Paulo who feared an epidemic of EMND in a large population of stabled cavalry horses.

Of a total of 405 cavalry mounts, to date 72 have died, resulting in substantial operational and financial losses. Pathological studies have confirmed EMND among the majority of cases.

Mohammed's team continues to work closely with the Brazilian cavalry. Team members have traveled to Brazil three times, and delegates from the Brazilian group have come to Cornell four times. Two fourth-year veterinary students have each spent two months in Brazil, helping collect samples from both unaffected horses and from those suspected of having the disease.



(left to right)
The official portraits
of former deans
Dr. George C. Poppensiek,
Dr. Robert D. Phemister,
and Dr. Edward C. Melby.

Celebrating Millennium 2000:

College To Honor Former Deans

During the year 2000, the College of Veterinary Medicine plans to celebrate the millennium with ceremonies to honor its fifth, sixth, and seventh deans and their major legacies to the college and the veterinary profession.

Dr. George C. Poppensiek, fifth dean, served the college as dean from 1959-1974.

Dr. Edward C. Melby served as sixth dean of the college, from 1975-1984. And Dr. Robert D. Phemister served as seventh dean of the college, 1985-1995.

As part of each ceremony, the portraits of the deans, now exhibited in the Flower-Sprecher Veterinary Library, will be rededicated in locations at the college that are representative of their respective heritage and impact on the college.

A memorabilia album will be given as a gift to each of the former deans. Those who knew Drs. Poppensiek, Melby and Phemister during their tenures as dean are encouraged to send photographs, letters, anecdotes, and other memorabilia for inclusion in the albums.

Please direct submissions to Mrs. Doris A. Smith, c/o The Office of the Dean, Schurman Hall S2-005, College of Veterinary Medicine, Cornell University, Ithaca, NY, 14853-6401.

George C. Poppensiek, MSc, VMD

During Dean Poppensiek's tenure, the college made major advances in veterinary research. The Veterinary Research Tower was funded and constructed and stands as testament to the foresight and legacy of Dean Poppensiek and his colleagues.

On Friday evening, March 24, during the college's 92nd annual Conference for Veterinarians, friends and colleagues of Dr. and Mrs. Poppensiek are invited to visit with them in the college's Centennial Room between 6 and 7pm. A brief ceremony will be held at 7pm to rededicate Poppensiek's portrait in a new location in the Veterinary Research Tower, as a tribute to his vision and the accomplishments of those who advanced the profession during his deanship.

On Sunday, March 26, at 12:30pm in the James Law auditorium, a special tribute will be given to Dr. and Mrs. Poppensiek. Invited speakers will include Lonnie J. G. King, dean of the College of Veterinary Medicine at Michigan State University.

Robert D. Phemister, DVM, PhD

Ceremonies to honor Dean Robert D. Phemister will be held during Reunion Weekend, June 8-10. In his deanship, Phemister focused attention on instruction and learning as critical elements of the college's mission and was instrumental in helping the faculty develop and implement a new paradigm for veterinary education. He also presided over the planning, funding, and construction of a major college addition, the Veterinary Education Center, which opened in 1996. In honor of the many accomplishments of Dean Phemister, his portrait will be rededicated in ceremonies during Reunion Weekend, which coincides with his own 40th class reunion.

Edward C. Melby, DVM

The college will honor Dean Edward C. Melby and all those who served to advance biomedical research during the period of his deanship, 1975-1984, at special ceremonies during Cornell's Homecoming Weekend, on September 21-23. Dean Melby's portrait will be rededicated in the Veterinary Medical Center, the building which was envisioned and planned during his tenure. ■

Millennium Celebration

Year 2000

March 24 to 26

92nd Annual Conference
for Veterinarians

Honoring Ceremonies for
former dean George Poppensiek

Preview of the college's
millennium video and portfolio
[early orders taken]

April 8

34th Annual Open House

May 27

DVM Hooding Ceremony

May 28

Commencement

June 8 to 11

Reunion Weekend

Honoring Ceremonies for
former dean Robert Phemister
Exhibit and sales of the college's
millennium video and portfolio

September 22 to 23

Homecoming Weekend

Honoring Ceremonies for
former dean Edward Melby
Scholarship reception

October 9 to 10

50th anniversary celebration
of the James A. Baker Institute
for Animal Health

Year 2001

June 7 to 10

Dedication of the college's
millennium sundial

Announcing: Cornell University Hospital for Animals

Cornell University's College of Veterinary Medicine recently announced a name change for its hospital facility. The new name — *Cornell University Hospital for Animals* — better reflects the hospital's primary mission, the medical care of animals, says Robert O. Gilbert, BVSc, MMedVet, the college's associate dean for clinical programs and professional service, in discussing the name change.

"The mission of the hospital has not changed — patient care still comes first and foremost," explains Bonita S. Voiland, the college's assistant dean for hospital operations. "Now we have a name that emphasizes what we do."

The mission of the hospital, formerly known as the Cornell University Veterinary Medical Teaching Hospital, is to provide leadership in patient care, education, clinical investigation, and scientific innovation.

The new name was approved by the executive committee of the Cornell University Board of Trustees this winter.

Cornell University Hospital for Animals, renowned as a state-of-the-art clinical facility, was renovated in 1994. The hospital comprises the Companion Animal Hospital, under the medical direction of William Miller, DVM; the Equine & Farm Animal Hospitals, under the medical direction of Norm Ducharme, DMV, MSc; and the traveling Ambulatory and Production Animal Medicine Service, under

the leadership of section chief Maurice (Pete) White, DVM.

"The professional excellence of our veterinary medical staff, combined with the newest technologies and advanced techniques in medicine and surgery, assures the best health care for all of our animal patients," explains Ducharme.

Clinical faculty total 61, with another 29 veterinary residents and interns; licensed veterinary technicians and other hospital staff add another 110.

The hospital serves the health-care needs of animal patients 24 hours a day, 7 days a week.

"Many of the hospital's patients are referred with complicated medical or surgical problems by their veterinarians for evaluation here by our faculty specialists," explains Miller.

Specialty medicine services at the hospital include anesthesiology, behavioral medicine, cardiology, dentistry, dermatology, emergency medicine and critical care, equine performance testing clinic, farriery service, intensive care, internal medicine (including a new comparative cancer program), medical imaging, ophthalmology, soft-tissue and orthopedic surgery, theriogenology (reproductive health), and wild-life and exotic animal medicine (including zoo animal medicine). ■

From *Helicobacter pylori* to *Helicobacter bizzozeronii*:

The Stomach Is Not a Sterile Place

by Metta Winter

Cornell Media & Technology Services

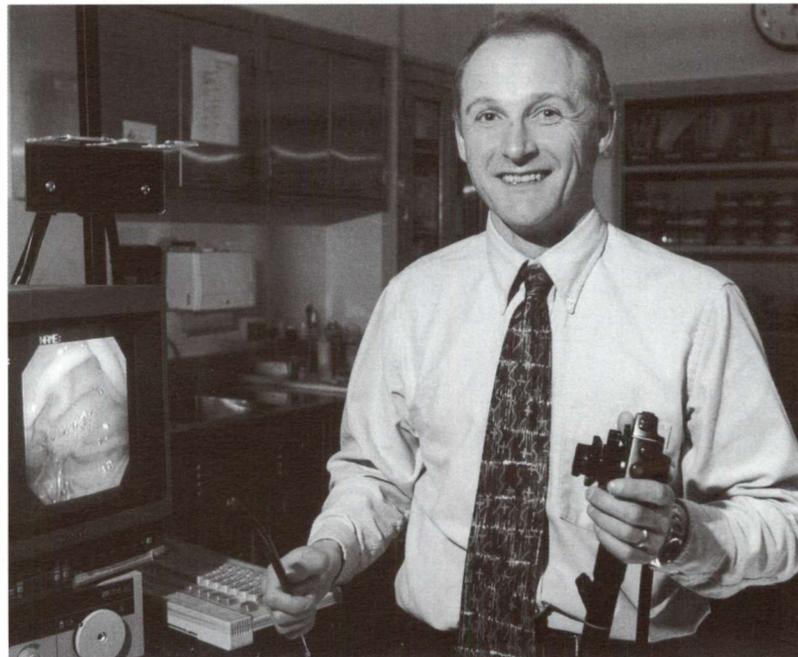
Last June, Kenneth Simpson sent off a note to the medical director of *Digestive Health and Nutrition*, a magazine published by the American Gastroenterological Association. In its "Pet Scoop" column, the magazine had published an article about a schnauzer that had been diagnosed with an ulcer reputedly caused by the bacterium *Helicobacter pylori*.

Simpson knew that *H. pylori* had never been isolated from pet dogs or cats.

"What most concerned me was that readers would think they could get *H. pylori* from their pets," says Simpson, BVM&S, PhD, MRCVS, an assistant professor of medicine in the college's department of clinical sciences.

Simpson, who is a diplomate of both the American College of Veterinary Internal Medicine and the European College of Veterinary Internal Medicine, first encountered *Helicobacter* in 1991 when he was a veterinary resident

Gastric spirals much larger than *H. pylori* are common in both cats and dogs. Until their association with disease is determined, pet owners should be advised to wash their hands after handling their pets, particularly when cleaning vomit or cleaning litter boxes, and to avoid letting pets lick their faces.



UNIVERSITY PHOTOGRAPHY/CHARLES HARRINGTON

Dr. Kenneth Simpson reads the results of an endoscopy exam.

endoscoping a cheetah. After coming to Cornell in 1995, he wrote a series of grant proposals to study the organism, and his research has had active funding through corporation, foundation, and private support ever since.

"When it comes to *H. pylori*, we have no reason to believe that pets pose a significant zoonotic risk [a risk of communicating the disease from animals to humans]."

Being clear on this point is particularly important because the bacterium, *H. pylori*, which is present in the stomachs of between 20 and 95 percent of healthy people worldwide, is now known to cause chronic gastritis and peptic ulcers. Just as importantly, these S-shaped organisms, a mere 2- to 5-microns long, are implicated in two cancers: gastric adenocarcinoma and gastric mucosal-associated lymphoma. Between

The World Health Organization classified *H. pylori* as a carcinogen in 1994.

one and three percent of the people infected with *H. pylori* will develop stomach cancer. This is six times the risk faced by uninfected people.

The confusion in the magazine article most likely stems from the fact that large (5- to 12-microns) gastric spirals are commonly found in the stomachs of healthy dogs (up to 100 percent of shelter dogs, for example). Using DNA techniques, scientists have classified these gastric spirals into distinct *Helicobacter* species such as *H. felis*, *H. bizzozeronii* and *H. salomonis*. These large *Helicobacter* species in dogs and cats may pose some zoonotic risk, but it is a relatively small problem as *H. pylori* accounts for more than 99 percent of *Helicobacter*-related disease in people.

“Rather than thinking that cancer is solely a product of oncogenes, we’re now considering that chronic inflammation might be a stimulus for tumorigenesis.”

Simpson is intensely curious about *Helicobacter spp* and their role in disease in dogs and cats.

“Clinically, the general lack of knowledge of the pathogenicity of these large gastric *Helicobacter spp.* has meant that veterinarians do not have a basis for decisions of whether to eradicate, or ignore, spiral bacteria observed in biopsies from their animal patients with chronic vomiting and gastritis.”

This clinical dilemma served as a catalyst for much of his research. At Cornell, as well as through collaborations with other institutions, Simpson is studying whether some of these other species of *Helicobacter* may be the culprits behind gastritis or even gastric cancer in animals, just as *H. pylori* is in people. And, if this is the case, what can be done to both treat the disease and prevent the infection.

In this endeavor Simpson sees himself as lucky. He points out that it’s very rare to have a circular research project like this that goes from the clinic to the bench and back to the clinic again, and, particularly, where it deals with a problem as frequently seen by veterinarians as chronic vomiting and gastritis.

“There are not many people who would be able to undertake these studies, because most clinicians don’t have laboratory experience, most research scientists have little clinical knowledge, and even fewer

people have the excellent collaborative support that I have enjoyed” Simpson explains.

In contrast to research programs where the animal is viewed solely as a model for a human disease, Simpson’s studies are directly relevant to cats and dogs, and also provide comparative insights on human *Helicobacter*-related disease.

Spiral bacteria are not a new finding in dogs and cats. Back as far as the 1890s, large gastric spirals were found to live in the stomachs of dogs and cats (and people, too). But they were largely ignored as a potential cause of disease until scientists first successfully cultured *H. pylori* just a decade ago. The species common to cats and dogs are even harder still to culture and require only recently perfected genetic tests to speciate them. Growing reliable cultures is still a taxing enterprise. At present, Simpson’s studies are centered on *H. felis* and *H. pylori*.

In his initial experiments Simpson looked at changes in both gastric structure and function in cats and dogs infected with *H. felis*. He found that while cats mount a response against *H. felis* that is characterized by the expansion of gastric lymphoid tissue, mild gastric inflammation, and the production of circulating antibodies against *Helicobacter*, their gastric function (in terms of an increase or decrease in acid secretion) remained unchanged. In dogs, the only clear consequence of infection was antibody production.

By contrast, when Simpson looked at cats infected with *H. pylori*, they had a much more severe inflammation of the stomach, yet still no changes in acid secretion.

In the United States each year, seven million people suffer *H. pylori*-related disease, including ulcers, and thousands die, primarily from gastric cancer.

“These variable outcomes may be related to differences in the pathogenicity of individual *Helicobacter* species, or the host response to them,” Simpson says. “Our findings suggest that most dogs and cats live in relative harmony with their indigenous bacterial flora such as *H. felis*. Disease, when it occurs, may be a consequence of a loss of tolerance to their normal flora.”

To further look at which species of *Helicobacter* are more pathogenic than others, Simpson is gathering a large sample of biopsies from cats and dogs with naturally acquired gastritis to see which species are present. An additional goal of this phase of his research is to use PCR (polymerase chain reaction) techniques to examine the mucosal inflammatory response in the stomachs of these animals to determine precisely what it is that cells produce to regulate inflammation.

In addition to his work with different species of *Helicobacter*, Simpson’s research program includes developing diagnostic tests, evaluating treatment regimes, and creating vaccines.

Although they are not yet commercially available, Simpson has pioneered the development of two types of diagnostic tests. One is a non-invasive test that involves collecting the animal’s breath or blood; the other is a blood test.

Helicobacter

CONTINUED FROM PAGE 9

Both tests predict the presence of all species of *Helicobacter* in the stomachs of naturally infected animals.

Important findings have come from a treatment trial in which dogs were given the same combination of antibiotics and antacids that has been 90 percent successful in ridding people of the bacterium. Simpson found that although four days after the end of a 14-day treatment no *Helicobacter* was present, 28 days later the level of infection was right back up again. Examination of the DNA of these animals over time showed that the bacterium had persisted throughout, merely dropping for a while to levels that were conventionally undetectable. (Researchers elsewhere have found the same finding holds true for cats.)

This year Simpson is embarking on a blind, placebo-controlled trial, involving several veterinary centers in the United States and Europe, to look at the effects of antibiotics in the treatment of animals that have gastritis and *Helicobacter*. Cats are first.

Studying animals before and after eradication of *Helicobacter*, Simpson says, is perhaps the best way to be confident about implicating *Helicobacter* as a cause of vomiting and gastritis in dogs and cats.

There is much debate in the human medical community about the use of vaccines to prevent *Helicobacter*. The

Stomach cancer is the 14th leading cause of cancer death in humans, worldwide.

argument hinges on whether *Helicobacter* might be beneficial in suppressing acid or in other ways damping down changes that contribute to gastroesophageal reflux disease.

But Simpson and his collaborators are hard at work looking for candidate genes in a variety of species of *Helicobacter* and evaluating different systems for delivering those genes to an animal's immune system. He believes that vaccines are likely the ultimate answer to diseases caused by pathogenic bacteria and may provide a lasting solution to diseases where the host is not living in harmony with indigenous flora.

"If you treat an animal with antibiotics and the organisms return, you're not going to be very successful," he explains, "not until you change the underlying immune response of the animal."

The more Simpson learns, the more his outlook is broadening, he explains. "Since various species of *Helicobacter* also colonize the liver and the intestines," he says with a smile, "the stomach is just the starting place!" ■



Conserving a Species

Since 1994, conservation biologists have been studying the tapirs of Central America, the largest land mammals on the continent and also an endangered and threatened species. Cornell's Sonia Foerster, DVM, a postdoctoral associate with the college's wildlife health program, is one of the biologists interested in finding ways to preserve the species.

Foerster, a member of the Tapir Taxonomy Advisory Group, studies 17 radio-collared Baird's tapirs in Corcorado National Park, Costa Rica. She is concerned with baseline health data: reproduction, mating habits, dispersal, and the nature of solitary and family groups. She collaborates with her husband, Charles, who studies the ecology of the tapirs. The project aims at describing this elusive, solitary, large rainforest herbivore's habitat use, home range, movement patterns, and health status.

"Our goal is to look at the impacts of habitat loss, hunting, and ecotourism on the conservation of the species," she explains. "We need to study the potential of disease exchange between populations (for example, tapirs and livestock), to look at boundary issues, and to determine the sustainability of activities in the tapir's overall habitat range." ■

Zoonotic Pathogens and Drug Resistance in Dairy Cattle

Salmonella Typhimurium is a major animal and human pathogen, which can be directly transmitted from animals to people. It is also the most common type of *Salmonella* in New York State dairy cattle.

Recent focus on improved farm management practices aims to minimize the transmission of the disease from dairy cattle to people. However, there is continued concern among public health officials and the dairy industry about the potential that certain antibiotics used in dairy herds — for disease prevention, treatment of illness, and growth enhancement — may help select for strains of *Salmonella* (including *S. Typhimurium*) resistant to antibiotics. Some of these drugs also are currently used in human medicine.

In a two-year study, funded by US Department of Agriculture, a research team from the college's department of population medicine and diagnostic science — led by Lorin Warnick, DVM, PhD, and including Patrick McDonough, MS, PhD, and Yrjo Grohn, BVSc, DVM, MPVM, PhD — is combining clinical, epidemiology, and bacteriology experience to analyze antibiotic use and treatment information for *S. Typhimurium*-infected dairy herds and to determine resultant levels of drug-resistant *Salmonella*. The study includes 65 herds in the state receiving clinical service from 45 different veterinarians.

"We are very appreciative of the support and participation of practicing veterinarians and farm owners who are working with us in this project," says Warnick.

The goal is to gather scientific data for use in developing additional management practices that might reduce the risk of emergence of drug-resistant zoonotic pathogens and to decrease food-borne and direct transmission of resistant strains from cattle to people.

In a second project funded by US DA, Warnick is collaborating with colleagues at Michigan State University, University of Wisconsin, and University of Minnesota to study risk factors for *Salmonella* and *Campylobacter* infections and antibiotic use and drug resistance in dairy cattle in US northern tier states. The three-year study will analyze data from 130 dairy herds.

"This is one of several large studies across the country trying to understand the ecology of enteric pathogens in livestock so we can make management practice recommendations to improve food safety," he says.

Cancer Research

CONTINUED FROM PAGE 1

called X-ray crystallography reveals the three-dimensional arrangement of atoms in molecules by bombarding them with intense bursts of X-rays.

The mammalian Cdc42 protein originally was purified and cloned at Cornell by researchers in Cerione's laboratory in 1990. Cdc42 is believed to play a dual role, alternating as an essential protein for normal cell growth and as a switch that allows protein from a mutated Ras oncogene to cause cancer.

Many of the current strategies for intervening against

cancer are directed at the Ras protein. The Cornell biochemists believe that, given the essential function of Cdc42 in Ras-induced malignant transformation, it should be possible to block signals that lead to cancer by modulating Cdc42 activity.

"We are not ready to start designing drugs yet," Cerione cautions. "This has been an extremely difficult biological problem. Just obtaining sufficient amounts of the proteins in functional form and figuring out how to crystallize them was a formidable challenge. The achievement is a real tribute to Greg and Nico's talents and dedication," he says of his scientific colleagues.

However, Cornell University is one of the few institutions in the world with the scientific capability to move a discovery from the basic-biology stage to the determination of molecular structure, the design of drugs, and finally to clinical trials, observes Douglas D. McGregor, associate dean for research in the College of Veterinary Medicine. He points to Cornell's expertise in chemical biology in the College of Arts and Sciences, the university-wide Genomics Initiative and MacCHESS, as well as to the veterinary college with its department of molecular medicine and Comparative Cancer program, its hospital where animal patients with cancers are treated, and its expertise and facilities for conducting clinical trials of new therapies in animal models.

Studies of the Cdc42/GDI complex were supported by grants from the National Institutes of Health and the international Human Frontiers of Science Program. ■

Scientist Uses Forensic 'Gold Standard' in Animal and Human Poisoning Cases

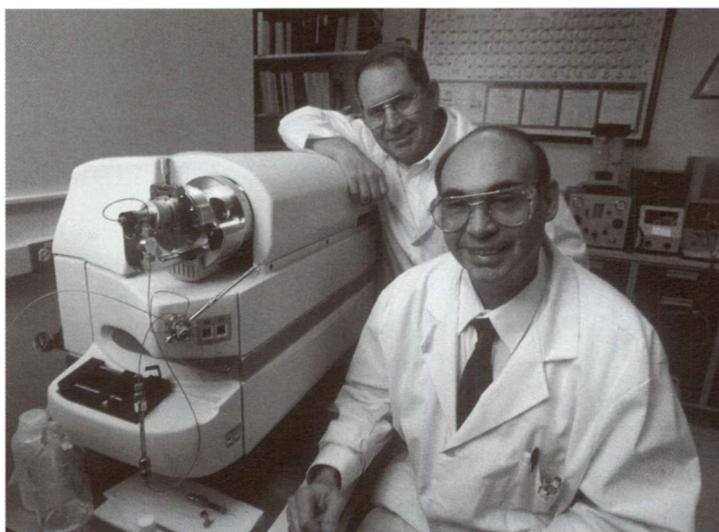
by Roger Segelken
Cornell News Service

Substances that are poisonous to animals can now be subjected to the same chemical scrutiny given to materials in high-profile human cases — such as the O.J. Simpson murder trial. That's because Cornell's College of Veterinary Medicine has equipped its analytical toxicology laboratory for forensic testing with LC/MS/MS, or liquid chromatography tandem mass-spectrometry.

"The state-of-the-art instrumentation can tell us — with scientific certainty that stands up in court — whether even the smallest amount of a particular chemical is present in animal tissue or other biological samples," says Jack Henion, professor of toxicology and director of the laboratory, a unit of the college's department of population medicine and diagnostic science. "Just as important, it can determine if a chemical is not present. This is truly the gold standard of forensic toxicology."

With colleagues Joseph Ebel, director of laboratory operations; Kerry Manzell, research support specialist; and a research group headed by Timothy Wachs, the team detects and characterizes toxic substances that cause poor health or death in animal cases.

The \$200,000 API 2000 LC/MS/MS system, on loan to the college from PE Biosystems of California, incorporates patented technology (an atmospheric pressure ionization LC/MS interface perfected at Cornell's toxicology research-



and-development laboratory) that allows scientists to measure intractable chemicals not possible to characterize with established instrumentation.

Henion and his colleagues have worked to develop better analytical tests for everything from illegal drugs in racehorses' urine to a telltale substance in a retired football player's blood.

In one case, the lab tested the system on a problem involving 100 horses. Several animals went off their feed and many became ill with severe colic in a 12-hour period after eating a newly delivered batch of feed, symptoms consistent with ionophore antibiotic toxicity. Using the API 2000 LC/MS/MS instrument, the lab positively identified the suspect culprit: the antibiotic compound, monensin, routinely added to poultry and cattle feeds as an antibiotic and a growth promoter. Monensin has no business being in horsefeed, Henion explains, because horses are extremely sensitive to very small amounts of the chemical.

The lab's technology and expertise also has the potential

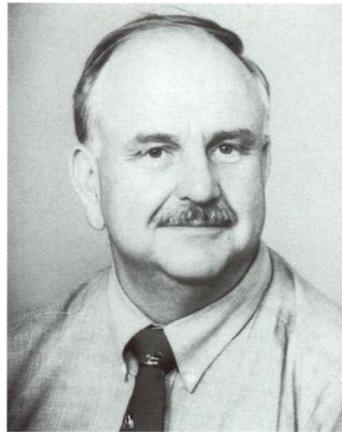
to help forensic toxicology for humans, Henion says, pointing to a few notorious cases: — in one dramatic incident, as reported in *Analytical Chemistry*, the college's toxicology lab analyzed decayed human tissue from an exhumed body, finding that it had not been poisoned with oleandrin, thus saving an accused man from a murder conviction and death penalty. — during the O.J. Simpson trial, Henion was prepared to fly to Los Angeles as an expert witness to explain the results of tests performed by the FBI lab, which found only trace levels of EDTA [an anticoagulant often found at very low levels in human blood] in blood from the scene, a fact that bolstered the prosecution's case by showing police had not planted previously collected blood to frame the suspect [EDTA is found in much greater quantities in blood collected by police in special tubes that contain the anticoagulant as a preservative]. But at 2am Ithaca time, Henion's phone rang and he was told not to fly west, as Judge Ito had heard enough science. ■

People, Honors, and Awards

Douglas Aspros, DVM '75, hospital director of Bond Animal Hospital, PC, in White Plains, New York, was named 1999 practitioner of the year by the America Animal Hospital Association Northeast Region.

Klaus W. Beyenbach, PhD, professor of physiology in the college's department of biomedical sciences, has been awarded the German National Order of Merit for his work with the Alexander von Humboldt Association of America. An offshoot of Germany's Alexander von Humboldt Foundation, the American association was formed in 1995 to promote scholarly, professional, educational, and scientific collaboration between the German and American academic and research communities. One of three founders, Beyenbach served as the organization's first vice-president and second president from 1997-99. Since 1953 the Humboldt Foundation has sponsored study in Germany by more than 19,000 scholars from some 125 countries in highly competitive programs. Beyenbach, whose research on kidney function and ion transport across cell membranes in the kidney is supported by the National Institutes of Health and the National Science Foundation, received a Humboldt Research Award in 1992 and was a visiting scientist at the Max Planck Institute for Molecular Physiology in Dortmund, Germany, from 1991 to 1992.

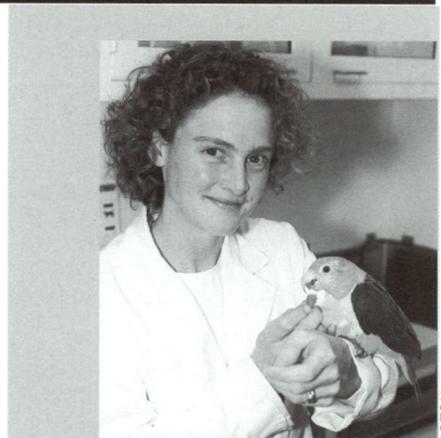
Roger G. Ellis, DVM '77, MSc, recently was named to the board of directors for Heifer Project International, a non-



profit development organization that works worldwide to alleviate hunger and poverty through gifts of livestock and training in its care.

Erla P. Heyns, MLS, PhD, has been named director of the college's Flower-Sprecher Library. Before joining Cornell, she was director of Indiana University's Health, Physical Education, and Recreation Library for seven years and a staff member of the university's library system since 1984. She holds a bachelor of arts (1979) in education and history from University of Stellenbosch, South Africa; a master of library science (1985) and a doctorate of philosophy from Indiana University; her dissertation focused on fundraising for land-grant university libraries.

Jonathan R. Hill, BVSc, PhD, has joined the college as assistant professor of theriogenology in the department of clinical sciences. He will provide clinical service and instruction in animal reproduction and conduct independent and collaborative research. His research focus is in improving the technique of nuclear transfer [cloning] by investigating the abnormalities found in cloned embryos, fetuses, and calves.



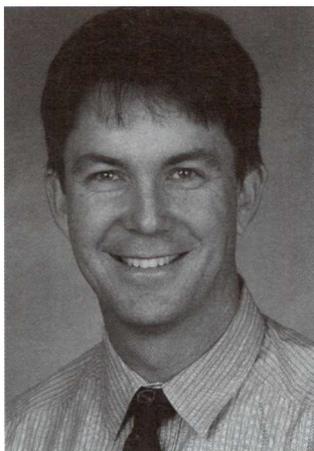
UNIVERSITY PHOTOGRAPHY/CHARLES HARRINGTON

Dedicated Scholars

Stacey Benton, Cornell DVM Class of 2002 (with parrot), and **Amy Johnson**, Cornell DVM Class of 2003 (with goat), are the 1999-2000 recipients of the college's Michele & Agnese Cestone Foundation Scholarships, full scholarships, awarded on the basis of academic merit, that provide tuition and living expenses for the academic year. The scholarship renews for each future academic year until the receipt of the DVM degree (provided that a grade-point average of 3.5 is maintained).

People

CONTINUED FROM PAGE 13



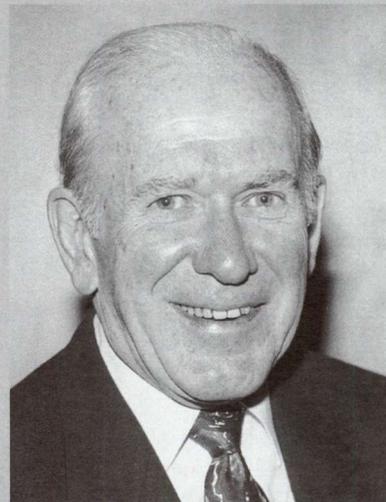
Hill has most recently served as a researcher and coordinator of canine and bovine cloning projects in the department of physiology and pharmacology at Texas A&M University's College of Veterinary Medicine.

Robert Hillman, DVM '55, professor emeritus in the clinical sciences department of Cornell's College of Veterinary Medicine, recently received the Outstanding Service Award from the NYS Veterinary Medical Society. He was a member of the faculty in the college's ambulatory clinic and department of reproductive studies for 30 years before his retirement in 1995. He initiated the equine reproduction program and was instrumental in establishing the neonatal intensive care unit in the college's hospital. In retirement, he continues to serve Genex Artificial Insemination Cooperative in Ithaca, New York, where he directs the animal health program.

Richard Jacobson, MS, PhD, associate professor of immunoparasitology, has been appointed associate chair for laboratory operations in the college's department of population medicine and diagnostic

Scholarship Established To Honor Robert E. Clark, DVM '52

The Miller-Clark Animal Hospital in Mamaroneck, New York, has announced the establishment of a scholarship fund at the College of Veterinary Medicine in honor of the retirement of Robert E. Clark, DVM. The scholarship, say his colleagues, is a tribute to Clark for his many years of dedication to the clients and animals whom he served so well. Nothing would mean more to him, they say, than to help needy veterinary students at Cornell. Contributions are being collected to establish a permanent endowment



science. In this position, he will continue to support the major functions of facilities planning, staff development, and daily laboratory operations.

Francis A. Kallfelz, DVM '62, PhD '66, the college's James Law Professor of Medicine, was elected as NYS Veterinary Medical Society president-elect for 2000, to serve as president in 2001. A faculty member at the college since 1966, Kallfelz served as director of the college's hospital from 1990-1998.

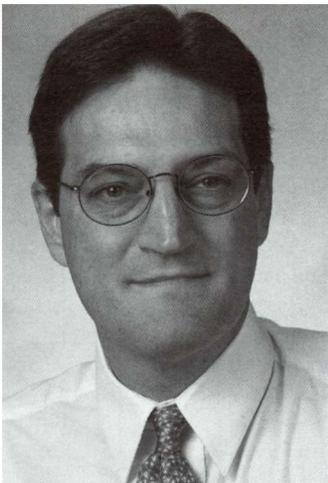
Melissa Kaltaler, an honor student at Liverpool High School in Liverpool, New York, has been presented a regional award for a project that she completed while studying Eastern house finches with Dr. George Kollias and Dr. Barry Hartup of the wildlife health program at Cornell's College of Veterinary Medicine. She received seventh-place honors in the 20th Annual Greater

Syracuse Scholastic Science Fair, in 1999, for her project titled, "The Effects of Mycoplasmosis on *Carpodacus Mexicanus* Have Been Devastating." She observed and recorded information about 83 finches at feeding sites during a two-week period and helped conduct laboratory tests to determine whether the birds had conjunctivitis.

Donald H. Lein, DVM '57, PhD, chair of the college's department of population medicine and diagnostic science and director of its diagnostic laboratory, has received the E. P. Pope Memorial Award from the American Association of Veterinary Laboratory Diagnosticians, Inc. A diplomate of the American College of Veterinary Pathologists, he has been director of the college's diagnostic laboratory, the official New York State laboratory, since 1987; he has been a member of the college faculty since 1974.

Syed A. Naqi, BVM, MS, PhD, professor of avian medicine in the college's department of microbiology and immunology, has received the 1999 Pharmacia-Upjohn Achievement Award for outstanding contributions to avian medicine research. Naqi, who joined Cornell as a faculty member in 1987, served as a professor at Texas A&M University's College of Veterinary Medicine from 1969-1987. A major expert on infectious bronchitis, he has devoted his research career to viral diseases in chickens and turkeys. One of his most important contributions is the development of serotype-specific monoclonal antibodies for the three most prevalent serotypes.

Franklin M. Loew, DVM '65, PhD, was honored by the college Alumni Association, which unveiled his official college portrait during Homecoming Weekend in November 1999. The association honored Loew for his service to the college and the profession during his tenure as 8th dean of the college, 1995-1997.



Rodney L. Page, MS, DVM, has joined the college as professor of clinical sciences and director of its comparative cancer program. He will integrate companion animal cancer manage-

ment with biomedical research programs in cancer throughout the college and university. He holds a master of science in medical physiology (1977) from Georgetown University School of Medicine, and a doctorate of veterinary medicine (1981) from Colorado State University's College of Veterinary Medicine. He is a diplomate of the American College of Veterinary Internal Medicine, with subspecialties in both internal medicine and oncology. He previously was professor of medical oncology at North Carolina State University's College of Veterinary Medicine. His research concerns mechanisms of drug resistance, targeted delivery of anti-cancer agents, and pharmacology.

William C. Rebhun, DVM '71, former professor of medicine and ophthalmology in the clinical sciences department of Cornell's College of Veterinary Medicine, posthumously received the Outstanding Service Award from the NYS Veterinary Medical Society. Rebhun served as a member of the college faculty for more than 20 years before his death. He was a diplomate of both the American College of Veterinary Ophthalmology and American College of Veterinary Internal Medicine.

Karel A. Schat, DVM, PhD '78, professor of avian medicine in the college's department of microbiology and immunology, is the recipient of the 1999 Pfizer Excellence in Poultry Research Award, given for sustained excellence in poultry disease and health research. A faculty member at the college since 1978, he has been devoted to research in Marek's disease, for which he developed the SB-1 vaccine strain.

John F. Wootton, PhD, professor of physiology and acting chair of the college's department of biomedical sciences, was a guest speaker at the 25th Congress of the Turkish Physiological Society at Firat University. He presented a paper titled "Inert, Soluble Precursors Which Release Cyclic Nucleotides Upon Photolysis."

Harold Zweighaft, DVM '56, director of West Parc Veterinary Clinic in New York City, has been elected to the judicial council of the American Veterinary Medical Association.

In Memoriam

Peter Poggi, DVM '62, of Pleasant Valley, New York, died on November 21, 1999, after a long battle with cancer. He is survived by his wife, Patricia, and four sons, Peter, Patrick, Paul, and Matthew.

Clarence R. Roberts, DVM '22, of Roanoke, Virginia, died on December 1, 1999; he was 99 years of age. He is survived by his wife, Florence, of Roanoke, and three children. His eldest son, Kent, of Blacksburg, Virginia, is a Cornell DVM '51. Roberts began his career as a practicing large-animal veterinarian in New Jersey, shortly after graduation from Cornell. When he and his wife decided that he needed work with more regular hours, he took a job with a company later bought by Sealtest Foods; he stayed and became president of Sealtest Foods and Breyer's Ice Cream Company in 1950. He retired in 1965 and spent the next 25 years as a volunteer for the American Red Cross. Roberts and his wife celebrated their 75th wedding anniversary in 1998.

C O R N E L L
Veterinary Medicine

College of Veterinary Medicine
Cornell University
Ithaca, New York 14853-6401

Nonprofit Organization
U.S. Postage
PAID
Ithaca, NY 14850
Permit No. 780

CORNELL
UNIVERSITY

Announcing Early Sales:

The Transforming Influences of Veterinary Medicine

Work is in progress at the college on two special projects that will capture veterinary medicine and its potential as we enter the 21st Century. Sales of these two special editions will benefit ongoing priorities of the college. Please support us by placing early orders.

On Video: The Perspectives of Five Deans

The college's five most recent deans reflect on the notable challenges and accomplishments of the college. A short video featuring commentary on the state of veterinary medicine, with images of research, education, and service activities at the college,

historic and current. The millennium video is being offered for early sales at a discounted price of \$15 for orders postmarked by June 1, 2000*. Order early for discount! [Retail cost for orders after June 1 is \$20. The video will be ready for shipment in early summer.]

In Print: A Unique Portfolio of Images and Ideas

Veterinary medicine and biomedical research, current and future. Large-format photographs, illustrations, essays, explanations, quotations. Featuring visions for animal and human health and medicine as we enter the 21st Century.

This unique portfolio publication is being offered for early sales at a discounted price of \$50 for orders postmarked by June 1, 2000*. Order early for discount! [Retail cost for orders after June 1 is \$65. The print portfolio will be ready for shipment in early summer.]

Buy Both! Video and Portfolio

Purchase the video and portfolio together. The combined set is being offered for early sales at a discounted price of \$55 for orders postmarked

by June 1, 2000*. Order early for discount! [Retail cost for orders after June 1 is \$75. The video and portfolio each will be ready for shipment in early summer.]

* or for orders placed at any time by Cornell DVM students

Please make checks payable to Cornell University College of Veterinary Medicine and mail with the attached form specifying the item(s) you wish to order to: Office of Public Affairs, Box 39, College of Veterinary Medicine, Cornell University, Ithaca, NY 14853-6401.

Yes, I would like to order a video, portfolio, or both.

_____ videos (at \$15 + \$3.40 shipping/handling = \$18.40 each, tax included)
_____ print portfolios (at \$50 + \$5.50 shipping/handling = \$55.50 each, tax included)
_____ sets of both the video and portfolio (at \$55 + \$6.50 shipping/handling = \$61.50 each, tax included)
TOTAL ENCLOSED = _____

Name _____ Phone _____

Email _____

Mailing Address _____ City _____ State _____ Zip _____

Please make checks payable to Cornell University College of Veterinary Medicine. Mail check and form to:
Office of Public Affairs, Box 39, College of Veterinary Medicine, Cornell University, Ithaca, NY 14853-6401

Discount prices apply only to orders postmarked by June 1, 2000; retail prices apply thereafter.

Order by June 1, 2000!