University of Florida
College of Veterinary Medicine

Research

Advancing Human, Animal and Environmental Health

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Whether developing new ways to restore sight and sense, pinpointing levels of toxicity in the environment, or investigating microscopic organisms and viruses to protect against disease, researchers at the University of Florida College of Veterinary Medicine are in the forefront of advancing animal, human and environmental health.

Improving quality of life for you, your pets, food animals and the world's endangered species is our primary goal, and our objectives for doing this unfold in multifaceted ways every day at the UF veterinary college.

We hope this document will enhance your awareness of what we do here at the college and how our multiple approaches to disease diagnosis and prevention come together to make up the whole of who we are as an institution and how we serve the public. Basic biomedical research aimed at improving human health, clinical research to improve domestic animal health and productivity, and conservation medicine and biology to improve the health and well-being of wildlife and our environment are all part of our overall college research program.

In this brochure, we've put faces to some of the individuals who make up these programs, and the stories you will read here offer unique insights into not only who's doing what, and why, but also food for thought as to why research makes a difference in our everyday lives.

Some of our individual researchers and their programs are better known than others. Many readers may know already that a vaccine against Feline Immunodeficiency Virus (Feline AIDS) was developed and patented by a UF researcher whose work into relationships between FIV and human AIDS is ongoing. Others familiar with the college's history may recall that one of the cornerstones of our research program was the infectious disease group focusing on devastating tick-borne diseases such as heartwater in livestock. This group's role in keeping such diseases at bay in sub-Saharan Africa and preventing them from taking root in the U.S. has received international recognition through continued funding from agencies such as the U.S. Agency for International Development. As a result of our team's dedication, a vaccine against heartwater is believed to be close at hand.

Introduction, continued on page 2

Dr. Joseph A. DiPietro, dean, and Dr. Charles H. Courtney, associate dean for research and graduate studies

Introduction, continued from page 1

The preferred animal model for the study of osteoporosis in women was developed by one of our faculty members in the mid 1980s. That same individual has helped evaluate several osteoporosis treatments now on the market. Mice that were part of his related studies involving bone loss and its relationship to weightlessness have flown on the Space Shuttle.

More recently, UF veterinary researchers made headlines when they reported in conjunction with the Centers for Disease Control that equine influenza virus had jumped species into dogs and was the likely cause of several racing greyhound deaths in Jacksonville. Mysterious greyhound deaths continue in Florida and elsewhere from respiratory illness, and so does our investigators' research into the cause.

Another of our researchers is well known locally and internationally for her advocacy of homeless cats and her studies of how to improve cat population control.

When West Nile virus began grabbing media attention a few years ago, another of our researchers soon became the point person for monitoring the incidence of outbreaks affecting horses at our Veterinary Medical Center and elsewhere in Florida. With funding from state and federal sources, she has helped to build a database that will help both horse owners and veterinary professionals better understand the potential for infection as well as how to better track West Nile disease spread.

In spite of all the public acknowledgments our researchers have received, much work continues without headlines or fanfare. In this collection of stories, a meaningful cross-section of research taking place here at the college, we celebrate all of these individuals and their commitment to keeping animals, humans and the environment healthy. We hope you will as well.

Best Regards,

Joseph A. DiPietro, D.V.M. M.S.
Dean, UF College of Veterinary Medicine

Charles H. Courtney, D.V.M. Ph.D.
Associate Dean for Research and Graduate Studies

The College of Veterinary Medicine at the University of Florida, the state's only veterinary college, offers comprehensive service to the public through a fourfold mission: teaching, research, extension, and patient care. Following graduation of its first class in 1980, the college has built on the university's reputation for excellence and is consistently ranked in the top 10 of all U.S. veterinary colleges by *U.S. News and World Report.*

The college is unique in that it is administered jointly by UF's Institute of Food and Agricultural Sciences and the Health Science Center, with the Dean of Veterinary Medicine answering to both the Vice President for Agriculture and Natural Resources and the Vice President for Health Affairs. Over half of college faculty hold both IFAS and Health Science Center faculty appointments. Organizationally, the college is divided into four academic departments.

The department of large animal clinical sciences is responsible for teaching, clinical service and research involving diseases of livestock, poultry and fish. Major programs include animal reproduction, food animal production medicine, equine colic and equine performance medicine.

The department of pathobiology is responsible for teaching, clinical service and research involving pathology, molecular biology, microbiology and parasitology of animal diseases. Major programs include tick-borne diseases, EPM in horses, the AIDS viruses of animals and mycoplasmal diseases. The department also hosts the college's comparative clinical immunology program.

The department of physiological sciences is responsible for teaching, clinical service and research involving basic physiology and toxicology. Major programs include environmental toxicology, forensic toxicology, the neurosciences, and respiratory and cardiac physiology.

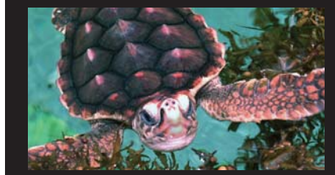
The department of small animal clinical sciences is primarily responsible for teaching, clinical service, and research involving diseases of pets and zoo animals, but some work is done with livestock, primarily in the field of ophthalmology.

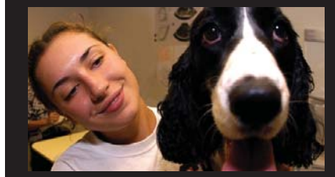
In addition to the above four departments, the college also is host to the Center for Environmental and Human Toxicology. Included within this center are the analytical core toxicology laboratory, the aquatic toxicology facility and the University of Florida Racing Laboratory. The racing laboratory, one of only five such internationally certified laboratories in the United States, is responsible for conducting drug screens on all horses and greyhounds raced at tracks throughout Florida.

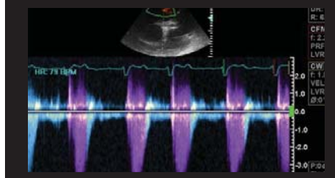
The college also hosts the university's marine mammal program jointly with the Whitney Laboratory. This interdisciplinary program supports research and training in the care of marine mammals with emphasis on manatees.

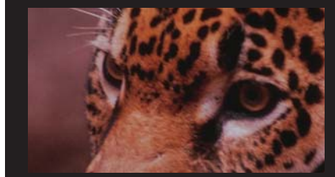
In the 10 years from 1994 to 2004, the dollar amount of grants and contracts awarded annually to UF College of Veterinary Medicine faculty nearly doubled, from $5,221,642 in 1994 to $9,616,498 in 2004 despite an overall decline in state-supported faculty numbers.

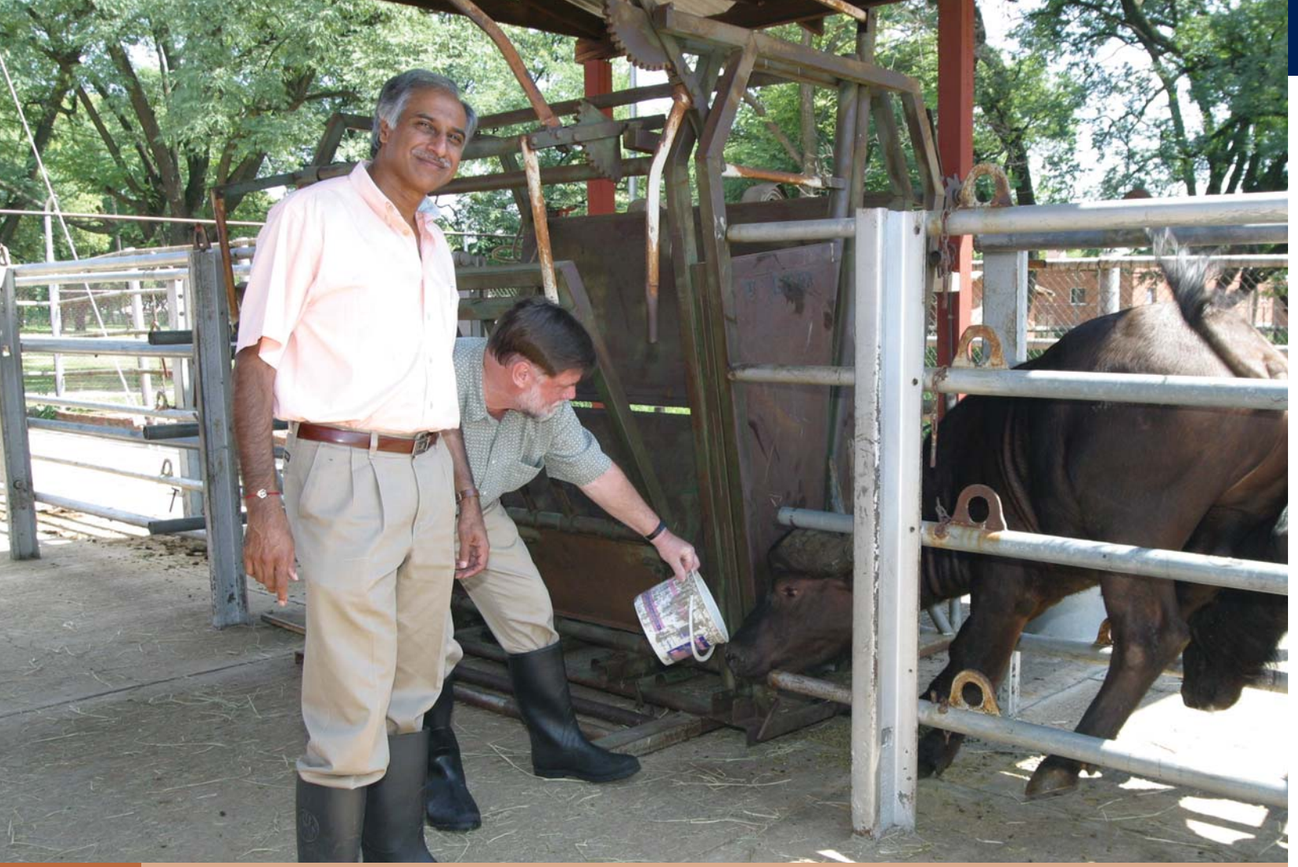
Most of the increase was a result of a 2.5-fold increase in federal funding, a 3-fold increase in corporate funding and a 3.5-fold increase in funding from charitable foundations, whereas research grant funding by the state of Florida declined to 80 percent of 1994 levels.











Keeping Tick-borne Diseases at Bay

Keeping the ticks that carry deadly heartwater disease from jumping U.S. borders and infecting livestock and wildlife might seem like an impossible task, the kind that would take a giant fence around the country.

But a research team at the University of Florida's College of Veterinary Medicine thinks a good vaccine to prevent heartwater would be better – and more effective – than any fence.

And after two decades of working with heartwater disease, the team is on the verge of marketing a conventional vaccine even as it works to develop an even better vaccine with genetic engineering.

Heartwater is spread to livestock and wildlife by the bont tick, a native of Africa. The transoceanic tropical bont tick has shown up in the Caribbean, lurking just off Florida's shores and making its arrival in the United States possible if not likely.

The UF Heartwater Research Project, led by pathobiology Professor Michael Burridge, has been in a 20-year race against time to understand the disease, develop better methods to diagnose it, control the ticks that carry it and invent a vaccine to protect against it if – or when – it arrives.

Heartwater can kill up to 90 percent of the animals it infects, decimating an entire herd. The disease damages the lining of blood vessels, allowing fluid to accumulate in the lungs and body cavities, causing an agonizing death for the infected animal. The tropical bont tick also is associated with acute dermatophilosis, a disease that causes the skin of cattle literally to peel off. Burridge said it is impossible to underestimate the threat to U.S. wildlife and livestock from the tropical bont tick.

"Heartwater is a potential bioterrorism or agriterrorism agent," Burridge said. "It's a disease we definitely need to keep out of the United States."

Burridge, a parasitologist and epidemiologist, points out that many emerging diseases today are tick-borne. While heartwater affects cattle, sheep, goats and deer – not people – tick-borne afflictions like Lyme disease and African tick bite fever do affect humans. Studying bont ticks may help in controlling other disease-carrying ticks, he notes.

Burridge has been horrified by the ease with which exotic ticks travel. In 1997, an injured tortoise from a reptile breeding facility in Central Florida was brought to UF's veterinary hospital for treatment and, almost by accident, found to be carrying exotic ticks. With the United States responsible for more than 80 percent of world trade in live reptiles in the 1990s, the threat of importing ticks via reptiles is very real.

The tropical bont tick also could jump borders by hitching a ride from the Caribbean to Florida on a migratory bird, like a cattle egret. Southern climates are ideal for the ticks which, with wild deer as a host, would be impossible to eradicate once they arrive.

The UF team has focused much of its research offshore. UF scientist Suman Mahan oversees the program in southern Africa, where much of the research has been successfully field-tested.

On campus in Gainesville, pathobiology professor Anthony Barbet, who has had breakthroughs in the study of the tick-borne disease anaplasmosis, brings biotechnology and its advances to the heartwater team. With Mahan and Burridge, Barbet has helped develop technology for a conventional vaccine that is on the verge of being marketed.

His focus now is on using genetic engineering to produce a recombinant DNA vaccine. Laboratory results have been promising, and the new vaccine would be the best tool yet in fighting heartwater.

Biotechnology also has yielded more advanced diagnostic tests for heartwater. Previously, diagnosing heartwater required a difficult and costly brain biopsy. In a huge advance, the UF heartwater team has developed two blood tests for detecting the disease.

> "Heartwater is a potential bioterrorism or agriterrorism agent."
>
> Dr. Michael Burridge

Another breakthrough has been in tick control. Burridge and colleagues invented a bont tick decoy, which can be attached to the ear or tail or worn in a collar around an animal's neck. The small, plastic tag attracts ticks with pheromones then delivers a tickicide. The decoy lasts three months and eliminates the need for ranchers to dip or spray whole herds, which releases toxic chemicals into the environment.

For tick control in wild animals, Burridge and his colleagues developed the AppliGator™, which can be attached to a feeding trough and applies pesticide passively as deer brush against it.

Both the decoy and the AppliGator are inexpensive and easy to use and the AppliGator is stress-free both for animals and the people who need to treat them, Burridge said.

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Intervet International of the Netherlands, the world's largest manufacturer of large animal veterinary vaccines, is working with the UF heartwater team to commercialize the vaccine.

The Heartwater Research Program has spawned more than a dozen patents and attracted more than $16 million in funding from the U.S. Agency for International Development alone.

Burridge says he is perhaps most gratified by the scope and completeness of the project.

"What we've done with this heartwater project is unique in the world. We've taken a disease and we've gone from the very basic science of understanding it at the cellular level and moved on to applied science and then on to commercialization of useful products," Burridge said. "I don't know of another project that has gone from the subcellular level to commercialization of products in the field in quite the same way."

If – or when – the tropical bont tick jumps the U.S. border, the UF Heartwater Research Team will be ready.

Photo left: Dr. Suman Mahan, left, and Dr. Michael Burridge are shown with wild African buffalo during a recent visit to South Africa.

Racing to Determine Causes of Greyhound Deaths

At first, Florida greyhound owners thought they had a particularly tough case of kennel cough on their hands. Then greyhounds started dying from the mysterious respiratory ailment.

For answers, the dog owners turned to University of Florida immunology and infectious disease specialist Cynda Crawford.

When Crawford began investigating, she found an epidemic of nationwide proportions. By June 2004, racetracks and kennels across the country were reporting hundreds of sick greyhounds, causing quarantines and putting a halt to racing in some locations.

No one liked what came next. Crawford's conclusion: equine influenza virus had jumped the species barrier from horses to dogs.

"In the veterinary profession, we had not identified influenza as a cause of respiratory disease in dogs before," said Crawford, a researcher in UF's College of Veterinary Medicine. "In fact, it has not been described in domestic species other than horses, pigs, and poultry. But our DNA analysis of the virus genome showed that this virus actually jumped from horses to dogs.

"When the influenza virus crosses a species barrier, it's a big deal because you don't know which species will be next down the line," Crawford said. "Are people subject to acquiring influenza from dogs now?"

Despite the surprising discovery, the diagnosis gave veterinarians a target. With the culprit identified, Crawford is now pursuing research on a vaccine for prevention of infection and use of antiviral drugs for treatment of sick dogs. Crawford works with a team that includes UF veterinary researchers Paul Gibbs, William Castleman and Richard Hill as well as researchers at the Cornell University College of Veterinary Medicine and the national Centers for Disease Control and Prevention. She is also working on developing a diagnostic assay to identify infected dogs in hopes of catching the disease earlier.

Crawford said respiratory disease outbreaks are the top cause of illness in racing greyhounds, but the severity and duration of these outbreaks led her to suspect a novel infectious agent.

"In the past, these outbreaks would shut down greyhound racing every five years or so," Crawford said. "But they started occurring annually and lasted for several weeks."

Influenza is highly contagious, especially for dogs kenneled in close quarters. It causes fever, coughing, nasal discharges and pneumonia, and can be fatal. Greyhounds have been dear to Crawford since her days as a student in the UF veterinary college. "I adopted my first greyhound here," said Crawford, who now owns three.

The College of Veterinary Medicine has particular expertise in racehorses and racing greyhounds through its Center for Veterinary Sports Medicine and is the only veterinary college with its own greyhound racing track.

During 10 years of private veterinary practice, Crawford ran a greyhound adoption group for retired racers in Tallahassee. Veterinary medical research beckoned, however, so she gave up private practice and returned to her alma mater. Her first posting was in a laboratory for feline immunodeficiency virus research and her work in that area continues today.

Lately, Crawford and UF researcher Julie Levy have been working to identify a diagnostic test that accurately detects feline immunodeficiency virus, or FIV, in cats. Cats infected with FIV are usually diagnosed by the presence of antibodies to the virus in their bloodstream, and the tests available for detection of these antibodies are accurate. However, the introduction in 2002 of a vaccine for protection of cats against FIV infection has created a problem for diagnosis.

"When the influenza virus crosses a species barrier, it's a big deal because you don't know which species will be next down the line."

Dr. Cynda Crawford

When a cat whose history is unknown shows up at a veterinary clinic or animal shelter and tests positive for FIV antibodies during a routine health screening, there is no other test available to verify whether the antibodies are due to infection or vaccination.

"We now have a diagnostic dilemma," Crawford said. "The antibodies the cat makes when it is vaccinated are indistinguishable from the antibodies the cat makes when it is infected with FIV."

It is important to identify the infection because it is contagious and lifelong. FIV-infected cats need to be segregated from other cats to avoid spreading the virus, a procedure particularly important in shelter cat populations. Shelter cats also face euthanasia – instead of adoption – if they test positive for FIV, making an accurate diagnostic test a life or death issue.

After three years, Crawford said, a test to differentiate between vaccinated and infected cats is no closer, but the work will continue.

Crawford also directs the blood donor program at the UF veterinary teaching hospital, which provides blood products for transfusion of their dog and cat patients. Her research is supported by grants from the Winn Feline Foundation, Morris Trust Fund, Alachua County Department of Health and the Division of Pari-mutuel Wagering.

"I very much enjoy what I do. Every veterinary researcher's big dream is to contribute something that improves animal health and welfare," Crawford said. "That's also my big dream."

Photo left: Dr. Cynda Crawford and her colleagues concluded in 2004 that equine influenza virus had jumped the species barrier from horses to dogs.

"I see my mission as improving equine health."

Dr. Steeve Giguère

When he was a boy, the formula seemed simple to University of Florida researcher Steeve Giguère: become a veterinarian, own a horse, keep riding.

Today, his research into equine neonatology brings him into contact with plenty of horses, although he doesn't own them or ride them. But that's OK with Giguère, who says he has found a new mission in helping frail foals survive. And he likes knowing his work makes a difference.

"If you do clinics, you deal with horses and their problems every day," Giguère said. "That way you know what kinds of research really will help, as opposed to something that is interesting fundamentally but not really helpful clinically."

Since the mid-1980s, Giguère said, the UF College of Veterinary Medicine has built up its neonatology program, publishing the first equine neonatal text in 1990. The university long has been a top referral center for clinical care of neonates and is playing a key role in equine neonatology research.

"The discipline of equine neonatology started here," Giguère said. "Every project helps in understanding better ways to treat equine neonatal diseases."

A big part of Giguère's research is focused on an anomaly that makes newborn horses highly susceptible to Rhodococcus, which causes pneumonia, while adult horses largely are immune to it.

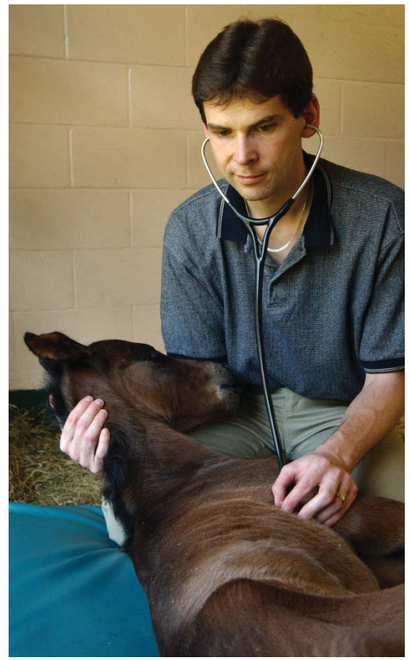
"With Rhodococcus, we are trying to discover why only the babies get it, not adults. What is different in the immune system of the babies?" Giguère said.

Rhodococcus is the leading cause of illness and death in foals in the United States and the leading cause of pneumonia in foals from 3 weeks to 5 months of age. It is financially devastating for horse breeders, who sometimes see 40 percent of their foal crop contract the disease. Foals that do recover are much less likely to race as adults.

Giguère says a long-term goal is to develop a vaccine to protect foals from Rhodococcus. But first, he needs to find the reason for foals' peculiar susceptibility to the infection. Preliminary results show that the immune systems of adult horses rapidly dispatch Rhodococcus infections. Foals' immune cells, however, fail to react, allowing Rhodococcus to cause pneumonia.

"Rhodococcus lives in the environment, so it's very difficult to get rid of. Oftentimes, foals don't show clinical signs till the disease is too advanced," Giguère said. "I want to try to find better ways to identify the disease earlier so we can start treating it sooner. One day maybe we can prevent it, possibly with a vaccine. It's a big challenge. Since the infection occurs so close to birth, there is a small window to build an immune response."

In his work in UF clinics, Giguère found himself faced with a need to measure blood pressure and cardiac output in critically ill foals, but with few well-standardized, non-invasive ways to perform those tests. So he embarked on studies to find more precise and less invasive ways to take the measurements.



In one study, he looked at the accuracy of blood pressure monitors and foals and he evaluated the effect of the site of cuff placement on the accuracy of the measurements. He found that most blood pressure monitors commonly used worked well but found that the best placement for the cuffs was on a foal's tail. The non-invasive monitors are portable and easily used on the farm or in a veterinary office.

To improve methods to measure cardiac output in critically ill foals, Giguère decided to evaluate many non-invasive methods. He found that ultrasound examination of the heart was very accurate in measuring cardiac output and easily used without causing distress to the sick foals.

Giguère also evaluated kits commonly used on horse farms to measure concentrations of antibodies in newborn foals. He found the kits varied widely in accuracy and made his results available to veterinarians and farm managers. Giguère also has been studying multiple antibiotics for use in foals in an attempt to improve treatment of bacterial infections. Systemic bacterial infection is the leading cause of mortality in foals.

Giguère's work has been funded by Morris Animal Foundation and Florida's Pari-Mutuel Trust Fund as well as the Florida Thoroughbred Breeders' and Owners' Association. In fact, support from the association allowed the college to establish a breeding herd of 17 mares that provide foals each year for research. Once the research is completed, the foals are adopted, Giguère said.

"With access to the foals, we can answer more questions so the breeding herd is very important," Giguère said. "These projects are practical for the horse owner.

"We can change the way we practice, discover better therapies," Giguère said. "I see my mission as improving equine health."

Photo left: Dr. Steeve Giguère and veterinary care technician Maria Gore monitor a foal using ultrasound technology.

Seeking Solutions to Cat Overpopulation Problems

University of Florida researcher Julie Levy has her eye on the big picture, a future in which there are no homeless cats because the cat overpopulation problem has been solved.

On her way to that future, Levy focuses on today, sterilizing and vaccinating feral cats at monthly clinics at UF's College of Veterinary Medicine. Operation Catnip sterilizes and provides veterinary care each year for about 2,000 cats, which are trapped, neutered and returned to their environment. The low-cost operation – Levy and other veterinarians, veterinary technicians and students donate their time and the college provides the facilities – is an attempt to make a dent in a problem of almost staggering proportions.

Since 1994, Operation Catnip's three chapters have sterilized more than 20,000 cats, yet estimates put the number of homeless cats nationwide at about 70 million.

"There is a huge cat overpopulation problem," Levy said. "A large number of strays are fed by people but receive no veterinary care. These people are trying to make a situation better that they had nothing to do with creating.

"We can help by providing free veterinary care for the cats. We're the machine that makes it all work," Levy said. "Our clinics are full every month."

Operation Catnip in Gainesville is modeled on a trap-neuter-return, or TNR, program Levy started while in graduate school at North Carolina State University. Similar clinics are scattered across the country and she concedes that surgical sterilization alone won't end the overpopulation problem.

But her outreach program has fueled her research. Levy evaluates contraceptive vaccines for use in feral cats. A successful vaccine would work by triggering antibodies that suppress fertility. One such vaccine that had been used on wildlife did not work in feral cats, and Levy says much work still needs to be done. Her research group currently is conducting studies on another vaccine that looks more promising. Questions that need to be answered with contraceptive vaccines include how soon they work and how long they provide contraception.

If a high percentage of feral cats in a colony can be sterilized – either surgically or with a vaccination – that will bring down the birth rate and eventually the population.

"With feral cats, you may only get to see them once in their life," Levy said. "So what we're looking for is herd immunity. And it will be important to have a product that works on both males and females.

"It's a population that is breeding continuously so somehow we need to increase our capacity to sterilize," Levy said.

Levy said few things spark a controversy in a community the way feral cats do. On one side are cat-lovers seeking a humane way to bring the population under control. On the other side are wildlife advocates who say that feral cats harm native animals like birds by hunting. In between is a lot of misinformation.

For example, one community's debate on feral cats centered on the notion that feral cats spread rabies. Not so, says Levy. Wild animals are the reservoir for rabies, and cats and dogs are incidentally infected during encounters with wildlife. To decrease the risk of rabid cats further, Levy recommends vaccinating all cats that are sterilized in TNR programs.

Levy also does research on feline infectious diseases and says feral cats serve as a sentinel animal and a window on what pet cats might face. So far, for example, surveys of cats exposed to West Nile virus, a mosquito-borne disease, show that cats are commonly exposed to the virus but seem to survive the infection. Levy's research also showed that, contrary to a common misconception, feral cats are not more likely than pet cats allowed outdoors to be infected with feline leukemia, feline immunodeficiency virus and other common feline diseases.

"Feral cats are a very poorly understood population in terms of infectious diseases, systemic infections, diseases that are a threat to other species or humans," Levy said.

The alternative to trap-neuter-return programs is euthanasia, a policy that does not work, Levy says. Even if a community wanted to remove all its feral cats, who would do it and who would pay for it, Levy asks. And studies show that as cats are removed from an environment, other cats take their place.

Levy's work on overpopulation of unwanted pets is so well-known that she was asked to join a team that went to the Galapagos for a wide-scale cat and dog sterilization program in 2004. In the past, the Galapagos had used euthanasia for animal control. In 2004, the islanders and the Park Service agreed to try neutering the animals.

"In a lot of ways it was the perfect place to do this, with no animals coming in from somewhere else to fill the void," Levy said.

After 15 years of working on the feral cat issue, Levy said she is beginning to notice more communities talking about the issue.

"It's a hugely controversial topic, but people are finally starting to do something about it," Levy said. "Veterinary schools are an important connection for training veterinary students how to work safely with feral cats and how to contribute to pet overpopulation solutions.

"It is society's problem; Operation Catnip is one solution," Levy said. "Trap-neuter-return is an example of the really wonderful altruistic instincts of human beings.

"It's the human-animal bond," Levy said. "We protect that."

Photo above: Dr. Julie Levy's outreach program, Operation Catnip, has fueled her research.

In 2001, University of Florida veterinarian Maureen Long became an expert on West Nile virus almost by accident.

That year, in clinics at UF's College of Veterinary Medicine, Long and other large animal medicine clinicians saw an increase in the number of horses coming in with the mosquito-borne disease. Prior to its arrival in Florida, there had been fewer than 100 cases of the disease diagnosed in the United States.

Intrigued, Long and her colleagues put together a proposal that was funded by the Pari-mutuel Wagering Trust Fund in Florida to study the disease outbreak. The timing could not have been better.

The next year, 14,000 cases of the dreaded equine disease were diagnosed and the demand for Long's expertise kept her crisscrossing the country, making her a national expert by the end of the year.

Today, Long runs biosafety level 2 and level 3 laboratories and is able to study the disease in horses under high-containment conditions. In just a few short years, UF has become a leader in West Nile research in horses.

"We became the go-to point by the accident of seeing a lot of cases in 2001 in our clinics," Long said. "Now, we're one of two places in the country to be able to house horses in a facility with special air flow and waste decontamination, and with two labs that offer the proper lab worker protection."

West Nile virus causes encephalitis, both in horses and people, adding a human component to Long's research. In horses, it has a 30 percent mortality rate and there is no treatment. The virus affects the central nervous system and symptoms can range from fever to paralysis to death. The level of infection in horses is important, too, because it's an indication of what people might face with the virus.

Long's research has spanned all aspects of the disease from something as standard as building a database to more complicated questions such as why one horse dies and another survives. Long and her colleagues have investigated testing procedures for the Florida Department of Agriculture and Consumer Services. All cases of West Nile in horses in Florida also are entered into a database of information obtained from a two-page questionnaire filled out at the time of testing.

The U.S. Department of Agriculture heard about the UF work and funded a follow-up questionnaire, which has become the foundation for research into the types of horses, husbandry and management practices that may affect a horse's chances of becoming infected with West Nile and other mosquito-borne viruses in Florida. The information collected – breed, age, vaccination history, clinical signs, location of the horse – is a valuable tool in tracking West Nile's spread, Long said.

The collected information also revealed that the horses that become sick are not vaccinated or not vaccinated often enough, leading to new recommendations, Long said.

Other research investigates the effectiveness of vaccines.

"Currently marketed are the first-generation vaccines for West Nile and Eastern Equine Encephalitis," said Long, referring to another mosquito-borne disease. "What we need now is a better class of vaccines for enhanced protection.

"We need to explore questions like what makes a protected horse, why the virus goes to the brain, whether we can breed for immunity," Long said. "Another question is which mosquitoes like horses compared to birds and which mosquitoes also share a taste for humans. Which mosquitoes are the biggest threat? We don't even know that basic information. A grant funded by the charity of the Florida Derby Gala is assisting in research that consists of vacuuming mosquitoes directly off horses.

> "Horses get the same diseases we do, so this is an excellent model of a human/animal disease."
>
> Dr. Maureen Long

"Horses get the same diseases we do," Long said, "so this is an excellent model of a human/animal disease."

Long said the West Nile outbreak was exciting because of the opportunities it offered to go deeper into basic science and research and to collaborate with other UF experts on emerging diseases, like virologist Paul Gibbs. But in the clinics, the disease only brought sadness.

"During the first couple of years, I had vets with 30 and 40 years of experience calling from all over the country, extremely upset over the devastation they were seeing," said Long, who has owned horses since she was 5 years old. "There is no treatment, so it was really hard on everybody. I felt very powerless when people asked me if their horse would get better."

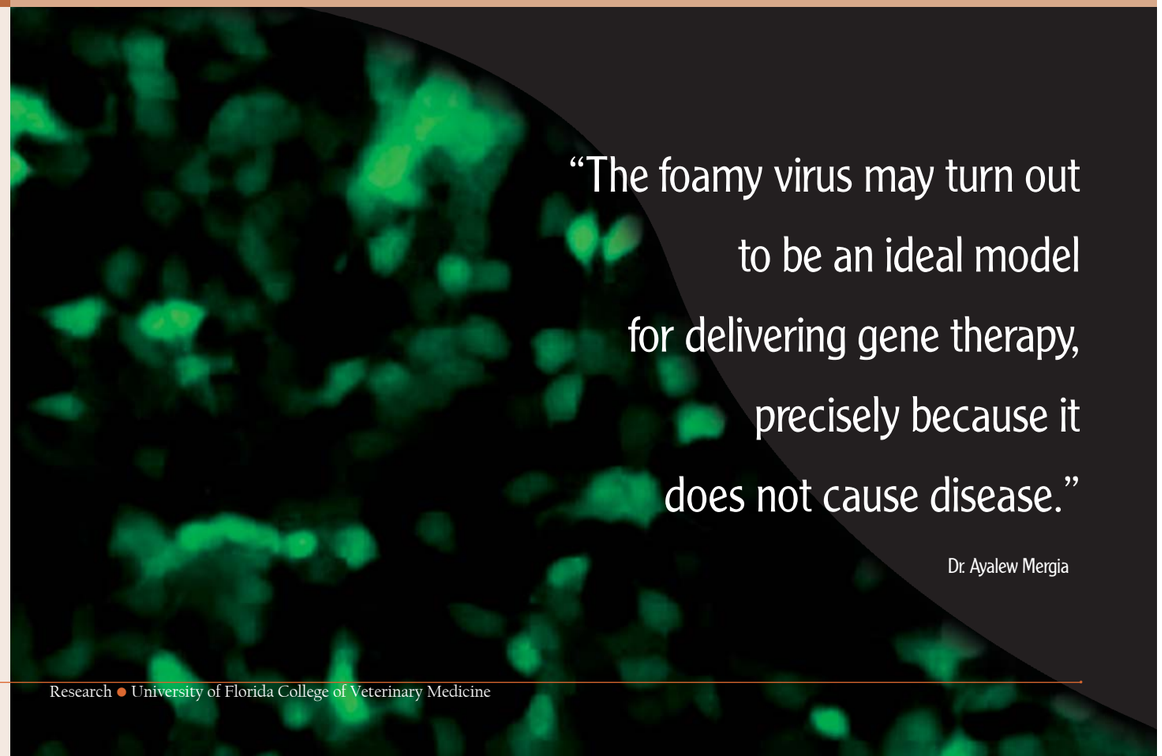
As West Nile has spread, other veterinary colleges and research institutions have turned to Long and her UF colleagues for advice on how to set up high-containment research facilities to study newly emerging diseases.

"Every veterinary school and every region of the country was touched by this outbreak," Long said. "It was a phenomenal outbreak."

Although the emergency has passed – there were only a handful of West Nile cases in 2004 – Long says Floridians should be braced for the next outbreak.

"We're stuck with the threat of new viruses in Florida because of our subtropical climate," Long said. "We're at risk of outbreaks from our common diseases on a cyclical basis every five to 10 years. Because we are an important import state we are also constantly at risk for new infectious diseases that threaten our animals, whether pets or production animals."

Photo left: Dr. Maureen Long has helped UF to become a leader in West Nile virus research in horses.



"The foamy virus may turn out to be an ideal model for delivering gene therapy, precisely because it does not cause disease."

Dr. Ayalew Mergia

Foamy Viruses Show Gene Therapy Potential

A Ayalew Mergia has spent the last 10 years working on a way to use the foamy virus as a delivery vehicle (vector) for gene therapy, the ultimate goal being gene therapy for HIV patients. In gene therapy, desirable genetic traits are delivered to a patient's cells, which then replicate the desirable traits and strengthen the body's defense against disease.

"The foamy virus may turn out to be an ideal model for delivering gene therapy, precisely because it does not cause disease," Mergia said.

Mergia points out that some virus vectors now being studied for gene therapy have problems with efficiently delivering genes to target cells. Others deliver genes but pose potential safety problems for use in human gene therapy. The ideal delivery system is a virus vector that doesn't cause any of its own problems as it delivers the benefits of gene therapy to a patient's cells.

"With every vector you use, there could be some kind of problem. Remember, these vectors are derived from viruses, and viruses can cause disease in humans," Mergia said. "So maybe this is where the foamy virus may have an advantage. It appears to be safe and effective."

Already, researchers have studied humans who have contracted the foamy virus accidentally from animals. These include hunters and animal caretakers, whose cells show the presence of the virus without any ill effects. There are no known instances of human-to-human transmission of the virus, Mergia said, thus a gene therapy treatment that uses a foamy virus vector should not spread unintentionally from the patient to other people. And animals that have the virus show no ill effects, either.

"There are many monkeys in primate centers that are infected with the foamy virus, and they're healthy," Mergia said. "Nothing happens to them."

So far in trials with mice, Mergia has used the foamy virus to deliver marker genes, which tell a scientist where the virus travels and which cells the virus enters. The ultimate goal of Mergia's research is to use the foamy virus in gene therapy for HIV patients.

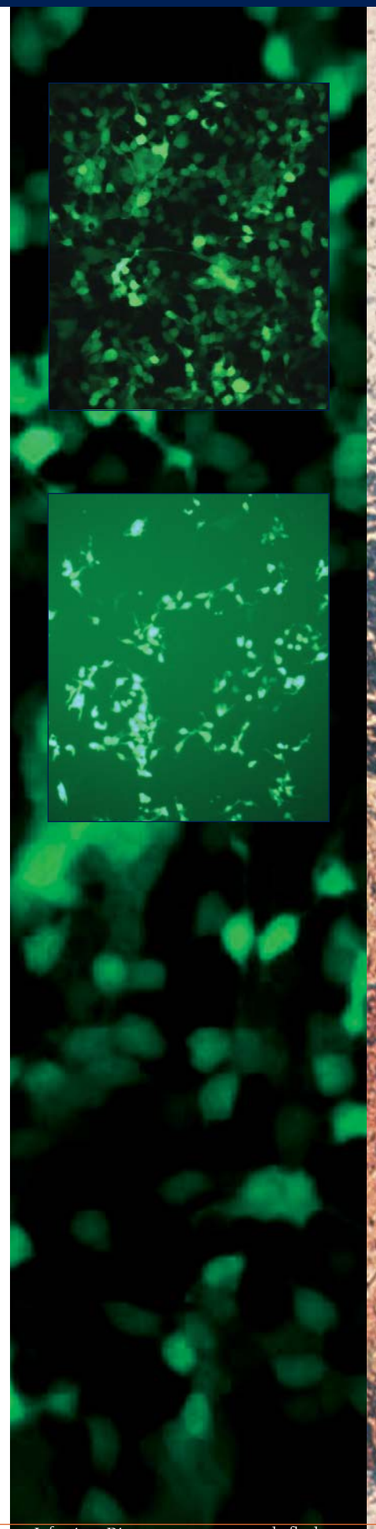
Mergia's work has been funded by the National Institutes of Health since 1995.

"We still have a significant amount of basic research we have to accomplish for the next five years to make the foamy virus vector an efficient gene delivery system. Furthermore, we need to be careful. What if there is something the foamy virus is doing that we haven't discovered?" Mergia said. "Gene therapy is a promising novel approach, and with an efficient and safe gene delivery system will help cure many diseases."

Photo top left: Dr. Ayalew Mergia, shown with post-doctoral associate Dr. Nadja Matvienko, has focused on research that may one day lead to advances in gene therapy.

Photo above: 293T Cells infected with Foamy Virus Vector containing Green Fluorescent Protein gene.

Photo bottom: Higher magnification of top image.



Could cats,
rather than dogs,
be man's best friend?

When it comes
to AIDS research,
the answer might be yes.

Charting New Territory With Immunodeficiency Virus Research

University of Florida immunologist Janet Yamamoto says the feline immunodeficiency virus, or FIV, has biological similarities to human immunodeficiency virus, or HIV, and those similarities could yield advances in efforts to develop an HIV vaccine.

Yamamoto says she has "always liked viruses." In the early 1980s, she worked on the virus that causes feline leukemia and in 1986, she and a colleague discovered FIV, the virus that causes AIDS in cats. Her work during the 1990s culminated in an FIV vaccine that became commercially available in 2002.

Yamamoto found her work on FIV often intersected with research on HIV. There are points in the structures of both viruses, in fact, where the two are so similar that research into one virus may help in research into the other.

"We are working on a new generation of feline vaccines that actually are made with HIV proteins," said Yamamoto, who directs the Laboratory of Comparative Immunology and Retrovirology at UF's College of Veterinary Medicine. "We've found that HIV proteins are closely related to FIV proteins and are useful in developing an FIV vaccine, so that leads us to ask whether FIV proteins can help humans."

Immunodeficiency viruses have "a good side and a bad side," Yamamoto said. People are familiar with the bad, which leads to AIDS, a disease that has killed 22 million people worldwide since it was identified in 1981, according to United Nations estimates.

Yamamoto said the virus likes to hide its "good" side, which provides protection against disease, making it very difficult to isolate it. But in people – and cats – who have an immunodeficiency virus for years without getting ill, the virus' good side is at work. These people and cats are called long-term nonprogressors and the strains they carry may provide a key to prevention, therapy or even a cure for the disease.

The work is painstaking. Imagine that FIV and HIV are long ribbons. One section of the ribbon may contain elements that cause disease or accelerate it. But the flip side of that section of ribbon may be "good" and hold elements that provide protection against disease or retard the disease. Then imagine five FIV ribbons and two HIV ribbons.

Researchers have found five distinct subtypes of FIV, each with its own characteristics that had to be understood and studied before moving forward on a vaccine. The protective properties in the subtypes had to be combined in numerous ways to bring out the most protective combination while suppressing the harmful properties.

"We were about to give up on an FIV vaccine when we combined subtype A and subtype D," Yamamoto said. "The overlap of those two gave us the protection we were seeking."

Cats can't get HIV infection, so Yamamoto now is researching ways to use the protective elements of HIV in a feline vaccine. Her research found a protective section of HIV that provides better immunity for cats than the protective sections of FIV. This section of HIV is so similar to FIV that it is usable in a feline vaccine. And since cats can't get infected with HIV, the HIV proteins that promote disease in humans do nothing to cats.

Since the reverse is also true – humans can't get FIV – she would like to continue her work by looking for FIV strands that trigger an immune response in humans without promoting the disease.

"It was important to find out that HIV proteins are so closely related to FIV proteins," Yamamoto said. "Hopefully, I can contribute to the human vaccine with my model."

Selecting the right strains to trigger immunity in cats is much easier than doing so with humans. As Yamamoto said, "In cats, we could immunize and watch. But there are no laboratory humans."

Yamamoto believes that tests with people who already have HIV would show whether a vaccine developed from FIV could be useful as therapy and perhaps eventually useful in a human vaccine.

"We have identified, so far, three regions of FIV that are similar to HIV-1, and these FIV regions could be tested with immune cells from people who have HIV," Yamamoto said. "If these regions are recognized by the immune cells from people with HIV, it would suggest that those regions may be useful as components for HIV vaccines for non-infected humans. However, more studies are needed not only in cats but also in monkeys to determine the significance of these FIV regions as components for HIV vaccines."

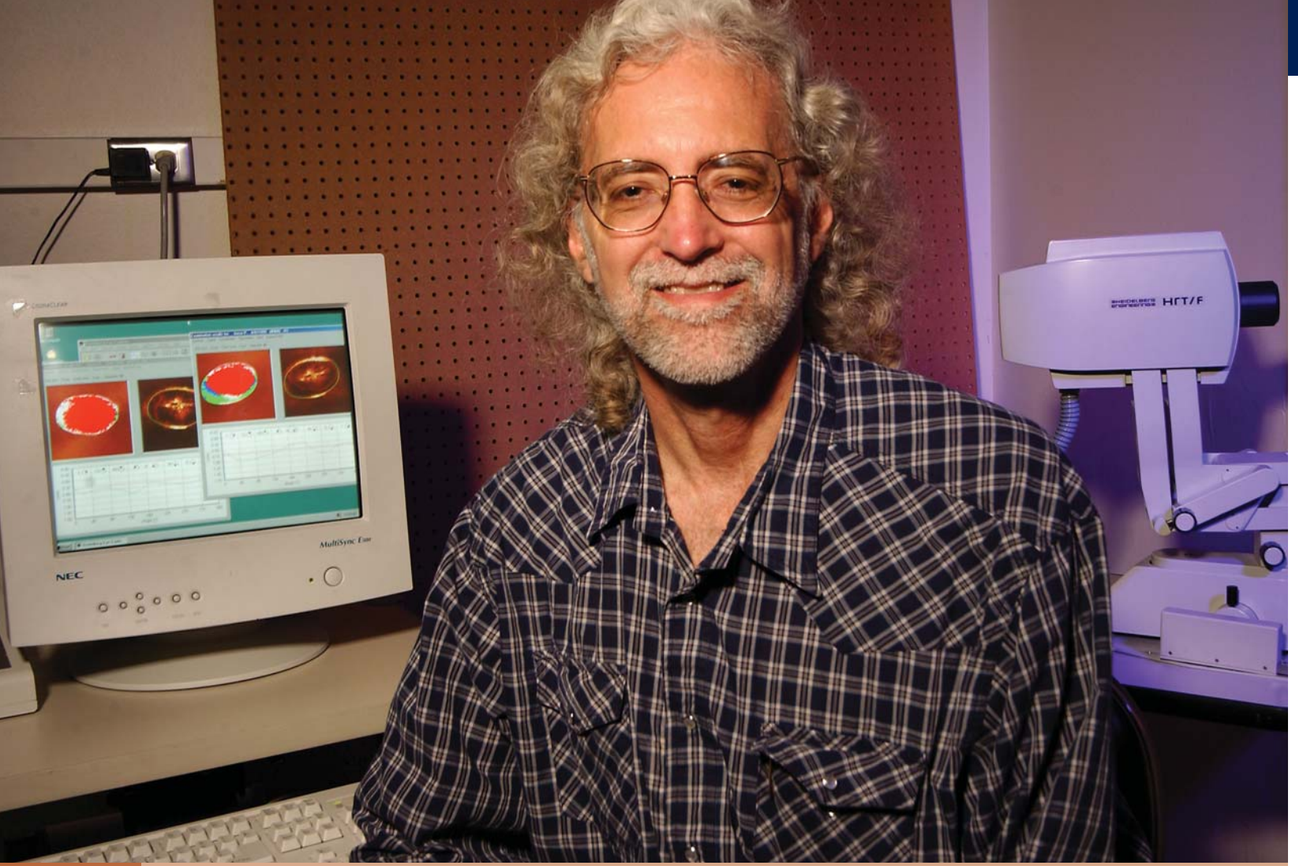
Yamamoto spent much of 2004 and will spend more time in 2005 collaborating with colleagues at the University of California at San Francisco and the University of Pittsburgh, as part of her strong belief that teamwork will be the key to further breakthroughs on immunodeficiency viruses. Her vaccine work has been funded with more than $3.4 million in grants from the National Institutes of Health since 1989. She also has funded her research with more than $1 million in royalties from her patents, including the patent on the Fel-O-Vax FIV™, which is marketed by Fort Dodge Animal Health, a division of Wyeth pharmaceuticals.

Yamamoto said she uses her patent money to explore ideas. When an idea bears fruit, she seeks grants. "NIH funding is taxpayer money, so we need to repay it with discovery."

She personally repays some of her laboratory cats, veterans of bone marrow transplants, by providing a home for them. But she would like to see her feline studies pay off for people.

"Seeing animals and people live longer, that's why we do this work," Yamamoto said. "I enjoy seeing my concept and products help. It's applied research. I believe the cats can benefit not only cats, but people, too."

Photo left: Dr. Janet Yamamoto's work on FIV often intersects with research on HIV.



“These animals can live without seeing, but they want to see. When you can give them sight, their personalities change big-time.”

Dr. Dennis Brooks

Veterinary ophthalmologist Dennis Brooks has fond memories of some of his patients, such as a blind foal that ended up in his University of Florida clinic a few years ago for an eye operation.

“We were taking the baby back to the mare, and when the baby got 10 to 15 feet from the mare, the baby dug in his hooves, just stopped, and would not go any closer,” Brooks recalled. “We were trying to push the baby gently toward the mare when a student figured out the problem. The baby had never seen his mother.

Changing Standards of Care While Improving Sight

“It took him a minute or two, but the baby figured out the huge animal in front of him was his mother,” Brooks said. “It’s a big high to restore sight.”

Brooks has spent a career working toward such success stories. He has performed cataract surgery on a Bengal tiger and used laser surgery to treat glaucoma in horses and dogs. At UF, Brooks and his colleagues have performed more cornea transplants on horses than anywhere else in the world.

While some pet and horse owners may focus on more routine veterinary care, vision problems are the fourth most common health problem for horses, and dogs are second only to humans in incidence of glaucoma, making the need for veterinary ophthalmology research easy to see.

Brooks has not only personally saved sight for many animals, his research has changed the standard of care other veterinarians provide for equine eye problems.

“We’re right here in the middle of Florida’s horse industry, and in the early 1980s we started seeing a lot of horses with eye problems at a time when no one was successful with horse eye problems. Horse eye problems scared people,” Brooks said. “So we started working harder to figure out why the horse eye healed so poorly, how we could help it heal.”

Eye problems in horses typically are worse than eye problems in other species, including humans. Brooks and his colleagues figured any advances in treating equine eyes might eventually benefit other animals and people. The researchers studied tears collected from horses’ damaged eyes and found high levels of enzymes. The enzymes, in effect, were causing the eyes to begin digesting themselves.

“The horse eye is so destructive,” Brooks said. “But once we knew the enzyme level was up, we could figure out how to reduce the enzyme level and allow the eye to heal.”

The research was published in January 2005 and resulted in changes in the legal standard of veterinary medical care for horse eye problems. A veterinarian now must address the enzyme level in a horse with a damaged eye, and failure to address it amounts to a failure to meet the new standard of care.

“We’ve changed the legal standard of care for these animals, and I’m pretty proud of that,” Brooks said.

Brooks’ research began with glaucoma in dogs. He was the first to start examining how the blood flow and blood pressure in the eye affects the optic nerve and currently is in the midst of a large grant project to examine electrical changes in the eye.

“It requires a very large team of people to make contributions in this area,” Brooks said. “I’ll be studying glaucoma my whole career. It’s a big puzzle, and what I’m trying to do is put some of the pieces together. I’m hoping someone comes along one day and puts all the pieces together.”

When Brooks’ career brought him to UF, he found himself in the midst of horse country and facing some of the most intransigent eye problems around. Not every horse’s eyesight could be saved, but Brooks has found inspiration among the blind animals as well.

One inspiration, a plucky Palm Beach County thoroughbred named Valiant, competes in dressage although he is blind. Brooks tried in vain to save Valiant’s sight and says he has been impressed by what Valiant and his owner have accomplished without sight. “A horse with no eyes can do better than you think,” Brooks said.

The Valiant Equine Ophthalmology Research and Development Center is named after the horse and helps to fund Brooks’ research.

“These animals can live without seeing, but they want to see,” Brooks said. “When you can give them sight, their personalities change big-time.”

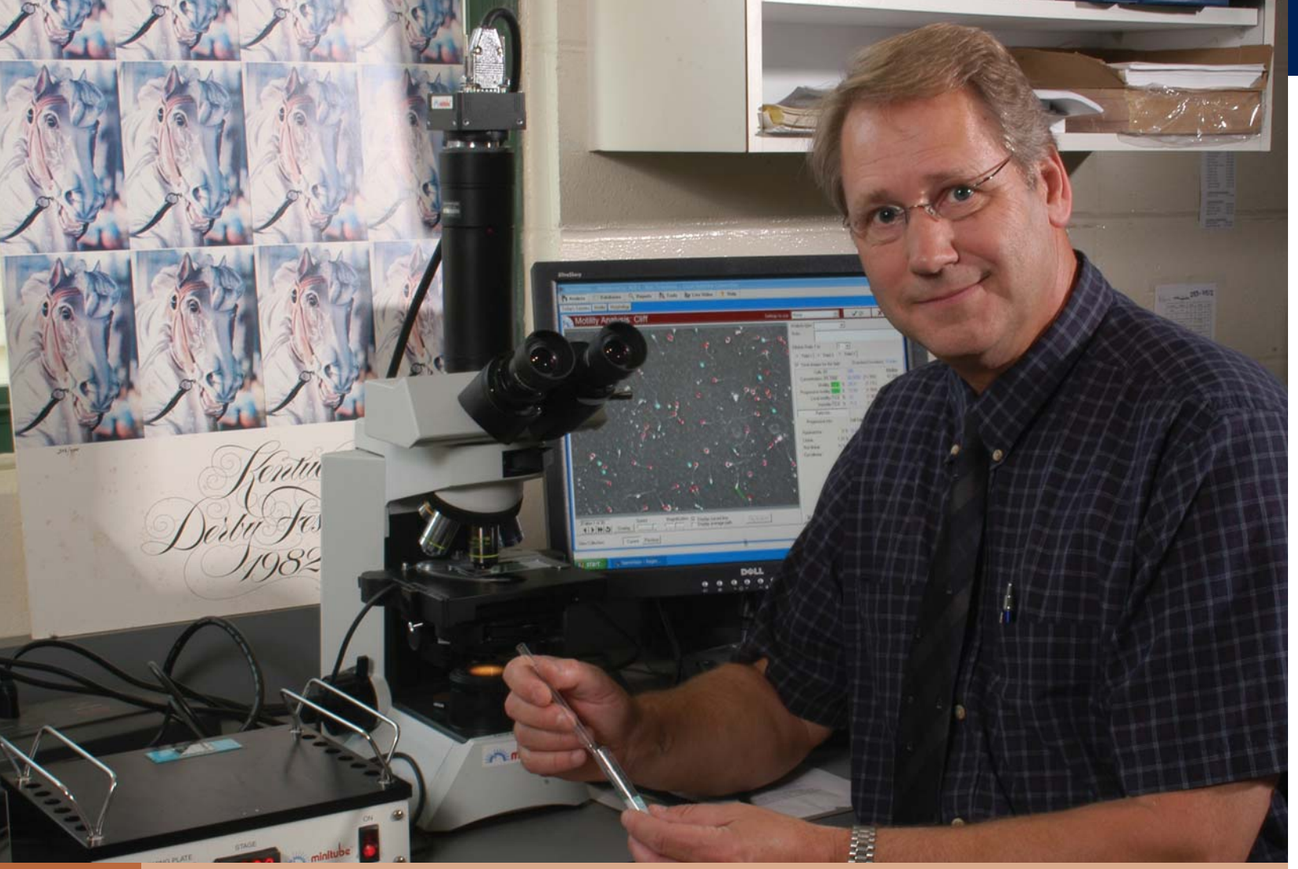
Brooks holds a veterinary medicine degree and a doctorate, making him part doctor and part scientist. He teaches as well and has written a text called “Equine Ophthalmology.” He praises his graduate students and the university environment.

“The graduate students make you better,” Brooks said. “If I worked all by myself, without colleagues or students, I would not be doing nearly as well as I am in working at a university.”

While Brooks’ work appears specialized – only about 10 veterinarians worldwide share his expertise – he says he doesn’t think he has narrowed his focus at all.

“I’ve opened a door to a whole universe of knowledge,” Brooks said. “It will keep me busy my whole career.”

Photo left: Dr. Dennis Brooks combines scientific aptitude with clinical knowledge in veterinary ophthalmology.



Advances in animal reproductive health have mirrored advances in human reproductive health. Horses, for example, get in vitro fertilization and have ultrasound examinations of unborn babies, just like people do.

While horse owners come to the University of Florida's Reproduction Service in the College of Veterinary Medicine for such procedures, some are now offered by veterinarians closer to home. Where does that leave UF's Reproduction Service? Poised to take the next step into the future, says service chief Mats Troedsson.

UF has done its job when it popularizes health care technology for animals, Troedsson said. The point of developing new treatments is to get the advances into the hands of veterinarians.

"People don't need to come here for ultrasound anymore," Troedsson said, although they can, if they like. "So we will develop new assisted reproduction technologies.

"And when those technologies are refined enough to go into the field, we will be one step ahead, working on the next technology."

Troedsson came to UF in 2002, attracted by the synergy between the college's clinical and research facilities. Being able to treat equine patients and conduct research into their reproductive health issues, too, was a key for him. He is one of five veterinarian-researchers, three working on equine reproductive issues and two on small animal reproductive issues. The staff is international: Troedsson grew up in Sweden, and recently researchers from Poland and Belgium have joined the staff.

"UF is one of the main veterinary colleges when it comes to both equine research and clinics," Troedsson said. "The proximity of the horse-breeding center in Ocala helps, too."

Troedsson's research has focused on equine endometritis, a leading cause of fertility problems in mares. In fact, uterine inflammation affects about 15 percent of mares, a high rate of incidence for any disease.

Troedsson started out looking for the part of the uterine defense mechanism that was breaking down. He found that mares susceptible to endometritis don't contract the uterus in the same way non-susceptible mares do. Susceptible mares were responding to an inflammation that caused them to fail reproductively.

At first, Troedsson thought bacteria caused the inflammation. But he found that sperm cells trigger a normal inflammatory response, too. In a normal mare, semen causes an inflammation that flushes out excess sperm cells from the uterus. The inflammation is modulated, however, by seminal plasma, ensuring a healthy environment when a fertilized egg descends into the uterus.

In a susceptible mare, the inflammation process continued, causing the embryo to be lost. Troedsson currently is trying to identify proteins in seminal plasma that protect sperm cells.

> "We can sort out the bad genes and save the good genetics."
>
> Dr. Mats Troedsson

The work could lead to better management of mares who are susceptible to endometritis.

"In the past, we believed that seminal plasma was just a vehicle," Troedsson said. "Now we recognize its importance."

Troedsson also is in the early stages of research into genetic testing of embryos to improve the health of future crops of horses.

Nearly all horse breeds suffer from a disease unique to that breed. Quarter horses have a debilitating muscle condition. American paint horses suffer from a genetic disease that kills foals just days after their birth. The roots of the diseases are genetic, and the key to curing them may lie in disrupting the genetic link from generation to generation.

Troedsson has started a project to do molecular genetic testing on embryos before they are implanted. The research calls for removing single cells from a five- or six-day-old embryo and testing the cells for genetic diseases. Only healthy, disease-free embryos would then be implanted in mares, leading to fewer genetic diseases in future generations.

"We can sort out the bad genes and save the good genetics," Troedsson said. "There are so many diseases. So we have to make a decision: What can they live with; what are the genetic traits that are so desired?"

Troedsson has collaborated with obstetricians and gynecologists at UF's College of Medicine and researchers in the Department of Animal Sciences, as well as with veterinary colleagues who study fertility issues in stallions.

Although there are few major grants for equine research each year, he says the Reproduction Service has been able to conduct research with a range of smaller grants from organizations like the American Quarter Horse Association, the Grayson Jockey Club Foundation and internal funding from the university.

"It's very difficult to get funding in equine research, with only a handful of national grants each year," Troedsson said. "But I like specializing in equine reproduction because it has great potential to apply basic research findings to clinical advances through assisted reproduction. It's a very results-oriented science."

Photo left: Dr. Mats Troedsson's research has focused on equine endometritis, a leading cause of fertility problems in mares.

> “There are profound regulatory differences between cough and breathing.”
>
> Dr. Don Bolser

It’s a nagging, hacking, wheezing, gasping problem, and it’s the second most common reason people in the United States see doctors, according to the Centers for Disease Control and Prevention.

It’s the cough, a common problem that is uncommonly complex, says University of Florida physiologist Donald Bolser.

“It’s a difficult problem to deal with clinically,” said Bolser, a professor and researcher in UF’s College of Veterinary Medicine. “Just because a patient is coughing doesn’t mean we know why.

“When I first started working on this issue, I was amazed at how little information existed, how much fundamental information is not known about cough and how cough-suppressant drugs work,” Bolser said. “It seems almost any experiment I devise will yield important and fundamental information.”

Bolser is among the relatively few scientists working on understanding how and why we cough and whether our treatments for cough do what we think they do.

“Codeine, for example, is one of the most widely prescribed drugs in the world, yet we know relatively little about what it actually does,” Bolser said. “It doesn’t work on everyone, and when it does work, no one knows exactly how it’s working.”

The issue, Bolser said, is finding out which areas of the brain trigger cough, then deciphering how they function and react to drugs. He has conducted research from both sides of the issue, working in pharmaceutical testing and development at Schering-Plough and moving to UF to study the science and physiology of cough.

Breathing is controlled in the brainstem, and scientists long have thought that the mechanism that controls cough originates there, too. However, drugs that suppress cough have no effect on breathing, so something more is at work. Bolser calls it a hidden regulatory element in the control system for cough.

“What is the nature of that element?” Bolser asks. “We have a lot of knowledge about breathing and the brainstem, and we know that the neural elements that govern cough are restricted to the brainstem, but there are profound regulatory differences between cough and breathing.”

In one model Bolser has proposed, he theorizes that there may be previously unidentified neurons that are active only during a cough. These neurons may have remained unidentified because they are located in a region of the brain not thought to be related to breathing. If that turns out to be true, it presents researchers with a challenge both in understanding cough and treating it. The challenge is magnified further because different coughs – for example, a laryngeal cough as opposed to a cough from the airways farther into the lungs – may well be controlled differently by the brain.

Cough suppressants like codeine and dextromethorphan act on the brainstem, but how they suppress cough – when they do – is not known.

Bolser is designing an experiment to inject codeine into the brainstem of laboratory animals to see where the codeine goes to work. Making the laboratory animals cough and then figuring out how to control the cough will yield new information that may eventually help in studying cough in humans, Bolser said.

Pharmaceutical companies recently have turned their attention from asthma medications to cough medications, Bolser said.

“Another medicine was not needed for asthma,” Bolser said. “So they started looking at cough. Our current array of medicines is inadequate, even codeine, the one thought to be the gold standard.”

Bolser collaborates with other researchers and UF’s own Brain Institute. He said medical research funding organizations, such as the National Institutes of Health, are receptive to research proposals on cough, partly because they recognize how unique the work is.

“When you see someone cough, what are they actually doing?” Bolser asks. “We have to explore the fundamentals, how cough is produced in humans and why drugs, while powerful, don’t always work. This is an emerging issue.”

Photo left: Dr. Donald Bolser, shown with scientist Melanie Rose, is among the relatively few scientists working on understanding how and why we cough.

Photo top: Dr. Paul Davenport, shown in his lab with graduate student Sarah Peiying Chan, is one of the few researchers in the college working on both humans and animals. Photo below demonstrates the use of a breathing device.

It's a common description, that something is as natural as breathing.

But for some children with severe asthma, breathing isn't natural at all. In fact, these children can't sense when they struggle with breathing and often end up in the emergency room on the verge of respiratory failure, said University of Florida Professor Paul Davenport.

For years, Davenport has been studying something most people take for granted: How you consciously know you are breathing. For healthy people, it seems automatic, but the brain is still at

work, regulating respiration. For some asthmatic children, those signals from the brain are faulty.

"If a patient can't sense a problem with their breathing, they can't compensate for it," said Davenport, a professor in UF's College of Veterinary Medicine since 1981.

So Davenport and colleagues in the UF College of Medicine developed the Respiratory Related Evoked Potential test in 1986. During the test, a patient's breathing is increasingly impeded with a mechanical device as scientists measure brain wave activity and breathing responses. The test helps identify children who lack the ability to sense difficulty breathing, so they can be monitored and avoid a life-threatening asthma attack.

Asthma is the top chronic disease of childhood, and 60 percent of the children who have life-threatening asthma have a reduced ability to tell the difference between a mild obstruction to their breathing and a severe obstruction, Davenport said. People who have had a double lung transplant or spinal cord injuries also have trouble sensing difficulties with their breathing.
"For most people, if you stop breathing for 2/10 of a second, it elicits a reaction," Davenport said.

"Most people can feel a chest tightness and treat themselves."

The reverse issue - patients who are *too* aware of their breathing, which leads to anxiety and overuse of medication – also is a topic of research for Davenport.

"One group can't perceive breathing problems, the other group is hyperperceptive about breathing problems," Davenport said. "So we want to understand the physiology of breathing. If you can't breathe, nothing else matters."

In the hyperperceptive group of asthma patients, the anticipation of a future breathing problem leads to anxiety. In effect, they prompt a respiratory event with their anxiety and panic and end up relying heavily on medication.

> "If you can't breathe, nothing else matters."
>
> Dr. Paul Davenport

"Nothing bothers you more than the sense of suffocation," Davenport said. "So these patients end up reaching for their inhaler at the slightest sign of tightening in their chests and end up taking in more medication than they need to regulate their asthma.

"We're wandering into a brand new area," Davenport said.

Davenport also has explored ways to strengthen respiratory muscles and has invented a device that amounts to a barbell for the lungs. The device can be used for healthy people, like tuba players in a high school marching band, and by people who have suffered a loss of respiratory capacity, such as people on ventilators or victims of spinal cord injuries. In fact, Davenport worked with actor Christopher Reeve and U.S. Navy divers in testing the device.

One advantage of the device is that it does not involve a drug; it's mechanical, so it can be used by just about anyone.

"We need to change the way we look at ventilation," Davenport said. "We don't want to just make a patient comfortable on a breathing machine, we want to rehab because it is possible to do respiratory rehabilitation."

Patients on ventilators have been anesthetized and immobilized and lose some of their respiratory capacity. That leads to fear when it's time for them to breathe on their own. But with therapy to strengthen their respiratory muscles, 90 percent of the patients who initially fail to wean from a breathing machine can come off ventilation.

Although he's a physiologist, not a veterinarian, Davenport is one of the few researchers in the college working on both humans and animals.

"There are some questions we can only address in humans and some questions we can only address in animals," Davenport said. "We can't answer all the questions in one species."

In addition to his research grants from the National Institutes of Health and the American Lung Association, Davenport also has won the Merck National Creativity in Teaching Award. He used the $25,000 grant to fund seminars on creative teaching strategies.

What Wronski has done with the rats to further osteoporosis research is groundbreaking.

Evaluating Treatments for Osteoporosis

During the last 15 minutes of the bone lecture in his musculoskeletal course, University of Florida Professor Thomas Wronski talks about a topic he hopes will save his students' health decades ahead. He lectures the women to get plenty of calcium and hopes the men will help the women they love do the same.

"Women develop their peak bone mass at 25 to 35 years of age," said Wronski, a researcher in UF's College of Veterinary Medicine. "So to avoid getting osteoporosis during menopause, they need to be very aware of getting calcium while they're young.

"I feel it's just to take 15 minutes to educate them," Wronski said. "If that little talk prevents just a couple of them from getting post-menopausal osteoporosis, that's more important than what I do with the rats."

That's saying a lot, since what Wronski has done with the rats is groundbreaking.

Wronski has established an animal model with ovariectomized rats that allows for the evaluation of osteoporosis treatments for humans. He has won awards for his work and sent an experiment into orbit on the space shuttle.

In his work, Wronski has shown that ovariectomized rats become estrogen deficient just as women do at menopause and, like menopausal women, the estrogen deficiency contributes to loss of bone density. The ovariectomized rats have proven to be such a good animal model in bone density studies that the Food and Drug Administration now requires new osteoporosis treatments to be tested first in ovariectomized rats before being used in women.

Wronski has played a key role in validating the animal model and helping evaluate several osteoporosis treatments now on the market.

"In the mid-1970s, bone loss was not well understood, and people had a hard time believing the ovariectomized rat could be a good model to use in osteoporosis research," Wronski said. "In my work since the mid-1980s, I've been able to show that it is a good model.

"Once the model was established, it could be used to evaluate treatments. Several drugs approved by the FDA for osteoporosis were evaluated in our studies here, so we've been able to make a contribution, and it's been a nice application of our research," Wronski said.

Wronski's work with rats attracted attention from NASA in 1996, when he won a grant to send an experiment up on the space shuttle to evaluate the causes of bone loss in space. NASA doctors had noted that astronauts returned from space with decreased bone mass and wanted to know if it was due to stress hormones, which inhibit bone growth, or lack of gravity, since bones need to bear weight to remain healthy.

"It had always been thought that stress increases levels of corticosteroids, which inhibits bone formation and leads to bone loss," Wronski said. "So I decided to test that theory."

In Wronski's experiment, six rats had their adrenal glands removed to eliminate the source of corticosteroids and six kept their adrenal glands. Their bone mass was evaluated upon their return. Based on the experiment, Wronski said it appears that bone changes in space are caused by a lack of mechanical forces rather than increased stress hormone levels.

The National Institutes of Health has continuously funded Wronski's work since 1986, and his current grant runs through 2008.

The NIH also awarded him its prestigious MERIT (Method to Extend Research in Time) award, which goes to fewer than 1 percent of investigators, for his sustained contribution to research on aging. In making the award, the NIH noted that Wronski's work "represents a splendid example of how beautifully simple good science can be when the investigator has the ability to ask the right questions and do the right experiments."

Photo left: Dr. Tom Wronski, shown with laboratory technician Mercy Rivera, established an animal model with ovariectomized rats that allows for the evaluation of osteoporosis treatments for humans. Photo above: Laboratory technician Melissa Rodriguez

It's no wonder that pathobiologist Mary Brown is one of the top-funded researchers in the University of Florida's College of Veterinary Medicine. Her specialty – microscopic organisms called mycoplasmas – show up just about everywhere.

Over the past 20 years, Brown has studied infections in creatures from alligators to humans. She has studied the role of mycoplasma in the premature birth of babies and in a respiratory ailment of tortoises. Mycoplasmas are at work in urinary tract infections in women and in economically important diseases of dairy calves.

Mycoplasmas are busy, and they keep Brown busy, too.

"Only a few hundred of us worldwide work on these microbes," Brown said. "We try to advance the basic science, and I always find there are so many questions to ask but so little time."

Mycoplasmas are the smallest free-living bacteria. They need intimate contact with a host, for instance in the respiratory or urogenital tract, and establish a chronic disease that usually is not fatal because they need the host in order to survive. The bacteria spread through direct contact, and "walking pneumonia" is one example of a mycoplasmal disease in people. Few could love mycoplasmas, but they have yielded a lifetime of research for Brown.

"There are so many interesting hosts in veterinary medicine, encompassing animal and human health as well as conservation issues," Brown said. "With this research we can not only help the animals but help humans, too."

Most recently, Brown has been studying the role of mycoplasmas in a respiratory infection that has spread rapidly among Florida gopher tortoises, a species of special concern. The gopher tortoise population has declined in part because of loss of habitat. The habitat loss also means gopher tortoises live in closer proximity to each other, a condition that likely allows infections to spread more easily.

Mycoplasmas Play Key Role in Disease of Humans, Animals

Well-meaning citizens have compounded the problem, Brown said. In one study site in Duval County, people were releasing tortoises displaced by development of a subdivision. The newcomer tortoises were sick with respiratory mycoplasmosis, which swept quickly through the existing gopher tortoise population.

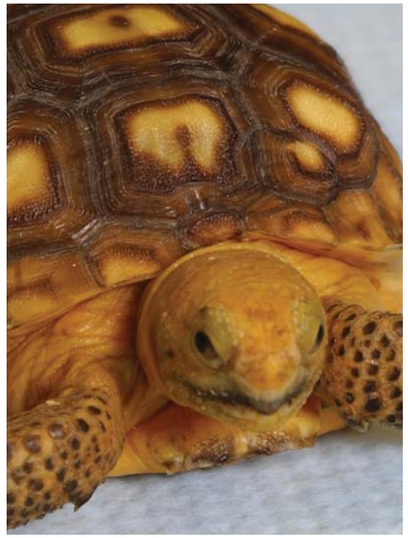
"This was a prime example of what happens when an acute disease comes through a population," Brown said. "We are seeing very sick animals and increased deaths. Some females also appear not to be producing eggs. Loss of reproductive-age adults, decreased reproductive rates and the low survival rate of young tortoise hatchlings combine to make it very hard for a tortoise population to recover from a population crash."

Brown and her team worked with regulatory agencies, state parks and water management districts to do a statewide survey of habitat status and changes in the gopher tortoise population. She and the team also developed a diagnostic test for the presence of mycoplasma.

Her work with the threatened species attracted a $2.2 million grant from the National Science Foundation to support further investigation.

"We're just beginning to understand the diseases in wildlife that are caused by mycoplasma," Brown said. "It's a very adaptive organism."

On the human side, women stand to benefit from Brown's research. Mycoplasma can take up residence in the urogenital tract, causing a variety of problems.



Brown has been awarded a National Institutes of Health grant to study the role of mycoplasma in recurrent urinary tract infections in women. Her research is centered on finding the factors that dispose some women to recurrent infections as opposed to one-time infection and whether mycoplasma plays a role in an exaggerated inflammatory response to an infection. She is also studying whether there are genetic factors in a woman's susceptibility to urinary infections.

Women also could gain from a study on mycoplasma infections in the genital tract and their role in pregnancy loss and premature birth.

In that study, Brown is questioning whether loss of pregnancy is the body's response to the infection. Her eventual goal is to develop a method to screen women for pregnancy loss. In the meantime, she is working on an animal model using rats infected with mycoplasma.

"Once we establish the model, we can ask and answer a lot of questions," Brown said. "Some strains of rats are more susceptible to adverse pregnancy outcome, so we will look into which genes are turned on in the placenta of those rats and when they are turned on and turned off."

"The data would help humans and animals, and that makes it a win-win," Brown said.

The U.S. Department of Agriculture has funded yet another study of mycoplasmal disease in food and fiber animals. In dairy cows, for instance, the bacteria cause mastitis. In young calves, a mycoplasmal infection can lead to severe disease and sometimes even death, and is an important herd cost for dairy farmers.

"There are as many different species of mycoplasma as there are hosts," Brown said. "All these projects require large teams, a real team approach. Science is not done in a vacuum."

Brown likes to share her success at getting grants by helping graduate students and other young researchers obtain grants of their own. For her, that's as rewarding as the basic science.

"When I watch the development of these young scientists," Brown said, "I can't imagine having a better job."

Photo left: Dr. Mary Brown, shown with scientist Dr. Lori Wendland, has been studying the role of mycoplasmas in a respiratory infection that has spread rapidly among Florida gopher tortoises, a species of special concern.

He is the go-to guy for people who want to help ailing reptiles, including endangered turtles at sea and tortoises on land. The plight of these mild-mannered creatures has taken University of Florida wildlife and zoological medicine Professor Elliott Jacobson from the Florida Keys to the Mojave Desert.

Jacobson has seen sea turtles with fibropapillomatosis – grotesque tumors that are benign in themselves but kill when they cover the eyes or mouth or interfere with the motion of flippers. In tortoises, both in the Mojave Desert and Florida, he has studied deadly respiratory ailments that can spread quickly.

Unlike veterinarians who treat better-known domestic animals, wildlife veterinarians often have little of even the most basic information, and that is where Jacobson's work begins.

"For many wildlife species we don't have reference values," Jacobson said. "So we need to establish a normal database in order to determine what is not normal for these animals.

"We're in the process of building a database on blood values for sea turtles in Florida and around the world, so we will know what's in their blood, the biochemical components of their blood," said Jacobson, who is collaborating on the project with the Archie Carr Center for Sea Turtle Research and the St. Lucie Power Plant. "This will become more and more important as we try to help these animals survive."

Jacobson and his colleagues began working on fibropapillomatosis in sea turtles in the mid-1980s when turtles with the bizarre growths began showing up at a hospital in Marathon. A single turtle can have more than 50 lesions, some as large as 12 inches across, on both soft body tissue and the shell. Sea turtles are endangered and reproduce slowly, so a disease like fibropapillomatosis, which affects more than 50 percent of some turtle populations, can be devastating.

Jacobson and a graduate student discovered herpes virus in the tumors. The student is now the head of Laboratory Animal Medicine at Albert Einstein College of Medicine in New York and is investigating a link between the virus and the tumors.

More recently, Jacobson has begun work on ways to improve diagnosis of maladies in wildlife. In November, he published the results of a study of the usefulness of magnetic resonance imaging and radiography in determining the presence of internal fibropapillomas in sea turtles.

At the turtle hospital in Marathon, veterinarians have been able to remove the exterior tumors from sea turtles and return them to the ocean. However, the possibility existed that the animals would go on to suffer and die from internal tumors. Most turtles with internal tumors need to be euthanized because the tumors interfere with the operation of organs and severely damage surrounding tissue.

Jacobson's study found radiography's benefits limited because internal views were somewhat obscured by the shell. However, MRI scans were not affected by the shell and provided detailed views of the turtle's organs and internal tissue, easily revealing the presence or absence of the tumors.

There are both practical and emotional reasons to do this work, Jacobson said.

"Sea turtles are important to Florida. We have the largest nesting beaches in the United States and more dead turtles wash up here than elsewhere," Jacobson said. "It's a federally listed, charismatic animal. You see a sea turtle laying eggs and people are fascinated by them. They are benign, long-lived animals."

Jacobson and a graduate student also have begun work on another problem plaguing sea turtles. Somewhere on their round-trip between Florida and the Mediterranean, the animals are picking up deadly parasites.

"Sea turtles have the most unique migration pattern of any animal on the planet," Jacobson said. "They travel from here to the Mediterranean and back, and sometimes it takes 10 to 20 years to complete that migration. These parasites don't exist in the Canary Islands, so that's an important part of this puzzle. They're picking them up when they come back."

Necropsies have shown clusters of parasites in the brain, but Jacobson and veterinary pathologist Brian Stacy are just beginning research to find out where the parasites come from.

On land, Jacobson's work with tortoises began in 1989 with an urgent call from a California preservation group worried about a strange upper respiratory tract disease that was causing a die-off of tortoises in the Mojave Desert. Jacobson put together a research team that discovered a microbe known as mycoplasma was responsible for the infections.

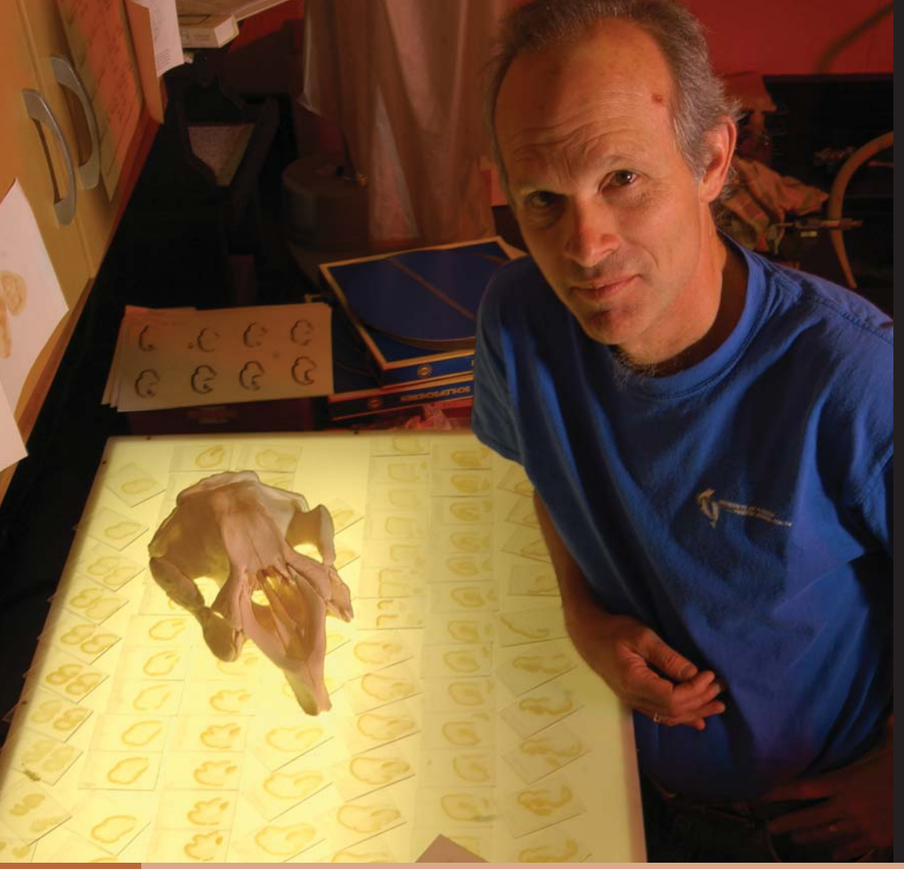
Soon after, the problem cropped up closer to home when Florida gopher tortoises began contracting the respiratory ailment. The research used in the desert tortoise studies was applied to the gopher tortoises and the presence of the mycoplasma was detected.

While scientists continue to study the disease in tortoises, which are species of concern due to sharp declines in their populations, Jacobson says some common sense guidelines would help control spread of the disease. For example, in high-growth areas it is common for well-meaning people to relocate the displaced animals to another wild area. What they don't realize, Jacobson said, is that they may be relocating a sick animal and spreading the disease.

With 260 species of turtles and tortoises, most in decline, more research and collaboration is needed, Jacboson said.

"We're seeing an extreme loss of tortoises and habitat," Jacobson said. "As populations dwindle, those populations will need to be more intensely managed. One of the most important outcomes of our work is to bring attention to these issues and educate people."

Photo left: Dr. Elliott Jacobson shown with a sea turtle that received rehabilitation after being drawn into a canal near the Port St. Lucie Power Plant. Jacobson works with many sea turtles, snakes and other reptiles both clinically and in his research.



"Are there parts of the brain that can be repaired?"

Dr. Roger Reep

Every 45 seconds, someone in the United States has a stroke – and a reason to be interested in the research of University of Florida physiologist Roger Reep.

Reep studies spatial neglect, a syndrome that robs stroke victims of the awareness of half of their world. A stroke on the right side of the brain, for example, takes away the victims' awareness of everything on their left. The problem isn't visual – their eyesight is fine – but they are not aware of the left side unless they turn around.

"Under normal circumstances, whether you pass on my right or my left, I will say hello," said Reep, a professor in UF's College of Veterinary Medicine and a researcher in UF's McKnight Brain Institute. "If I've had a stroke in the right hemisphere of my brain, I'll neglect to say hello to you if you pass on my left.

"The interesting thing is that people with neglect don't even realize they're missing half the world, and since they're unaware of the problem, they aren't motivated to seek therapy."

Filmmaker Federico Fellini, who suffered a stroke at 73, posted notes everywhere as reminders to "look left." Artists with spatial neglect show a strong bias toward the right side of a painting or sculpture. But for the bulk of stroke victims, mostly the elderly, it's the everyday manifestations of spatial neglect that alter their lives: Stroke victims in nursing homes, for instance, may eat only the right half of a meal until a worker turns the plate around.

During 20 years of research, Reep and his colleagues developed and used a model in rats that allows for the study of spatial neglect syndrome. The researchers located a region of the brain in rats that is similar to the region of the human brain affected by spatial neglect syndrome. They induced damage to this region in the rats, then administered monoclonal antibodies, which override a protein that prevents neuron growth. Their preliminary findings indicate that

the antibodies encouraged neurons in the damaged regions of the rats' brains to sprout. Over time, in some rats, the new neurons appeared to take over the work the damaged tissue used to do and restored normal behavior.

"By investigating mechanisms of neural repair in rats, there's hope for developing a therapy to promote recovery in humans," Reep said.

"Our question is what kinds of changes can the brain make to compensate for injury from stroke? Are there parts of the brain that can be repaired?"

For the 700,000 Americans who have a stroke each year, the answers will be vital.

Florida conservationists, too, have reason to pay attention to Reep's research. Reep also studies evolution of the brain and recently has focused on the manatee brain, in hopes of developing insights that can help in conservation of the protected animals.

"I guess you could say I lead two research lives," Reep said. "I'm a Florida native, and because of that and my own sensibilities, I want to preserve what I can of the natural domain of Florida, and that includes the animals."

Reep says the order Sirenia, to which manatees belong, evolved independently from other lines that led to elephants and hyraxes, beginning about 50 million years ago. There are striking differences between manatee brains and the brains of animals of similar size. Every brain even a third as large as a manatee brain becomes convoluted, with folds of matter. Manatee brains are smooth and their brains are smaller relative to their body size.

"It's not so much that their brains are small but their bodies have become large because of the need to eat large amounts of plants per day, and to conserve heat," Reep said.

In recent years, researchers also have discovered that manatees use tactile hair – a sense of touch – to detect underwater currents and vibrations. Reep and his colleagues at Mote Marine Laboratory are currently using behavioral testing to determine the capacities of this system to detect significant water movement, such as the approach of other animals from behind.

Reep's group also works closely with the state marine mammal pathology laboratory and Sea World so that the scientists can examine manatee brains quickly following a manatee death. The postmortem examinations show that manatees have specific clumps of cells on the cerebral cortex that deal with tactile information transmitted from the hairs.

"What we have is an indication that manatees have an elaborate system to process tactile information," Reep said. "It's a neurobiological solution for living in the world. By understanding more about the kind of information the animal has to work with, we can more effectively design protective habitat and alter our behavior in a way that is meaningful to them."

The research could have implications for regulators who have designed no-wake zones to protect manatees, Reep said. Scientists are asking whether manatees can sense fast-moving boats better than they sense slower boats.

The common thread in Reep's work is the brain and using basic science to understand it. The National Institutes of Health is a major source of funding for his research, which has been published in the journal *Brain Research*.

"Purely as science, this is fascinating," Reep said. Of his work with spatial neglect, he added, "As the population ages, more people will get this, and we will need to learn more about the higher order regions of the brain. In a person with stroke, we have an opportunity to learn from the nature of their deficits."

Photo left: Dr. Roger Reep has focused on the manatee brain in hopes of developing insights that can help in conservation of the protected animals.

Protecting the health of Florida's people and environment is a huge task, and policy makers often lack the expertise to tackle scientific questions.

How much of a chemical is harmful and how much is acceptable? Does the hazard posed by a toxin change depending on whether it is present in water or in soil? How does the cost to clean up a hazardous waste site balance with the likelihood of public exposure?

Environmental policy makers on the state and national level place such issues in the hands of scientists at the University of Florida's Center for Environmental and Human Toxicology, an interdisciplinary center housed in the College of Veterinary Medicine.

"We have a lot of strength in toxicology across the campus, so the center's role is to take those strengths and foster research, education and service," said center Director Stephen Roberts. "We draw from the health science center, engineering, agriculture and others. We're the go-to point for human and environmental toxicology."

The center has contracts with the Florida Department of Environmental Protection to provide advice on risks posed by environmental contaminants and is involved in the evaluation of virtually all major contaminated sites in the state. Roberts stresses that the center's role is informational and advisory; the decisions on how to manage the risks posed by chemicals in the environment remain in the hands of policy makers.

A case in point involved a controversy in 2001 over pressure-treated lumber used in playgrounds. The lumber was treated with chromated copper arsenate, or CCA, a pesticide that contains arsenic, which can cause neurological problems, cardiovascular disease and even cancer.

The state asked the center to investigate the issue and evaluate risk assessments that had been conducted on exposure to arsenic from pressure-treated wood, particularly exposure of children using wooden play structures. The center found that a critical weakness in the assessments was the absence of data regarding how much arsenic children actually receive from contacting CCA-treated wood. Estimates of exposure and risk varied widely, making it unclear the extent to which the wood posed a health problem.

The U.S. Environmental Protection Agency decided to conduct its own assessment of risks to children from pressure-treated wood. Roberts provided technical advice to the agency on how to perform the assessment through his role as a member of the EPA's Scientific Advisory Panel. Ultimately, amid mounting concern, the pressure-treated wood industry voluntarily agreed to withdraw CCA-treated wood from the market for most uses.

"Our role is to provide sound, objective technical advice. Most of the time we're out of the limelight," Roberts said. "We don't want to be portrayed as a crusader."

The issue of arsenic contamination in Florida doesn't stop at playgrounds. Roberts said the state has thousands of agricultural sites contaminated with arsenic, dating back to an era when cattle tick fever was treated by dipping cattle in vats of arsenic. Golf courses, too, can be contaminated with arsenic. The fodder for toxicologists is endless.

"If arsenic is in drinking water, we know its toxicity," Roberts said. "But if it's in soil, is it as toxic? Does the soil bind it? We're doing studies to find out what is an acceptable level for arsenic in soil. And the results could mean the difference of millions in cleanup costs."

The work of the center extends well beyond arsenic. A health department official might ask for help explaining the hazards of benzene in drinking water. An environmental manager overseeing cleanup of a contaminated site might ask for guidelines on chemical concentrations in soil (the center has issued guidelines for 500 chemicals). A military installation might need help evaluating the risks from unexploded ordnance on old training fields. In between, Roberts travels to Washington, D.C., every six weeks or so for meetings of the EPA Scientific Advisory Panel.

> "It's exciting for UF to be a main player."
>
> Dr. Stephen Roberts

"Our role is science advice, not policy," Roberts said. "We want to understand what chemical substances do from the level of molecules up to entire populations of individuals. We give regulators the science to decide whether there's a health problem."

Among the newest research initiatives for the center is nanotechnology. The center collaborated with the College of Engineering last fall to put on UF's first seminar on nanotoxicology.

Nanotechnology is the science of creating materials on an extremely small, molecular scale, called nanoscale. The size of the molecules is measured in nanometers, or one billionth of a meter. Nanotechnology can be used to create computer chips, for example, that are thousands of times smaller than current methods allow.

"The federal government is spending billions on nanotechnology," said Roberts, "but there's been almost no research on the environmental effects of nanotechnology."

Roberts said nanotechnology is a big concern for the EPA and U.S. Food and Drug Administration because eventually materials, chemicals and foods produced with nanotechnology will get into the environment. Already, sports equipment and fabrics are being produced with nanotechnology.

UF is uniquely positioned to contribute to the science of nanotoxicology because the center can draw together the resources of the health science center and UF's strength in particle engineering. The center is using Department of Defense grants to conduct pilot studies on penetration of nanoscale particles through the skin and inhalation of the particles.

"What do we know? It's a basic question," Roberts said. "When you produce something on a nanoscale, the properties of matter change. Do biological properties change, too? And if so, does our conventional wisdom about what's toxic and what's not change, too?"

"It's a brand new, emerging field," Roberts said, "and it's exciting for UF to be a main player."

Photo left: Dr. Steve Roberts and scientists at UF's Center for Environmental and Human Toxicology are key players on the state and national scene when it comes to environmental policy.

Gift Opportunities

The College of Veterinary Medicine recognizes the need to advance animal and human health through research programs that generate new knowledge, both basic and applied. Because of the similarity in physiology between humans and animals, the college has conducted comparative studies that are instrumental in shedding light on the mysteries of both animal and human disease.

Its major strengths include both animal and human health infectious disease research, gene therapy approaches, vaccine development, basic and applied food safety research, research on comparative medicine, and the commitment to support the nation's need to advance the career development of veterinarians and graduate students who wish to pursue clinical and/or basic research as a career aspiration.

To further these efforts, support from the private sector is always welcome.

Ways you can help

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