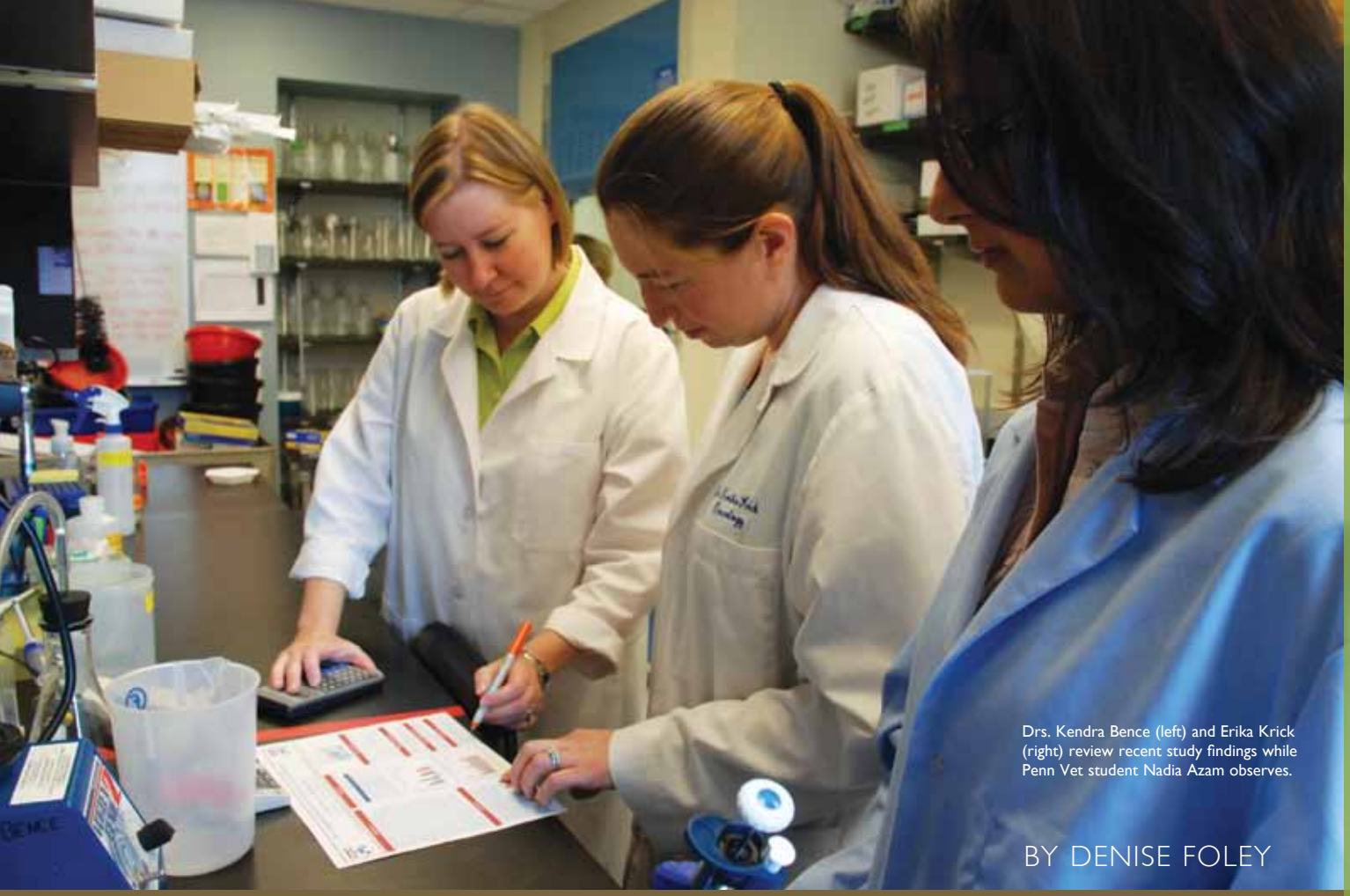
Bellwether Magazine

Volume 1
Number 75 *Fall 2011*

Article 5

10-1-2011

Advancing the Field Together



Drs. Kendra Bence (left) and Erika Krick (right) review recent study findings while Penn Vet student Nadia Azam observes.

BY DENISE FOLEY

Advancing the Field {TOGETHER}

A hallmark of Penn Vet, collaboration is a daily exercise for researchers, students, clinicians and colleagues

You can't whistle a symphony, a wise man once said. It takes an entire orchestra to play it. At Penn Vet, the ability to collaborate with others has allowed researchers to create some beautiful music, not to mention elegant science, together with colleagues, researchers from around the world, industry and even students from other academic institutions. Collaboration can yield valuable results, as these examples illustrate.

Combating Cachexia in Cats

Kendra K. Bence, PhD and Erika L. Krick, VMD joke that they met "speed dating." That's what organizers called the ice-breaking exercise at an annual faculty retreat that threw together staffers with similar interests who otherwise might never talk to one another. That day, Drs. Bence and Krick found themselves at the same table; today, they're at the same bench. The two are collaborating on a translational study looking at the similarities in cats and humans of cachexia, a metabolic wasting syndrome that occurs in cancer — often GI cancers — and other diseases.

It's the perfect melding of professional interests. Dr. Bence is an assistant professor in the animal biology department where she studies the cellular mechanism of feeding and obesity in mice that serve as stand-ins for the humans caught in the double epidemic of obesity and diabetes. Dr. Krick is a clinical veterinary oncologist with a special interest

in studying and treating cats with lymphoma and cachexia. They've been joined by second-year Penn Vet student Nadia Azam (V'14) who was awarded a Merial scholarship to participate in the research. The Veterinary Clinical Investigation Center (VCIC) is also involved.

Dr. Krick examines a patient with cachexia.

Patients with cachexia — both feline and human — experience a loss of appetite, weight and muscle mass that isn't remedied by supplements or extra calories. They also respond poorly to cancer treatment.

"Cats who are skinny and not feeling well from their cancer may not tolerate standard chemotherapy doses. Sometimes they are given lower doses of chemotherapy, which could decrease the chance that they will respond," said Dr. Krick, who is also collaborating with researchers at Texas A&M University on a study of feline lymphoma. "Also, we have found that cats that lose weight during treatment have a significantly shorter survival time than cats that don't lose weight."

In fact, she says, as many as 30 percent of people with cancer cachexia die from the condition.

The villain? Likely pro-inflammatory cytokines, elevated in cancer cachexia patients, that speed muscle loss, decrease intestinal motility and gastric emptying leading to early satiety, and alter production of hypothalamic neuropeptides that govern appetite.

The first aim of the study is to discover if cachectic cats with cancer have different inflammatory markers than healthy cats and those with cancer but who aren't cachectic. The researchers are also looking at the gene expression of appetite controlling peptides in the brain, specifically the orexigenic neuropeptides NPY and AGRP that stimulate eating, and the anorexic neuropeptides POMC and CART that suppress the desire to feed. Preliminary results have been partially unexpected, but intriguing.

"Surprisingly we found no change in NPY and AGRP with fasting, but we did see the expected suppression of POMC and CART," said Dr. Bence. "As we go on, we may need to expand the number of neuropeptides we examine. It may have been that the fast we did [overnight] with the cats wasn't long enough to see changes in orexigenic peptides. Or it may be that cats utilize alternate neuropeptides in their response to feeding and hunger compared to other species."

Ultimately, the researchers would like to discover a marker that would alert a clinician — like Dr. Krick — that an animal is more likely to develop cachexia.

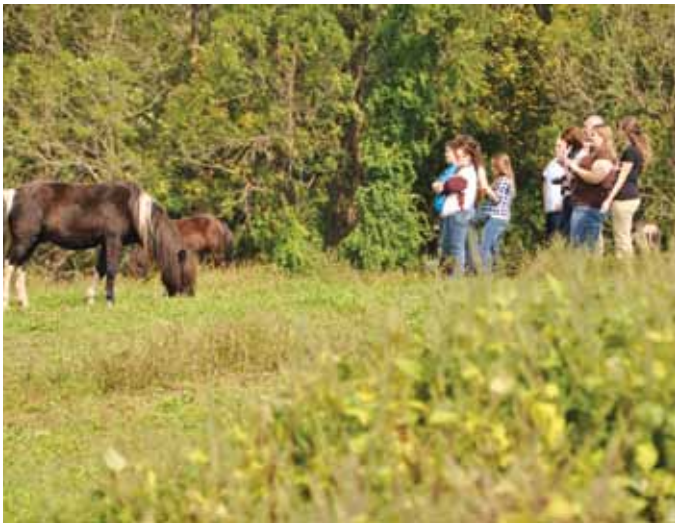
"Then," said Dr. Bence, "it's not out of the question that we could design new treatment strategies for our feline patients that can be translated to humans."

Sharing a Living Laboratory

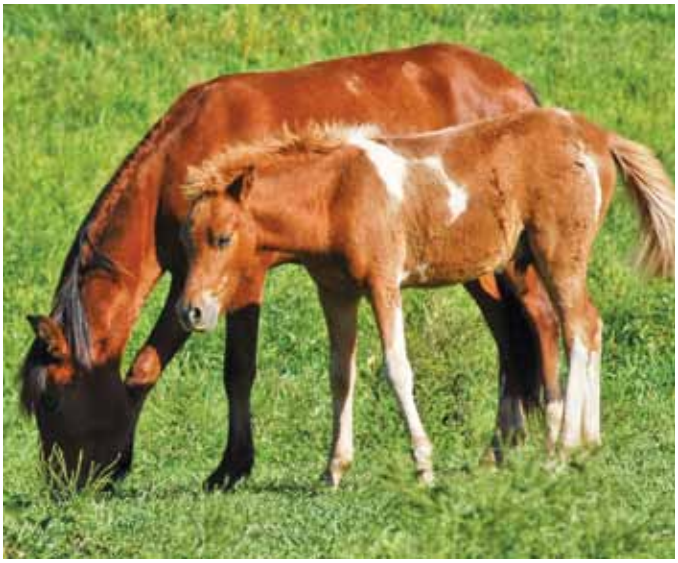
Sue McDonnell, PhD, head of the Havemeyer Equine Behavior Research Program at Penn Vet's New Bolton Center, has learned that when you build a better herd, everyone will beat a path to your pasture.

The herd, in this case, is made up of 95 semi-feral ponies that roam 35 acres of lush grassland at the New Bolton Center in Kennett Square. Since the herd was started in 1994 (with 13 mares and 13 stallions from domestic stock), it has become a living laboratory, drawing not only equine researchers and clinicians from around the world, but high school students, university undergrads and graduate students, and vet tech and nursing students who might never have an opportunity to observe horses in the wild.

Or, in this case, the semi-wild. Penn Vet's ponies forage, mate when they want to, get plenty of exercise because they're never indoors, but, unlike wild horses, are acclimated to humans who provide some minimal veterinary care — and come to watch. (With a housing development abutting one



Dr. McDonnell's semi-feral pony herd serves as a living laboratory for Penn Vet students and researchers as well as for area universities.



Mare and foal behavior is just one of the many interactions Dr. McDonnell and her team study in the semi-feral pony herd.

pasture, they likely also get supplemental treats from young neighbors despite a large "don't feed the ponies" warning on the fence.)

"It's not exactly like going to see wild horses. They are contained, but that's the beauty of it," said Dr. McDonnell, who has been at Penn Vet since 1981. "We've seen them every day since 1994, and because their wandering is limited to the pasture enclosure we can observe the whole herd so we know a lot more about their natural social organization than we would if they were out west where the terrain is so tough and the forage is so sparse that the horses are spread out. There, the best you can do is stay with one family at a time, so you are unable to readily understand the social interactions among families."

But it's more than just convenience that lures researchers and students (from places like the University of Delaware, Delaware Valley College of Science and Agriculture, Penn State, Cazenovia College and Penn's own psychology department) to this classroom on the hoof. It's also what's been — and can be — learned there.

"Once you get students attuned to natural horse behavior, they see that most health problems in horses have resulted from how we manage them," said Dr. McDonnell.

The Penn Vet herd doesn't experience the same health problems as domestic equines. There's no colic, no laminitis and no sexual dysfunction, the bane of many breeders who also come to consult with Dr. McDonnell.

Since the herd has become a lure for students, said Dr. McDonnell, the center has created short courses specifically for them that their own institutions have neither the resources nor faculty to provide. As a bonus, she says, "these courses generate funds that help to support the herd."

There have been some other unanticipated benefits of what could be called Penn Vet's open pasture gate policy.

Ensuring a Safer Egg

Penn Vet researcher leads charge in developing safe-egg testing kit for FDA

In August 2010, an outbreak of *Salmonella* Enteritidis (SE) was responsible for illness in almost 2,000 people in at least 25 states. More than 550 million eggs were recalled from the market. While methods have been in place to test for the presence of SE in eggs, the traditional methodology is time consuming, requiring up to 10 days to determine the presence or absence of SE in egg samples.

Recognizing that this timeframe wasn't acceptable, the microbiology laboratory at Penn Vet's New Bolton Center has played a significant role in the development of rapid SE-specific molecular diagnostic methods. The polymerase chain reaction (PCR) test developed at Penn Vet allows quick determination of the presence or absence of SE in egg samples, and provides accurate results in approximately 27 hours – a tenfold reduction in waiting time for results.

This methodology came in handy for the Federal Egg Safety Program, which requires all large-scale producers in the US to test for SE before products reach consumers.

As a result, the *Salmonella* Enteritidis Detection Kit was developed by Shelley Rankin, PhD, associate professor of microbiology at Penn Vet and chief of NBC's microbiology, in collaboration with The Life Technologies Corporation, which allows producers to quickly test their eggs for SE. FDA-approved for use in the Federal Egg Safety Program in early 2011, the kit was validated by Dr. Rankin's lab.

"Penn Vet has been collaborating with the Commonwealth of Pennsylvania to ensure food safety for decades," said Joan C. Hendricks, VMD, PhD, the Gilbert S. Kahn Dean of Penn Vet. "The adoption of our egg-testing protocols by the FDA illustrates our researchers' success in their field and the importance that veterinary researchers play in ensuring public health and food safety. I am thrilled that Penn Vet is continuing to lead the way in setting the standard in food safety and public health."

"The FDA equivalence determination for this test marks a milestone for the egg industry in this country," said Dr. Rankin. "The Commonwealth was the first state in the nation to initiate a voluntary egg quality assurance program and the Pennsylvania Animal Diagnostic Laboratory System will be the first to implement this new level of testing. It's very exciting that the FDA has adopted this test for the Federal Egg Safety Program. This action demonstrates their commitment to delivering the safest quality food to the consumer and I'm proud to be a part of that trend."

Penn Vet has been active in the development and implementation of the state's PEQAP (Pennsylvania Egg Quality Assurance Program), and much of what has been learned and shared by PEQAP forms the basis for the national Egg Safety Program. Dr. Rankin has more than 20 years experience in the detection and characterization of *Salmonella* from human and animal sources.

—Sally Silverman

"We get the opportunity to meet some real star students, some of whom are inspired to study vet medicine and apply to Penn," said Dr. McDonnell.

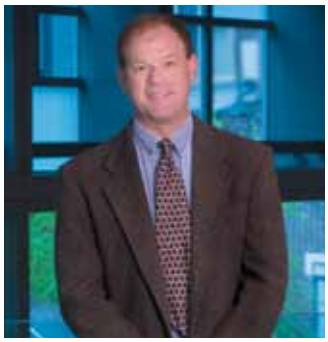
And in one case, a student from the University of Delaware launched an ongoing independent study based on a Penn Vet project using recorded stallion vocalizations and stallion scent for estrus detection in mares. It's allowing Dr. McDonnell and her colleagues to find a solution for a problem that faces small farmers but which can't be tested in the Penn Vet research and teaching herd.

"Our mares are exposed to stallions on the property, but what if you're out in the middle of nowhere with no stallions around," she said. "At the University of Delaware, they had only a few mares at the time and no stallion. This project by one of our student visitors gives us the opportunity to do a real-world test of the problem."

Predicting Epileptic Seizures for Novel Treatment Options

When it comes to epilepsy, dogs and humans have much in common. Their rate of idiopathic epilepsy is about the same. And their treatment options are similar — and equally inadequate.

"The problem for people with epilepsy is they may have a seizure once or twice a year, but they're on medication all year," said Charles Vite, DVM, PhD, assistant professor of neurology and neurosurgery in the Department of Clinical



Drs. Brian Litt and Charles Vite are working together to help humans and animals with epilepsy.

Studies at Penn Vet. "These drugs are not benign. They can have side effects, including cognitive dysfunction, depression and liver failure."

And for over 30 percent of people — and dogs — the drugs don't adequately control seizures.

But here's where dogs and people differ. Epilepsy doesn't usually dramatically circumscribe a dog's life. It does for humans.

"People with epilepsy can't drive, they have a hard time holding down certain jobs and they take a lot of drugs," said Dr. Vite. "But what if they could predict when they were going to have a seizure, or when a seizure was likely to happen? If they had a box that would flash blue when they were okay they could say, 'Great, it's blue today, I can drive,' that would be a wonderful thing."

Through a collaboration involving Penn Vet, NeuroVista, a premier medical technology developer with Penn Vet connections, and researchers at the Mayo Clinic, University of Minnesota and the University of California at Davis, that "wonderful thing" is one step closer to reality. The team is expecting to receive a translational research grant this fall and are awaiting a funding decision.

Dr. Vite, Penn neurologists Kathryn A. Davis, MD, and Brian Litt, MD, along with the VCIC, joined Mayo, University of Minnesota and UC-Davis researchers to test an implantable device in dogs that may predict a "perfect storm" in the brain's electrical system that signals a seizure — before it even happens. The device was developed by NeuroVista, a Seattle firm specializing in implantable neurological products. Dr. Litt is a scientific advisor to the company; its vice president of clinical research is Penn Vet alum and Medical Scientist Training Program graduate W. Douglas Sheffield, VMD, PhD.

The device includes implantable (subdural) strip monitoring electrodes and a sub-dermal telemetry unit which wirelessly transmits EEG signals to an external personal advisory device (PAD), much like a pager, with colored lights — including the blue one Dr. Vite was talking about — as well as vibrating and audible alarms. The data is collected on ordinary flash memory cards and can be downloaded to a computer for storage and analysis.

The results of the first test, in six dogs with naturally occurring epilepsy, was published this year in the journal *Epilepsy Research*. Analyzing more than 11,000 continuous hours of iEEG data and clinical observation, the researchers found that canine epilepsy is "a promising model" for human epilepsy for testing implantable devices: When having seizures, dogs and humans share similar patterns in brain activity and observable symptoms.

Though far from market-ready, the device has the potential to exert profound effects on epilepsy research and care.

"If we are able to give people with epilepsy or a dog owner one-to-two hours notice before a seizure occurs, this will represent a massive change in how we treat epilepsy," said Dr. Vite.

Instead of taking drugs every day, a person with epilepsy may be able to take a fast-acting antiepileptic drug only on days when a seizure warning is sounded.

While the long-range goal of the study is to find better ways to treat human patients, Dr. Vite said, "As I remind everyone, I'm a vet. I'm here to help dogs and cats." In fact, he says, he has about 600 active epilepsy cases and this month [October] he launched a weekly clinic strictly for epileptic animals.

Fortunately, whatever the research in dogs uncovers to help humans will also help animals.

"It could give us more options to offer when we get calls from owners and breeders asking if there's anything new for epilepsy," said Dr. Vite.