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First successful multi-organ gene therapy

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When I went back to my alma mater, Bristol University in England, for my 40th reunion last summer, I couldn’t help but reflect on how much clinical veterinary medicine has changed in the intervening years; the veterinary medicine of today was unimaginable when I graduated in 1962. Every inch of this progress has come from research, both basic and clinical research; from scientists working at the lab bench on fundamental questions of biology to astute clinicians recognizing patterns of disease among their many cases.

Penn has contributed substantially to these advances and the School continues to lead the profession in research. This was brought home forcefully last month as we had an accreditation site visit from Council on Education of the AVMA and were required to provide outcomes, benchmarks, to measure our progress and achievements. To assess our research productivity, we tallied the numbers of papers published by our faculty in 73 of the most frequently quoted and prestigious scientific journals in the world and compared this with the numbers from faculty at Penn. Between the years 1981 to 1994 there was a total of 117 papers, of which 46, (40%) came from our faculty. The nearest rival was Glasgow University Veterinary School with 5% of the papers.

The findings set the School apart from every other veterinary school but they are largely unknown to the profession for there are few clinicians who have the time or inclination to read journals like Nature, Genetics, Cell, or Annual Reviews of Immunology. So this edition of Bellwether highlights the School’s research program and celebrates its preeminence.

Alan M. Kelly
The Gilbert S. Kahn Dean of Veterinary Medicine

Class of 2006 Alumni Legacy Students
Penn Veterinary Medicine takes pride in the admission of alumni legacy students. They provide a vital link through the generations of the School’s alumni. Photographed in Classroom A, clockwise from bottom: Sarah R. Zimmerman, daughter of George F. Zimmerman, V’76, and sister-in-law of Hubert-Jan Karreman, V’95; Anne R. Heskel, daughter of Linda E. Aiken, V’78 and Neil Stuart Heskel, M’78; Holly J. Schroll, daughter of H. James Schroll, V’74, and Jane Sparacino Schroll, V’74; James L. Widmann, son of Raymond J. Widmann, V’52; and Wesley A. Baff, son of Frederic K. Baff, V’63.

Photo by Addison Geary

In this issue of Bellwether we highlight some of the research projects at the School. During the last fiscal year, faculty pursued 134 sponsored research projects and garnered $22 million in sponsored support from the NIH, the Commonwealth of Pennsylvania, USDA, and a number of foundations.

As we cannot discuss every research project, we selected a few to illustrate the diversity of the research work by our faculty. This is just a small sample and we hope, in future issues, to bring you more on basic and clinical research projects.
Teaching and Research Building News

Prices for goods and services increase over time and the new Teaching and Research Building is not exempt from this trend. The cost for the five-story building is now estimated at $50.7 million. The School has raised $42.7 million and is working hard to meet the June 30, 2003 deadline to complete the funding for the building.

The University’s Board of Trustees has reviewed the preliminary plans for the building and has approved the project. Dean Kelly has appointed a building committee headed by Dr. Richard O. Davies, professor of physiology. Several architectural firms have been invited to submit design proposals for the building to be reviewed by a University committee. An architect will then be selected. It is planned to have that process completed by the end of 2002. Groundbreaking is anticipated for December 2003.

Of special note since our last report is more than $300,000 raised from School’s faculty and staff through the “Take A Seat” campaign. More than 100 have pledged $3,000 each for a seat in the two, 150-seat classrooms in the new building. This money was raised in less than one month and many members of the faculty and staff have yet to be approached. There are 300 seats available and it is anticipated that many will be “reserved” by the School’s faculty and staff. In early 2003, this special opportunity will be available to alumni to reserve a seat and leave a legacy.

Veterinary School Buildings in Philadelphia

- **Quadrangle Building**
  - 1907

- **Gladys Hall Rosenthal Building**
  - 1963

- **Veterinary Hospital of the University of Pennsylvania**
  - 1981

- **Site of Teaching & Research Building**
  - Planned Groundbreaking
  - 2003

This site is bounded by University, Woodland and Baltimore Avenues.
A glimpse into the future

By Allen Arndt

In 50 years, pet health insurance will be nearly universal in the United States, with deep implications for both the practice of veterinary medicine and veterinary research.

That is just one prediction offered by the School's four department chairs and two hospital directors when Bellwether asked them to peer 50 years into the future of veterinary medicine and research.

Their vision finds veterinarians playing a leading role in protecting public health and developing advances in healthcare for animals and humans alike.

And progress in genetic research could eliminate genetic diseases while paving the way for new treatments for a range of other diseases and conditions.

But despite the dramatic advances on the horizon, the need for veterinarians and the skills they wield will not subside.

“Animals will likely still be getting traumatized,” says Dr. Gail Smith, V’74, chair of the Department of Clinical Studies in Philadelphia. “There will still be bones to fix, although the rate of bone healing will be hastened by application of osteogenic factors.”

A Surge in Pet Health Insurance

A rapidly growing number of pets with health insurance will drive many changes in veterinary medicine, predicts Barry Stupine, vice dean and director of VHUP.

“In the next 50 years, pet insurance will become as common in the United States as it is in Europe today,” giving vets and pet owners the freedom to provide first-class care regardless of out-of-pocket costs, Stupine says. “Vets want to help animals and it is very frustrating when they can’t because of cost. No vet wants to put an animal down.”

With insurance defraying the cost, sophisticated diagnostic and medical procedures will be performed more frequently. As a result, the cost to perform these procedures will fall as the rate of bone healing will be hastened by application of osteogenic factors.

But Stupine anticipates a downside to the proliferation of pet health insurance. As veterinarians perform sophisticated procedures more frequently, the cost of malpractice insurance will increase.

“We are likely to see more lawsuits and bigger damage awards pushing increases in malpractice insurance premiums,” he says.

One factor in damage awards that will undoubtedly change, according to Stupine, is the legal view of the relationship people have with their pets. Currently, the legal system does not allow for damages for emotional suffering resulting from the loss of a pet.

“We’re learning a lot about the beneficial relationship people have with their pets,” he says. “It’s just a matter of time before a judge, for the first time, awards damages in a malpractice suit for emotional suffering resulting from the loss of a pet.”

Another trend to watch, Stupine says, is economic forces—including pet health insurance—driving veterinarians into larger and larger group practices as solo and small group practices diminish. Those same economic forces will also likely result in more specialists in veterinary medicine.

“In an economic sense, veterinary medicine follows human medicine by a few years,” he says. Just as the insurance industry has prompted medical practitioners to seek efficiencies and economies of scale, so too will pet health insurance force veterinary practitioners to seek similar efficiencies.

Protecting Public Health

The next 50 years will see a growing public awareness that veterinary medicine is the leader in public health issues ranging from communicable diseases to food safety, according to Bruce Rappoport, associate dean of New Bolton Center and director of the Widener Hospital for Large Animals.

“Veterinary medicine benefits everyone, whether they have animals, whether they are in agriculture or not,” he says. “Things like Lyme disease, rabies and West Nile virus aren’t just animal issues. They are public health issues, and veterinary medicine will be the leader in solving these public health problems.”

Dr. David Nunamaker, V’68, chair of the Department of Clinical Studies at New Bolton Center, agrees, saying that veterinary medicine will be on the forefront of solving the world’s expected shortfall of energy and food supply, as well as making that food supply safer.

“In Great Britain, for instance, Foot and Mouth disease and Mad Cow disease were both big problems,” Nunamaker says. “And with threats from E. coli and salmonella—things that need constant attention—veterinary medicine will play a much bigger role in solving.

Similarly, veterinary research will contribute not just to animal health, but also to human health, according to Dr. Phillip Scott, chair of the Department of Pathobiology.

“Veterinary medicine is where advances will happen, because veterinary training is a broader training and more rigorous scientific training than medical training,” Scott says. “Veterinary medicine shouldn’t be marginalized as a type of research. It’s an important part of understanding how things work in a biomedical sense.”

The veterinary school trains scientists in comparative medicine in order to understand comparisons between species while providing a broad background in many animals—a background that is much broader than that provided to those who are trained in treating humans, he says.

“Vets are trained in such a way that they will understand linkages in diverse fields,” Scott says. “Those veterinarians who choose to have a scientific career should be making great contributions in biomedicine—contributions that can be applied to humans.”

Indeed, at least one portion of the federal government will soon change its view of veterinary research, reflecting the growing role veterinary research plays in developing advances in human medicine, according to Avadhani.

“Currently, the National Institutes of Health will only fund research focused on human diseases,” Avadhani says, “but within 10 years I predict that the NIH will recognize that veterinary medicine and research is an important component of disease research and allow funding for veterinary research and training.”

Cancer is one area of research where veterinarians are likely to develop innovations that can be applied to humans.

“Cancer diagnosis and treatment is becom-
ing a greater concern for both people and animals,” says Dr. Smith of the Department of Clinical Studies in Philadelphia.

He predicts that biomedicine will advance to a point where a simple blood test can detect biomarkers of many different cancers in both animals and humans. “Similar to the PSA test for prostate cancer in humans, I believe we’ll get to a point where there will be tests like that for early diagnosis of many types of cancer.”

Similar advances will be made in treating cancer. Current chemotherapy techniques, for example, destroy harmless cells along with cancerous cells. Smith points to research in targeted chemotherapy, where molecular-level treatments are designed to attack just the cells that have been identified as cancerous.

It is natural for these advances to come from veterinary research, Scott says.

“Working on humans has real limitations, just as working on mice has limitations,” he says. “One can study cancer in mice, but those aren’t spontaneous tumors. And cancer research on humans is limited for ethical reasons. But a small mammal, such as a dog, is a good model because the tumor is spontaneous. It’s a good place to study.”

**Cracking the Genetic Code**

Within 50 years, researchers will sequence the complete genome for most common animals, leading to new treatments for genetic diseases and changing the way medication is prescribed or administered, predicts Avadhani.

“Gene therapy and stem cell therapy will be commonly used to treat various diseases in animals, including diseases of the muscles and nervous system as well as cancer and cardiac diseases,” Avadhani says.

Genetic research will also help determine the efficacy of drugs, as researchers studying pharmacogenomics uncover the genetic variations that result in different responses to various drugs.

“Some people show resistance to certain drugs while others are more sensitive,” explains Avadhani. “This is a very important factor in both human medicine and veterinary medicine. Even within a given breed of animal, minor mutations in genes can make one either more or less responsive to a particular drug.”

In the future, healthcare providers will be able to perform a genetic analysis on an individual patient in order to find genetic variations that might cause the patient to respond differently to various drugs. The result will be drug therapy designed specifically for that patient.

Smith sees even more applications for genetic research. For example, DNA analysis will soon allow breeders to pick better breeding candidates using genetic analysis rather than the macro-screening processes currently in use.

Likewise, Smith foresees a day when a genetic analysis will be routinely performed on an individual pet before it is purchased, allowing potential owners to make purchasing decisions based on genetic vulnerabilities uncovered by the analysis.

And advancements in genetic research will ultimately lead to the ability to create transgenic animals—animals created as a result of splicing a new piece of DNA in place of an existing portion in order to correct a problem or make an animal that is less disease-prone, Smith says.

“This is uncharted territory and it is our obligation to inform the public and heed the opinions of ethicists as we progress.”

Regardless, Nunamaker predicts that the ability to create transgenic animals will help bring infectious diseases under control.

**From the Bench to the Clinics**

Nunamaker also sees research discoveries making their way into clinical practice much faster than today, a trend he says the School, bolstered by the planned Teaching and Research Building, will lead.

“The new facility will be a vibrant teaching component that will allow us to develop new modes of teaching using the Internet and other technologies,” Nunamaker says.

For Scott, the new building will strengthen both the most basic research and translational research.

“For example, in my lab, if I’m working on vaccine development, I might do some studies and find out that the right kind of protection will develop if I immunize in a certain way,” Scott says. “This may work with experimental model, but the key to translational research is taking something that you’ve learned at the bench and applying it in a way that will be useful in the clinics.”

“Translational research provides the underpinning of everything we do in the clinics,” Smith says. “In clinical studies, my goal here is to pursue specialization to the ultimate endpoint and to make those specializations every bit as sophisticated as they are in human medicine.”

Smith has a no-less ambitious vision for the hospital.

“I want our hospital here to become the Mayo Clinic of veterinary medicine, a place where not only pet owners bring their pets, but where other veterinary professionals and specialists send animals to receive the ultimate in veterinary care.”

**Living Longer, Healthier**

“Animal welfare will take a larger place in our thinking as a society,” Smith predicts. “Not just companion animals, but agricultural animals as well. It makes sense that this thinking be centered in the veterinary school.”

Companion animals feed our sense of self and our emotional well being, Smith says. “During the next 50 years it will become clear that companion animals have a huge benefit to people and the public. We’ll recognize the health benefits that pet ownership brings to people.”

Smith believes that pet sitters will be as common as baby sitters, supplemented by electronic monitoring devices.

“We know that pets are traumatized by getting out of their contained environment,” Smith says. “Electronic monitoring will be a common tool used to keep pets from physical harm. We can’t do this to people, but we could, for example, implant a microchip in an animal in order to identify it from a great distance.”

While researchers seek ways to use technology to protect animals from physical harm, others are studying how lifestyle habits influence the health and longevity of animals.

In a study Smith just completed, for example, he found that diet is an important factor in protecting the health of smaller mammals.

“They benefit greatly from staying lean. They live longer and have a much lower frequency of health problems.”

The key, he says, is developing diets that make animals feel full without making them fat.

Because of these many factors—from pets with health insurance and electronic tracking devices to gene therapies and lean diets—animals will be living longer and healthier lives.

“Animal life span will increase substantially, perhaps as much as 25 to 30 percent longer,” Avadhani says. “Cats and dogs particularly will live much longer.”

Still, despite these advances, the need for veterinarians will not subside. After all, Smith says, there will still be bones to fix.
Gene therapy treats a disease affecting multiple organ systems

By Stephen Bradt

For the first time, researchers have successfully used gene therapy to treat a disease that affects organs throughout the body of a large animal.

The study, led by Dr. Mark E. Haskins, V’69, of the School and Dr. Katherine Parker Ponder of the Washington University School of Medicine in St. Louis, involved dogs with a rare disorder in which an enzyme deficiency causes clouding of the corneas, cardiac disease and bone abnormalities leading to loss of mobility by six months of age. Newborn dogs treated with hepatic gene therapy maintained near-normal mobility throughout the 17-month study and showed little evidence of the other debilitating signs normally associated with the disease.

“While gene therapy has been used previously in dogs, this is the first use to treat a disorder affecting multiple organ systems throughout the body,” said Haskins, professor of pathology and medical genetics at the School. “Previous applications of gene therapy in dogs have targeted disorders affecting a single bodily function, such as vision or blood clotting. Like many diseases that we might eventually like to treat with gene therapy, this one has complex, multisystemic effects.”

The experiments involved seven dogs with mucopolysaccharidosis VII, a disorder in which the enzyme β-glucuronidase is deficient in activity. Also known as Sly syndrome, MPS VII is among a constellation of lysosomal storage diseases; in humans, such disorders include Tay Sachs disease and Gaucher disease.

“In theory, the approach should be applicable to other lysosomal storage diseases, with the exception of those that affect the central nervous system,” said Ponder, associate professor of medicine and assistant professor of biochemistry and biophysics at Washington University. “We’re hopeful that the approach might also be applicable to hemophilia.”

Lysosomal storage diseases such as MPS VII can be treated through enzyme replacement therapy, but that approach requires regular intravenous injections and is prohibitively expensive. Bone-marrow transplantation is another option but is risky, and compatible donors are often unavailable.

MPS diseases affect 1 in 27,000 live births among humans, but the disease is debilitating for patients and emotionally wrenching for their families. Human symptoms include growth retardation, mobility problems, facial deformities, corneal clouding, liver and heart valve abnormalities and mental retardation, among others. Most patients die in childhood.

“The gene therapy research of Drs. Haskins, Ponder and collaborators involving MPS VII dogs has significant implications for all MPS disorders,” said Barbara Wedelhase, executive director of the National MPS Society, an organization of parents of children with MPS. “Their current and ongoing research will provide new insights into the treatment of individuals affected with these devastating disorders.”

In these experiments, two- to three-day-old dogs with MPS VII received four injections of a retroviral vector expressing canine β-glucuronidase. The vector was made from the Moloney murine leukemia virus with a liver-specific promoter; at several days of age, canine liver growth is so rapid that transduction occurs readily and β-glucuronidase is secreted continuously into the bloodstream.

The enzyme’s activity was subsequently found at normal, stable levels for up to 14 months in the treated dogs; one dog has produced 60 times normal enzyme for 17 months. Unlike other dogs with MPS VII, the treated dogs gained weight normally, attaining nearly 90 percent the weight of their unaffected littermates, and avoided the serious side effects normally associated with lysosomal storage diseases. The β-glucuronidase gene does not appear to have been inserted into the germ line.

Haskins and Ponder were joined in the research by Drs. John R. Melniczek, V’92, Margaret A. Weil, Thomas M. O’Malley, Patricia A. O’Donnell, Van W. Knox, Hamutal Mazrier, N. Matthew Ellinwood, Meg Sleeper, V’93, Susan W. Volk, V’95, Jean Zweigle and John H. Wolfe, V’82 of Penn’s School of Veterinary Medicine; Albert M. Maguire of Penn’s School of Medicine; Lingfei Xu and Robert L. Mango of Washington University’s School of Medicine; and Gustavo D. Aguirre, V’68 of Cornell University’s College of Veterinary Medicine. The work was funded by the National Institutes of Health.
Cell transfer restores sperm production in infertile mice

By Stephen Bradt

Scientists at the School have successfully transplanted specialized cells that are critical to sperm development in mice, restoring sperm production in once-infertile animals. The research may give scientists a better understanding of how Sertoli cells—which surround spermatogenic stem cells—nourish sperm production and the survival of stem cells.

“Spermatogenesis is a highly organized process, requiring just the right environment, or ‘niche,’ around the germ line stem cells,” said Ralph L. Brinster, V’60, professor of reproductive physiology at the School. “The Sertoli cells are essential to this environment, and it appears that by replacing them, we can essentially reconstruct the niche in which sperm development takes place.”

Much of the volume of a mammalian testis consists of tightly coiled seminiferous tubules that hold mature sperm. Sperm development also occurs within these tubules, which are home to spermatogenic stem cells, the seeds from which spermatogenesis arises. Seminiferous tubules are lined with Sertoli cells, which are thought to nurture sperm cells as they develop and facilitate their eventual passage out of the testis.

Brinster and colleagues worked with Steel mutant mice, which are congenitally infertile due to a Sertoli cell defect. Before inserting healthy Sertoli cells, the researchers treated the mice’s testes with busulfan and cadmium to remove any defective germ cells and Sertoli cells. The seminiferous tubules remained, likely providing the structural support needed to completely reconstitute spermatogenesis from donor cells.

The Brinster group’s technique for transplanting Sertoli cells will likely allow scientists to study stem cells’ specialized environment in a way that has not been possible before. Currently, the best-studied stem cells are those that generate blood cells, even though these cells, which reside in bone marrow, are relatively inaccessible to researchers.

“I believe Dr. Brinster’s new results have catapulted the spermatogenic stem cell system into a position of maximum experimental flexibility among all other stem cell systems in the body,” said John R. McCarrey, professor of cell and molecular biology at the University of Texas at San Antonio, who was not involved in this work. “This may lead to significant new insight into the manner in which the spermatogenic stem cell works in particular as well as to additional information about how all stem cells work in general.”

Brinster’s work could eventually prove useful in the treatment of certain types of infertility in men, although complete spermatogenesis was established in only 1.5 to 3 percent of seminiferous tubules in this experiment.

“Male infertility can be caused either by defective germ cells or by a testicular environment that fails to promote proper spermatogenesis,” Brinster said. “While several assisted reproductive technologies, such as in vitro fertilization or intracytoplasmic sperm injection, are now available for patients with low sperm counts, infertile patients with Sertoli cell defects have limited options.”

The technique developed by Brinster and his colleagues may provide a new way of replacing defective Sertoli cells with healthy ones, which may initiate normal spermatogenesis in some infertile patients.

Brinster was joined in the research by Takashi Shinohara, now at Kyoto University, and Kyle E. Orwig and Mary R. Avarbock in Penn’s School of Veterinary Medicine. The work was funded by the Japan Society for Promotion of Science, the National Institute of Child Health and Human Development, the Commonwealth and General Assembly of Pennsylvania and the Robert J. Kleberg Jr. and Helen C. Kleberg Foundation.

PennHIP®

Dear PennHIP Members, Veterinarians, Pet Owners, and Dog Breeders:

I am pleased to announce that the University of Pennsylvania has once again become the home of PennHIP. Synbiotics and the University of Pennsylvania have reached an agreement that transferred the PennHIP license back to Penn on November 15, 2002. We at PennHIP would like to recognize Synbiotics (and before that, ICG) for the years of good management, helping to grow PennHIP to the size it is today. We are hopeful that this friendly departure will strengthen both entities. Like the OFA, PennHIP will now be a “not-for-profit” organization and we look forward to working with the American Kennel Club and other breed clubs.

We anticipate some confusion in the transition and we thank you in advance for your understanding and tolerance through this period. Penn’s acquisition of PennHIP is an exceptional opportunity to put PennHIP on equal footing with other not-for-profit screening methods. The expanding body of published scientific articles provides comparative evidence that PennHIP is the superior screening method for hip dysplasia. We are excited about this new development and we look forward to widespread utilization of PennHIP to improve the hip quality of all dog breeds afflicted with hip dysplasia.

Visit our web site for periodic updates.

Thank you,

Gail K. Smith, V.M.D., Ph.D.
Director, PennHIP
MRI screening to characterize tumors in dogs

Masses in spleens or livers of dogs are relatively common findings for the veterinarian. They are often noted during the routine physical exam or during ultrasound imaging of the abdomen. These lesions may be a result of trauma, hyperplasia, and benign or malignant tumors. Benign lesions in the liver are more common than malignant ones, though clinicians cannot automatically assume that a mass is benign. To determine the character of a lesion, ultrasound and biopsies are used as diagnostic tools.

Ultrasound is an excellent modality for determining the presence of a mass but often the ultrasonographer cannot say whether it is truly benign or malignant. That is determined definitively only by biopsy. In human medicine, for a number of years, MRI imaging has been used to characterize lesions in the liver and spleen. MRI images have advantages over ultrasound images in providing a much more defined, soft tissue imaging modality. MRI is considered the “Gold Standard” of imaging for the liver and spleen in people. MRI in people can not only determine whether a lesion is benign or malignant, but can further define whether it is a primary or metastatic (cancer spread) lesion. To determine whether canine benign and malignant tumors in the spleen and liver can be diagnosed through MRI, clinicians at VHUP and at HUP, (the hospital for humans a few blocks away), designed a study for MRI screening of dogs with focal splenic or liver lesions.

Dogs, unlike humans, have to be anesthetized for an MRI as they are required to be perfectly still. Cases were selected from patients presented at VHUP’s clinics. The study examined 20 dogs that had been scheduled for a splenectomy and/or liver biopsy.

The dogs were taken to a research MRI at HUP. Technicians and clinicians from VHUP accompanied the animals to handle anesthesia and contrast medium infusion. The MRI images were read by two radiologists (Drs. E.S. Pretorius and E. Siegelman) from HUP who used guidelines established for liver and splenic tumors in humans.

The animals then underwent a liver biopsy and received the Clinical Research Award.

In two cases the MRI found pulmonary metastasis not seen on radiographs. MRI also showed the exact location of the tumor, making it easier for surgeons if removal was required in several cases.

“It appears that MRI imaging maybe a useful screening method for canine patients with focal splenic or liver lesions,” says Dr. Craig Clifford, resident in oncology and primary investigator. “We are enlarging the study to look at a bigger group. If the results hold true, then it is possible that some biopsies and surgeries of benign lesions can be prevented. The MRI modality also shows a more exact location of a mass, making it easier for the surgeon, in several cases, MRI provided the surgeon with valuable information. One additional benefit of MRI and its superior soft tissue imaging is that we can use it to follow a tumor while it is treated with chemotherapy; the MRI allows us to see whether the tumor is shrinking. This is particularly important when new drug regimens which are designed to kill the blood vessels supplying the tumor are tried, for example, for hemangiosarcoma” (blood vessel tumor).

The clinicians participating in the initial pilot study are Drs. Clifford, Chick Weisse, V’98, and Karin Sorenmo of VHUP, and E.S. Pretorius, E. Siegelman and J.A. Solomon of HUP. This study was presented by Dr. Clifford at the 22nd Annual Veterinary Cancer Society Conference in New York this past September and received the Clinical Research Award.
Scientists find a gene that’s key to cloning success

By Stephen Bradt

A team led by K. John McLaughlin and Hans R. Schöler at the School has found that the activity of a single gene is a powerful predictor of whether newly cloned mammalian embryos will survive and thrive, but the gene’s sporadic expression in cloned mouse embryos casts fresh doubt on prospects for reproductive human cloning.

Despite the successful cloning of sheep, pigs and cats, mammalian cloning— in which an ordinary cell’s nucleus is transferred to an egg whose nucleus has been removed—remains remarkably inefficient. Fewer than three in 100 cloned mouse embryos survive to birth.

McLaughlin and Schöler’s groups showed that the activity of the gene Oct4 correlates strongly with the viability of cloned embryos but also found that in only one-tenth of cloned mouse embryos is the gene expressed at the right level in the right place at the right time. Without Oct4, embryos cannot survive; even if Oct4 expression is a tad high or low, an embryo will die.

“Cloning requires the precise reprogramming of the nucleus inserted into an enucleated egg,” said Schöler, professor of animal biology and director of Penn’s Center for Animal Transgenesis and Germ Cell Research. “This nucleus must abandon its former genetic program and adopt the genetic profile of an embryonic nucleus; failure to do so dooms the embryo.”

To evaluate the accuracy of this genetic reprogramming, the Penn group analyzed Oct4 expression in cloned mouse embryos derived from cells that surround ovulated eggs in adult mice, cells that would not normally express Oct4. The result: Only 34 percent of embryonic cells correctly reprogrammed to express Oct4, and just 10 percent showed levels of Oct4 expression conducive to further development.

Even as it suggests new hurdles for reproductive human cloning, the Penn work offers new support for the feasibility of therapeutic cloning using embryonic stem cells.

“The small number of clones that did adequately express Oct4 were capable of forming embryonic stem cell lines,” Schöler said, “supporting existing evidence of the scientific feasibility of therapeutic cloning even as it shows the infeasibility of reproductive human cloning.”

The Penn team chose Oct4 as a marker because its expression is tightly regulated throughout the mammalian life cycle. Oct4, which encodes a protein critical to normal embryonic development, is expressed only in the portion of the embryo that eventually gives rise to fetal tissues; in the adult, Oct4 is expressed only in germ cells.

Although improper expression of Oct4 can single-handedly obstruct embryonic development, Oct4 is likely not the only gene expressed incorrectly in cloned embryos.

“When we started the study, we thought Oct4 misexpression might account for a fraction of clone failures,” Schöler said. “The big surprise was that Oct4 alone can explain most of the failures, although Oct4 is probably just one gene of many whose misexpression can cause cloned embryos to fail.”

The research team was a combined effort of the laboratories of McLaughlin and Schöler, both faculty in the School’s Department of Animal Biology, with major efforts from post-doctoral researchers Michele Boiani and Sigrid Eckardt, all part of the Center for Animal Transgenesis and Germ Cell Research at Penn’s School of Veterinary Medicine. Their work is supported by the Marion Dilley and David George Jones Funds and the Commonwealth and General Assembly of Pennsylvania.
Stress on tiny cell component has dire consequences

Various life sustaining metabolic processes of animals and humans are powered by energy converted from food and oxygen by mitochondria. A complex cycle converts glucose and oxygen into the energy required by cells. Mitochondria, tiny organelles in cells, have their own DNA, most of which is inherited from the mother.

Mutations in mitochondrial DNA are either passed from mother to child or they may also occur somatically during the early life of the animals. Within the organelle there are many copies of the DNA so a mutation may remain dormant because there are many mitochondria within a cell. However, over time mutated DNA gets enriched due to various biochemical factors. Mutations in mitochondrial DNA also occur due to external influences like chemicals, drugs, radiation, and the like, and they become cumulative as the animal or human ages. When mutations interfere with the proper function of the mitochondria disease results.

Dr. Narayan Avadhani, Harriet Ellison Woodward Professor of Biochemistry at the School, studies mitochondria. Currently he and his group are examining the effects of stress, caused by interruption of the function of the organelle. It has been known for a number of years that mitochondrial DNA is the direct and preferential target of attack by varied carcinogens, which cause mutations to the DNA. The mutations accumulate and eventually interfere with the oxygen utilization and energy production. Recent work in Dr. Avadhani’s laboratory also showed that mitochondrial DNA or membrane damage also triggers a stress response cascade through the altered cellular Ca²⁺ (calcium ions) pool that causes a major change in the expression of nuclear genes and cell morphology.

While investigating mitochondria-to-nucleus stress signaling, the group found that some of the genes implicated in tumor progression are activated and overexpressed in otherwise non-malignant cells when mitochondria are stressed. The chemistry within the organelle and hence in the whole cell is changed as a result of mitochondrial stress signaling. A change in mitochondrial membrane property and reduced energy production in some cells of a tumor mass leads to increased intracellular calcium. This in turn leads to the activation of genes that make cells more invasive or metastatic. Such cells show increased resistance to apoptosis (cell death) and keep proliferating. The study shows the existence of a new pathway for cancer progression, which is activated as part of the mitochondrial genetic and metabolic stress signaling. The researchers found that reversal of the mitochondrial stress in these tumor cells also partly reversed the mitochondrial stress-induced phenotypic changes and invasive behavior.

“The stress signaling may therefore be a critical factor in the ability of some cells within a tumor mass to acquire invasive phenotypes and undergo morphological changes leading to tumor progression and metastasis,” explains Dr. Avadhani. “In summary, mitochondrial dysfunction and the resulting alterations in nuclear gene expression through mitochondria-to-nucleus stress signaling might be an important factor in cancer progression and tumor cell metastasis.”

NIH/Merck Summer student research program

Veterinarians play an important role in all aspects of biomedical research, in industry, government agencies and academia. To encourage students to consider research as a career, the School, in 1990, initiated a summer student research program with a grant from the Merck Foundation, supplemented by School funds. That year, six students participated in the program. Now the program receives support from NIH and Merck and the number of students who received grants in the summer of 2002 grew to 17.

Students receive a stipend and gain research experience in all phases of biomedical research. They work in the laboratories of clinical and basic researchers at the School as well as at other locations within the University.

The program enables students to perform research full time during June, July and August and participate in weekly seminars as well as a national meeting in August. Students make short oral presentation to peers and write a paper at the end of the summer that is submitted to the School’s Phi Zeta Day.

The program, under the direction of Dr. Michael Atchison, professor of biochemistry and director of the V.M.D./Ph.D. program, in 2002 generated such diverse research projects as those studying detailed molecular-biological mechanisms of growth control, to studies on the dynamics of West Nile Virus infection in the United States. The caliber of the research performed was outstanding and the application pool continues to grow each year. Since inception of the program, over 20 research papers and 11 meeting abstracts have been published. Considering the short training period, this is an excellent level of productivity.

Since the inception of the program, 156 awards have been funded for 136 students (some students participate more than once). Many of the students pursue research careers after graduation. The current positions of 47 recent graduates (1998-2001) show that 32% are pursuing post-graduate education (postdoc, graduate program, residency, internship), 57% are in clinical practice, 2% other and the pursuits of 9% are unknown. Looking further back to students at least five years out of the program (1990-1997), current positions are distributed as follows: 12% academic faculty, 14% post graduate education (postdoc, graduate program, residency, internship), 57% in clinical practice 5% industry, 5% other, 7% unknown pursuits.

Continued funding is expected for the program in 2003 since Merck Foundation funding has been continuous over the past 13 years and the NIH competitive renewal grant received an outstanding score. Dr. Atchison hopes for even more applicants and awards than in 2002.
Bacteriophage: an old weapon against bacteria reemployed

Strains of bacteria resistant to most available antibiotics have raised the possibility that veterinary medicine may soon be confronted with untreatable bacterial infections. Researchers are looking for other treatments of such infections and are investigating the use of bacteriophage (phagein: Greek, to eat) to combat bacterial infection.

Bacteriophage are small viruses that infect bacteria and kill them by multiplying and basically filling the bacterial cell to bursting. They don’t affect the infected host, because bacteriophage activity ceases once the bacterial cells are killed. Bacteriophage, which exist in many varieties, do not attack bacteria indiscriminately, they each usually attack only one specific kind.

Dr. Charles Benson, professor of microbiology, is working on utilizing bacteriophage to treat bacterial infections in dairy cows. He has identified several phage that work against specific organisms causing infections.

Bacteriophage were discovered accidentally early in the 20th century by Frederick W. Twort, working at the Brown Institution (London), who was looking for filterable agents that were nonpathogenic virus. He reported them in Lancet as the filterable agent that had preferential activity against micrococci. The speculation offered was that nonpathogenic viruses grew in bacteria while the pathogenic strains grew in animals. In 1917, Felix d’Herelle rediscovered Twort’s lytic principle. d’Herelle had isolated his agent from cultures of patients with bacillary dysentery (shigellosis) and concluded that the filterable agent was an obligate bacteriophage.

He proposed and utilized these bacteriophage as “true microbes of immunity” in therapies. His work continued for years up to his death in 1949. Twort, having never been seriously involved with phage therapy nor properly credited for his initial observations, died in 1950. Sinclair Lewis fictionalized the use of bacteriophage as a therapeutic agent in his 1926 book entitled “Arrowsmith.”

The study of bacteriophage during the 40’s through to present day has lead to a number of observations that suggest reconsideration of phage therapy might provide a mechanism for circumventing the rising concerns about the growing spectrum of resistance to antibiotics by using a new approach. “In actuality, the approach is not new but an old process to be revisited and modified based on the discoveries since Twort and d’Herelle presented their initial findings,” says Dr. Benson. “There are many advantages: to name a few, the cost of isolating and preparing phage solutions is considerably less than the discovery and production of antibiotics, cost of testing the activity of the phage against a pathogen is much lower than defining antibiotic activity spectrum, phage are not harmful to the animal, resistance to phage does not impact on human health medicine as does the developing resistance of the pathogen in the animal to the drug and, an important factor, there are no significant withdrawal times involved when phage are used to treat a disease in food animals.”

Dr. Benson has treated seven cows with Pseudomonas aeruginosa mastitis. In all instances the mastitis infection was resolved although experimental and collaboration difficulties prevented following the animals through the drying-off period. More recently, Dr. Benson has collaborated with Dr. Michaela Kristula to evaluate and experimentally treat Staphylococcus mastitis in cows in the Marshak dairy herd. They have experienced success but not to the extent that Dr. Benson had anticipated and he is working now to modify the preparation to provide Dr. Kristula with a more effective solution.

V.M.D./Ph.D. program

Penn’s NIH-supported VMD-PhD program was initiated in 1969 and is the only such program in the nation. Penn’s School of Medicine offers an NIH-funded MD-PhD and veterinary and medical students attend many of the same lectures and courses and interact in research laboratories on campus. The program is highly competitive and each year only one or two students are admitted (although plans are in place to expand the program). The School is providing limited, additional funds to attract more students as there is a great need for veterinary medical researchers at universities, in industry and government agencies.

Since its inception, the program has graduated 47 individuals. It generally takes seven to eight years to complete the program. In the VMD curriculum students receive a thorough training in the basic sciences as they relate to veterinary medicine. They are exposed to and involved in scientific research through the Graduate Groups at the University and can select courses in any one of the following subjects: biochemistry and molecular biophysics, cell and molecular biology, epidemiology and biostatistics, genomics and computational biology, immunology, neuroscience, parasitology, pharmacological sciences, biology, and bioengineering. They are able to participate in research projects with outstanding scientists across the University. The VMD-PhD students also receive training in clinical medicine as they rotate through the clinical services at the two hospitals.

After completion of the program, about fifty per cent of the graduates go into internships or residencies, and the balance pursue postdoctoral training. Of the 47 graduates of the program, eighty-five percent are pursuing careers in research: 26 serve on academic faculties, seven of these are chair, chief or head of a department; six are active in the pharmaceutical industry, three as directors and two as presidents of companies; seven are postdoctoral fellows, interns, or residents; two are on clinical faculties; one is with a government health agency; and five are in private practice.

Currently there are 14 students in various stages of the program. Four new students joined the program in the 2002 academic year. The School would like to expand the program to at least five to six new students each year as there is a great need for medically trained researchers. What hampers the expansion of the program is lack of funds, as these students need financial support to complete the program. Ideally, the School would like to provide full funding for each student, and efforts are underway to secure the funds needed for this goal.
Effects of early exposure to MSG and Phenobarbital

Newspaper and television ads extol the benefits of a multitude of drugs and supplements, diet products, and flavor enhancers. People take herbal remedies to fight everything from a cold to depression, if those don’t work, they obtain a prescription for one of the many drugs to elevate or alter their mood. Nobody knows yet the long-term effects of all these substances on the human body, and in particular on the highly vulnerable perinate. What may be therapeutic or safe for the mother, could be toxic to the fetus and nursing infant. Many of these compounds are too new to have been studied for a long period of time.

There are two substances that have been widely available for many years, and they, for 25 years, have been one of the subjects of Dr. Bernard Shapiro’s funded research. Shapiro, professor of biochemistry, has studied the influence of MSG on prenatal and perinatal development. Fifteen years ago, he added the drug phenobarbital to his investigations. Why those two? MSG, commonly known as monosodium glutamate, is a food additive that cannot be avoided. It’s in prepared foods, and has been widely used in the United States since the 1940s as a flavor enhancer—it is estimated that Americans consume 200 million lbs. of MSG or related products annually. Phenobarbital, a barbiturate, is frequently prescribed to infants in intensive care and to pregnant women for a variety of commonly occurring maladies, among them convulsive disorders that complicate one out of every 200 pregnancies. Prescriptions for pregnant women were particularly common between the 1950s and 1970s exposing more than 23 million children in the United States alone. Neither MSG nor phenobarbital produce visible birth defects, however, it is thought that they interfere with the production of a number of liver enzymes, known as CYPs that are vital to the body’s ability to metabolize drugs and other potentially toxic substances.

The expression of these drug metabolizing enzymes is controlled by growth hormone produced by the pituitary. Levels of the hormone in males and females are different as males secrete the hormone in an episodic on-off rhythm with periods where the hormone cannot be detected. Women produce growth hormone continuously and it is always present in circulation. Because of these profiles, the levels of drug metabolizing enzymes are different in males and females; this may in part explain the difference in response to drugs, for example women take longer to emerge from anesthesia than men. To complicate matters, levels of growth hormone decline as a person ages.

In earlier studies, Dr. Shapiro’s group had shown that neonatal administration of normal, exposure-like levels of both phenobarbital and

Extracorporeal High Energy Shock Wave Therapy

Lithotripsy, the fragmentation of bladderstones by shock waves, is an established treatment in human medicine. Now these shock waves are utilized in equine medicine to help heal specific ligament and bone injuries. Dr. Olga Seco, lecturer in sports medicine and imaging, and other ultrasound specialists at the Allam Center for Equine Sports Medicine at New Bolton Center are compiling data on horses they are treating with Extracorporeal High Energy Shock Wave Therapy (ESWT).

The Scott Equine Sports Medicine Building houses the ESWT equipment. Horses with suspensory ligament desmitis and stress fractures, and other musculoskeletal problems are treated with ESWT. In the condition known as suspensory ligament desmitis, the ligament originating in the palmar/plantar aspect of the canon bone has sustained an injury. This injury can affect only the ligament, or have an associated avulsion fracture (piece of bone pulled up at the area of attachment of the ligament by the stress caused by the pulling on the ligament). A stress fracture is an incomplete fracture that occurs as the result of repetitive overload and microfractures in one area of the bone. They frequently occur in the dorsal aspect of the canon bone in thoroughbred racehorses.

ESWT is thought to speed healing as well as relieve pain. Pulsated pressure waves (shock waves; not electric) are sent to the targeted area via a probe contained in a head that also incorporates an ultrasound transducer that helps localize the area of injury during the treatment and focus very accurately in the area of interest. Horses with soft tissue injuries usually receive three treatments at three weeks intervals. For bony injuries, there is usually one treatment, but sometimes depending on the response to the treatment, there can be additional sessions. Each treatment usually consists on 2,000 shocks delivered to the area of injury. Horses received this treatment under sedation as the shock waves cause some pain while being administered.

Many chronically lame horses become sounder with ESWT treatment, although no one knows with any degree of certainty why the treatment seems to work. It is thought that increased blood flow may help with the healing process.

Dr. Seco and Dr. Virginia Reef will present their findings at the Sports Medicine Symposium in the spring of 2003.
MSG to laboratory animals can produce delayed, but permanent defects in hormone secretion and drug metabolism, contributing to long-term, serious health consequences. Another of their studies found that prenatal administration of either one of the two substances can result in a multitude of long-term reproductive, growth, hepatic and neural dysfunctions. One finding, in particular, is disturbing: neonatal administration of phenobarbital can induce a delayed but permanent elevation in the activities of several hepatic drug metabolizing enzymes. These enzymes break down specific substances, when their activities are elevated, these drugs are broken down faster. One would expect such elevated activity right after administration of phenobarbital, but not much later. However, it appears that at sexual maturity, when gender dependent differences in drug metabolism appear, the hepatic drug metabolizing enzymes are induced again and remain overexpressed for the rest of life. In rats exposed as neonates to phenobarbital this results in a shorter lifespan, and a great increase in tumor formation.

Neonatal exposure to MSG has a different effect on growth hormone production. It causes a permanent reduction in the secretion of growth hormone which leads to a reduced production of the drug-metabolizing enzymes. This hampers the metabolism of drugs and toxic substance. The reduced quantity of growth hormone leads to stunted growth and irreversible obesity. Like phenobarbital, defects resulting from neonatal exposure to MSG are not apparent until adulthood.

Dr. Shapiro and his group are currently working to answer these questions: How do the chemicals induce the defects? How are the defects expressed? The group has observed that, when the production of growth hormone is disturbed, the level of drug metabolizing enzymes is affected. They found that in male and female rats, prenatally exposed to phenobarbital, there were permanent defects in the expression of these enzymes. The mechanism by which the abnormal profile of growth hormone disrupts the enzyme expression is not known, and the group proposes to investigate it.

It is known that men, exposed perinatally to phenobarbital, have a considerable higher incidence of delayed puberty, undescended testes, and genital abnormalities. In women this exposure of delayed puberty, undescended testes, ovarian dysfunctions and genital abnormalities. In women this exposure of delayed puberty, undescended testes, ovarian dysfunctions and genital abnormalities.

Dr. Shapiro. “It is estimated that children consume almost 100 mg of aspartame per kg of body weight per day, a level approaching the adverse doses found in animal studies. Children under the age of five are particularly vulnerable, their hepatic and neuroendocrine differentiation are still incomplete and early constant exposure to low levels of food additives could permanently alter hormone secretion, the expression of hepatic drug metabolizing enzymes and/or their responses to inducing agents. Such effects could unknowingly affect the efficacy of drug therapy or the susceptibility to chemically-induced cancers in adulthood.”

Sports Medicine Symposium for Equine Practitioners
Saturday, March 22 and Sunday, March 23, 2003

Registration/participation fee: $175 Saturday only; $200 Saturday plus Sunday wet labs.

**March 22: Lecture Topics**
- Performance problems in the Race Horse—Dr. Ben Martin
- Performance problems in the Sport Horse—Dr. Elizabeth Davidson
- Cardiovascular Problems in the Equine Athlete—Dr. Virginia Reef
- Obscure Lameness Problems in the Equine Athlete—Dr. Mike Ross
- Exercise Physiology: What You Need to Know—Dr. Ric Birks
- Evaluation of Cardiac Output and Myocardial Function in Exercising Horses—Dr. Mary Durando
- Muscular Problems associated with Poor Performance—Dr. Jill Beech
- Motion Correction for Standing Equine MRI—Dr. Lexi Lawrence
- Suspensory desmitis and its response to treatment with high energy extracorporeal shock wave therapy—Dr. Olga Seco
- Where we stand and where we are moving toward with respiratory surgery—Dr. Eric Parente

All presenters with exception of Dr. Mary Durando are New Bolton Center faculty/clinicians

**March 23: Wet Labs**
- **Station A** - High speed treadmill demonstration
- **Station B** - Endoscopic evaluation of upper airway dysfunction detected at speed
- **Case discussions at 2 stations - half of participants in each group**
- **Station C** - Lameness videos
- **Station D** - Scintigraphic case evaluations

CE credits: 8 hours
Registration limited to 80 for Saturday sessions, 60 (max.) for Sunday wet labs
Saturday Sessions will be held in Woerner Amphitheatre, George D. Widener Hospital for Large Animals, New Bolton Center, Kennett Square, Pa.
Wet Labs to be held in the new Scott Equine Sports Medicine Building, Jeffords Treadmill Building, Scintigraphy station, New Bolton Center.
Please contact Office of Development, New Bolton Center, for detailed information and registration forms. Tel: 610-444-5800. ext. 2500 or email Patricia Hall at <phall@vet.upenn.edu>
Optimal phosphorus management technologies on dairy farms

Phosphorus (P) management is a national issue with respect to water quality and the sustainability of animal agriculture. A major problem facing dairy farms is the surplus of phosphorus resulting from the excess quantity of the element in feeds and minerals. The cow can only utilize a small fraction of the nutrient, excess phosphorus is excreted in manure. It accumulates in soils, increasing the potential for phosphorus losses in runoff, which in turn contributes to accelerated water quality deterioration.

The traditional approach to reduce phosphorus problems is focused on the management of manure at the end of the production cycle, i.e. after manure is excreted. A more efficient and cost-effective approach of managing phosphorus on dairy farms is to eliminate excess of it in diets with optimal nutrient balances in the rations. This front-end approach minimizes phosphorus excretion in manure without impairing cow performance and farm profitability. This approach saves feed cost for the farmer.

In fact, phosphorus is an essential nutrient, needed by all plants and living species. The problem is that in many areas soils already have phosphorus buildup to levels far exceeding crop needs. Manure added as fertilizer compounds the problem. Run-offs from these high-phosphorus soils to rivers, streams, and the Chesapeake Bay impede the water quality and interfere with balance of plant and marine life in the watershed.

To help dairy farmers better manage phosphorus for enhanced farm profitability and environmental quality, a multi-state, multi-disciplinary project ($1,797,000 for year 2002-2005) supported by the USDA-IFAIS Program was recently initiated to develop optimal phosphorus management technologies on dairy farms. The long-term goal is to develop and deliver practical, scientifically sound, and economically viable phosphorus source control measures and management tools that sustain dairy farming and protect the environment.

Penn is the lead institution with Dr. Zhengxia Dou as the project director and Dr. James Ferguson the co-director. Researchers from five other institutions are collaborating on the project. They visit farms in their areas and collect samples, then send farm information and samples to Penn for processing and analyses. Drs. Dou and Ferguson are in charge of project planning, monitoring, implementation, evaluation, supervising, and reporting findings to USDA. They are also working with 20 dairy farms in Southeast Pennsylvania and Delaware to collect farm information and samples, just like the collaborators do for this project.

The specific objectives of the project are:
(A) Determine the dietary P range adequate for optimal cow performance but not in excess of animal needs by combining farm data across five states (PA, NY, DE, MD, VA) with research findings.
(B) Develop easy-to-use management tools including a fecal P testing procedure for

The five states participating in the project make up much of the Chesapeake Bay watershed.

The results of the study will be disseminated rapidly through existing multiple outreach channels. Project findings will be equally applicable on small, medium, or large farms. Project impact will be large-scale and long-lasting beyond the project period.

The principal investigators are Dr. Zhengxia Dou and Dr. James D. Ferguson at the School. The collaborating scientists are: Dr. L.E. Chase, Cornell University, Dr. K.F. Knowlton, Virginia Polytechnic Institute, Dr. R.A. Kohn, University of Maryland, Dr. J.T. Sims, University of Delaware, Dr. Z. Wu, Penn State University.

Clinic to bench

Christopher Hunter’s lab on the second floor of Rosenthal is overflowing with equipment and people. In the broadest sense, the work here focuses on the role of cytokines in triggering immune responses. Cytokines, soluble messenger proteins, tell cells when to mount an immune response or when to stop such response. Cytokines are indispensable for the ability to fight diseases.

A major aspect of the basic research work here involves Toxoplasma gondii, a protozoan parasite that infects most warmblooded animals, including birds and man. Cats, domestic and wild, are the only known definitive host of the organism and serve as the main reservoir. Toxoplasmosis occurs world-wide. It is a major concern for pregnant women because the disease causes birth defects in fetuses. The disease is also a major concern for people with immune system dysfunction; here it causes meningoencephalitis.

Hunter’s laboratory is home not only to bench scientists but also to clinicians who are pursuing basic research to enhance their clinical work. Dr. Lillian Aronson, V’92, assistant professor of surgery and head of the feline kidney transplant program at VHUP, and Dr. Nicola Mason, on leave from the section of medicine, and in the process of earning a Ph.D., are both working with Dr. Hunter’s group to learn more about the immune complex.

Dr. Aronson came to the lab to evaluate the effects of a drug CTLA4-Ig on feline lymphocyte function. The theory behind this drug is that it is more specific in its mechanism of action, i.e. it can hopefully still prevent rejection (suppress T lymphocytes that are specifically involved with rejection), but also allow a patient to fight off an infection (not have an affect on memory T cells).

Some of her patients, after a kidney transplant when they received regular doses of cyclosporine and prednisolone as immunosuppressants to prevent rejection of the new kidney, suddenly developed acute generalized toxoplasmosis (because of a reactivation of a latent
Basic research projects often involve narrow, focused aspects of basic processes. One such piece is the process by which certain viruses move from one cell to then spread and infect additional cells.

To replicate, viruses turn host cells into “virus factories.” The new viruses then move on to infect other cells and the whole process begins again. The mechanism that allows a virus to be released efficiently from one cell and move to another is the main interest of Ronald Hartoy’s laboratory at the School.

Viruses are released from a cell through a process called budding. The virus pushes the lipid membrane of the cell outward so that it enfolds the virus. This budding virus separates from the cell and the new virus particle is ready to infect the next cell.

The mechanism that governs this process is not well understood and scientists have been trying to understand this process of budding as it could help in combating viral diseases. Dr. Hartoy, assistant professor of microbiology, and his colleagues, two years ago identified a sequence of amino acids that is instrumental in the movement of Ebola virus out of a cell. “We discovered a short sequence of four amino acids contained in the matrix protein of Ebola virus that is instrumental to budding,” says Dr. Hartoy. “If this sequence or motif, as it is called, is changed, the budding process slows down significantly.”

This motif not only is present in the matrix protein of the Ebola virus, but also in the matrix proteins of vesicular stomatitis virus (VSV) and HIV. All three viruses are RNA viruses with different characteristics and they represent three different virus families: Ebola is a filovirus, one of the biggest viruses; VSV is rhabdovirus, this family includes rabies; HIV is a retrovirus. The motif is interchangeable between these different virus groups, such that the motif from one initiates budding in another group when implanted in that matrix protein.

“We have found that budding occurs if we move the motif from one place to another on the matrix protein,” says Hartoy. “The protein by itself also causes budding. It is thought that the motif interacts with specific cellular proteins for budding to occur. We are trying to identify these cellular proteins. Because budding doesn’t completely cease if the amino acid sequence of the motif is changed, we know other interactions are involved in the process.”

Most of the work in the laboratory occurs with VSV, a RNA virus with an RNA genome of about 11,000 bases, considerably smaller than the Ebola virus genome of 19,000 bases. VSV, a reportable disease, afflicts cattle and equines. Symptoms in cattle resemble foot and mouth disease and animals must be quarantined until an accurate diagnosis is made.

“Although we work with VSV, we do not work with actual Ebola virus, just with DNA plasmids that make the proteins we are studying,” says Hartoy. “These plasmids are just pieces of DNA that are not infectious. We could not work with Ebola virus or any other lethal virus as that requires the highest grade secure laboratory which we do not have.”

The members of Dr. Hartoy’s laboratory working on the Ebola virus project are Jill Licata, Ph.D. student and Dr. Ziyng Han, a post doc. Recently, Dr. Hartoy and Dr. Bruce Freedman, V’87, assistant professor of pathobiology, received a NIH grant to examine Ebola virus proteins that may have channel activities in the cell during budding. These may well be another piece needed in the budding process. It may bring scientists closer to a means that can prevent the spread of virus from cell to cell. Dr. Hartoy’s research on the amino acid motifs is also supported by a second NIH grant.

infection; 30-40% of cats in the NE are carriers for the infection) that they could not overcome because they were immunocompromised.

“Right now we give cyclosporine and prednisolone to our transplant patients to prevent rejection of the new kidney,” explains Aronson. “Unfortunately, long term use of these immune system suppressing drugs can make a patient more susceptible to infection and cancer. This has been seen in people and we have also seen it in our transplant patients.”

The new drug, CTLA4-Ig, is being used in clinical trials in human transplant patients. It is hoped that it does not have the long-term effects of the drugs currently used. “The drug has been shown to prevent rejection in many research models. Hopefully, its more specific mechanism of action will allow a patient to respond to an infection as well,” says Aronson. “We are now investigating the drug in vitro to determine its effect on feline lymphocytes, a group of infection-fighting cells. It appears that the drug suppresses feline lymphocyte proliferation, but allows some cells to remain intact. Some of the cells that remain intact appear to be cells (memory cells) that have previously seen the infectious agent and are present to respond to the infectious agent again. Eventually, we have to determine if the degree of immunosuppression seen in vitro using CTLA4-Ig is enough to prevent rejection in an in vivo model.”

Aronson hopes the drug will provide an alternative to cyclosporine and prednisolone so that her feline transplant recipients remain able to suppress a latent toxoplasmosis infection and fight of any other infections.

Mason is looking at another factor involved in the immune response to *Toxoplasma gondii*. In Hunter’s lab, she is studying the role of c-Rel, a gene that controls the production of the cytokines interferon gamma (IFN-g) and Interleukin 12 (IL-12), both essential for resistance to toxoplasma infections.

“The cytokines are important in resistance to toxoplasmosis,” says Mason. “We are studying the immune response to toxoplasma in mice that lack the c-Rel gene. When these mice are infected with *Toxoplasma gondii*, their resistance to the disease is very low. They have normal levels of IL-12 and reduced levels of IFN-g early on during infection. This may allow the parasite to establish itself in the mouse and result in a reduced survival time compared to wild type mice.”

To know the role the gene c-Rel plays in the immune response is important as this gene is also involved in producing resistance to Leishmania, another protozoan disease that is devastating to people and animals, and to viral infections. Once this role is completely understood, scientists may be able to develop treatments that reinforce c-Rel and help people and animals overcome these infectious diseases.

Aronson and Mason are just two clinicians at the School who are taking advantage of the proximity of the basic scientists to the clinical facilities; there are many more clinicians, at VHUP and at New Bolton Center, who work closely with bench scientists, incorporating basic science findings into clinical applications.
The 2002 Rush Shippen Huidekoper Society Dinner, which recognized Penn Veterinary Medicine’s most generous donors and friends during the 2001-02 fiscal year, was held on November 2 at the Independence Seaport Museum at Penn’s Landing in Philadelphia. It was a wonderful evening as the School’s alumni, grateful clients, and other friends came together to celebrate Penn Veterinary Medicine.

The dinner also brought together Opportunity Scholarship student recipients and their donors/mentors. Established in 1998, the Opportunity Scholarship Program fosters scholarship support and mentoring opportunities by pairing a donor, who commits to giving $2,500 per year for four years—a total of $10,000—to a single student, who is selected based on strong academic qualifications and financial need. More than 30 students attended this year’s dinner, and Nathan D. Harvey, V’03, spoke movingly on behalf of them when he thanked the donors/mentors for their generous support of the students’ veterinary educations.

According to Nate, having grown up in New Hampshire near his grandfather’s dairy farm, he has always had the dream of attending veterinary school and returning to New England to practice dairy medicine. He looks forward to taking what he has learned at Penn about progressive production medicine, and applying it in the context of the important lessons and values that he learned working on his family’s farm. Nate emphasized that he could not have achieved these goals without the tremendous generosity of the School’s alumni, and he expressed particular gratitude toward Benson B. Martin, Jr., V’80, associate professor of equine sports medicine at New Bolton Center, his Opportunity Scholarship donor and mentor. Nate concluded his remarks with his plan to give back to students following in his footsteps by funding an Opportunity Scholarship himself.

The dinner’s special guest, University President Judith Rodin, C’66, was unable to attend in person, however she recorded a message on video that was shown at the dinner (see page 18 for her remarks). “On Any Given Day,” a new 15-minute video that follows a day in the life of New Bolton Center, was also shown at the dinner. The video helps to mark New Bolton Center’s 50th anniversary, and showcases the high-level of research, teaching, and clinical service that occurs everyday on campus.

Named after the first dean of the School of Veterinary Medicine, the Rush Shippen Huidekoper Society recognizes those donors who contribute $1,000 or above to the School in the fiscal year. The generosity of the School’s alumni and friends advances the School’s mission to better the health and welfare of animals and humans. For information to support Penn Veterinary Medicine, visit the Alumni & Friends website at <http://alumni.vet.upenn.edu> or contact Joshua E. Liss at (215) 898-1481 or via e-mail at <lissj@vet.upenn.edu>.


Mary McMahon Stewart, PT’66, Robert W. Stewart, Sr., V’68, Amy Hinze, V’03, and Raymond Patsch.
Remarks by Judith Rodin at the 2002 Rush Shippen Huidekoper Society Dinner

Good evening. While I am unfortunately unable to join you in person this evening at the Independence Seaport Museum, thanks to modern technology, I can share some of my own thoughts with you as we celebrate Penn Veterinary Medicine and its record of wonderful excellence.

By every measurable standard in teaching, research, and care, Penn’s School of Veterinary Medicine is among the best in the world. Admittedly, some of my own standards are somewhat subjective and based on my personal experiences and observations. Our family’s beloved dog, Butterfinger, received outstanding care at VHUP. For that alone, Penn Veterinary Medicine will always hold a special place in my heart.

I also had the pleasure of touring the Scott Sports Medicine Building at New Bolton Center, an amazing facility that gives Penn the inside post position in equine sports medicine, service, teaching and research.

And I know from the time I have spent with Dean Alan Kelly and our outstanding faculty and students that the road to major discoveries and breakthroughs in clinical research and care will pass through the Veterinary School at Penn.

But I am also aware that it takes the time and talent and resources of our alumni and volunteers and grateful clients to keep the Veterinary School and its two campuses moving in the right direction.

I am happy to report that this past year was one of the best ever for fundraising. The Veterinary School ranked fifth among the 18 schools and centers at Penn for new gifts and commitments, which surpassed $13.6 million. I was especially pleased that the new Teaching and Research Building received the lion’s share of the School’s gift support last year.

With $7.5 million to count on, University Trustees have given the official go-ahead for the building, and I know that Dean Kelly and his team are hard at work on finding the right architect to move this project forward.

By 2006 our Veterinary School facility will have it all. It will provide state-of-the-art classrooms and group study areas for our students. It will house the finest laboratories for faculty to study infectious disease, cancer, medical genetics, and germ cell biology. Rising at least five stories over University Avenue, this new building will establish a dramatic presence for the Veterinary School.

However, a great university is more than state-of-the-art buildings and much more than the sum of its outstanding research centers and professional and graduate schools.

What makes Penn great is how these different parts work together to boost our intellectual firepower. A dynamic and collaborative spirit permeates our whole campus. For example a faculty member from the Veterinary School is always just a short walk away from partnering with colleagues from the Medical School, the Wistar Institute, and Children’s Hospital of Philadelphia.

We have veterinary students who earn dual degrees at Wharton or pursue doctorates at one of the more than 500 laboratories located throughout the campus. These opportunities for synergy set Penn and the School of Veterinary Medicine well apart from our peers.

But these synergies are not restricted to Dean Kelly, the faculty, or our remarkable students. You are a critical part of our synergistic swagger. Your philanthropic support strengthens the School’s ability to fight disease while saving lives and improving the health of all animals, large and small, including Homo sapiens.

Whether you funded scholarships, physical plant improvements, faculty research, or unrestricted support to meet current and pressing needs, you have kept the Veterinary School on its upward trajectory.

On behalf of the University of Pennsylvania, I thank you for all that you do to sustain and promote the best School of Veterinary Medicine in the world.
Dean Alan M. Kelly has been appointed co-chair of the Commonwealth of Pennsylvania Agricultural Transition Team by Governor-elect Ed Rendell. The other co-chair is Dean Robert D. Steele of the College of Agricultural Sciences, Penn State University.

Dr. Peter Dodson, professor of anatomy in the School of Veterinary Medicine and professor of earth and environmental science in the School of Arts and Sciences, has been elected a fellow of the American Association for the Advancement of Science. Election to AAAS fellowship recognizes efforts to advance science or foster applications that are scientifically or socially distinguished. Dr. Dodson was cited for distinguished contributions to vertebrate paleontology, especially in discoveries about dinosaur biology, and for the education of the public about dinosaurs and evolution.

Dr. Mark Haskins, V’69, professor of pathology, presented a talk “Animal Models of MPS” at a conference entitled The Mucopolysaccharidoses: Therapeutic Strategies for the Central Nervous System. It was held in September at the NIH, Bethesda, Md. In October, he presented at the American Society of Human Genetics meeting in Baltimore, a Plenary Session, “Substantial Long-Term Clinical Improvement in Dogs with Mucopolysaccharidosis VII Following Neonatal Retroviral Vector-Mediated Gene Therapy.” Dr. Haskins’ paper “Marked clinical improvements in mucopolysaccharidosis VII dogs after neonatal administration of a retrovector expressing β-glucuronidase,” was the cover story of the October 1 issue of Proceedings of the National Academy of Sciences.

Dr. Andrew Wood, Professor of Radiology, retired October 31, 2002 and has returned to Sydney, Australia.

Dr. Vickie Hoffman, lecturer in pathology, is a diplomate of the American College of Veterinary Pathologists.

Dr. Gerhard Schad, professor of parasitology, was elected a Life Member of the Helminthological Society of Washington. The award was presented in October in Washington, D.C.

Dr. Brett A. Dolente, V’96, lecturer in medicine at New Bolton Center, has become board-certified in Internal Medicine-Large Animal by the American College of Veterinary Internal Medicine.

A number of faculty appointments recently became official: Dr. Jennifer Baez, V’92, as assistant professor of oncology; Dr. R. Avery Bennett as associate professor of surgery; Dr. Rosario Cerundolo as assistant professor of dermatology; Dr. Robert Gilley as assistant professor of surgery; Dr. Christiane Massicotte as assistant professor of neurology; and Dr. Margaret Sleeper, V’93 as assistant professor of cardiology.

Dr. Gary Smith, professor of population biology and epidemiology, was on the organizing committee of a conference held at the National Press Club in Washington called “Agenda for Action: Veterinary Medicine’s Role in Biodefense and Public Health.” It took place November 1-3, 2002. Dr. Smith served on the steering committee as the Veterinary School representative for a University-wide Masters of Public Health program. He now serves on the admissions committee for the program.

Dr. David Heller, intern, received a departmental grant to be matched by the Oncology Society of the American Association of Veterinary Parasitologists.

The conference on the Advances in Canine and Feline Genomics: Comparative Genome Anatomy and Genetic Disease was held in St. Louis in May 2002. This represented a follow up to the successful first international conference on feline genetic diseases held here at Penn in 1998. The joint conference was co-organized by Dr. Steven O’Brien’s group at the Division of Genomic Diversity, NIH, Dr. Elaine Ostrander at the Fred Hutchinson Cancer Center, Nestle Purina PetCare, and Dr. Urs Giger at Penn. Several invited presentations were given by members of Penn’s Section of Medical Genetics, including Drs. Ellinwood, Giger, Haskins, Henthorn, Mazrier, Patterson, and Werner.

Dr. Gail Smith, V’74, professor of orthopedic surgery presented data that showed the beneficial effects of keeping dogs lean at a special symposium titled: “Advancing Life Through Diet Restriction: When Less is More,” organized by Nestle Purina Pet Care in St. Louis in September. This one-of-a-kind study followed 48 Labrador retrievers for life.

Barry Stupine, vice dean for administration and finance, has been named interim associate dean for administration and finance at the School of Dental Medicine. He will serve in this position until an individual is appointed which is expected to take six months. He will continue to serve in his regular position as vice dean for administration and finance of the Veterinary School and VHUP director while serving at the Dental School.

Dr. Tobias Schwarz, lecturer in radiology, presented an invited lecture entitled “Imaging in Fish Patients” at the Norwegian Veterinary College in Oslo in September; he also participated in a research project on short-tail-syndrome in Atlantic Salmon by performing computed tomography in affected salmon.

Dr. Gary Althouse, associate professor of swine herd health and reproduction, was program-chair for the 2002 Society for Theriogenology Annual Conference held in September in Colorado Springs. At this meeting, he was elected president of the Society for Theriogenology (www.therio.org). This is a ~2,400 (continued on page 20)
International award

Dr. Urs Giger was presented the Scientific Achievement Award by the World Small Animal Veterinary Association at the organization’s meeting in Granada, Spain in October. The award is given annually to an outstanding veterinary researcher for his/her lifetime scientific contributions to the health of small animals. Dr. Giger, the Charlotte Newton Sheppard Professor of Medicine and chief of the Section of Medical Genetics at the School, has a strong research program in hereditary blood and metabolic diseases. His group has identified a number of hereditary diseases in dogs and cats, developed many diagnostic hematologic, biochemical and molecular tests for hereditary disorders which are offered through the Josephine Deubler Genetic Disease Testing Laboratory. He also contributed to the understanding of feline blood types to assure safe and effective transfusions and to avoid hemolysis of the newborn in these species.

Scholarships

Jason Cordeiro, V’03 and Tony Ebling, V’03 each received a SCAVMA Community Services Grant. The William Goldman Foundation awarded scholarships to Gina Marie Cairone, V’03 and Jason Cordeire, V’03 and the following members of the Class of ’04: Kristen Hart, Caitlin Heinez, Laura Javicas, Michael Koch, and Kelli Russell. Three members of the Class of ’06 each received a Donald E. Cross Scholarship for Large Animal Medicine: Lauren Greene, Caitlin Roberts and Alison Wolfgram.

Jannie Carr, V’05 received the American Veterinary Medical Foundation Scholarship. Victoria Achenbach, V’03 was awarded the Ginnie Leiblein Memorial Scholarship. Darah Resh, V’03 received the Lalitta Nash McKaig Foundation Scholarship. The Barnstable County Agricultural Society awarded a scholarship to Kate Johnson, V’03. Mary Kwacz, V’03 is the recipient of the Union County Kennel Club scholarship.

Todd Brooks, V’03 and Erik Herrema, V’03 received scholarships from the Pennsylvania Veterinary Foundation as did the following members of the Class of ’04: Jill Compton, Josh Eaton, Caitlin Heinez and Laura Javicas. Holly Edwards, Megan Manfredi, Regina Pellegrin and Erin Wright, all members of the Class of ’04, each received a Ethel H. Mitchell Dean’s Scholarship.

Jill Compton, V’04 and Erik Herrema, V’03 each were awarded a Harry B. Roshon Memorial Dean’s Scholarship. Laurie Prober, V’04 received a scholarship from the Mispillion Kennel Club.

The Oncology Section of VHUP attended the 22nd annual conference of the Veterinary Cancer Society and presented the following research abstracts:

1) Magnetic resonance imaging of canine splenic and hepatic lesions: A pilot study. C.A. Clifford; C. Weisse; E.S. Siegelman; J.R. Solomon; K.U. Sorenmo and E.S. Pretorius. Department of Clinical Studies, Veterinary Teaching Hospital and Department of Radiology, Hospital of the University of Pennsylvania. (Won the resident presentation for clinical research).

2) Case-Control study of Hormonal Influences on the development of feline mammary gland carcinoma. B. Overley, D. Sherer, F. Shofer, M. Goldschmidt and K. Sorenmo. Departments of Clinical Studies and Pathobiology, School of Veterinary Medicine, University of Pennsylvania.

3) Clinical Characteristics of mammary carcinoma in the male feline. K. Skorupski, B. Overley, F. Shofer, M. Goldschmidt, K. Sorenmo. Department of Clinical Studies and Pathobiology of the School of Veterinary Medicine of the University of Pennsylvania. (for publication only)

4) Immunohistochemical characterization and correlation with neuter status/time, treatment response and outcome in canine prostatic carcinoma. K. Sorenmo, M. Goldschmidt, C. Goldkamp and F. Shofer. Departments of Clinical Studies and Pathobiology of the School of Veterinary Medicine of the University of Pennsylvania. (for publication only)

5) Cross-immunoreactivity of goat anti-human angiogenin antibodies with canine serum haptoglobin. D. Narvaez, C. Clifford, K. Sorenmo, C.M. Otto, T. Melgarejo. University of Pennsylvania, School of Veterinary Medicine, Kansas State University, Comparative Alimentary Tract laboratory. (poster)

Rosettes and Ribbons (continued from page 19)

member veterinary organization dedicated to furthering advances in the science and practice of animal reproduction. Dr. Althouse received a grant from the Pennsylvania Department of Agriculture to investigate artificial insemination as a route for the spread of porcine circovirus type-2 in swine herds.

Dr. Ronald Harty, assistant professor of microbiology, was awarded an NIH Grant from NIAID to study the role of the VP24 matrix protein of Ebola Virus. Dr. Bruce Freedman, V’87, assistant professor of pathobiology, is co-principal investigator on this grant. Dr. Harty was an invited speaker at Louisiana State University Medical Center to give a seminar on the functions of Ebola virus matrix proteins.

Dr. Fabio Del Piero, assistant professor of pathobiology, presented an invited lecture about West Nile flavivirus at the University of Barcelona, Spain. He lectured at the University of Turin, Italy, on West Nile flavivirus, bovine and equine herpesviruses. He presented a lecture about infectious diseases of horses at the European Section of the Charles Louis Davis Foundation for the Advancement of Veterinary Pathology. At the annual meeting of the European Society of Veterinary Pathology in Turin, he presented three abstracts at the annual meeting of the about infectious and neoplastic diseases of equids.

Dr. Edward Pearce, associate professor of parasitology, was honored by the American Society of Tropical Medicine and Hygiene with the 2002 Bailey K. Ashford Medal. This award is presented to a scientist who has made important scientific contributions to the field of tropical medicine.

Dr. Adrian R. Morrison, professor of behavioral neuroscience, spent two weeks in November in Jos, Nigeria with the World Health Mission. He taught and consulted at the Jos Medical School and Teaching Hospital. He was honored by being appointed by a tribal chief as Sarkin Yaki (war chief) of Butura for the war on illiteracy in Africa.
For two brothers, twin degrees sow divergent paths

by Joan Capuzzi Giresi, C'86 V'98

Marvin, C'46 V'48, and Irwin Rothman, C'40 V'41, know a thing or two about animals. But the two brothers, both Penn Veterinary Medicine graduates, probably don't know the same thing or two.

Take birds, for instance. Marvin can treat liver problems in parrots and excise feather cysts in cockatiels. But big brother Irwin, now a psychiatrist, is more apt to display his avian acumen in a more esoteric way: he can explain how woodpeckers are able to bang on trees without knocking themselves out.

Two entirely different approaches to animals, yet a common education and a shared upbringing.

The Rothman home in North Philadelphia, Marvin remembers, was never without cats and dogs: “Our parents were very fond of pets back when it wasn't so au courant, as it is today,” he says.

For the Rothman boys, animals were an endless source of discovery and intellectual fascination. When young Irwin raised tadpoles, he would fast-forward their metamorphosis by administering thyroid hormone to them. Also enthralled with hypnosis, Irwin would commission Marvin to help him hypnotize the pets—and the other children—in the neighborhood.

True to their eastern European farming heritage, the elder Rothmans exposed their two children to livestock, with frequent visits to friends’ homesteads in rural New Jersey. Marvin, 77, recalls his parents, who owned a small furniture store in Philadelphia, stoking their sons’ desire to pursue veterinary medicine. “It was an unusual profession for immigrants' children to go into,” he says.

As a veterinary student, Irwin questioned the risk vs. reward ratio of drugging animals for routine treatments, such as dental prophylaxis. Encouraged by the Penn faculty to find an alternative to chemical anesthesia, Irwin turned to his childhood hobby, hypnosis. Through hypnosis alone, he was able to adequately anesthetize birds and other small animals for minor procedures. Over the years, Irwin has become the Dr. Doolittle of hypnosis, producing trance-like states in everything from horses and monkeys to snakes and alligators.

After Penn, Irwin operated his own small animal practice out of his parents’ home. Although not yet a psychiatrist, he applied psychiatric principles in handling late-night calls from distressed pet owners. Often, he says, all these clients really wanted was to talk and be comforted.

During this time, Irwin also tried—unsuccessfully—to promote animal hypnosis within the veterinary profession. But, he says, his colleagues “wore hip boots and their attitude was if you couldn’t step in it, it wasn’t real.”

Irwin realized that if he wanted to pursue hypnosis, it would have to be within the realm of human medicine. So, a decade after becoming a veterinarian, he earned the degree of Doctor of Osteopathic Medicine from Philadelphia College of Osteopathic Medicine and became board certified in psychiatry. (The University of California, Irvine later granted him a medical degree based on educational requirements already fulfilled.)

While maintaining several Philadelphia-area hospital affiliations and teaching posts through the years—with an emphasis on hypnosis—Irwin, 83, used his work to explore the evolutionary connection between man and other animals. “There’s a tremendous dislike of seeing human problems in an animal context.” But, he continues, “man isn’t a vegetable or a mineral. He is another animal.”

Through his understanding of “comparative psychiatry,” Irwin has helped smokers, stammerers, overeaters and impotent men “retrain” themselves, just as pets can be retrained. And he credits his veterinary background with aiding him to read between the lines with his human patients, like the woman who fiddled with her wedding ring while insisting that her failing marriage was blissful.

“You learn as a veterinarian to be much more observant of body language. In people, I pay as much attention to body language and facial expressions as I do to spoken words.”

Irwin says that the veterinary “school” of thought, which stresses signs versus symptoms, has enabled him to distinguish physical from psychosomatic afflictions in his patients.

And his appreciation for the human-animal bond has been invoked in counseling sessions, even helping him to prevent a patient, distraught over the death of her dog, from committing suicide. His veterinary expertise has also been called into play by patients in whom he has diagnosed zoonotic infections that had confounded their family doctors, and by lawyers who have referred dog-bite victims to him for therapy.

Recently retired from private practice, Irwin, a widower, is researching his theory that war might be prevented if men are excluded from political negotiations. To do this, he is studying animals that have peaceful and matriarchal social structures.

Marvin traces his own veterinary roots back to his brother. “He was my hero figure and he went to vet school,” Marvin says. “That inspired me a little.”

Thanks to Irwin, Marvin was able to begin veterinary school with a full set of hand-me-down books and an accurate set of expectations. Both brothers recall experiencing subtle anti-semitism from some of the faculty and fellow students. At the time, the two percent quota for Jews was an unwritten but widely-known rule at the School.

Marvin maintains that the School today is nothing like the institution he attended. “It was during the war years,” he recalls, “and they still had a lot of the old professors who were not so current.”

Although Penn had a good small animal clinic, Marvin says, the School’s emphasis was

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For two brothers, twin degrees sow divergent paths

(continued from page 21)

clearly farm animals. Hands-on experience was basically limited to a large and a small animal rotation, and an ambulatory clinic.

Marvin went on to an internship and residency at Boston’s Angell Memorial Animal Hospital, at the time a far more sophisticated veterinary institution than Penn. He remained on the staff there for three years before being called into service with the Army Veterinary Corps during the Korean War. At Angell, Marvin rounded out his clinical experience through exposure to the newly-burgeoning veterinary specialties and the hospital’s vast caseload, which included birds.

It was at Angell where veterinary medicine really “clicked” for Marvin, but he says that Penn gave him a solid foundation in the basic sciences. And his natural compassion for animals was deepened by example from some of his Penn professors.

“If you understand the human-animal bond,” he says, “you know you’re there to provide compassionate, quality medicine.”

And that is what Marvin has been doing for almost five decades at Rothman Animal Hospital in Collingswood, N.J. He sold the practice, which still bears his name, 12 years ago to Mark Esser, V’86, but continues to work there. His lightened work schedule—35 hours a week, which he works alongside his wife Betty, who is the longtime office administrator, and four other doctors—leaves him plenty of time to participate in local charity work.

He says his proximity to Penn has given him access to advanced veterinary technologies, exposure to new techniques, and a constant influx of fresh knowledge from the new grads he hired through the years.

For Marvin and Irwin, veterinary medicine is the proverbial egg cooked in two vastly different ways. The one element that has always fascinated both brothers is the human-animal bond, which they often explore through traded stories and insights. Despite their divergent paths, the bond between Marvin and Irwin also remained strong.
Join your fellow alumni for Alumni Weekend 2003 at New Bolton Center on Saturday, May 17!

Event Schedule (as of November 2002)

9:00-10:30 a.m.
Concurrent Continuing Education Courses in Companion Animal and Large Animal Medicine

11:00 a.m.-12:00 p.m.
Veterinary Medical Alumni Society Annual Meeting
See your Alumni Society at work, help to honor the 50th year reunion of the Class of 1953, and celebrate the presentation of the 2003 Alumni Award of Merit, awarded to three graduates celebrating a class reunion in 2003, and the 2003 Excellence in Teaching Award, awarded to an educator recommended by recent graduates.

12:00-3:00 p.m.
Alumni Day Picnic
Enjoy a buffet-style luncheon with alumni; special activities will be available for children.

Tours of New Bolton Center
Visit the George D. Widener Hospital for Large Animals, the Marshak Dairy Facility, and the Scott Equine Sports Medicine Building.

6:00-9:00 p.m.
All-Alumni Dinner at the Brandywine River Museum, which features regional and American art. U.S. Route 1 and PA Route 100, Chadds Ford, PA

Hotel Reservations and Tourist Information
Make your hotel and travel plans early! A limited number of rooms have been reserved for Friday, May 16, and Saturday, May 17, at the hotels below. Please mention that you are calling to reserve rooms held for the University of Pennsylvania School of Veterinary Medicine. For other Chester County lodging options and to get tourist information, visit the Chester County Conference and Visitors Bureau website at <www.brandywinevalley.com/pyv.htm> or call toll-free (800) 228-9933.

Best Western Concordville Hotel
Route 322 and U.S. Route 1
Concordville, PA 19331
(610) 358-9400 Phone
(610) 358-9381 Fax
$109 single plus tax; $119 double plus tax; additional guests are $10 each (up to four people per room). Reserve by April 1, 2003, to obtain reduced rate. Must cancel reservation by May 8, 2003, to get refund; ask for cancellation number.

Hilton Garden Inn Kennett Square
815 E. Baltimore Pike (U.S. Route 1)
Kennett Square, PA 19348
(610) 444-9100 Phone
(610) 444-9186 Fax
$104 plus tax. Reservation must be guaranteed to a credit card by April 1, 2003, to receive reduced room rate. Reservations not canceled at least 24 hours prior to arrival will be billed to the credit card.

Mendenhall Hotel
Route 52, Kennett Pike
Mendenhall, PA 19357
(610) 388-2100 Phone
(610) 388-1184 Fax
$105 single or double plus tax; additional guests are $20 each (up to four people per room). Reserve by April 15, 2003, to obtain reduced rate. Must cancel reservation by May 8, 2003, to get refund; ask for cancellation number.

An Alumni Weekend 2003 brochure with an event reservation form will be sent to all alumni in March 2003. If you have any questions or need more information about Alumni Weekend 2003, please contact Joshua E. Liss, Director of Alumni Relations and Annual Giving, at (215) 898-1481 or via e-mail at <lissj@vet.upenn.edu>. For updated information, visit the Alumni Weekend 2003 website at <http://alumni.vet.upenn.edu/alumniweekend2003.htm>.
Pets can have a positive impact on the human condition. This we know. But at the Centers for Disease Control and Prevention (CDC) in Atlanta, veterinarians are also doing their part to improve human health.

Charles E. Rupprecht, V’85, Cathleen (Lanutti) Hanlon, V’87 GR’94, and Peter M. Schantz, C’61 V’65, have taken their veterinary training to the CDC in Atlanta, where they work to combat zoonoses that threaten public health worldwide.

Charles Rupprecht isn’t sure if it’s the dog bite he received as a youngster, the bat that invaded his childhood home, or the occupational hazards that rabies sometimes poses, but some powerful force triggered the mythos of rabies for him. Today, Rupprecht is chief of the Rabies Section of the CDC’s National Center for Infectious Diseases, where he heads up national efforts to eradicate rabies both at home and abroad.

As a child growing up in Trenton, N.J., Rupprecht wanted to be a paleontologist. Armed with a bachelor’s degree in ecology from Rutgers University and a master’s degree in zoology from the University of Wisconsin, Rupprecht went to Panama to study neotropical bat ecology. While there exploring potential Ph.D. projects, he met a veterinarian who was working with night monkeys … Rupprecht’s fate was sealed.

“I’d never thought about combining veterinary medicine and basic biology or zoology before,” he says, “but I knew when I came back from Panama, I wanted a happy marriage between veterinary medicine and biology.”

Upon his return home, Rupprecht enrolled simultaneously in veterinary school at Penn and a doctoral program in biology at the University of Wisconsin, where he wrote his dissertation on the epidemiology and antigenic characterization of rabies virus variants in North America. Serendipitously for Rupprecht, raccoon rabies was first discovered in Pennsylvania in the spring of 1982, during his first year in vet school. Intrigued by the development, he teamed up with noted researcher Hilary Koprowski, M.D., who was developing rabies vaccines across the street at The Wistar Institute.

While Rupprecht enjoyed his clinical work at Penn, his prior experiences in the rain forest left him with little intention of becoming a traditional veterinarian.

“Given the biodiversity that exists, I found a sole focus on cats and dogs to be intellectually limiting,” he says.

Rupprecht adds that his professional endeavors have benefited greatly from Penn’s emphasis on the basic sciences, its diverse faculty, and its flexible rotation schedule that left him time to pursue his research interests while in school.

At the CDC—the lead federal agency for protecting the health and safety of people at home and abroad, and also the national reference center for rabies—Rupprecht, 47, oversees research on the pathogenesis, epidemiology, diagnosis and prevention of rabies in the United States. And as head of the World Health Organization (WHO) Collaborating Center for Rabies Reference and Research, he combats the disease on an international front.

Rupprecht is proud to report that national rabies cases are now at an all-time low, with just 89 last year, down dramatically from over 9,000 annually in dogs alone during the World War II years.

But Rupprecht is not ready to breathe a sigh of relief. “I don’t yet feel fulfilled because the task in front of us is still quite formidable,” he laments. “These very small RNA viruses are constantly evolving.

“We live in a sea of rabies, and we need to be always on guard for new cases.”

While noting that some confusion regarding rabies titers, booster vaccines and quarantine regulations still exists among veterinarians, Rupprecht says, “The veterinary community deserves a huge pat on the back for the decline in cases.”

Cathleen Hanlon, who works with Rupprecht as the veterinary medical officer in the Rabies Section, says that veterinarians are uniquely poised to pull the plug on rabies.

“They are the first and most critical line of contact when there’s a potential exposure to rabies,” she explains.

Veterinarians, she adds, generally are far more knowledgeable about rabies than are their counterparts in human medicine. And from her experience working side-by-side with both veterinarians and medical doctors, she has concluded that their respective academic curricula render veterinarians more suited to transitioning into the field of public health than medical doctors are to working in animal health.

Hanlon, who holds a bachelor’s degree in animal science from Rutgers University, was first drawn to epidemiology during a veterinary school work-study project on transitional cell carcinoma in animals. Then during the last two years of her veterinary education—the raccoon rabies epidemic at its height—she worked as a research assistant in Wistar’s Rabies Unit with Rupprecht and Koprowski. There, Hanlon worked in the lab developing vaccines, and in the field live-trapping raccoons.

After she graduated, Hanlon stayed on at Wistar as a veterinarian associate, while she conducted rabies research to earn her Ph.D. from Penn in comparative medicine. She then joined Rupprecht and Koprowski at Thomas Jefferson University’s Center for Neurovirology. When the rabies epidemic hit Albany, N.Y., she was hired there as acting state public health veterinarian.

Hanlon credits her Penn experience for much of her professional success. “The rigorous, high-quality education at Penn provided me with the tools to branch into many different areas in addition to the fundamentals in clinical care,” she says.

The veterinary courses that Hanlon has found to be most applicable to her job, she says, are physiology, epidemiology, public health, medicine, microbiology, neurology and surgery. She spends almost half of her time in the lab, and the remainder divided between telephone consultations and animal colony work. She also trains state health personnel around the country in techniques for live-trapping, sedating and testing wild animals.

True to her veterinary nature, Hanlon, 43, enjoys the “touchy-feely” aspect of her job the
most, working with the lab animals to assess their clinical condition, evaluate their temperament, make handling and sedation judgments and determine appropriate routes of medication.

“My job runs the gamut, from the ivory-tower, sitting-at-your-desk thinking to fundamental research in the lab to clinical care and field work,” she says.

Hanlon’s work comes with the obvious occupational hazards. She will probably never forget being bitten by a vampire bat she was removing from a net while investigating a rabies outbreak among cows in Venezuela. The rabies virus has earned Hanlon’s healthy respect for the “interesting way it can navigate through the central nervous system of its host in order to affect its behavior—causing aggression, inquisitiveness and vocalization—for transmission before killing it.

“A rabid animal would be useful for everyone to see at least once in their life,” she says. “It would make the hair on the back of your neck stand on end.”

Peter Schantz is just as fascinated with his pathogens of choice—zoonotic helminths. He finds them biologically intriguing because of their transmission dynamics and their interaction with the human population. In his job, Schantz travels the world, collecting samples in butchered animals, collaborating with local health officials and veterinarians to develop educational materials for local distribution, and supervising research on disease pathogenesis.

“I enjoy the fact that my career has enabled me to do lab and field work, collect epidemiologic data in humans and animals, present the data, and see my work get published and then result in measurable disease reduction,” he says.

Schantz points to the success he and his colleagues have had in reducing the incidence of trichinosis in the United States by educating the pork industry on healthier production methods. He is also encouraged by the demonstrable impact his group has had on *Echinococcus granulosus* in Argentina, Peru and Chile by working with local veterinarians and physicians to develop effective parasite control programs.

Schantz, who holds a bachelor’s degree in anthropology from Penn, says he enjoys studying zoonotic diseases whose propagation is rooted within different cultural traditions like sheep herding, and often within grim poverty.

“Whether you’re talking about transmission of echinococcus in Tibetan nomadic sheep herders or toxocara in American children who have a new litter of puppies with roundworms, it’s a natural follow-up for a person trained in anthropology and veterinary medicine,” he explains.

Growing up in southern New Jersey, Schantz channeled his childhood love of animals into a yearning to become a veterinarian. He became interested in a career in public health when he spent the summer after his first year of vet school working for the California Department of Health Services to help eradicate *Trypanosoma cruzi*—the “kissing bug”—which causes allergic reactions in the people it bites.

He also remembers his interests in public health being nurtured by his veterinary school professors. “Penn’s academic tradition was inspirational to me,” says Schantz. “The faculty was interested that I was interested in research and public health, and they fostered this.”

After earning his veterinary degree, Schantz headed to the University of California, Davis, School of Veterinary Medicine for a job as an epidemiologist. Although he also worked part-time as an associate at a local animal hospital, he says he regrets not spending more time in private practice before moving into public health exclusively.

Schantz recalls that, at the time, he ascribed the “Peace Corps mentality: I became interested in the world outside the U.S.” After spending four years investigating helminthic zoonoses in South America, he returned to the United States in 1974 to work for the CDC. Schantz’s work with the CDC has spanned many countries and types of helminthic diseases, from cystercerosis and intestinal nematodiases in Mexico and Ecuador, to hydatid disease in China and Tibet, to Guinea worm infections in Nigeria, to leishmaniasis in the United States.

Schantz, 63, enjoys the regular interaction he has with veterinarians in many different professions, including those who work at the state and local levels, and those in academia and private practice. Dr. Schantz returns to the School every spring to teach a seminar on zoonotic diseases.

“I have one foot in the veterinary arena and one foot in the human medical arena,” he says.

Schantz believes that local veterinarians hold the key to disease control for zoonotic helminths. “Veterinarians in private practice,” he says, “can every day do good things for human health.”

**CDC Rotations for Veterinary Students**

The CDC offers six- to eight-week epidemiology rotations for fourth-year veterinary students. The project-based rotations include desk, lab and field work. Applications are due by the end of the third year, and applicants may specify an area of interest within public health. Travel and accommodations in Atlanta are not provided by the CDC, but listings of housing options are furnished upon request. Interested students may contact the CDC’s Epidemiology Program Office via e-mail at <pbellamy@cdc.gov>.
Class Notes

1941  
**Glenn D. Gates** was inducted into the Mississippi Veterinary Medicine Hall of Fame by the Mississippi Veterinary Medical Association (MSVMA) in June 2002. Only six other Mississippi veterinarians hold this distinction, which recognizes excellence in veterinary practice and community service. After graduating from Penn, Dr. Gates joined his father in practice in Clarksdale, Miss. They both served as president of the MSVMA, and Dr. Gates was appointed by the governor to succeed his father on the Mississippi Board of Veterinary Medicine. Clarksdale honored Dr. Gates as Citizen of the Year in 2001 for his service to the community.

1943  
**Albert D. Thorp** is the author of “Volunteers for Glory,” a historical Civil War novel, published in 1999. The book is a living history of the major players who participated in the Army of the Potomac.

1961  
**Peter Theran** was quoted in *The Boston Globe* on October 1, 2002, about Chimp Haven, which is building a sanctuary in Shreveport, La., to provide a permanent home to the hundreds of chimpanzees no longer needed in biomedical research, entertainment, or as pets. The National Institutes of Health have awarded Chimp Haven a $24 million grant over 10 years to help build the sanctuary. According to Dr. Theran, a member of the Chimp Haven’s board of directors, “It’s really exciting.” The NIH advisory group “worked seven years to find this perfect spot, a rainforest where the weather is great and protected from hurricanes,” he said. Dr. Theran is the vice president of the Health and Hospital Division for the Massachusetts Society for the Prevention of Cruelty to Animals/American Humane Education Society.

1973  
**Richard A. Carnevale** visited the School of Veterinary Medicine and spoke to students in November 2002. Dr. Carnevale was the kick-off speaker for the School’s new Alumni Career Speaker Series. He has worked for more than 25 years in the regulatory, scientific, and international arenas of animal health and food safety. Currently, Dr. Carnevale serves as the vice president for regulatory, scientific, and international affairs at the Animal Health Institute (AHI) in Washington, D.C. AHI represents the manufacturers of animal drugs and veterinary biologicals before federal agencies, Congress, and international health and food safety organizations.

1975  
**Harvey R. Bendix** was quoted in the October 1, 2002, edition of the *Pittsburgh Post-Gazette*, about a client’s cat that received a kidney transplant at VHUP.

1978  
**Gregory D. Bossart** was featured in the November 1, 2002, issue of the *Journal of the American Veterinary Medical Association* in an article on papillomaviruses in manatees. Dr. Bossart is the director of marine mammal research and conservation at the Harbor Branch Oceanographic Institution in Ft. Pierce, Fla. In 1997, he identified a manatee-specific papillomavirus, and is part of a team of veterinarians and physicians studying the virus in manatees to help prevent and cure the infections in human and other animal species.

1979  
**David L. Foster** was profiled by the *Examiner* newspaper of Millstone, N.J., in May 2002. Dr. Foster specializes in equine dentistry, and opened Equine Dental Services in 1996. According to Dr. Foster, “Horse teeth are highly specialized. They are dependent on even wear. Most don’t wear evenly and must be kept balanced by dentistry.”

1980  
**Robert A. Cook**, chief veterinarian and vice president of Wildlife Health Sciences at the Wildlife Conservation Society, was recently appointed to the Morris Animal Foundation’s Wildlife Scientific Advisory Board. The Board guides the Foundation in evaluating, selecting, and monitoring wildlife health studies chosen to receive Foundation funding. In addition, the Board uses its expertise to provide guidance in the administration and operation of the Mountain Gorilla Veterinary Project, based in Central Africa. Dr. Cook’s Wildlife Health Sciences division is responsible for the health care of more than 17,000 wild animals at five New York City parks (Bronx Zoo, New York Aquarium and Central Park, Queens and Prospect Park Zoos) and the Wildlife Survival Center on St. Catherines Island, Ga. In addition, the division’s services and critical research efforts benefit free-ranging wild animals in native habitats around the globe.

**John C. Kimmel** visited the School of Veterinary Medicine and presented a Friends of New Bolton Center lecture, “Thoroughbred Racing—Views from a Veterinarian Turned Trainer,” in November 2002. His father, Caesar P. Kimmel, a horse owner, introduced him to racing. Dr. Kimmel was honored by the New York Turf Writers Association with the Woody Stephens Award for Outstanding Trainer in 1999 and as a co-recipient in both 1997 and 1998.

1983  
**Marcella D. Ridgway** has become board-certified in Internal Medicine-Small Animal by the American College of Veterinary Internal Medicine. Dr. Ridgway is a clinical assistant professor in the Department of Veterinary Clinical Medicine at the University of Illinois at Urbana-Champaign College of Veterinary Medicine.

**John D. Young, Jr.**, is chairman of the Americans for Medical Progress, a non-profit organization founded in 1991 in response to a growing concern about the impact of animal rights activism on biomedical research. Dr. Young is director of Comparative Medicine at Cedars-Sinai Medical Center in Los Angeles.

1984  
**Gary J. Patronek** was featured in the October 15, 2002, issue of the *Journal of the American Veterinary Medical Association* in an article about animal hoarding. Dr. Patronek is the director of the Tufts University Center for Animals and Public Policy and the founder of the Hoarding of Animals Research Consortium (HARC). A collaborative effort involving investigators in the disciplines of psychology, sociology, social work, psychiatry, veterinary medicine, epidemiology, and animal protection, HARC is currently engaged in several efforts to better understand the phenomenon of hoarding of animals. According to the HARC web site <www.tufts.edu/vet/cfa/hoarding.html>, animal hoarding transcends simply owning or caring for more than the typical number of pets and is not about legitimate sheltering or rescue, and has serious consequences for animal health and welfare, as well as human health and welfare.

1988  
**Patrice Noelle Klein** is a new diplomate of the American College of Veterinary Preventive Medicine.
During the Pennsylvania Veterinary Medical Association’s (PVMA) Annual Meeting in August 2002, Timothy J. Ireland was elected Vice-President. Dr. Ireland and his wife, Lynda, live in Wrightstown, Pa., with their three children Timmy, age 6, Abby, age 5, and Angelina, age 2. In November 2002, Dr. Ireland celebrated the 10th year anniversary of his purchase of Newtown Veterinary Hospital in Newtown, Pa. Three Penn Veterinary Medicine alumni work with him: Nicholas James Volkman, V’89, Judith E. Palm, V’90, and Angela C. Summers, V’02.

During the PVMA’s Annual Meeting in August 2002, Michael R. Moyer was elected President-Elect. Dr. Moyer and his wife welcomed the arrival of their first child in August 2002.

Gillian R. Gibson has become board-certified in Internal Medicine-Small Animal by the American College of Veterinary Internal Medicine. Dr. Gibson practices at Wingrave Veterinary Surgery in Sutton, Surrey, United Kingdom.

Larisa C. Chavin married Michael Tempero on September 7, 2002. Dr. Chavin is currently working as a medical director for a small animal hospital in Boston.

Eveline Han has become board-certified in Internal Medicine-Small Animal by the American College of Veterinary Internal Medicine.

William W. Bush IV has become board-certified in Internal Medicine-Neurology by the American College of Veterinary Internal Medicine.

Carol Frollo is an associate veterinarian at Allegheny Veterinary Emergency Associates, P.C., in Pittsburgh.

Angela E. Frimberger, a daughter, Ivy, on August 8, 2002, who joins brother Alexander, age 3.

Hubert-Jan Karreman, a daughter, Emily Faith, on October 13, 2002. Emily’s Penn Veterinary Medicine alumni relatives include grandfather George F. Zimmerman, V’76, and aunts Grace A. Karreman, V’82, and Sarah R. Zimmerman, V’06.

Hillary R. G. Israeli, a daughter, Naomi

Henry Sussman on April 4, 1990.
Harlan W. Fenimore on September 7, 1998.
Philip P. Metzger on August 16, 2002.

John E. Martin on September 22, 2002. Dr. Martin joined the School of Veterinary Medicine’s faculty in 1946 as assistant instructor in physiology and pharmacology; in 1956 he was appointed associate professor of therapeutics. He served as associate dean from 1961-62. Dr. Martin left the School in 1963, and he returned briefly as professor of therapeutics in 1968-69.

In 1980, Dr. Martin returned to the School as special assistant to the dean. He served as director of the Centennial Office and as supervisor of the student financial aid program. Dr. Martin was the founding editor of the School’s newsmagazine, Bellwether, and he is the author of A Legacy and A Promise, a book about the School’s first 100 years; it was published in 1984, the School’s Centennial. In recognition of his contributions to the profession and the School, Dr. Martin was awarded the Veterinary Medical Alumni Society Alumni Award of Merit in 1987.

Jack O. Whitaker on September 3, 2002.
Harry H. Hanshaw on September 28, 2002.
William A. Limberger, Jr. on March 27, 2002.
Special Gifts to the School

THE FOLLOWING GIFTS WERE MADE TO THE VETERINARY HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA:

In memory of a special pet:
Ms. Joan M. Auten in memory of “BASSIE”
Ms. Regina Berard in memory of “PRINCESS”
Mr. Robert Bosco in memory of “MOUSHKA”
Mr. and Mrs. John Bussolini in memory of “BUDDY”
Mr. Frankle L. Carothers in memory of “TIRA”
Cherry Hill Animal Hospital, P.A. in memory of “ASHLEY”
Ms. Victoria Stigari Dawson in memory of “MADDIE”
Mr. and Mrs. Carl J. Deinhart in memory of “MEGHAN”
Ms. Helen W. Depenbrock in memory of “WINDSOR” & “ABBEY”
Ms. Gertrude Dukeman in memory of “PRINCESS”
Mr. and Mrs. Ted C. Fochlain in memory of “TIRA” & “TAI”
Ms. Susan Goll in memory of “BANDIT”
Mr. and Mrs. Wilson Hipley in memory of “PAL”, “MAJOR”, “GARETH”, “PHELAN”, & “NICCI”
Victoria Johnson, V.M.D. in memory of “DIEGO”
Marilee King in memory of “THOR” & “ELKIE”
Ms. Joan Kistler in memory of “BRANDY”
Ms. Joan Kistler in memory of “WOODY”, Mr. and Mr. George Kostik in memory of “LIBBY” & “MISTY”
Ms. Arlene Kress in memory of “CORKY”
Ms. Maria Leone in memory of “SNOWEY”
Mr. Christopher A. LeVan and Ms. Kate Clancy in memory of “BIGGER”
Tom I. McCann, M.D. in memory of “BUDDY”, “PEDO”, “SWEET PEA”
Dr. Jill McCracken in memory of “DRIFTER”
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Mr. and Mrs. William Sauerwine in memory of “OSCAR”
Ms Anne Sheppard and Mr. Hal Real in memory of “KARLA”
Ms. Ronni Schwartz in memory of “SPATS”
Ms. Victoria Dawson in memory of “TOMMI” & “DAISY”
Ms. Anne Sheppard and Mr. Hal Real in memory of “BUDDY”, “PEDO”
Ms. Arlene Kress in memory of “CORKY”
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Mrs. Victoria L. Dawson in honor of “MADDIE”
Mr. and Mrs. John Purnell in honor of “TEQUILA”
Mr. and Mrs. Herbert O. Sonz in honor of “BREEZY”

In honor of those listed:
Mr. and Mrs. Bryan Cooper in honor of VHUP’s wonderful work
Mr. and Mrs. Paul E. Cope in honor of Dr. David Holt
Ms. Jean K. Goodman in honor of Dr. Stephen Atwood
Mr. James Koch in honor of Dr. Chick Weisse
Mr. James Koch in honor of Dr. Tona Thinh Melagerajo
Judy Hansen and Ed Millerick in honor of Joe and Debra Baumann
The Kauffman Family in honor of Mr. Mark Sheft’s Birthday
Ms. Beth E. Liddle in honor of Dr. Dan Morris
Ms. Anne Sheppard and Mr. Hal Real in honor of Drs. Curt Heyde, Lillian Giuli and the wonderful staff at Pets First

In memory of those listed:
Ms. Mary Jane Allen in memory of Sue Mudler
Ms. Christine Cook in memory of Cecelia Arts
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The following have made gifts in memory of Aida:
De Lage Landen - The West Team
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Ms. Victoria Roberts
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The following have made gifts supporting the Cardiomyopathy study in memory of a those listed:
Dr. and Mrs. Thomas J. Weiner in memory of Matthew Weiner

The following have made gifts to the Special Species Clinic in memory of a special pet:
Mr. and Mrs. Denis Roark in memory of “DJ”, “SNEEZIE”, “SARAH”, & “ADAIR”
Teoco Corporation in memory of “DJ”, “SNEEZIE”, “SARAH”, & “ADAIR”

The following have made gifts to the Behavior Clinic in memory of a special pet:
Mr. Wayne Carey in memory of “BARKLEY” & “RAGS”

The following have made gifts supporting Neurology Research in memory of a special pet:
Mr. and Mrs. Barry B. Miller in memory of “FLUFFY”

The following have made gifts supporting Oncology Research in memory of a special pet:
Ms. Marla Tocker in memory of “MOLLIE”

The following have made gifts supporting Oncology Research in honor of those listed:
Mr. and Mrs. R.V. Schumacher, Jr. in honor of Dr. Craig Clifford & VHUP Staff

The following have made gifts supporting Oncology Research in honor of a special pet:
Mr. and Mrs. R.V. Schumacher, Jr. in honor of “ALEX”
The following have contributed gifts to the Feline Research in memory of a special pet:

Barbara Lynn Vail, M.D., V.M.D. in memory of “SKIMBLE”

THE FOLLOWING CONTRIBUTED TO THE DEAN’S FUND:

In honor of those listed:
Ms. Beth E. Fand in honor of Dr. Julie Robb
Letitia O. Principato in honor of F.D. Masiocco, D.D.S.
Brooke Roberts, M.D. in honor of my friends at the Veterinary School, past and present

In memory of a special pet:
Mr. and Mrs. Peter Hanos in memory of “MAURICE”

GIFTS WERE MADE TO VETERINARY STUDENT SCHOLARSHIP:

In memory of those listed:
Karen Kessler, V.M.D. in memory of Eric Tilluners, V.M.D.
Dr. Jacob Kolodner in memory of Israel Kolodner
Julie M. Dade in memory of Dr. Thomas J. Jones

In memory of a special pet:
Ms. Jolita Campbell in memory of “BEAR”
Ms. Catherine H. Giorgio in memory of “BODO HAAS”
Miss Kathleen M. Lombard in memory of “BARON” & “CHARLIE”
Ms. Corita A. Peabody in memory of “PUPPY PEABODY”
Susan V. Westmoreland, V.M.D. in memory of “RUBY”

In honor of a special pet:
Ms. Cindy H. Davis in honor of “CHESTER”
The following have contributed gifts to the Karen Spiegel Memorial Fund in memory of Karen Spiegel, V.M.D.:
Ms. Maureen M. Spiegel

The following have contributed gifts to the Dr. David H. Knight Memorial Fund in memory of Dr. David H. Knight, V.M.D.:
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Jeffrey A. Wortman, V.M.D.
Ms. Zoe D. Zampana

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Marsha and Jeffrey Perelman in honor of Dr. Susan Volk
Dogs fed a reduced-calorie diet live longer

By Stephen Bradt

A 14-year study of canine diet and health has found that dogs fed a calorie-restricted diet live a median 1.8 years longer than dogs allowed to eat more and are slower to develop chronic diseases such as osteoarthritis.

The findings add to the growing body of evidence that caloric restriction in a wide range of species significantly boosts longevity. Dogs are the only large mammals—and the closest human relatives—for which a diet-restriction study has been completed. Similar studies involving primes are ongoing.

The results, from scientists at the Penn’s School of Veterinary Medicine, Nestle Purina PetCare Company, University of Illinois, Cornell University and Michigan State University, was the subject of a Sept. 20-21 symposium in St. Louis. Partial results were published in May in the Journal of the American Veterinary Medical Association.

The study involved 48 Labrador retrievers from seven litters. Littermates were paired, with one dog fed 25 percent fewer calories than its sibling starting at 8 weeks of age. The researchers found a median life span of 13 years among dogs whose food intake was reduced, while dogs in the group fed a diet higher in calories were uniformly overweight and had a median life span of 11.2 years.

“Impressive as they are, the life span figures are only part of the story,” said Gail K. Smith, professor of orthopedic surgery and chair of the Department of Clinical Studies at the School. “The study also showed that lean body conformation forestalls some chronic illnesses, most notably osteoarthritis, and that diet can either mitigate or exacerbate the expression of genetic diseases.

“This study should reinforce for dog owners the importance of keeping their dogs lean, with palpable ribs and an obvious waistline,” Smith said. “Avoid giving dogs too many high-calorie treats and consider a brand of balanced dog food formulated to be low in caloric content while providing a sense of satiety.”

Smith said that while simply reducing a dog’s food intake, as in this study, can also be effective in maintaining a healthy weight, this approach often leads to begging—a behavior that many owners find themselves unable to resist in their canine companions.

The team of researchers has reported previously that the onset of osteoarthritis, an often painful and occasionally debilitating condition for many large-breed dogs, was delayed significantly by reduced food intake. Overall frequency of the condition was also reduced: At age 2, only one of 24 calorie-restricted dogs had developed radiographic osteoarthritis of the hips, compared to six of 24 dogs in the unrestricted group. By age 10, six restricted dogs (42 percent of that study group) and 19 unrestricted dogs (79 percent of that study group) had hip osteoarthritis.

“Dogs in the calorie-restricted group didn’t require treatment for osteoarthritis until a mean age of 13.3 years, fully three years later than the dogs in the control group,” Smith said. “Because osteoarthritis is painful, this deferral represents a substantial boost in quality of life.”

Caloric restriction also significantly delayed the onset and severity of other ailments. Dogs on a restricted diet who developed such conditions were 2.1 years older, on average, than their overfed counterparts.

Dietary restriction has been shown to have a positive effect on the life span of rodents and invertebrates. Research spanning decades has found that dietary restriction is the only nutritional change that consistently extends the life span of animals.

Smith was joined in the study, funded and conducted by Nestle Purina PetCare, by Darryl N. Biery at Penn; Richard D. Kealy, Dennis F. Lawler and Joan M. Ballam at Nestle Purina; Elizabeth H. Greeley and Mariangela Segre at Illinois; George Lust at Cornell; and Howard D. Stowe at Michigan State.

The following have made gifts supporting the Dr. Josephine Deubler Bridge in honor of Dr. Josephine Deubler
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Randi Semanoff and Family in memory of "TIMBERLYN & WHITE OUT" AKA "TIMMY"

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Patricia Hall
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Elizabeth McNamara
Timothy Rupe
Mark Stuart
Helma N. Weeks
Andrea Withers

The following have made a gift in memory of "TRAPPER," beloved horse of Anne Katein:
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Jim Morelli
Cleen Murphy
Nancy & Stephan Murphy
Sandy O’Brien
Monicah Otieno
Karen Palermo
Deb Wescott

Some recently published papers


Animal Crackers

Free-Roaming Cats

It has been estimated that nearly half of the cat population consists of unowned, free-roaming and not neutered animals. A lot of the cats live in feral colonies and are provided with food by caregivers. Trap-neuter-return programs are one of the methods being used to control the problem. Traps can be borrowed from animal welfare organizations who will perform the neutering. The cats are then returned to the area where they were trapped and where there is a caregiver. Removing the tip on an ear has become internationally accepted as the sign of a neutered free-roaming cat.

The American Veterinary Medical Association's position statement on abandoned and feral cats supports action aimed toward reducing overpopulation. Among the recommended requirements are education and training of caregivers, restricting colonies to an area away from wildlife and screening for infectious diseases.

Further information may be obtained from a local SPCA. They may have traps available. There are many different opinions about what to do about overpopulation. The spay-neuter program is a step in the right direction.

West Nile Virus

West Nile Virus (WNV) was first identified in Africa (Uganda) in 1937 and appeared in New York City in 1999. At first, only humans, horses and birds were considered susceptible. Most human infections are mild with flu-like symptoms. In horses, the most common sign is weakness in the hind legs. Infected birds are most often found dead. Studies in dogs suggest they are susceptible to infection, but do not develop clinical signs of disease. Antibodies to WNV have been reported in cattle but to clinical signs were described. WNV has been isolated from a cat with neurological signs.

Mosquitoes transmit the virus through bites. The disease is not transmitted directly from person to person, person to animal, animal to animal or animal to person. It has been estimated that less than 1% of people bitten by an infected mosquito become ill. New information is published almost daily. It appears that horses are more severely affected.

There is a vaccine for horses. Prevention requires limiting exposure to mosquitoes and elimination of mosquito breeding sites (areas of standing water).

Testing for WNV in pets is available at Cornell Diagnostic Lab.


Book Reviews


This is an excellent all-purpose basic book beginning with what to consider when adding a dog to the household and continuing with advice about selection, care, training, health as well about AKC events if you become interested in competing in conformation, obedience, agility and other events. Any fancier can find something of interest. There are excellent drawings covering anatomy and faulty conformation. Ten different tails are shown. Abbreviations for AKC titles are given—25 are prefixes and 42 are suffixes. A glossary defines commonly used terms. There are excellent photographs throughout, some in color.

From the text—“When you select a breed, be sure that the adult is what you really want… A part of being a responsible dog owner is making sure your dog has proper identification … AKC Companion Animal Recovery (CAR) is dedicated to providing lifetime recovery service for microchipped and tattooed pets, regardless of species, age or size… AKC Website (www.akc.org) will teach you what you need to know about specific breeds… The American Kennel Club has been the dog breed expert since 1884.”

New Secrets of Successful Dog Show Handling by Peter Green and Mario Migliorini. Alpine Publications. $19.95

This book covers what is involved in showing dogs, from assessing show potential through conditioning, training, trimming and ring techniques. Numerous photographs show proper presentation.

The authors have many words of advice for the novice handler, particularly the importance of observing other dogs and handlers as well as knowing all about your breed. It takes time and hard work but the amateur can do as well as the professional if he or she masters the art of making a good dog look its best.

Webster defines a secret as “something kept from public knowledge.” In this book, two successful handlers share their expertise with those who want to know as much as possible about handling at dog shows, particularly the amateur. Even spectators might find something of interest.

Bellwether
University of Pennsylvania School of Veterinary Medicine

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Open House

The School's biennial Open House on September 21 at New Bolton Center drew huge crowds—the estimate is that about 13,000 people came to tour the campus and to enjoy the exhibits and entertainment. It was a beautiful, sunny and warm day and New Bolton Center sparkled. People toured the new Scott Equine Sports Medicine Building, the swine facility and the Marshak Dairy in addition to the other buildings of the George D. Widener Hospital for Large Animals.
Upcoming Events

January 2003

11-18 Penn Farm Show 2003
Visit the School of Veterinary Medicine's booth at the largest indoor agricultural event in America. For information, contact Jeanie Robinson-Pownall at (610) 444-5800 x2182 or via e-mail at <jeanierp@vet.upenn.edu>.

March 2003

19 2:00-4:00 p.m.
Veterinary Medical Alumni Society Executive Board Meeting
Alumni Hall
New Bolton Center

May 2003

14 2:00-4:00 p.m.
Veterinary Medical Alumni Society Executive Board Meeting
Veterinary Hospital of the University of Pennsylvania

29-30 2003 Penn Annual Conference
Adam's Mark Hotel
Philadelphia, PA
For information, visit <http://alumni.vet.upenn.edu/pennannualconference.htm>.

Important Phone Numbers

VHUP
24-Hour Emergency Service (215) 898-4685
Specialist Clinic Appointments (215) 898-4680

George D. Widener Hospital for Large Animals
24-Hour Emergency Service and Specialist Clinic Appointments (610) 444-5800

School of Veterinary Medicine
General Information (215) 898-5438

In 2003 we will not offer the Canine Symposium and the Feline Symposium. We are evaluating the events and hope to bring back these two educational seminars in a different format to attract a wider audience.