The UW School of Veterinary Medicine helps make both animal and human lives better. Our discoveries have advanced cancer treatments, we’ve created new ways to fight the flu, and we’re a world leader when it comes to figuring out what keeps cows healthy and happy.

We have trained over half of the veterinarians in the state and serve as a resource and referral clinic for all.

Our teaching hospital provides exceptional care for animals throughout the state. Of our 27,000 patient visits last year, 80% were from Wisconsin.

Our scientists conduct 75% of the infectious disease research at UW-Madison, including work to prevent pandemic influenza.

Our livestock experts launched The Dairyland Initiative, a program that works directly with farms to optimize cow comfort, health, and production.

AnimalsNeedHeroesToo.com
A Leg to Stand On
At 10 years old, Ferguson has a new lease on life. And a new leg. Previously plagued by chronic pain due to a deformity in his lower left leg, today the rescued miniature donkey is standing strong after receiving the first amputation with a prosthesis at UW Veterinary Care’s Morrie Waud Large Animal Hospital. Page 9

A Shot at Preventing Cancer
Can a vaccine prevent cancer before it starts? The UW School of Veterinary Medicine is part of a clinical trial now underway to evaluate a vaccine strategy for the universal prevention of canine cancer, utilizing the body’s own immune system to mount a watchful defense. Page 14
Thank You All!
Welcome to the winter issue of On Call.

In this issue, we highlight many of the latest advances at the School of Veterinary Medicine and, importantly, we dedicate the magazine to the many friends, alumni, and donors who support all that we do here at the school.

Whether it is improving our students’ education, enhancing the research that we conduct to benefit both animal and human health, or improving the excellent care we provide to the nearly 27,000 patients who visit our hospital, our success is dependent on the support of friends such as you. With heartfelt gratitude, I thank you for your support, generosity, and leadership.

You will find in this issue several highlights of the transformative research our faculty are conducting here at the school. We’ve launched the Vaccination Against Canine Cancer Study, the largest clinical trial conducted to date in veterinary medicine. Two recent discoveries carry important implications for potential therapies for bladder-related diseases and for female infertility. And Professor Yoshihiro Kawaoka and his team have developed a new tool called FluVision that allows scientists for the first time to witness influenza infection in a living animal and better understand how the body responds.

Notable stories from our hospital include the adorable Ferguson, the first large animal to receive an amputation and prosthesis at UW Veterinary Care, and a blue crane named Periwinkle who received life-saving surgery and is now reunited with her mate Kito at the International Crane Foundation.

We continue to remain focused on providing an outstanding education to our veterinary medical students and graduate students, and on preparing these cohorts — as well as pre-college students — for the broad array of career possibilities in our amazing profession. Along these lines, this summer we were able to host seven local high school students for an internship in our teaching hospital through a Madison Metropolitan School District program focused on careers and curriculum in the health sciences.

Lastly, each year the school is proud to produce an annual report detailing the impact of the school’s accomplishments across teaching, research, clinical care, and public service. I hope you will take a moment to read our 2018 report with pride, viewable at vetmed.wisc.edu/annual-report-2018.

Enjoy the winter issue of On Call!

Mark D. Markel, Dean
Concerns About FIP in Multi-Cat Household

This expert response comes from Michael Wood, board-certified specialist in small animal internal medicine and clinical assistant professor.

**Question:** In February our kitten stopped eating and went into complete kidney failure. Because of her stunted size, our vet tested her markers for feline infectious peritonitis (FIP) and they came back over 2,000. We had no choice other than to put her to sleep. We still have her littermate sister, who has been healthy, as well as a four-year-old cat. We were thinking of bringing in another young cat, but I’m terrified at the thought of losing another to what may have certainly been FIP. I have done extensive research on this disease and just about every article quotes a different amount of time to wait. What is the general consensus among staff there for the waiting period?

**Answer:** Unfortunately there is not a set timeframe by which you can ensure that your cats (or cats introduced to your household) will not develop FIP. FIP is caused by a variant of feline coronovirus (FCoV) that is ubiquitous in cat populations. FCoV usually causes either no signs or mild gastrointestinal signs like diarrhea. Upon exposure to the virus, most cats are either resistant to the virus or are transiently affected and shed the virus for months before returning to normal. However, about 10 percent of cats will chronically shed the virus in their feces. These cats may show no clinical signs while others will develop chronic diarrhea as they age. While these cats rarely develop FIP, their persistent shedding of the virus can infect cats that contact their feces.

Given that you have had a cat in your household with FIP, I would be suspicious that all of your cats have been exposed to FCoV and that perhaps one of your cats may be a chronic shedder of the virus. This does not mean your cats will get FIP, as the virus undergoes the necessary mutation to cause FIP in only one to three percent of cats. However, it does mean that if one of your cats is a chronic shedder, your ability to permanently eradicate FCoV from your household is low.

There are measures that may reduce the risk of FIP, but they involve identifying and separating FCoV-shedding cats from their uninfected housemates. If a household of cats was tested as FCoV-free, then it is possible to reduce the risk of FIP by screening any new cats for FCoV before introducing them to the household.

Questions

Have a question for our veterinary medical experts? Please send it to the On Call editor at oncall@vetmed.wisc.edu. We cannot guarantee responses to all submissions. For any urgent pet health issue, please contact your veterinarian directly.
A Leap Forward for Local High School Students

For six weeks this summer, seven incoming juniors from the Madison Metropolitan School District (MMSD) gained hands-on skills in the UW School of Veterinary Medicine’s small animal hospital. Their work was part of LEAP Forward, a paid internship hosted by UW–Madison and MMSD to expose high schoolers to careers and curriculum in the health sciences.

For Lizzy Schmidt, a junior at La Follette High School, the opportunity was a “once in a lifetime experience” that showed her what it’s like to be a veterinarian. Now she hopes to become one in the future.

UW Veterinary Care was one of the only internship sites on campus that allowed interns to work in an actual clinical setting. The students had many responsibilities including documenting patient data, cleaning and stocking examination rooms and wards, assisting veterinary technicians, and interacting with animals. Ruthanne Chun DVM’91, director of UW Veterinary Care, says the program also got high schoolers outside of their comfort zones and taught them practical skills beyond the medical field.

Schmidt is a testament to the internship’s impact. “I’m a very shy person and I don’t like asking for help,” she says. “But by being in this environment, I’ve learned that you have to put yourself out there and you have to know how to ask a lot of questions.”

Kayla Huynh

School Says Farewell to Three Exceptional Teachers and Mentors

After 28 years of service to the UW School of Veterinary Medicine (SVM), Linda Sullivan DVM’87, an alumna of the inaugural SVM class, retired in July.

As a clinical instructor in the Department of Pathobiological Sciences, Sullivan led the laboratory sections of a broad range of courses including bacteriology, parasitology, and clinical pathology. In addition to her impact in the classroom, students could always count on Sullivan for a sympathetic ear and wise counsel.

Sullivan also served as the long-time coordinator of the Dog Jog, a two-mile walk/run founded by the SVM’s inaugural class that raised more than $500,000 over 30 years for Madison-area shelters and humane organizations. She plans to return to the classroom occasionally and will continue her work with Pet Pals, a program that brings volunteer dogs to visit pediatric patients at American Family Children’s Hospital in Madison.

Tim Yoshino, a professor of parasitology, also retired this fall after 30 years at the SVM. Yoshino served as coordinator and instructor for the Veterinary Parasitology course and led a research laboratory, funded by the National Institutes of Health (NIH) for more than 35 years, studying the cellular and molecular interactions between parasites and their invertebrate hosts. His research into schistosomiasis — a disease that infects more than 200 million people worldwide — provided important insights for global human health.

Yoshino was also the long-time director of the NIH-funded Parasitology and Vector Biology Training Grant, which supported the research training of many graduate students and postdoctoral trainees at UW–Madison.

Finally, Michael Collins, a professor of microbiology, will retire in January after 36 years with the school. Collins, who was part of the original cohort of SVM faculty, has long taught the Veterinary Bacteriology course. His innovative and engaging teaching style has equipped thousands of students with practical knowledge of the bacterial pathogens they will encounter in veterinary medicine.

Collins is a global leader in the study of paratuberculosis, or Johne’s disease, a prevalent, costly infectious disease affecting cattle and other ruminants. His research has revealed new information about the causative agent behind the disease and led to improved methods of detection. He ran the Johne’s Testing Center that handled more than 20,000 clinical samples annually (in anticipation of his retirement, Johne’s testing has shifted to the Wisconsin Veterinary Diagnostic Laboratory).

Collins will continue to oversee the Johne’s Information Center website (johnes.org), which provides comprehensive, scientifically reviewed information on disease prevention, treatment, zoonotic potential, and more.
Becoming Bladder: Cells Regenerate and Now We Know Why

The bladder is a master at self-repair. When damaged by infection or injury, the organ can mend itself quickly, calling upon specialized cells in its lining to repair tissue and restore a barrier against harmful materials concentrated in urine.

But a new study in mice from researchers at the UW School of Veterinary Medicine (SVM) shows for the first time that non-bladder cells from a nearby anatomical structure called the Wolffian duct can actually provide an assist. It can contribute cells that migrate to the bladder, adopt bladder-like characteristics, and help restore the organ’s function.

“We saw these other cells come in to compensate for the loss of bladder cells,” says Diya Joseph, a UW–Madison doctoral student and lead author of the study, published in July in the Proceedings of the National Academy of Sciences.

The surprising discovery carries important implications for potential therapies for bladder-related diseases and for patients’ quality of life related to bladder function and incontinence. These are often overlooked areas of study, says Chad Vezina, professor of comparative biosciences at the UW SVM, who led the new work.

In the study, the research team was investigating the role of a specific gene called DNA methyltransferase 1 (Dnmt1). This gene modifies cell behavior during bladder and urethra development in mouse embryos. By removing it, Joseph says, the scientists could better understand the role the gene plays in the formation of the urinary tract.

“The organ is saying ‘I need help.’ And neighboring cells come in to make an assist.”

The team is now working to identify the specific cues that marshal this defense, as well as opportunities to utilize those cues for improved bladder replacement therapies. For instance, the researchers would like to know what signals the bladder epithelium is producing that results in the reprogramming of Wolffian duct cells. “Those signals could maybe be used to convert stem cells to bladder-like cells, and then you could use those cells to make an artificial bladder,” says Joseph.

Vezina notes that this helping-hands relationship could also exist between other organs, opening new avenues for exploration: “Now as researchers try to figure out ways to regenerate and repair tissue, we don’t need to only think about that specific organ. This might be something that happens elsewhere too.”

Meghan Lepisto

In Memoriam

Rudolf “Tass” Dueland, a founding faculty member of the UW School of Veterinary Medicine and former chair of the Department of Surgical Sciences, passed away in September. Throughout his career, Dueland taught hundreds of students, impacted the lives of thousands of animals with his medical and surgical skills, advanced orthopedic research through the publication of approximately 70 scientific papers, and received a U.S. patent for his work measuring hip dysplasia in dogs.
Cellular Communication System Helps Control Female Fertility

Research published in August in the journal *PLOS Genetics* provides a new piece of the puzzle of female infertility. Joan Jorgensen DVM’93 of the UW School of Veterinary Medicine, graduate researcher Anqi Fu, and others discovered that two genes work together to construct a cellular communication system in the ovaries of mice to maintain healthy eggs.

The researchers describe this system as a series of junctions between the eggs and the cells that surround and support the eggs, known as granulosa cells. Both reach out to form multiple junctions that exchange information and ensure the proper development and survival of the egg leading up to ovulation.

Jorgensen, an associate professor in the Department of Comparative Biosciences, looks to build off the findings to uncover more information on fertility problems like premature ovarian failure. This condition leads to an early loss of viable eggs and affects as many as three percent of all women, according to the National Institutes of Health. In most cases, the cause is unknown. Problems with the development of follicles — the combination of an egg and its surrounding granulosa cells — are likely behind many cases of premature ovarian failure.

Jorgensen’s lab had previously found that mice missing two genes, Irx3 and Irx5, had defective follicles. In the current study, they looked for how these genes work together to keep follicles healthy. Jorgensen and Fu collaborated with researchers at the University of Melbourne, Monash University, and the University of Toronto to complete this work.

The researchers showed that mice with either Irx3 or Irx5 deleted had fewer pups, which led the team to suspect that communication within the follicle was breaking down. Looking within the ovary, they tracked the expression of each gene.

Early on, the researchers saw that Irx3 and Irx5 were expressed throughout the follicle. But as the follicle began to mature, Irx3 became isolated to the egg, while Irx5 was only expressed in the granulosa cells.

From their separate vantage points, these two genes synchronize the two cell types to help them establish communication networks. Jorgensen’s team saw that the granulosa cells and the eggs extend parts of their membranes to form junctions with each other. These junctions allow signals to be transported in both directions. With Irx3 or Irx5 deleted, these junctions fell apart, interrupting communication within the follicle and destabilizing it.

“We think of Irx3 and Irx5 as the supervisors in connecting these two cells,” says Jorgensen. She and Fu say the next step will be to evaluate exactly how these genes direct these key cell-to-cell interactions.

“If we can figure out how those networks are placed, we think that will be a major step in understanding the basic foundations of how follicles are built,” says Jorgensen. “That will go a long way towards helping women that have infertility, especially those that undergo premature ovarian failure.”

Tyler Fox
A Leg to Stand On

Previously plagued by a leg deformity, Ferguson is now standing strong with an artificial limb — the first large animal to receive an amputation and prosthesis at UW Veterinary Care

The crowded surgery room hums with excitement as a rotary saw buzzes through the fiberglass cast encasing the left front leg of a supremely cute, extra fuzzy, little-bit-sassy miniature donkey. More than 20 surgeons, veterinary technicians, students, and other observers have gathered to see the small but mighty Ferguson fitted with a custom-made prosthesis.

Five weeks earlier, the 10-year-old donkey’s disfigured lower left leg was amputated at the fetlock. The procedure was the first amputation with a prosthesis at UW Veterinary Care’s Morrie Waud Large Animal Hospital.

Ferguson — or Fergie for short — may not know that he’s made history, but he’s certainly aware of his ever-growing fan club. During his extended stay in the teaching hospital, he gained an affinity for handfuls of sweet feed, crisp carrots, and frequent neck scratches. Now back at Holyland Donkey Haven near Fond du Lac, Wisconsin, where he will have lifelong sanctuary, he is the object of daily adoration from both people and fellow donkeys, frequently seen scratching the neck of his equine stablemates as they return the favor — mutual grooming that he wasn’t strong enough to do pre-amputation.

Simply put, Ferguson’s leg deformity could have cut his life short. Amputations are rare in equids and other four-legged large animals due to their size and fight-or-flight nature. “They need four legs that they can run around on at all times,” says Samantha Morello, clinical associate professor of large animal surgery at the UW School of Veterinary Medicine. And amputations of front limbs, which bear about 60 percent of a four-legged animal’s weight, are even more challenging and extremely rare as a result.

But Ferguson was a special case. His easygoing, sweet demeanor and his petite stature (he weighs about 250 pounds), combined with the tremendous pain he was experiencing due to the chronic leg deformity, made him a perfect candidate for a prosthetic device according to Morello.

“It’s his best shot at getting back to a good quality of life,” she said in April ahead of Ferguson’s surgery.

In the photos that follow, see this rescued donkey’s extraordinary journey.
1: When Ferguson was rescued by Holyland Donkey Haven in 2015, his hooves were overgrown and he could barely walk. Holyland brought Ferguson to UW Veterinary Care for evaluation and advice, then worked with their local farrier to reconstruct his deformed left front hoof through trimming and corrective shoeing every four weeks over several years. But in spring 2018, with the deformity still present (pictured) and causing substantial pain, UW Veterinary Care large animal surgeons determined that a partial limb amputation was the best path forward. “No less aggressive measure is likely to provide the comfort and stability that he needs in that limb,” said large animal surgeon Samantha Morello, who led the operation.

2: Ferguson’s chronic pain caused him to walk in an irregular way that placed pressure on the skin and soft tissue at the base of his heels. This subsequently began to cause deformity in his right hoof, as well. To help realign Ferguson’s conformation and balance his weight, in March UW Veterinary Care farrier Dean Johanningmeier trimmed Ferguson’s right hoof and attached a special shoe (similar to a human orthotic). This was a critical step for the amputation to proceed. “That provided a good foot to stand on,” said Morello.
Radiographs revealed that the bones in Ferguson’s lower left leg (pictured) were chronically deformed and infected and of a different density than those in his right leg. Veterinarians believe the middle phalangeal bone, which normally extends into the hoof capsule, may have been missing from Ferguson’s left leg since birth.

Holyland Donkey Haven did everything possible to manage Ferguson’s left front hoof deformity, but exposed soft tissue and abscesses were an ever-present concern and source of pain. Before his amputation, Ferguson spent the majority of his days lying down due to discomfort.

On April 18, Ferguson’s lower left leg was amputated below the cannon bone, at the fetlock joint. Here a member of the surgical team uses sterile solution to clean the amputated limb, which after several weeks of healing in a cast became the stump for Ferguson’s prosthesis.

Immediately following the amputation, a team from the UW Health Orthotics and Prosthetics Clinic made a mold of Ferguson’s left leg and took measurements of both limbs to plan the construction of a custom-fit prosthetic foot. Next (not pictured), Morello placed two large stainless steel pins through the cannon bone of the left front leg. These pins were incorporated into a cast placed around Ferguson’s leg for five weeks, helping to distribute weight away from the healing stump.

On May 23, Ferguson’s leg cast and pins were removed and he was fitted with the prosthesis. Here, Amy Paulios (center) of UW Health checks the height and angle of the bottom of the artificial limb as compared to Ferguson’s right hoof. The team also ensured that Ferguson could fully flex his leg without rubbing and that the prosthesis was easy to put on and take off. “It’s a perfect fit,” Morello (left) said as the device was slid on. “It’s so cool.”
Orthopedic surgeons at the SVM also assisted in Ferguson’s case, using the school’s 3D printer to create plastic models of the bones that were to be amputated. These 3D-printed bones, modeled off of radiographs of Ferguson’s right front limb, were placed in the left leg cast below the amputated stump to help mirror the height of the sound leg.

Amy Paulios, a board-certified prosthetist, holds an early iteration of Ferguson’s prosthetic device (she later added additional, stronger straps, along with a clamshell backing to create a cleaner, closed environment). This was Paulios’ first time producing a prosthesis for an animal. Constructed of carbon fiber and acrylic resin, it’s light to allow for easy movement, while durable enough to withstand outdoor elements. She was assisted with socket fabrication by Patrick Shea at UW Health and Beau Marek at the Hanger Clinic. “I’m proud of our teamwork,” she said.

Just minutes after being fitted with the prosthesis and waking from anesthesia, Ferguson was on his feet, standing strong on the prosthetic device. “You got a brand new foot,” said Angela Langoski (left), founder and president of Holyland Donkey Haven. Throughout Ferguson’s stay at the hospital, Langoski made the 90-minute drive to UW Veterinary Care at least twice a week.
On June 13, the day before Ferguson headed home to Holyland, Morello and large animal surgery resident Kelly Shaw took the valiant donkey out for a final jaunt. “He’s walking so well,” Morello said as she strolled beside him. While Ferguson grazed and basked in the sun, the surgeons reflected on his journey. “It takes a special patient to be able to come through and do well,” Shaw said. “It’s a testament to Ferguson and his toughness and tenacity.”

“There’s an inverse relationship between Ferguson’s personality and his size, and that personality has just grown with every day that he’s been recovering,” Morello added. “We knew that his attitude was going to be what saved him as much as anything else.” Morello is grateful for the chance to assist Holyland and credits the group’s unwavering dedication to Ferguson. “It’s been an awesome opportunity for a group effort to do the right thing.”
Could the body’s own immune system be primed to prevent cancer through a quick vaccine?

A clinical trial launched this fall aims to bring new clarity to this complex question.

“We’re testing a totally novel way of creating an anticancer immune response,” says David Vail, a board-certified oncologist with UW Veterinary Care.

The Vaccination Against Canine Cancer Study will evaluate a vaccine strategy for the prevention, rather than the treatment, of cancer in dogs. With more than 800 patients enrolled as participants, it is the largest clinical trial conducted to date for canine cancer and across the history of veterinary medicine.

The UW School of Veterinary Medicine is one of three participating institutions, together with Colorado State University and the University of California, Davis.

Cancer is the number one cause of illness and death in the aging dog population, with approximately one out of every three dogs affected and six million new cancer diagnoses made in dogs each year. If the trial is successful, it could not only provide a new strategy to prevent a critical health concern in canine companions, but it could also provide justification for studying a similar approach in people.

“The holy grail would be to prevent cancer as opposed to waiting for it to start and then treating it,” says Vail.

Much like an influenza vaccine bolsters the body’s readiness to fight the flu, this preventative cancer vaccine follows the same principle — “to have the immune system primed such that if a cancer cell develops, it will attack,” Vail says.

Traditionally, vaccines work by introducing into the body a protein found on the surface of the virus that the vaccine is protecting against. The immune system sees the protein as a threat, establishes a memory of it, and then, if there is a later infection, recognizes that protein and is primed to react.

“It’s almost like putting up a wanted poster for that particular virus,” Vail explains. “When that virus infects you, then the immune cells recognize it because of the ‘poster,’ go out, and kill it.”

The anticancer vaccine now being tested targets approximately 30 abnormal proteins found on the
surface of cancer cells. These proteins, a result of improperly coded RNA (so called frame-shift mutations), are generally only found in patients with cancer (both dogs and people) and are agnostic of cancer type, meaning that a patient with breast cancer has the same abnormal proteins as a patient with bladder cancer. By injecting this cluster of proteins into healthy patients, along with a substance that stimulates an immune response, it’s theorized that the vaccine could serve as a universal defender against cancer by “turning on” the immune system.

“Those proteins act as the wanted poster for the good guys, the killer cells, to be primed so that if they ever were to see that abnormal protein develop in a patient, they’re already primed to recognize it as bad,” Vail explains. “They have little receptors that will fit that protein, come along and attack the cancer cell, and essentially explode the cell.”

Stephen Johnson, a professor at Arizona State University and director of the Center for Innovation in Medicine, developed the technology behind the vaccine.

Several cancers that are common to dogs are targeted by the vaccine, including lymphoma, a cancer of the lymphatic system; osteosarcoma, or bone cancer; hemangiosarcoma, a deadly cancer that originates in the blood vessels and is almost exclusive to dogs; and mastocytomas, or mast cell tumors.

The potential to preventively target several types of cancer at the same time with a single vaccine series would be a revolutionary development and a major paradigm shift in veterinary and human medicine, according to Vail.

“It’s a whole new way of looking at anticancer vaccines,” he says. “The key is that you don’t have to personalize the vaccine to an individual, which is a very expensive proposition. This is more of a global vaccination.”

The trial is slated to run over five years, with cancer-free, healthy dogs between the ages of six to 10 randomized to receive either a series of the investigational vaccine or placebo vaccines. Two sets of vaccines will be given every two weeks, for a total of four treatments, and then annually. While no side effects other than those typical to any vaccine, such as moderate local pain or swelling at the site of injection, have been observed in mice or dogs to date, the study will also characterize any unanticipated adverse reactions in the larger study population.

Participating dogs will live at home and be checked two to three times yearly for five years after enrollment to monitor for the development of any cancers. This medical care will be covered by the study, which is funded by a $6 million grant from the Open Philanthropic Project. About 280 dogs will be treated at UW Veterinary Care, with the remainder of participants at the other two trial sites.

“Even if a patient is randomized to the placebo group, they will enjoy five years of the best medical care available at no cost,” Vail notes. “And funds are available to diagnose and treat cancers that may develop in dogs in both the treatment and placebo group.”

A number of anti-cancer vaccines have been developed in recent decades, including by researchers at UW–Madison, for the treatment of cancer after it has been diagnosed. But those vaccines are tailored to a specific cancer type and are often produced for an individual patient, making broad deployment worldwide both time- and cost-prohibitive.

“It would be far superior of course to prevent a wide range of cancer types before they develop,” Vail says. “There will be nine million human deaths resulting from cancer in the world this year, with 70 percent of those patients in poor or third-world countries, where there’s no way they could afford the type of cancer treatment currently available. A preventative vaccine can be applied globally at low expense, so this could have a tremendous effect.”

Initial trials of the vaccine in mice suggest that this new strategy could be successful, but many in the scientific community remain unsure.

“It’s so outside of the current box, but that’s how breakthroughs and paradigm shifts happen,” says Vail. “Based on what we know right now about the immune system, there are several reasons why this vaccine shouldn’t work and there are several reasons why it could work.”

“I go in with healthy skepticism, but if this works, or even if this is one step in the correct direction, I will be thrilled,” he adds. “With the possibility to prevent several cancer types before they develop, somebody absolutely needs to do the study.”

And, Vail notes, the array of information gleaned throughout the trial will advance scientists’ understanding of cancer, the immune system, and how it responds.

“This is a team project involving dozens of researchers across the country and hundreds of pets and pet owners. We’re so thankful that they’re with us and that they want to strive to push the envelope as far as what we can do to prevent cancer in the future.”
Scientists Take a Journey Into Lungs Infected With Influenza

In the 1966 novel, *Fantastic Voyage*, written by biochemist and author Isaac Asimov, a crew of people become miniaturized in order to travel through the body of a scientist and save him from a blood clot in his brain.

For University of Wisconsin-Madison virologist and flu expert **Yoshihiro Kawaoka**, recently seeing real, active influenza infection in the lungs of living mice for the first time was reminiscent of this 50-year-old piece of science fiction, which was also adapted into a film.

Publishing in the *Proceedings of the National Academy of Sciences*, Kawaoka and his team describe a new tool they call FluVision, which allows them to witness influenza infection in a living animal in action. Moreover, it provides a window into a world none have seen before, allowing scientists to observe and better understand what happens when a virus infects the lungs and the body responds.

“Now we can see inside of the body in real time in virus-infected animals,” says the professor of pathobiological sciences and faculty trainer in the Comparative Biomedical Sciences graduate program at the UW School of Veterinary Medicine. “It’s like we can shrink and go inside the body.”

In so doing, the scientists have documented differences in the action of two different strains of flu, witnessed influenza viruses as they spread in the lungs, showed a reduction in blood flow in infected areas of the lungs, watched the activation and behavior of immune cells called neutrophils, and revealed some of the damage that can be caused by infection with a highly-pathogenic flu strain.

Notably, infection with a highly pathogenic strain of influenza — the “bird flu,” H5N1 — proceeds more quickly and causes more damage than infection with a milder, mouse-adapted human strain — H1N1.

Pathogenicity refers to the ability of a virus to cause disease.

To microscopically peer inside the lungs of living mice, Kawaoka’s team had to overcome several challenges. The first was to find technology that allowed them to see through the lungs. Another group had pioneered this with an approach called two-photon excitation microscopy, and Kawaoka’s team adapted it for its study.

The team had to build a system that allowed it to work with influenza viruses at a high level of biosafety — biosafety level three — while also allowing technicians access to the laser source required to see objects of interest in the lungs. Lead author Hiroshi Ueki helped design a system in which the laser is located outside of the high-containment lab space, aimed through a small glass window to a microscope inside the lab, all built on stabilized platforms that had to be physically separated but virtually connected.

Kawaoka’s team also had to create fluorescently labeled viruses that could be used to infect the mice and viewed with the laser under the microscope, but which also functioned similarly to viruses found in nature. They call the technology Color-flu.

In addition, the researchers had to develop a method for keeping a portion of the lung still while the mouse breathed so they could get high-quality images and videos. The team had a small, custom-crafted device made called a thoracic window, which Kawaoka says has been patented, that uses a vacuum to stabilize a small portion of surgically exposed lung during imaging.

For the study, the researchers infected mice with either fluorescently labeled H5N1 or H1N1. Two days after infection, they could see cells in the lung infected with virus particles. The numbers of these cells reached their peak three days after infection and were higher in H5N1-infected lungs.

Blood flow in the capillaries of influenza-infected lungs slowed down after infection with either virus, though to a lesser extent in H1N1-infected mice. This suggests the viruses affect the vascular system before causing lung damage.

The lungs of mice infected with H5N1 also became “leaky” two days after virus exposure, whereby the contents of the capillaries permeated into the tiny air sacs of the lungs, called alveoli. This was also associated with an increase in the number of dead cells in the lungs.

“Clearly, something is wrong with the pulmonary capillaries,” says Kawaoka, who is also a professor at the
University of Tokyo, where the work was performed. “The reason why we see this leakage is that the junctions between endothelial cells (which make up the vessels in the lungs) loosen for some reason. We have documented this for the first time.”

Studying the mechanisms of infection can be something of a chicken-and-egg endeavor, because once infection starts, so does the body’s response, triggering a cascade of actions that can also cause some of the damage associated with the pathogen. Some of it, like the pulmonary leakiness Kawaoka’s team observed, may help the body respond, he says.

His team chose to look at immune cells called neutrophils, one of the body’s first lines of defense. Their action can cause inflammation. In mice infected with H5N1, neutrophils were recruited to the lungs on the first day after exposure, becoming six times more prevalent. They doubled in the lungs of mice infected with H1N1.

After the number of influenza-infected cells peaked on day three, neutrophil numbers dropped, but those that remained behaved differently than neutrophils in healthy mice.

The team found that neutrophils show two kinds of motion: slow and rapid. In influenza-infected lungs, the neutrophils that remained after the peak day showed a decrease in rapid motion and spent more time moving slowly, as if scouting for infected cells.

“We don’t yet know why and what they’re doing,” says Kawaoka, but, he notes, this is the first time this behavior has been documented. And for him, it is motivation to dig even deeper, and adapt the technology for other respiratory viruses.

“We are seeing the mechanisms of the immune system at work,” he says. “These are the things you discover and it’s exciting, but now we have to figure out what’s going on.”

Kelly April Tyrrell

FluVision provides a window into a world none have seen before, allowing scientists to observe and better understand what happens when a virus infects the lungs and the body responds.

From the CBMS Director

Celebrating Students and Training of the Highest Caliber

It is hard to fathom that five years have passed since I assumed the directorship of the Comparative Biomedical Sciences (CBMS) graduate program. It has been an exciting time to pilot the program and I am pleased to report on its current state. I am delighted that CBMS continues to garner the distinction of a top 10 national ranking among 51 programs in veterinary medical sciences, according to the Academic Analytics database.

In parallel with the constantly changing academic landscape, CBMS has evolved into a dynamic and vibrant interdisciplinary graduate program. The range of training spans the fields of infectious disease, genomics, biomedical engineering, neuroscience, oncology, and developmental biology at the cutting edge of each discipline. The program currently has 95 faculty trainers from a wide array of departments at UW–Madison. Its interdisciplinary nature is a substantial strength, particularly in light of the current shift toward pursuing science as part of multi-disciplinary teams.

We continue to recruit a highly talented and diverse pool of graduate students. Notably, among the program’s current 45 PhD and 14 MS students, 12 percent are domestic underrepresented students and 36 percent are international students. Our students have successfully competed for fellowships from the National Science Foundation, American Heart Association, Morris Animal Foundation, and American Association of Immunologists, among others, reflecting the excellent caliber of students in the program.

And I am happy to share that CBMS students complete the PhD program an average of one year before our Association of American Universities (AAU) peer institutions. The average CBMS time to degree completion is currently 4.3 years compared to AAU peer data of 5.2 years. Sixty one percent of CBMS PhD students finish within five years, compared to 34 percent of all PhD students campus-wide at UW–Madison and 41 percent of all biological science PhD students. This reduced time to degree is bolstered by strong mentor/student relationships and support from the CBMS community and the School of Veterinary Medicine.

I am excited about the trajectory of CBMS and strongly believe that the program is poised for sustained success in training scientists at the leading frontiers of biomedical research.

M. Suresh
Director, Comparative Biomedical Sciences Graduate Program
John E. Butler Professor, Department of Pathobiological Sciences
Poulsen Named Director of Wisconsin Veterinary Diagnostic Lab

The Wisconsin Veterinary Diagnostic Laboratory (WVDL) has a new director. As of September 1, UW–Madison veterinarian Keith Poulsen DVM’04, PhD’12 assumed official leadership of the lab, which plays a critical role in preserving animal health and the integrity of the state’s animal production industry.

“I think we have a very important mission for the state and for the university,” says Poulsen, who had served as interim director of WVDL since March 2018. He first arrived at the agency in 2014 as a clinical professor at the UW School of Veterinary Medicine (SVM), practicing large animal internal medicine. Poulsen continues to hold a second appointment as a clinical assistant professor in the Department of Medical Sciences at the SVM.

The WVDL was first established in the early 1930s with the goal of providing animal disease diagnostic services to the state’s veterinarians and animal producers. It is located and administered by the UW–Madison campus as part of the University of Wisconsin System and is specifically funded as a line item in the state budget.

Poulsen describes WVDL as “a hybrid of a state agency and a business.” With between 120 and 130 employees, the lab runs roughly 600,000 diagnostic tests each year, handling upwards of 38,000 cases. Nine out of 10 of these cases serve the state’s bovine genetics and dairy industries.

Beyond bovines, WVDL also supports the state’s poultry industry by helping respond to outbreaks of avian influenza, participating in the federal Salmonella Action Plan and the National Poultry Improvement Plan, and playing a role in maintaining flock health. It promotes health among all other animal species as well.

Though Poulsen has a passion for animals, he says it is the people at WVDL who have helped make his new role rewarding. “We have a great team of people and we are very focused on the working culture of our organization,” he says.

Among his first priorities is investing in these people, shifting to a team-based approach, and ensuring his employees know they are valued. He is also focused on engagement, inclusion and diversity. Mark Markel, the dean of the SVM, says Poulsen helps reinforce a welcoming environment and has created a climate where people want to show up for work every day, in part because he promotes good work-life balance.

“I came to the university because I wanted to be in the marching band and when I got here I said I wanted to be a biochemistry major,” Poulsen explains. “But my advisor said I couldn’t do both, so either pick a different major or don’t....
Gratitude for the School and for You

In this season of Thanksgiving I can’t help but reflect on the many reasons I have to be grateful. Personally, I get to work on behalf of incredibly intelligent, hard-working, and compassionate people who are making a difference every day in the lives of animals and people.

From our clinics to our classrooms, from the research labs to the farms, our faculty, staff, and students are providing exceptional care to animals and their owners, making discoveries that improve animal and human health, and training outstanding veterinarians and graduate students. This issue of On Call touches on just a few ways the UW School of Veterinary Medicine is making a difference. (You can find more examples at animalsneedheroestoo.com/our-impact.)

I am also grateful for you and the many ways you give back to the school. Since 2013, nearly 450 alumni have made a gift to the school. In addition, numerous alumni participate in our Companion Animal Fund clinic sponsor program. Many of you volunteer your time by being a part of our alumni advisory board, by hosting student interns, by speaking with our students, and sharing your experience and expertise. This past year some of you have contacted your state elected officials about the importance of the school and the need for an expansion. You’ve invited us to speak with your local veterinary medical and industry groups. For all this and more, thank you.

In gratitude,

Kristi V. Thorson
Associate Dean for Advancement and Administration
In this issue of On Call, we would like to thank our individual and corporate donors by listing those who made gifts or pledges of $100 or more to the UW Foundation between July 1, 2017, and June 30, 2018. Cumulative donors, alumni of the UW School of Veterinary Medicine and the Veterinary Sciences and Comparative Biomedical Sciences graduate programs, and veterinary medical clinics that participated in the Companion Animal Fund are thanked separately.

We're Grateful for Donations Made Between July 1, 2017, and June 30, 2018

We are deeply grateful to all who have contributed. Your gifts make an impact on the lives of animals and people. Whether you have chosen to direct your gift towards studies to improve animal health, scholarships for students, facility upgrades, or an unrestricted fund that helps us meet emerging needs, your gifts go a long way. Your generosity makes the difference and allows us to maintain the school’s tradition of excellence.

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The UW School of Veterinary Medicine receives tremendous support every year from veterinary medical clinics that make a donation to our Companion Animal Fund when a client’s pet has passed away. These donations are kind and thoughtful gestures by a client’s veterinarian at times of great sadness and loss.

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We would like to thank our alumni who have donated $100 or more to the UW Foundation between July 1, 2017, and June 30, 2018, whether for the benefit of animal health or aspiring veterinarians, or simply to maintain the excellence of their school.

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“I cannot say nice enough things about the care and compassion we received! It’s clear that everyone cares about animals and their owners.”

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One Health: Myers Aids Poultry Vaccination Project in Madagascar

Laurel Myers DVMx’20 was still in elementary school when a shipment of goats to her family’s farm in Bridger, Montana, left everyone sick with fever. “So I grew up thinking of the connections between human and animal health,” she says.

This summer, Myers, a dual doctor of veterinary medicine and master of public health candidate at UW–Madison, spent a month with Madagascar Health and Environmental Research vaccinating chickens as part of a project to improve human health. Her work was supported by the first Henry A. Anderson III Graduate Student Award from the UW Global Health Institute.

“You’re improving human nutrition, avoiding environmental degradation and cutting down on disease spread,” Myers says of the village poultry health project. “Chickens are also seen as a source of women’s empowerment. Men bring in meat. Women keep chickens.”

In work that looks at the many factors that can influence health and disease, Myers and Anderson are kindred spirits. Anderson, a 1972 graduate of the UW–Madison medical school, established Wisconsin’s environmental and occupational health program.

For Myers, the idea of occupational or environmental health fits perfectly into the concepts of One Health and Planetary Health, both centered on the idea that human, animal, and environmental health are interlinked. “I really believe everything is connected,” she says.

In Madagascar, Myers put her belief into action. Chickens are an important alternative protein source to bush meat and can help protect the environment by limiting hunting. The chickens in Makira Natural Park, however, are infected with Newcastle disease, a virus that spreads through the air and can wipe out flocks. In addition to vaccinating chickens, Myers helped to educate residents about animal husbandry and food safety, and will research other communities’ responses to the disease.

While she appreciates the financial portion of the Anderson award, Myers was even more grateful for the vote of confidence. “I felt for so long that I was going into a field people were not pursuing and combining things (veterinary medicine and public health) that people weren’t combining,” she says. “It makes a tremendous amount of difference to see elders endorse what I’m doing and believe in the things I believe in.”

Ann Grauvogl
Awards & Honors

Lewin Receives Veterinary Graduate Award

Andrew Lewin, who recently completed his residency in comparative ophthalmology at UW Veterinary Care, was presented with the 2018 Boehringer Ingelheim Veterinary Graduate Award at the National Veterinary Scholars Symposium in August. The award recognizes an exemplary research project by a graduate veterinarian.

Lewin was honored for his research into infectious ocular disease and glaucoma. His work as a shelter veterinarian before starting his residency inspired him to pursue this area of focus.

As part of his research, Lewin established a nationwide network of cat shelters to provide clinical scores and eye swabs for cats with ocular and respiratory infections, helping to determine the distribution of these pathogens nationwide — something that had never been done before. He also obtained viral samples for genomic sequencing and analysis. These samples and the data set will now make other downstream analyses possible.

Dulli Awarded Compassionate Care Scholarship

Kelly Dulli DVMx’20 earned second place in the Humane Society Veterinary Medical Association (HSVMA) 2018 Compassionate Care Scholarship competition, recognizing her academic achievements and dedication to animal welfare, in particular her passion for helping community cats.

Dulli serves as veterinary student coordinator for monthly spay days at Madison Cat Project, an organization that works with area animal rescues and shelters to offer adoptions and care for feral and under-socialized cats. She is also a patient care volunteer with the Dane County Humane Society and this summer she traveled to Washington state with Rural Area Veterinary Services, a nonprofit outreach program that brings free veterinary services to underserved rural communities.

As president of the HSVMA Student Chapter at the UW School of Veterinary Medicine, Dulli led the most active HSVMA chapter in the country, overseeing several speakers, a suture lab, and a spay lab.

Support for Study of Rabies Prevention

Elsa Cardenas Canales, a doctoral candidate in the Comparative Biomedical Sciences program, earned a 2018 Graduate Student Research Award from UW–Madison’s Global Health Institute for her work evaluating the feasibility of an oral rabies vaccination for vampire bats in Mexico. The funding will allow Cardenas Canales to travel to Mexico for fieldwork. Her mentor in the project is Jorge Osorio, a professor of pathobiological sciences at the UW School of Veterinary Medicine.

Vampire bat-transmitted rabies is a burden to the livestock industry in Mexico and a significant public health concern. Current rabies control measures in the country include culling vampire bats; however, this practice does not seem to be effective.

In previous studies, the Osorio lab developed a novel, topically delivered rabies vaccine that protected big brown vampire bats against rabies. The technology could be adapted to target other bat species, including vampires. Elsa’s project aims to be the first to assess the practicality of vaccinating free-ranging vampire bats to prevent rabies in Mexico.

Cardenas Canales will also evaluate public knowledge and perceptions about vampire-transmitted rabies in four Mexican communities, as well as the social impacts of the disease. Results will help to tailor public outreach efforts, educational campaigns, and control methods for rabies.

Other Notable Honors

- Hannah Carey, a professor of comparative biosciences, was named president-elect of the Federation of American Societies for Experimental Biology, the nation’s largest coalition of biomedical researchers.
- Peter Muir, the Melita Grunow family professor in companion animal health, is part of the 2018 cohort of Fellows of the Royal College of Veterinary Surgeons, recognized for meritorious contributions to knowledge in the field.
- Alyssa Karklus DVMx’20 won the Morris Animal Foundation 2018 Veterinary Student Scholar Program Poster Presentation Competition for her research into mitochondrial DNA lineages in Bornean and Sumatran orangutans in North American zoos.
- Shannon Gildersleeve DVM’18 received a 2018 Veterinary Student Innovation Award from Merck Animal Health and the American Veterinary Medical Foundation.
Periwinkle, a 7-year-old female blue crane from the International Crane Foundation (ICF) in Baraboo, Wisconsin, received a life-saving surgery at UW Veterinary Care earlier this year.

In May, ICF aviculturists found Periwinkle in respiratory distress while choking on a pebble from her enclosure. Barry Hartup DVM’93, the foundation’s director of conservation medicine and a clinical instructor of zoological medicine at the UW School of Veterinary Medicine (SVM), performed a tracheostomy, creating an opening through the neck into the trachea, and successfully removed the pebble from the airway so Periwinkle could breathe.

Though Periwinkle healed outwardly from the surgery, her respiratory distress returned in early July. Due to suspicion of a tracheal stenosis (a narrowing of the airway and common complication in birds after a tracheostomy) and the complexity of a crane’s respiratory system, Periwinkle was transported to the SVM for further evaluation.

With the assistance of zoological medicine clinical instructor Grayson Doss and resident Taylor Yaw, as well as specialists in anesthesia, a CT scan was performed, revealing a large mass within Periwinkle’s trachea at the base of her neck. An endoscopic camera showed that abundant scar tissue at the previous surgical site was impeding Periwinkle’s airway.

The veterinary team determined that this portion of the trachea would need to be removed or Periwinkle would be unlikely to survive much longer. Sara Colopy DVM’04, PhD’12, clinical instructor of small animal surgery, was joined by a team of experienced technicians who prepared Periwinkle for surgery.

Since the surgery involved the trachea, the anesthesia team placed Periwinkle’s breathing tube into one of her abdominal air sacs, a respiratory structure unique to birds, to be able to breathe for her throughout the two-hour surgery.

Colopy isolated the area of the trachea that was of concern, removed it, and reattached the two healthy, unobstructed ends. This is the first reported case of a blue crane successfully receiving a tracheal resection and anastomosis, or reconnection, procedure.

Within the first few hours after surgery, Periwinkle recovered well, was driven back to the International Crane Foundation, and reunited with her mate, Kito, in her enclosure. She can now be observed daily using her surgically repaired trachea to make various calls with Kito while on public display.

Taylor Yaw and Barry Hartup

Large photo: Periwinkle, two days following her surgery.
Inset photo: Periwinkle (right) and her mate Kito (left) on public display at the International Crane Foundation.
WILL YOU BE A HERO?

Morrie Waud, long-time friend and donor, has committed $5 million to match gifts and pledges toward the School of Veterinary Medicine’s Animals Need Heroes Too building expansion campaign — the most important project the school will undertake in the next 30 years.

To date, alumni and friends have completed $3.5 million of this special opportunity, but we need your help to complete the match. DON’T MISS YOUR CHANCE TO BE A HERO.

All gifts and pledges of $5,000 or more qualify for the dollar-for-dollar Morrie Waud Match.

To learn more and make your Morrie Waud Match gift today, visit vetmed.wisc.edu/morriewaudmatch.

To make a multi-year pledge, contact:
Heidi Kramer
Director of Development
heidi.kramer@supportuw.org
608-327-9136
Meet the Artist

Kathy Esch is a professional artist who specializes in animal portraiture. Working in a variety of media, her particular interest lies in capturing that special bond between humans and their animal companions. She resides in Oregon, Wisconsin, where her art studio is located.