

On an average day, the University of Michigan is home to more than 142,000 research animals — including about 7 cats, 14 dogs, 45 chickens, 100 primates, 140 sheep, 200 frogs, 400 guinea pigs, 7,600 rats, 25,000 zebra fish and 108,700 mice. This is their story.



Myths, Realities, Benefit Beyond Measure

Animal research might not be what you think

BY SALLY POBOJEWSKI

When U-M surgeons Jeremiah Turcotte, M.D., and C. Gardner Child, M.D., walked into Old Main Hospital's surgical suite on March 30, 1964, they knew this was going to be much more than an ordinary operation. Not only were they about to attempt the first human kidney transplant in the state of Michigan, but if the procedure didn't work, a 15-year-old girl was going to die.

Turcotte was new to the U-M faculty. He had just finished his general surgery residency the previous year. But when it came to organ transplants, Turcotte was the more experienced surgeon. During

his residency, he was one of several U-M physicians who used research animals to perfect the techniques and procedures required for transplant operations.

Turcotte already had performed kidney transplants in dogs, monkeys, sheep and rats. He'd just never done one in a human being before.

"I was familiar with the operation and with the immunosuppressive drugs that had to be used, so Dr. Child asked me to assist him," recalls Turcotte, who went on to chair the U-M Department of Surgery and now is a professor emeritus. "Human transplants had been attempted at other places, but only a few were successful. We were still working

out the best way to do the surgery and there were issues with organ rejection and immunosuppressive drugs."

Fortunately, the operation was a success and his patient became the first person in Michigan, and one of the early patients in the country, to receive a kidney transplant.

Since that first U-M transplant in 1964, another 4,252 U-M patients have received a kidney transplant and a second chance at life. Without knowledge gained from research with animals, none of these people would be alive today.

"Before you start doing something new in patients, it's a great help to have done the procedure in a good-sized animal a few

times to get some idea of what the technical problems will be,” Turcotte says. “Without animal research, there would have been a lot more morbidity and mortality in human organ transplants, and much more delay in the process.”

A Century of Essential Service

For the past 100 years, animal research has been an essential part of the advances in human and veterinary medicine we take for granted today. Every new life-saving drug, medical device or surgical procedure was tested for safety and efficacy in animals before it was even considered for use in a human being.

Like organ transplants, much of the early research that led to artificial hip implants and cardiac pacemakers involved research with dogs. Cats and rats were crucial to scientists’ early efforts to understand vision, cognitive development and neurological disease. Monkeys and chimpanzees were vital to the development of polio vaccines and drugs to slow the deadly progression of the HIV virus. Not to mention millions of laboratory mice — the workhorse of the genetics revolution.

“Animal research allows us to make great steps forward in our understanding of the causes of disease and how to treat it,” says Howard G. Rush, D.V.M., associate professor of laboratory animal medicine and director of ULAM — the U-M Unit for Laboratory Animal Medicine.

Rush leads a staff of 164 animal husbandry technicians, veterinary technicians and veterinarians who provide daily hands-on care for most of the nearly 460,000 animals used in U-M research studies every year. It’s not a glamorous job. These are the people who feed and water the animals, clean their cages, nurse sick and post-surgical animals back to health, and do whatever it takes to keep the animals in their care as healthy as possible.

“The role of ULAM is to be the animals’ advocate,” Rush says. “We go to great lengths to ensure that animals used in research are well cared for, are treated humanely and don’t suffer. It’s a correlate to the same kind of regulations put in place to protect humans who participate in medical research.”

“We look for people who genuinely care for animals, and who understand the process of research and how the animals are involved in it,” says Lynn Thiry, a licensed veterinary technician and animal husbandry supervisor who has worked in ULAM for seven years.

People who work in ULAM don’t just like animals — they *love* animals. Most staff members have several pets of their own at home, and snapshots of cats and dogs adorn desks and bulletin boards throughout ULAM’s suite of offices in the Medical School.



Lori Roberts with Wiley

A few of these family pets originally were research animals. Although it doesn’t happen often, occasionally healthy dogs, cats or other U-M animals no longer are needed for research studies. Then an informal network of ULAM employees starts working to find the animal an adoptive home. That’s how Lori Roberts, a ULAM veterinary technician, became the proud owner of a “real nice, sweet dumb dog” named Wiley. Not to mention a rabbit named Carrots, two guinea pigs and a former U-M lab rat that now live with Roberts and her family.

Before Roberts adopted Wiley — a 110-pound, 11-year-old dog of mixed ancestry, Wiley spent three years in a U-M

research laboratory helping scientists study the growth of new bone after an injury. Research with dogs like Wiley is one reason that veterinarians had the knowledge and procedures to save the life of Barbaro, the famous race horse recovering from a broken leg.

“Ten years ago, the horse would have been euthanized immediately,” Rush says. “Many of the treatments used with Barbaro were originally tested in animals, became part of human medicine and are now coming back to animal medicine again.”

Fifty to 100 years ago, many Americans considered animals to be little more than property — valuable only as a source of income, work or food. Today, people are more likely to see animals as much-loved companions and family pets, and to develop deep emotional attachments to them.

So it’s not surprising that people have mixed feelings about animal research. They know it’s necessary, but it makes them uncomfortable. So they’d really rather not know anything about what goes on inside a research laboratory. Unfortunately, ignorance has led to many widely accepted misconceptions about animal research.

For example, many people believe that the animals’ lives are filled with suffering, ended only by a slow and painful death. While no one would claim that the quality of a research animal’s life is the same as that of a family pet, Rush emphasizes that preventing pain and suffering is ULAM’s top priority.

“Just like people, animals are given anesthesia during surgery or invasive procedures,” Rush says. “We use the same pain-killing medications used in veterinary clinics or human hospitals.”

ULAM animal technicians inspect every animal at least once a day, and more often after surgery. If an animal shows signs of pain, infection, sickness or injury, a veterinarian or veterinary technician is called to provide immediate medical care.

A typical research mouse costs between \$10 and \$30, according to Rush, but one U-M investigator paid \$330 for a mouse used in research on cystic fibrosis. Even 10-dollar mice add up to a sizable investment when you order hundreds of thousands of them every year. Providing ➤

high-quality care makes good business sense, in addition to being the right thing to do.

Sometimes, research animals live out their natural life spans and experience few medical procedures, other than giving blood, until they die of old age. Such was the case with Yoda, U-M's most famous research mouse, who died in 2004 at the ripe old age of 4 years and 12 days old. (That's the equivalent of 136 in human

years.) Part of a colony of geriatric mice in the Medical School, Yoda's long life was devoted to helping scientists learn more about the effects of aging.

Another U-M research mouse named Sebastian contributed to research by fathering as many offspring as possible with his unique genetic make-up. Born in 1997 in a laboratory at the U-M Medical School, Sebastian helped U-M scientists find a genetic mutation that

changes the normal development of inner ear cells. He also helped scientists identify a nearly identical mutated gene that causes a form of congenital deafness in humans.

Lab Animals Increasingly Purpose-bred

Another common misconception is the belief that research laboratories are full of lost, stolen or unwanted dogs and cats purchased from animal pounds or shelters. (Researchers call them random-source animals.) Although this may have been true 30 years ago, Rush emphasizes that it is no longer the case today.

Responding to pressure from animal welfare organizations, research institutions increasingly are using what they call purpose-bred dogs and cats ordered from commercial vendors that breed and raise animals specifically for use in research.

"The animal welfare community prefers that animals used in research be purpose-bred," Rush explains. "They feel it's unfair to use an animal that was once a pet in research, because it's a betrayal of our responsibility to that animal.

"When I came to the U-M in 1972, 100 percent of our dogs and cats were random source," Rush adds. "Today, 70 percent of our dogs and nearly all our cats come from licensed dealers who breed animals for research. Nearly all rodents and rabbits used in research are purpose-bred, and vendors even provide some purpose-bred farm animals now."

Another trend during the last 30 years is that research laboratories are using fewer large animals. Today, more than 95 percent of all research animals are rodents, frogs or fish, many with specific genes or physical characteristics that make them especially valuable for research.

Guinea pigs, for example, often are used in hearing research, because their ears are large and their inner ear structure is virtually identical to that of humans. Zebra fish, one of the newest animal models, are especially useful for research



Photo: Martin Vloet

Howard Rush




Zebra fish are especially useful for research in genetics and developmental biology.

in genetics and developmental biology. Because fish embryos develop outside the body, scientists can actually watch organs as they form inside an embryo.

This shift from large to small animals is reflected in the University of Michigan's annual animal census report for 2005. Of 459,635 research animals in the U-M laboratories during 2005, there were 312,643 mice and 33,339 rats, but only 251 dogs and 28 cats.

It is sad, but true, that most research animals must be euthanized at the end of a study. Sometimes surgery is so extensive, it would be cruel to allow an animal to wake up from anesthesia. Other times, tissue or organs from an animal must be removed and analyzed to determine whether or not a new drug treatment is working.

When an animal must be euthanized, research technicians or ULAM staff use specific procedures to do it quickly and in the most humane way possible. "We are all trained in how to euthanize an animal without stressing it out," Thiry says. "We try to be as gentle and quiet as possible and just be at peace with them for that moment.

"You do get attached to the animals," she adds. "Even working with mice, you get to know the mice you work with every day and when you have to euthanize them, it's hard. But we keep in mind that these animals are here for a special purpose — the advancement of research — and that, while they are here, we have given them the best possible care." 

Regulations, Rules and Training

The U-M has a long and distinguished history in laboratory animal care that started in the 1960s with its first ULAM director, Bennett J. Cohen. Cohen was one of several authors of the first edition of *Guide for the Care and Use of Laboratory Animals* — the most widely accepted reference on animal research issues. Revised and updated several times since the 1960s, it can be found in nearly every American research laboratory, including those at the U-M.

In the United States, animal research is strictly regulated by the Animal Welfare Act, which is administered by the U.S. Department of Agriculture, and by a Public Health Service policy governing research institutions that receive funding from the National Institutes of Health. Regular inspections by USDA officials are mandatory, and the government can and does shut down research programs if institutions don't adhere to these standards.

The Animal Welfare Act requires research institutions to create committees that review and approve in advance all research protocols involving animals. At the U-M, it's called the University Committee on Use and Care of Animals, or UCUCA.

Made up of scientists, veterinarians, administrators and commu-

nity volunteers, the committee reviews hundreds of detailed applications from U-M scientists each year. UCUCA has the authority to modify an experimental protocol to ensure that animals are treated humanely. If necessary, a scientist's research privileges can be terminated by UCUCA.

The committee also provides mandatory training for all U-M personnel who work with research animals. Classes cover the biology, handling and care of animals, as well as the basics of rodent surgery and procedures for euthanization.

In addition to caring for the animals and providing services to research investigators, ULAM has another important role — training the next generation of laboratory animal veterinarians and veterinary scientists.

"The United States is facing a severe shortage of veterinarians engaged in public practice involving research, teaching and public health," Rush says. "There's a critical need for more veterinarians trained to work in biomedical research, on food safety and animal disease control issues. There are only a handful of academic programs like ours that combine research, service and teaching in one program."