

The Moral Status of Mice

THE USE OF ANIMALS IN SCIENCE

If, in evaluating a research program, the pains of a rodent count equally with the pains of a human, we are forced to conclude 1) that neither humans nor rodents possess rights, or 2) that rodents possess all the rights that humans possess. Both alternatives are absurd.

-CARL COHEN

Here was the human body writ small. -ALLEGRA GOODMAN

My first brush with the moral complexities of animal research was in my second year of graduate school. I had been assigned to work as a lowly assistant in the laboratory of a biochemist. One of my jobs was to collect molecules from the skin surface of earthworms. The procedure involved dropping worms into 180-degree water. Two minutes later, I would remove their inert bodies from the hot water and freeze little vials of *eau de worm* for chemical analysis. I had performed this procedure several times and viewed it as just another lab chore, one that I did not enjoy, but which also caused me no moral discomfort. The worms died instantly, and, after all, they were just worms.

for his collections. He was horrified by some of his own studies. He wrote of his pigeons, "I love them to the extent that I cannot bear to skin and skeletonise them. I have done the black deed and murdered the angelic little Fan-tail Pointer at 10 days old."

In the 1870s, the war on animal research heated up in England, and advocates on both sides of the issue sought the support of their country's most renowned scientist. Darwin, however, gave mixed messages. He once referred to physiology as "one of the greatest of sciences." Yet Darwin complained to a friend that surgery on animals should never be performed "for mere damnable and detestable curiosity."

Ultimately, however, Darwin sided with his fellow biologists. His views on the value of animal research are reflected by a subtle change he made in the second edition of *The Descent of Man*. In the first edition, he wrote, "Everyone has heard of the dog suffering under vivisection, who licked the hand of the operator; this man, unless he had a heart of stone, must have felt remorse to the last hour of his life." Three years later, however, he amended the sentence, adding: "*unless the operation was fully justified by the increase in our knowledge.*" In 1881, he laid his cards on the table, writing in a letter to the *London Times*, "I feel the deepest conviction that he who retards the progress of physiology commits a crime against mankind."

Although Darwin put his weight behind animal research, it was his theory of evolution that muddied the moral waters by undermining the views of the seventeenth-century French philosopher René Descartes. Descartes believed that animals are biological robots and their behaviors mere reflexes. Thus scientists can slash and burn as they wish. This perspective was exemplified by the nineteenth-century French physiologist Claude Bernard, who wrote, "The physiologist is not an ordinary man: he is a scientist, possessed and absorbed by the scientific idea he pursues. He does not hear the cries of animals, he does not see their flowing blood, he sees nothing but his idea, and is aware of nothing but an organism that conceals from him the problem he is trying to resolve."

Darwin pointed out that if humans and other animals are similar in our anatomy and physiology, we also share similar mental experiences. Most modern ethologists agree. The list of psychological traits that other species

share with humans is growing. Scientists have reported that elephants grieve their dead, monkeys perceive injustice, and cockatoos like to dance to the music of the Backstreet Boys. The ethical consequences of Darwin's notion that the mental capacities of humans and animals differ by degree rather than kind are inescapable. If animals have perceptions, memories, emotions, and intentions, if they can feel pain and suffer, if they dance, how can we justify using chimpanzees or dogs or even mice in experiments? Is it simply a matter of might makes right?

Thus animal researchers face a conundrum. Often, the more similar a species is to humans, the more useful it is as model for our afflictions. Because chimpanzees share about 98% of their genes with humans, they offer a better model for some human disorders than mice do. But because chimps are so similar to us, their use in research is especially problematic. In other words, often the more justified the use of a species is scientifically, the less justified is its use morally. This is the paradox of Darwin's legacy.

Animal activists sometimes claim that modern scientists are no different than their eighteenth-century counterparts in believing that animals do not feel pain. For example, in his book *Dominion: The Power of Man, the Suffering of Animals, and the Call to Mercy*, Matthew Scully, who served as special assistant to former president George W. Bush, writes, "It remains the working assumption of many if not most animal researchers that their subjects do not experience conscious pain or, for that matter, conscious anything else." Scully is wrong. For an article I was writing on animal consciousness, I once asked fourteen animal researchers if they thought mice were capable of experiencing pain and suffering. All of them said yes when it came to pain, and twelve felt that mice could suffer. In a more systematic survey of British scientists, all but two of 155 animal researchers said that animals experienced pain.

Because most animal researchers do not view animals as biological robots, they do not get off the ethical hook as easily as their nineteenth-century predecessors did. My friend Phil is an example. He studies how cells make use of glucose and fatty acids, the fuels they need to do their jobs. Phil is a basic researcher, but he hopes that his studies might someday lead to treatments for metabolic disorders such as diabetes. I asked

Phil if he ever felt guilty about using mice for his experiments. Only once, he said.

Phil had been a member of a research team that was using knockout mice to discover how cells use energy. Knockout animals are genetically engineered so that some of their genes are turned off. Phil's group was using a knockout line of mice to show that a protein called a transporter helped fatty acids and glucose cross into muscle cells, where they could be used as fuel. Because the transporter gene was inactivated in the knockout mice, the researchers predicted that they would tire more quickly than normal animals.

Phil was charged with measuring how long it took the mice to run out of gas. One way to measure fatigue in rodents is to see how long they can swim. The problem is that air gets trapped in a mouse's fur so they can float around forever, like a kid lying on an air mattress in a pool. "You have to make them swim for their lives," Phil told me. The solution is to rig up a miniature harness with just enough weight so that the mouse has to swim to keep his head above water.

Phil learned the procedure from a researcher who worked in another lab. First, take a four-inch-diameter graduated cylinder and fill it with water to within a couple of inches from the top. Then strap the mouse in the weighted harness, lower him into the water, and start the timer. After swimming a few minutes, the mouse will begin to tire. He will start to sink but then he will fight his way to the surface for a gulp of air. The trick is to let the test continue until it is clear that the animal is going down for good. Then quickly grab the beaker and dump out the water before the mouse drowns. The guy who taught Phil this procedure admitted that a couple of his animals did not make it.

Phil only tested one mouse.

He told me, "At some point I could tell that the mouse knew the score, that he had said to himself, 'OK. I know I am going to die, and I just can't do it anymore.' I was supposed to let the test continue to the point where the mouse gives up and sinks and does not try to fight anymore. I dumped the water out and the mouse just lay there panting. He was so exhausted."

Phil had had enough. He told the professor he was working for that he

would not take part in the study. The task of administering the swim test was reassigned to one of the new graduate students.

Like most scientists who use mice as models of fundamental biological processes, Phil neither likes nor dislikes them. They just happened to be the best animals for him to use in order to learn how muscle cells operate. Phil has killed a lot of mice over the years with no remorse. Some by cervical dislocation (he holds their heads down with the blunt side of a pair of heavy scissors and breaks their necks by yanking their bodies backward), others by decapitation (there was a mouse guillotine in lab he worked in; it looks like a miniature paper cutter).

But when push came to shove, Phil was no Cartesian. He looked a drowning mouse in the eye and saw a creature with a will to live. "The part that bothered me was that the mouse had given up, that the mouse knew it was going to die. I would have loved to be able to do the experiment, to measure their muscle fatigue. But I could not do it. I didn't want to test their will."

THE MORAL STATUS OF SPACE ALIENS

AND HANDICAPPED INFANTS:

THE PROBLEM OF MARGINAL CASES

While most scientists do not deny that mice are sentient beings, I expect that most animal researchers don't spend much time fretting over the morality of their work. But every now and then, something turns your head around. In my case, it was a space alien.

It happened one rainy afternoon when our five-year-old twin daughters were bored and starting to get whiny. To placate them, I drove to the video store and rented the movie *E.T.: The Extraterrestrial*, Steven Spielberg's 1982 film about a space alien who becomes stranded in a California suburb. I figured it was just the ticket to keep them occupied for a couple of hours so I could finish writing an article about some experiments I had recently completed on snake behavior. They were immediately hooked and so was I. I quit working on my research report and watched the movie with

them, not knowing that it would change the way I thought about the use of animals in science.

You probably know the plot. For most of the film, E.T., who has huge puppy eyes and a heart that glows, runs around Southern California with his new human pal, a boy named Elliott. The film ends when E.T.'s mom shows up to fetch her errant son. In the final scene, Elliott reaches out to E.T., pleading, "Stay?" E.T. wistfully shakes his monstrous head, looks deeply into Elliott's eyes and croaks, "Come?" But, alas, they both know it is not to be. As E.T. creeps into the flying saucer for the long ride back to the home planet Zork, Elliott blinks back a tear. So do I.

I could not get the movie out of my head. That evening over dinner, I conjured up a perverse new ending that I tried out on Betsy and Katie. I asked them, What if the movie ended differently? E.T. asks Elliott to come back to the home planet with him, and just like in the film, Elliott says no. The extraterrestrial, however, does not take no for answer. Instead, he grabs Elliott by the arm and drags the boy kicking and screaming into the alien spaceship. The doors close and as the movie ends, you hear Elliott shouting "Mommy, help me!" as the ship zooms off into space.

The reason for Elliott's abduction, I explain to the girls, is that a fatal disease is ravishing the population of Zork. Their scientists have come up with a potential cure, and humans, while not as intelligent as the Zorkians, are so biologically similar that they are good subjects for testing potential treatments. The real reason E.T. was in California was to collect humans for these important studies.

"Betsy, what do you think? Should E.T. use Elliott in painful experiments which could help save millions of Zorkians?"

"No, Daddy, no!!"

"But think about it. Zorkians are a lot smarter than humans. After all, E.T. made a space telephone out of junk, and he has special powers that we humans don't have. He could even make a dead plant bloom."

Katie chimed in, "I don't care, Daddy. It would be wrong for E.T. to put Elliott in a cage and use him for some stupid experiments."

I was not so sure. Like my daughters, I was repulsed by the specter

of Elliott sitting forlornly in the alien animal colony where he is injected with an experimental drug that might save the super-smart Zorkians. But as an animal researcher, I had a problem my daughters did not share. The movie made me realize that the justification for animal experimentation, including my own research, ultimately rests on the premise that organisms with bigger brains have the right to conduct research on creatures with less developed mental capacities. Ergo, E.T. has a perfect right to haul Elliott off to Zork.

Philosophers have a different version of the E.T. dilemma that raises a similar issue. It is called the *argument from marginal cases*. Our use of animals in research is predicated on the assumption that nonhuman species lack certain abilities that humans possess—complex emotions, or abstract thinking, or the ability to learn language. But what about humans who do not possess these traits? Thousands of children are born each year with severe intellectual impairments that render them permanently incapable of ever saying a sentence or thinking about the moral status of mice. The unfortunate truth is that some people are not nearly as smart as the average chimpanzee and some humans don't have the mental capacities of a mouse. I cannot see any way to set the moral bar so it is high enough to exclude all nonhuman animals, low enough to include all human beings, and be based on morally relevant traits—the ability to feel pain counts; having two legs does not.

Would it be better to test a drug on an anencephalic infant born with no cerebral cortex, a human infant who is blind, deaf, and incapable of experiencing pain, than on a perfectly healthy mouse? My gut tells me that we should not conduct research on profoundly impaired humans in lieu of animals. But when I posed this question to the philosopher Rob Bass, he wrote back: "My gut delivers a different verdict. It seems obvious to me that research on never-to-be conscious anencephalic children is preferable to making mice suffer." Many of my students also disagree with me: They want to save the mice and conduct our biomedical experiments on death-row prisoners. That's the problem with moral intuition.

WHAT CAN WE LEARN FROM MOUSE RESEARCH?

While a few philosophers have actually argued that scientists should conduct research on severely handicapped children, most people would prefer that we use animals like mice. But supporters and opponents of animal research disagree on how much we can learn from mouse research. Geneticists say that mouse research has led to breakthroughs in organ transplantation, immunology, and our understanding of cancer and cardiovascular disorders and the causes of birth defects. They want you to know that fourteen Nobel Prizes in physiology and medicine have been awarded for studies conducted on mice. On the other hand, groups like the National Anti-Vivisection Society and the Physicians Committee for Responsible Medicine claim that studies on mice are worthless because they are hopelessly flawed and are even detrimental to human health.

Like it or not, modern biomedical research is built on the backs of mice—millions of them. As lab animals, mice have a lot going for them. They are fertile, docile, and have fast generation times (one mouse year equals thirty human years). Females become sexually mature when they are only a couple of months old and go into estrus every four or five days. They produce litters of six to eight pups after three weeks of pregnancy and will happily copulate again just two days after they give birth.

There is another reason that mice make good research animals—most people do not get in a twit about their rights. In her book *Caring: A Feminine Approach to Ethics and Moral Education*, the philosopher Nel Noddings, who believes that ethics are based on interpersonal relationships, explains why she feels no moral obligation to rodents. She writes, "I have not established, nor am I likely ever to establish, a relationship with a rat . . . I am not prepared to care for it. I feel no relation to it. I would not torture it, and I hesitate to use poisons on it for that reason, but I would shoot it cleanly if the opportunity arose." Most people feel the same way about mice. A 2009 Zogby survey found that 75% of Americans would gladly kill a mouse that showed up in their house. Only 10% indicated they would

try to catch the mouse and release it outside, and no one said they would just let the mouse coexist in their home.

The transformation of the mouse from pest to model organism began in 1902 when a Harvard biologist named William Castle obtained inbred mice from a retired Boston schoolteacher for his studies of animal genetics. Castle was not the first scientist to use mice as subjects. The Austrian monk Gregor Mendel bred mice for his first tentative foray into genetics, only shifting to garden peas after his bishop deemed it unseemly for a man of God to share his living quarters with copulating animals. The laboratory mouse was officially born in 1909 when a student of Castle's named Clarence Little developed the first purebred line of lab mice. Named DBA for their coat color (*dilute brown non-agouti*), DBA mice are still used in biomedical research.

Mouse research mecca is the Jackson Laboratory, located in Bar Harbor, Maine. Founded in 1929 by Clarence Little with help from Edsel Ford (son of Henry Ford), it is a rodent factory that produces 2.5 million mice a year—nearly 40 tons of inbred, mutant, and genetically engineered mice. Scientists have their pick of over 4,000 strains of Jax mice, and, if none of them suit your needs, Jackson scientists will genetically engineer a new strain to your specifications. Making mice can be expensive, however. Developing a new strain can take a year and run \$100,000. While most Jax mice are shipped out as live animals, researchers with space limitations can order their mice as flash-frozen embryos to be thawed out as needed. The names of the colors of Jax mice remind me of the muted tones on the paint-chip samples at Lowe's—"misty grey," "light chinchilla," "gunmetal."

The variety of Jax mouse infirmities is even more impressive than the colors of their fur. Hundreds of strains are afflicted with rare cancers, others are prone to facial deformities, and some are born with malfunctioning immune systems. There are Jax mouse models for defects of vision, hearing, taste, and balance. Jax mice come with high blood pressure, low blood pressure, sleep apnea, and Parkinson's, Alzheimer's, and Lou Gehrig's diseases. Researchers trying to cure infertility have their pick of

eighty-eight strains of Jax mice with defective reproductive organs. Then there are the mice that just don't fit in—obsessive-compulsive, chronically depressed, addiction-prone, hyperactive, and schizophrenic mice.

Animal research advocates emphasize the successes. Liz Hodge of the

Foundation of Biomedical Research tells me that without animal research we would not have immunizations for polio, mumps, measles, rubella, or hepatitis. Nor would there be antibiotics, anesthetics, blood transfusions, radiation therapy, open-heart surgery, organ transplants, insulin, cataract surgery, and medications for epilepsy, ulcers, schizophrenia, depression, bipolar disorder, or hypertension. Your pets, she says, would also suffer. We would not have immunizations against rabies, distemper, parvo, or feline leukemia, nor treatments for heartworm, brucellosis, cancer, or canine arthritis.

Mouse researchers claim that almost everything we know about the operation of mammalian genes, including human genes, is rooted in mouse studies. True, the evolutionary paths that led to mice and to men diverged 60 million years ago. My brain weighs 1,500 times more than the brain of the little fellow that lives behind the filing cabinet in my basement office. But while we have different numbers of chromosomes (he has 40; I have 46), we have roughly the same number of genes—22,000, more or less. More important, 99.9% of mouse genes have a known human counterpart.

According to Rick Woychik, president and CEO of the Jackson Laboratory, this makes mice the organism that will allow scientists to develop treatments for killers such as juvenile diabetes, breast cancer, and Alzheimer's disease. "It is," says Woychick, "a bench-to-bedside continuum. You start with basic concepts, and then these concepts mature and get translated into clinical concepts and ultimately get delivered as innovative new therapies at the bedside."

Jackson researchers are particularly enthusiastic about the new field of personalized medicine. Genes play a role in your susceptibility to nearly every disorder, from tooth decay to AIDS. Genes also affect how your body responds to medications. Some people receive no benefit from a drug but suffer serious side effects (for example, those four-hour Viagra-induced penile erections that require an immediate trip to the emergency

room). Other people, however, experience few side effects and have excellent treatment results from the same medication. The goal of personalized medicine is to tell who will and who will not benefit from a drug. Woychick believes that studies based on mouse genetics will eventually enable doctors to tailor the right drug and the right dose to meet each patient's individual needs.

Carl Cohen, a University of Michigan philosopher, also believes that animal research is the key to the advancement of medicine. He is the author of a 1986 *New England Journal of Medicine* article regarded as the classic defense of animal testing. Cohen writes, "Every advance in medicine—every new drug, new operation, new therapy of any kind must sooner or later be tried on a living being for the first time. . . . The subject of that experiment, if it is not an animal, will be a human being. Prohibiting the use of live animals in biomedical research, therefore, or sharply restricting it, must result either in the blockage of much valuable research or in the replacement of animal subjects with human subjects. There are consequences—unacceptable to most reasonable persons—of not using animals in research." That's the party line, and I admit that I generally buy it—though I would like to see fewer mice killed for yet another minor variation of Claritin and instead used in the search for treatments for the neglected tropical diseases.

Opponents of animal research frame the debate differently. They throw thalidomide and Vioxx in your face as examples of the failures of tests on rodents to screen drugs that later turned out to be harmful to humans. (Mouse researchers dispute these claims.) They say scientists have exaggerated the contributions of animal research to improvements in our health. The anti-vivisectionists argue that 90% of the decline in the mortality rates for childhood killers such as scarlet fever and diphtheria came before the advent of vaccinations for these diseases. Animal research opponents argue that improvements to human well-being are really attributable to better nutrition and sanitation. They think studies on mice often lead down blind alleys and actually retard medical progress.

I support animal research and would like to dismiss the anti-vivisectionists as naïve and uninformed. However, they do have some

legitimate points—including, for example, the problem of replication of research results. One reason researchers use inbred strains of mice is that they allow scientists in different labs to check each other's findings by independently confirming their results. In 1999, the world of mouse researchers was shaken up by an article that appeared in the journal *Science*. Researchers in Portland, Oregon; Edmonton, Canada; and Albany, New York, ran eight strains of mice through a series of behavioral tests using exactly the same procedures. The animals in each lab were obtained from the same sources; they were born on the same day, fed the same food, reared on the same light-dark cycle, and put through identical procedures at exactly the same age. The experimenters even wore the same brand of surgical gloves when they handled the mice.

Despite the extreme lengths the researchers took to ensure that the animals were treated alike, in some tests the mice behaved remarkably differently. A dose of cocaine completely wired the animals in the Portland lab. Their coked-up brethren in Albany and Edmonton, however, showed little response to the drug. The authors concluded that subtle differences between laboratories mean that researchers can arrive at different conclusions even when studying genetically identical animals. I filed the article in my filing cabinet under "inconvenient truth."

There is also the contentious issue of how much we can generalize from mice to humans. Biologically, there are some big differences between us and them. We live forty times longer than mice and weigh two thousand times as much. A mouse's metabolism is seven times faster than a person's. Our two species have not shared a common ancestor since the age of dinosaurs. Writing in the journal *Immunology*, Mark Davis, a professor of microbiology at the Howard Hughes Medical Institute, argued that while dozens of experimental treatments work on mice with immune system diseases, few of these have been successful on humans. He has concluded that rodents make poor models for immune disorders.

Ditto neuroscience. Amyotrophic lateral sclerosis (ALS) is a degenerative nerve disease for which there is no cure. The dead include Yankee slugger Lou Gehrig and Bob Waters, the late Western Carolina University football coach who, toward the end, was calling plays from a wheelchair,

breathing through a respirator. Among its living victims are the Cambridge University theoretician Stephen Hawking. Disheartened that there are no effective treatments he could offer his ALS patients, Michael Benatar, a clinical neurologist from Emory University, read all the published mouse studies of ALS. He was surprised by the results. First, he concluded that most of the research was flawed. Often the samples were too small or the experiments poorly designed. Secondly, he found that nearly a dozen drugs that increased the life spans of mice with the rodent version of ALS had no effect when tested on humans. In fact, one drug that worked in four mouse studies made people with ALS sicker. Benatar says that using mice to study ALS is like searching for your missing keys at night under a street lamp because that's where the light is.

The anti-animal research faction, however, should not take too much comfort in the fact that some scientists are questioning the usefulness of the mouse as a model for human neurological disorders. Some neurobiologists have forsaken mice and have turned to animals whose brains are more like ours—monkeys.

HOW LABELS AFFECT OUR ATTITUDES TOWARD ANIMALS: GOOD MICE, BAD MICE, PET MICE

A recurring theme in anthrozoology is that the ways humans think about animals are mired in an uncomfortable mix of logic and emotion. Some of our decisions about the use of animals in science are perfectly reasonable. For example, an individual's attitudes about animal research depend, in part, on their perception of the potential payoff of the experiments, the degree of suffering they think the animals will experience, and the species used in the research. A survey conducted in England found that two-thirds of people approved of painful studies on mice aimed at developing a cure for childhood leukemia, but only 5% supported using monkeys to test the safety of cosmetics.

At other times our views on the moral status of animals are more convoluted. Consider the effect of labels and categories on how we think about

mice. I once spent a year as a visiting scholar in the University of Tennessee Reptile Ethology Laboratory. The lab is located in the Walters Life Sciences Building, home to hyperactive marmosets, cooing White Carneau pigeons, beady-eyed albino rats, spiky green tobacco worms, and 15,000 mice. The mice were housed in spotless cedar-smelling rooms in the building's basement, where they were cared for by a competent and fully certified staff. But while all mice in the building belonged to the same species, they were not afforded the same level of moral consideration.

The vast majority of these animals were *good mice*—the subjects in the hundreds of biomedical and behavioral experiments that were conducted by faculty, post-doctoral fellows, and graduate students. Most of these projects were directly or indirectly related to the search for treatments for the various afflictions that affect our species. Though they did not have any say in the matter, these animals lived and died for our benefit. Because the university received grants from the National Institutes of Health, these mice were treated according to the Public Health Service *Guide for the Care and Use of Laboratory Animals*. Each research project involving the good mice was approved by the university animal care committee charged with weighing the costs and benefits of the experiments.

There was, however, another category of mice that inhabited the building, the *bad mice*. The bad mice were pests—free-ranging creatures you would occasionally glimpse scurrying down the long, fluorescent-lit corridors. These animals were potential threats in an environment where a premium was placed on cleanliness and in which great care was taken to prevent cross-contamination between rooms. The little outlaws had to be eliminated.

The staff of the animal facility had tried several techniques to eradicate bad mice. Snap-traps were ineffective and the staff was reluctant to use poison for fear of contaminating research animals. Thus they settled on sticky traps. Sticky traps are rodent flypaper. Each trap consists of a sheet of cardboard about a foot square, covered with a tenacious adhesive and embedded with a chemical mouse attractant—hence their other name, glue boards. In the evening, animal care technicians would place glue boards in areas where pest mice traveled, and check them the next

morning. When a mouse stepped on a sticky trap, it would become profoundly stuck. As it struggled, the animal's fur would become increasingly mired in the glue. Though the traps did not contain toxins, about half of the animals were dead when they were found the next day. Mice that were still alive in the morning were immediately gassed.

Animals caught in sticky traps suffer a horrible death. I doubt that any animal care committee would approve an experiment in which a researcher requested permission to glue mice to cardboard and leave them overnight. Thus a procedure that was clearly unacceptable for a mouse labeled "subject" was permitted for a mouse labeled "pest."

This paradox was magnified when I discovered where the pest mice came from. The building, it seemed, did not have a problem with wild rodents, but in a facility housing thousands of small creatures, leakage is inevitable. Thus virtually all the bad mice were good mice that had escaped. The animal colony manager told me, "Once an animal hits the floor, it is a pest." And *poof*—its moral status evaporates.

In the Walters building, the moral status of a mouse depended on whether a creature was labeled a subject or a pest. I was quick to criticize this seemingly arbitrary distinction until I realized that the same theme was playing out in my home. For our son's seventh birthday, I kidnapped a mouse who was destined to become a meal for IM, the two-headed snake, from our lab and gave him to Adam as a birthday present. Adam named the mouse Willie and set up a home for his new pet in a cage in his bedroom. We liked Willie. He was quiet and affectionate. But mice have short life spans, and one morning Adam woke up and found Willie dead on the bottom of his cage. We held a family discussion, and the children decided a funeral ceremony would be appropriate. We put Willie in a little box and buried him in the flower garden with a piece of slate for a headstone. We stood around his grave and said a few nice things about him. Betsy and Katie cried a little; it was their first encounter with death.

A couple of days later, Mary Jean, a neatnik, discovered mouse droppings on the kitchen floor. She looked at me and said, "Kill it." That night, I put a dab of peanut butter in a snap trap on the floor between the refrigerator and the stove. I found the mouse the next morning. It was a clean

kill. This time, there was no funeral. As I tossed the little guy's body into the bushes not far from Willie's grave, it struck me that the labels we assign to the animals in our lives—pest, pet, experimental subject—affect how we treat them more than the size of their brain or whether they experience happiness.

THE WASTED MICE

A woman named Susan who worked in a rodent breeding facility recently convinced me that I needed to add a new category to my typology of lab mice. In addition to good mice, bad mice, and pet mice, there are "surplus mice" that are never used in experiments. Lots of them. Some of them will be fed to snakes and owls at a zoo; most will be incinerated. Susan said that in the animal colony where she worked, surplus mouse babies were euthanized nearly every day. One of the senior techs would put handfuls of them in a clear plastic bag, insert the end of a hose that was connected to a tank of carbon dioxide, and turn on the gas. How many mice would be killed in a typical day? Susan said that it varied, but usually about fifty.

I wanted confirmation so I called John, a veterinarian I had met at a conference on the care of laboratory animals. He runs the animal colony at a major research university where many scientists use mice to figure out how genes work.

"John, I just found out that in some animal colonies, mice are killed without ever being used for research. Is that true?"

"Sure."

"Do you guys cull surplus mice?"

"Yeah. We have a carbon dioxide chamber."

"How many animals?"

"Well, four thousand litters are born here every month. There are usually five pups per litter, so that would be a quarter of a million mice a year. We euthanize about half of them. I'd guess about 10,000 mice a month."

"Holy shit."

There are several reasons for the proliferation of surplus mice. According to Joe Bielitski, former chief veterinarian for NASA, most males are euthanized because they are prone to fight. Besides, you only need a couple of males to keep a genetic line going. He estimates that 70% of male lab mice are never used in experiments. But the most important reason for the large numbers of wasted mice is the explosion of research on genetically modified (GM) animals that began in the 1990s. Ninety percent of animal GM studies use mice. These experiments have led to important scientific breakthroughs. (A gene that affects the part of the human brain responsible for language was recently inserted into a line of GM mice. The mice did not talk, but they did squeak at a lower pitch and the gene changed the structure of their brains.) From a mouse's point of view, GM studies are terribly inefficient. It is not easy to slip a piece of DNA into the chromosome of a different species and have it be successfully incorporated into the genome. The efficiency rates of attempts to create a strain of transgenic mice range from 1% to 30%. In other words, sometimes only one animal in a hundred can be used for research. The other ninety-nine will be killed when they are a few weeks old. They are the junk mice, collateral damage.

According to calculations by Andrew Rowan, executive vice president of the Humane Society of the United States and an expert on the use of animals in research, more genetically modified mice are gassed each year in rodent production facilities than are actually used in experiments. But we actually don't know the exact number for sure because according to Congress, lab mice in the United States are not animals.

ARE MICE ANIMALS?

In 1876, the British Parliament enacted the world's first law governing the use of animals in research. The United States caught up ninety years later. The events that precipitated congressional action were a pair of articles on dogs. The first was a 1965 *Sports Illustrated* story about Pepper, a Dalmatian

who disappeared from her yard one afternoon, apparently abducted by a dealer who provided animals to laboratories. Pepper's distraught owners finally located their dog, but only after she had been euthanized at the end of an experiment in a New York hospital. A year later, an article appeared in *Life* magazine titled "Concentration Camp for Dogs." Again, the story focused on the treatment of family pets who wound up as laboratory subjects. Members of the House and the Senate were bombarded with letters from constituents worried that their cats and dogs might suffer a similar fate. For a couple of months, Congress received more mail about animal research than about the two great moral issues of the time, the war in Vietnam and civil rights. The House and Senate quickly enacted the Animal Welfare Act of 1966. (It was not until 1974 that the government took steps to ensure that human research subjects were treated ethically.)

The bureaucratic gyrations of the Animal Welfare Act exemplify the convoluted ways humans think about other species. Perhaps the strangest aspect of the legislation concerns an apparently straightforward question—what is an animal? The Act's definition of the term *animal* starts reasonably enough: "Animal means any live or dead dog, cat, nonhuman primate, guinea pig, hamster, rabbit, or other such warm-blooded animal, which is being used, or is intended for use for research, teaching, testing, experimentation, or exhibition purposes, or as a pet." The smoking gun is in the next sentence. "This term excludes: birds, rats of the genus *Rattus* and mice of the genus *Mus* bred for use in research . . ." *duh*

That's right, according to Congress, mice are not animals. Nor are rats or birds. This means that 90 to 95% of the animals used in research in the United States are not covered under the main federal animal protection legislation. (Mice and other vertebrates used in research at institutions that receive grants from the National Institutes of Health are covered under a separate set of guidelines.) Federal Judge Charles Richey called the mouse/rat/bird exclusion in the Animal Welfare Act arbitrary and capricious. He was right. For instance, the congressional definition of the word *animal* means that a researcher who unobtrusively videotapes the sexual behavior of white-footed mice (genus *Peromyscus*) has to jump through all the federal legal hoops. His friend down the hall who deliv-

ers electric shocks to brain-damaged lab mice (*genus Mus*), however, is exempt from the regulations.

It is instructive to compare how the Animal Welfare Act treats mice, a species most people do not like, with our best friend, the dog. Because mice are not animals, they have no standing under the law. End of story. Dogs, in contrast, are singled out for special treatment. They are entitled to a daily dose of "positive physical contact with humans" (I think this means play). Ironically, because the act applies to dead as well as living animals, dead dogs have more legal protection than live mice. (A footnote in the Animal Welfare Act, however, exempts dead dogs from the husbandry and cage-size requirements.)

The mouse/rat/bird exclusion means that we have no idea how many animals in total are used in research each year in the United States. I can tell you that exactly 66,314 dogs, 21,367 cats, 204,809 guinea pigs, and 62,315 apes and monkeys were used in biomedical and behavioral experiments in 2006. But no one has a clue about the number of mice used in research in American laboratories. Some experts say 17 million. Others, including Larry Carbone, a lab animal veterinarian at the University of California San Francisco and author of the book *What Animals Want: Expertise and Advocacy in Laboratory Animal Welfare Policy*, say the number is much higher. Larry puts it at well over 100 million. The larger number is probably closer to the truth.

The Animal Welfare Act has been tweaked often over the years, but the most important amendments were added in 1985 when Congress took on the issue of which studies were worth doing. In Great Britain, every animal experiment must be approved by the Home Office in London. Congress took a different route and placed the responsibility for ensuring the ethical treatment of lab animals on the institutions where the research was conducted. They directed each institution to establish a local Institutional Animal Care and Use Committee, or IACUC.

Serving on an IACUC is a tough job. At major research universities, animal care committee members can spend hours each week poring over the fine print in proposals that can run fifteen or twenty pages. Every couple of months, they get together and play God. The members thrash

out which proposals to approve, reject, or request more information about. The lives of animals hinge on their decisions, as do scientific careers. Being an IACUC member is a good way to lose friends. But can a committee accurately weigh the benefits of an experiment against the costs in terms of animal suffering?

JUDGING THE JUDGES: HOW GOOD ARE THE DECISIONS OF ANIMAL CARE COMMITTEES?

Some years ago, I received a phone call from Scott Plous, a social psychologist from Wesleyan University who is an expert on decision making. Both of us were interested in how people think about other species, and we had once run into each other while handing out surveys to activists at an animal rights demonstration in front of the Capitol in D.C.

"Hal, have you ever considered doing a study where you would ask different animal care committees to evaluate the same proposals?" he asked. "Of course," I replied. After all, it would be nice to know that the system Congress set up to ensure the welfare of research animals worked, that the University of Texas Animal Care Committee and the Johns Hopkins Animal Care Committee would make the same decisions about the same experiment. "But, Scott, it would be impossible. Scientists are busy. You would never get them to cooperate."

Scott disagreed. He thought committees would happily participate if you offered them money they could use to enhance animal care at their university. I was skeptical, but said, OK, count me in. Scott pitched the idea to the National Science Foundation and they approved the proposal. He was right—by offering institutions extra funds for animal care, we easily recruited fifty randomly chosen university IACUCs to participate in our study. Indeed, the committees were enthusiastic about the project. In the end, roughly 500 scientists, veterinarians, and community members took part in the study, nearly a 90% response rate.

Each committee chairperson sent us three animal researchers' proposals their group had already reviewed. After removing identifying in-

formation, we sent them the proposals to be re-reviewed by a second committee. The research ranged from studies of how bats find water to the development of eating disorders in mice. In all, the 150 proposals involved over 50,000 animals, mostly mice and rats, but also a smattering of other species—chimpanzees, frogs, buffalo, egrets, pigeons, dolphins, monkeys, sea turtles, bears, lizards, you name it. When the data were in, I flew up to Connecticut to help Scott crunch the numbers and figure out what they meant. I had served as an animal care committee member, and I was sure that there would be fairly high levels of agreement between the first and second IACUCs. I was so wrong.

There are moments of truth in science. For me, it is the fraction of a second between the time you push the enter key on the computer and when the results flash on the screen. Scott and I sat in his office, our eyes on the monitor. I was antsy, feeling a little rush of anticipatory adrenaline, like an offensive lineman waiting to hear the quarterback yell “Hut!”

Scott pushed the button. The numbers popped up. Our jaws dropped.

About 80% of the time, the second committees made a different decision than the first. Our statistical analysis indicated that the committees might as well have made their decisions by flipping a coin. Clearly, the system was inadequate. Why, I wondered, should it be OK to shock dogs at one university, but not at another one? In retrospect, I should not have been surprised to find that the decisions of animal care committees are wildly inconsistent. It is harder than you think to tell good from bad research. In his novel *Zen and the Art of Motorcycle Maintenance*, Robert Pirsig laid the issue out nicely: “But, if you can’t say what Quality is, how do you know what it is, or how do you know that it even exists?” This is a question that can keep a scientist up at night.

Our findings that different animal care committees often make different decisions were not an anomaly. Studies showing large inconsistencies in peer-review judgments of quality in science go back thirty years. They include studies of ratings of grant proposals, journal article submissions, and the decisions of both human and animal research ethics committees. The truth is that scientists have problems discerning the quality and importance of research. This is a little secret that researchers do not like to think about.

Put simply, the system Congress enacted to oversee the treatment of research animals is fraught with inconsistencies. Why are white-footed mice but not lab mice covered by the Animal Welfare Act? Why are dogs but not cats entitled to a play session every day? Why can a project be given full approval by one animal care committee and flat-out rejected by a different one? Unfortunately, these nagging problems give credence to the charges by anti-vivisectionists that the fox is presently guarding the henhouse.

What can we do? For starters, Congress should extend the Animal Welfare Act to include all vertebrate species—mammals, birds, reptiles, amphibians, and fish. (British animal research regulations even extend to octopuses.) Our data suggest that most scientists also want mice, rats, and birds covered under the Animal Welfare Act. Three-fourths of the animal researchers who participated in our animal care committee study said they disagreed with the Animal Welfare Act's definition of the word *animal*.

Of course, we could just dump the present system. We could either let scientists conduct animal research without any external oversight or we could throw a pair of dice to decide which animal experiments should be conducted. Both choices are unacceptable. Some animal rights activists argue for a third alternative. They would have us ban animal research altogether. But people who oppose all animal experimentation are up against their own inconsistencies and paradoxes.

THE ANIMAL RESEARCH PARADOX: USING ANIMAL EXPERIMENTS TO SHOW THAT YOU SHOULD NOT CONDUCT ANIMAL EXPERIMENTS

The argument against animal research is based on the premise that mice and chimpanzees fall within the sphere of moral concern but that tomato plants and robots do not. That's because animals have mental traits that plants and machines don't possess. For example, the philosopher Tom Regan restricts the possession of rights to species that have consciousness, emotions, beliefs, desires, perceptions, memories, intentions, and a sense

of the future. But how do we know which animals have these attributes? The answer, of course, is animal research.

The legal scholar Steven Wise is one of the few animal rights advocates who has seriously grappled with the moral implications of differences in mental capacities among the species. In his book *Drawing the Line: Science and the Case for Animal Rights*, Wise developed a 0 to 1.00 "autonomy scale" on which species are rated according to their cognitive abilities. The rankings are based on Wise's review of scientific studies of animal behavior and cognition. Humans are assigned a 1.0 on the scale; chimpanzees, .98; gorillas, .95; African elephants, .75; dogs, .68; and honeybees, .59. Wise argues that creatures scoring above .90 (great apes and dolphins) are entitled to basic legal rights, while animals with scores below .50 are not. The strength of this approach to animal ethics is that a species' moral standing is based on evidence of their cognitive capacities, rather than naïve conjectures about their abilities or how much we like them. For instance, after reviewing the science, Wise concluded that African gray parrots have a slightly stronger claim to basic rights than do dogs.

There is, however, a paradox associated with this empirical approach to animal rights—you need to conduct animal research to determine if it is immoral to use a species in animal research. Wise, for instance, assigns dolphins an autonomy scale score of .90, which puts them in the highest category of nonhuman creatures that deserve legal rights. He writes, "Dolphins have concepts and spontaneously understand pointing, gazing, and the holding up of replicas. They instantly imitate actions and vocalizations." His assessment of the cognitive abilities of dolphins is based on the finding of a University of Hawaii psychologist named Lou Herman. Over three decades of research, Herman has demonstrated that dolphins have extraordinary memories, understand human gestures better than chimpanzees, and have such sophisticated linguistic skills that they will correct your grammar.

Given that Wise bases his case for dolphin rights on Herman's research, you might think he would be fan of these studies. Wrong. In fact, he vehemently argues that Herman's dolphin research is unethical, that Herman exploits his animals, and that he treats them like prisoners. The

irony, of course, is that without these studies of dolphin cognition, Wise would not be able to argue that the mental abilities of dolphins are comparable to those of chimps and thus dolphins are entitled to legal rights.

What about mice? Where do they fall on the autonomy scale? Wise does not mention them in his book, so I sent him an email: *Professor Wise: Where do mice rank on your scale? They are, after all, the most common mammal used in research.*

Wise replied that the omission of mice was a matter of time constraints. The autonomy rankings, he said, are based on an objective review of the available evidence for the capacities of each species. This task requires tracking down the latest research reports and interviewing leading scientists who have studied the behavior and cognitive abilities of each species. Wise said that in the cases of apes and dolphins, the data fit his preconceptions. On the other hand, honeybees scored much higher than he ever anticipated. The evaluation process takes roughly three months for each animal, but there are only twenty-four hours in a day and thousands of species.

DO MICE EXPERIENCE EMPATHY?

THE MCGILL PAIN STUDIES

Wise freely admits that we don't know enough about the minds of most species to accurately place them on his moral status scale. This would seem to mean that we need more, rather than less, animal research. Some of these studies would certainly discover that some animals have unexpected capacities. Researchers at McGill University's Pain Genetics Laboratory, for example, recently conducted a series of experiments that they think show that mice are capable of empathy. I am not convinced that mucine empathy is analogous to the human experience of empathy, but their findings do raise interesting ethical issues.

The purpose of the studies was to discover whether mice would react to pain inflicted upon other mice. The researchers used several procedures to induce pain in the animals. Most of the mice were given the unfortu-