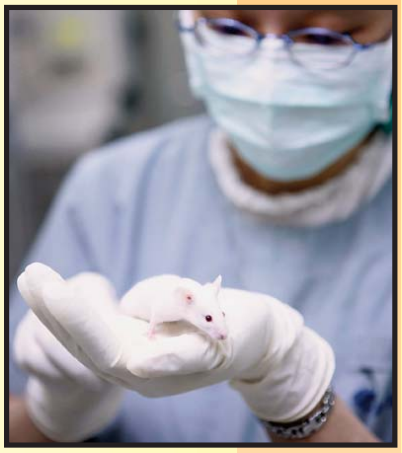
Animal Research

Finding cures,

Saving lives



The American
Physiological
Society

What is Physiology?

Physiology is the study of how living systems function. It is the foundation of modern medicine.

Physiologists study how life works at the level of the molecule, cell, tissue, organ, or whole organism. They also study how different animal species adapt to challenges such as an extremely hot or cold environment, high altitude, drought, or endurance exercise.

Studies of Gila monster saliva led to the development of exenatide, a drug that helps people with type 2 diabetes maintain stable glucose levels and lose weight.

Scientists study animal models of disease because it helps them understand what goes on inside the body and how illnesses can be treated or prevented.

Why do researchers study animals?

Researchers study animals to learn more about how living organisms work and how diseases affect the body. Biological processes are surprisingly similar across different organisms so researchers can learn about biological processes by studying simple organisms. What we now know about genetics began in the garden of a 19th century Austrian monk: Gregor Mendel identified the fundamental laws of inheritance by observing pea plants. Later researchers learned more about how genes work by studying bacteria, yeast, worms, fruit flies, and mice.

Animals get many diseases similar to ones that affect people. By studying these animals, medical researchers can learn what causes diseases and how to prevent, treat, or cure them. These findings help both humans and animals. Researchers also study animals to understand how they adapt to different environments. This can help threatened or endangered species.

Want to learn more?

For more about why researchers study animals see the *Living Laboratory Fact Sheet* at:
http://www.nigms.nih.gov/publications/modelorg_factsheet.htm

To find out how animal research contributed to discoveries awarded the Nobel Prize in Physiology or Medicine, see:
http://www.fbresearch.org/Education/NobelPrizes/tabid/427/Default.aspx

Why can't researchers use computers instead of animals?

Computers cannot replace animals, but they can reduce the number of animals needed. Researchers build computer models based upon what they already know about biological processes and use the models to predict what may happen under a different set of circumstances. But living organisms are far more complex than any computer model we have today. Computer modeling speeds new discoveries and reduces the numbers of animals needed. Nevertheless, animal studies are still needed to provide real-world data about what actually happens.

Want to learn more?

For details on why computers, cell lines, and other non-animal techniques can reduce, but not completely replace, animal models, see:
http://speakingofresearch.com/extremism-undone/alternatives

Diabetes: A Family Story

When she was nine, Kayla almost died. Fortunately, her doctor suspected that Kayla might be sick with more than a virus. That was how she and her family learned that she has diabetes. In type 1 diabetes or juvenile diabetes, the body's immune system destroys cells that produce insulin, a hormone that enables the body to turn food into energy. Without insulin, cells starve and excess sugar builds up in the blood, damaging tissues and organs. Diabetes is fatal if left untreated, and even with treatment, diabetes causes about 73,000 deaths a year. It is the sixth leading cause of death in America.

Diabetes was described in ancient times, but no one knew how to treat it. In 1889, a German physiologist named Oskar Minkowski removed the pancreas of a dog and found that the animal immediately developed the classic symptoms of diabetes: excessive thirst, hunger, and urination, along with fatigue and weight loss. He tried to figure out why, but it was not until 1921 that Frederick Banting and Charles Best isolated insulin from the pancreas of a dog. Banting and Best also showed that the insulin injections could eliminate the symptoms of diabetes. In 1923, Banting was awarded a share of the Nobel Prize in Physiology or Medicine for this discovery.

Kayla pricks her finger several times a day to test her blood sugar level and gives herself daily shots of insulin. She has to be very careful about what she eats and how much she exercises. Kayla hates the finger sticks and shots, but she knows she has to do these things to stay healthy.

Kayla is not the only member of her family with diabetes. Last year her Nana was diagnosed with type 2 diabetes. In this disease, the pancreas doesn't make enough insulin, or the body cannot use it effectively. Type 2 diabetes often occurs in people who are overweight and inactive. It used to affect mostly people middle-aged or older, but today even some children and teenagers develop the disease. For some patients, eating the right foods, losing weight, and exercising is enough to bring their diabetes under control. Researchers have also developed medications that increase the body's insulin production, reduce blood sugar, and make the body more sensitive to insulin. Some people—including Kayla's Nana—take these medications, but these drugs have risks, and many type 2 diabetics still need insulin anyway.

Kayla's cat Mr. Purrfect also has type 2 diabetes. He has to eat special food and gets daily insulin shots too. Kayla plays with Mr. Purrfect to keep him active and keeps track of how much water he drinks and how much he uses the litter box. Their veterinarian says if the family takes good care of him, Mr. Purrfect should stay healthy for a long time.

Kayla, her Nana, and Mr. Purrfect aren't real, but their stories are typical of the 20 million people in the United States who have diabetes.

Want to learn more?

For more about diabetes in humans and animals, visit the websites of the Juvenile Diabetes Research Foundation: **http://www.jdrf.org/** and the American Diabetes Association: **http://www.diabetes.org/** or the Nobel Foundation: **http://nobelprize.org/educational_games/medicine/insulin/**

For more about diabetes research, see *New Weapons to Combat an Ancient Disease: Treating Diabetes:* **http://opa.faseb.org/pdf/diabetes.pdf**

Many treatments that were developed for human diseases are also used to treat animals with similar conditions.

A Revolutionary Model

The 2007 Nobel Prize in Physiology or Medicine was awarded to three researchers whose work led to the creation of genetically modified mice. This in turn made it possible to learn what genes do by studying what happens when they are missing. During the 1980s, Mario Capecchi and Oliver Smithies each found ways to "knock out" genes and replace them with new genetic material. Meanwhile, Martin Evans developed a technique to remove stem cells from mouse embryos and grow them in the lab. These cells are important because they can become any kind of cell. Evans and his colleagues then figured out how to put embryonic stem cells into a mouse embryo to produce hybrid animals whose tissues contain two sets of genetic material. Some hybrids had stem cell DNA in their sperm or eggs so when two of these animals mated, their offspring carried stem cell DNA in every cell. When Evans collaborated with Capecchi and Smithies, the result was the "knockout mouse."

Mice are the most commonly used vertebrates in research for good reason: Over 95% of mouse genes are similar to ones found in humans. Image courtesy of Understanding Animal Research.

What types of animals are needed for medical research?

Specially bred rats and mice are the mammals used most often in medical research. Because rats and mice have so many biological similarities to humans, they make up 90–95% of the mammals in biomedical research. Some strains of rats and mice are susceptible to diseases such as cancer or high blood pressure. In addition, rodents develop diseases over a span of days or weeks instead of months or years. In the 1980s, major research discoveries made it possible to create strains of mice whose genetic make-up has been altered so that they carry specific disease-causing genes. (See *A Revolutionary Model*)

Other mammals commonly found in research are guinea pigs, rabbits, hamsters, and farm animals such as pigs and sheep. Most of these animals are specifically bred and raised for research. Researchers choose the species that best parallels the biology of what they want to study. For example, sheep provide a model to study osteoarthritis, a breakdown of cartilage that occurs as people age, causing pain and inflammation in the joints. Pigs offer a model for research on skin problems, including what may happen when medicine or a toxic substance is absorbed through the skin.

Species such as dogs, cats, and non-human primates account for less than 1% of all mammals in research.

Researchers increasingly rely on species such as zebrafish, fruit flies, and worms for basic research about gene function and biological processes. (See also *Why do researchers study animals?* pg. 1)

Want to learn more?

For an overview of what species are needed in various kinds of research, check out *How Animals Help* at:
http://www.statesforbiomed.org/animals.htm

For a list of common and not-so-common species of research animals, see *An A to Z of laboratory animals* at:
http://www.understandinganimalresearch.org.uk/about_research/types_of_animals/a_to_z

For more about how zebrafish contribute to research, got to:
http://www.fishforscience.com/

Who makes sure that research animals are treated well?

The U.S. has many laws and regulations that require research animals to be treated humanely. Treating animals well is an ethical imperative and the foundation of sound science. Animals that are sick or stressed are not good research subjects. There are four main sources of animal welfare oversight authority in the U.S.:

Animal Welfare Act (AWA)
The AWA regulates the care of many warm-blooded vertebrates (animals with an internal skeleton made of bones) including guinea pigs, hamsters, rabbits, dogs, cats, and non-human primates. Research laboratories and those who supply these animals for research must follow AWA regulations to provide them with appropriate food, housing, and veterinary care. The U.S. Department of Agriculture enforces the AWA through regular inspections of research labs and animal suppliers.

The AWA does not cover rats, mice, and birds that are bred for research, but most of these animals are covered by one of the other oversight authorities listed below.

Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals
Most money for basic research on diseases comes from government grants. To qualify for government funds, institutions that conduct research with vertebrate animals must follow the PHS Policy. The Policy requires a comprehensive animal care and welfare program that follows the *Guide for the Care and Use of Laboratory Animals*. The PHS Policy is broader than the Animal Welfare Act because it also applies to rats, mice, and birds and to cold-blooded vertebrates such as fish and reptiles. If an institution fails to provide good care for its animals, it must give the money back to the government.

Guide for the Care and Use of Laboratory Animals
This is a handbook that provides expert advice on how to care for research animals. It is published by the National Academy of Sciences, a prestigious organization that advises the government on scientific issues. The *Guide* is updated periodically by experts in laboratory animal medicine.

Association for the Assessment and Accreditation of Laboratory Animal Care (AAALAC), International
AAALAC, International was founded in 1965 by veterinarians and scientists who wanted to give the public assurance that laboratory animal research was conducted professionally and humanely. AAALAC offers accreditation to institutions with high quality programs of laboratory animal care.

Want to learn more?

To read the *Guide for the Care and Use of Laboratory Animals* go to:
http://www.nap.edu/openbook.php?record_id=5140

For an overview with links to laws, policies, and other key documents, see the *Timeline of Laws Related to Animal Subjects* at:
http://history.nih.gov/about/timelines_laws_animal.html

Zebrafish are widely used as a model of embryonic development and genetic disease because they are easy to observe and many of their organs are like those of humans. Image courtesy of Understanding Animal Research.

All of these oversight authorities require that every research proposal be reviewed and approved in advance by an institutional animal care and use committee that looks out for the welfare of research animals.

Why do some people say that animal research is wrong?

People have different views about the use of animals for food, fiber, companionship, and research. One widely shared belief is that people may use animals for these purposes if in return they provide them good food, housing, and treatment. To hold that people have an ethical responsibility towards animals in their care is to support animal *welfare*.

Supporters of animal *rights* believe it is wrong for people to remove an animal from its natural environment or interfere with its life. Animal rights advocates oppose eating meat, eggs, or milk; wearing leather, fur, or silk; or putting animals in zoos. Some even object to pet ownership. They also oppose animal research as a matter of principle regardless of its potential benefits for people and other animals.

Most of those who believe in animal rights try to end practices they oppose by influencing public opinion, getting laws passed, or using the legal system. However, the animal rights movement has also attracted a fringe element willing to use violence to advance their cause. Extremists have harassed researchers; threatened them and their families; vandalized laboratories, homes, and cars; set fires, and planted bombs to intimidate researchers into stopping their work.

People have a duty to treat animals humanely, but we also have a duty to relieve suffering. Research with animals has saved many lives and improved the quality of life for millions of people and animals.

Want to learn more?

For more information on animal welfare, see these materials from the American Veterinary Medical Association (AVMA):

http://www.avma.org/issues/animal_welfare/default.asp

http://www.avma.org/issues/animal_welfare/animal_welfare_brochure.pdf

http://www.avma.org/advocacy/state/default.asp#help

Scientists and veterinarians are dedicated to animal welfare.

Why do companies test cosmetics or other products on animals?

Drugs and cosmetics contain chemicals that can have dangerous side effects. U.S. law has required animal safety testing of drugs and cosmetics since 1938 when Congress passed the Food, Drug, and Cosmetic Act in response to public outcry after several tragic incidents involving untested products. In the 1930s more than a dozen women went blind because of Lash Lure, a mascara that was made with a chemical that could burn the skin. One woman had such severe burns that she died due to infection. In 1937, more that 100 people died after taking a new cough syrup called Elixir Sulfanilamide because the medicine was dissolved in diethylene glycol, which is toxic.

Today the Food and Drug Administration (FDA) oversees the safety of cosmetics, drugs, medical devices, and foods. Other federal agencies require safety tests for products that will be used in the home, workplace, and the environment. These agencies together with industry are trying to find ways to get reliable drug and product safety data through non-animal tests or tests that minimize the number of animals needed. Once it can be shown that new tests are as effective as the current ones, government agencies can approve their use to replace animal tests.

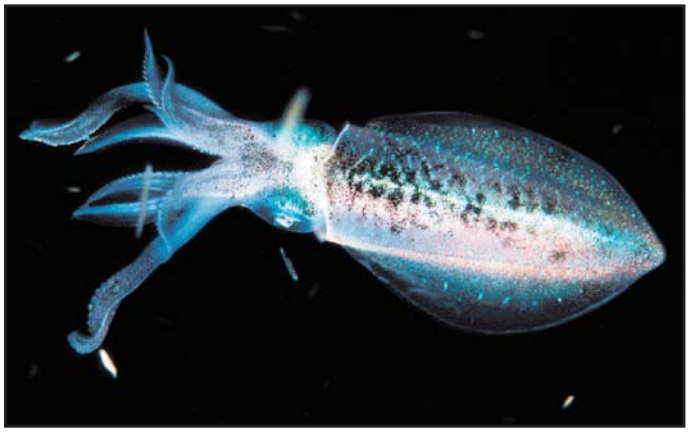
Want to learn more?

For the history of the Food and Drug Administration, see:

http://www.fda.gov/AboutFDA/WhatWeDo/History/default.htm

For more on the government committee to approve non-animal alternatives, see:

http://iccvam.niehs.nih.gov/



A squid's axons, the part of the nerve cell that sends signals out to the brain, are one hundred times larger than those of a human. This makes it easy for scientists to observe and study basic neurological processes in a squid model.

If animal testing is supposed to make sure that drugs are safe, why do some new drugs have serious side effects?

Although animal tests help screen out drugs with dangerous side effects, the results of tests with a small number of animals cannot predict what might happen when a drug goes into widespread use. U.S. law requires new drugs to go through pre-market testing involving two different species of animals. Very often a drug that works well in isolated cells is harmful to animals. If the risks outweigh the benefits, the drug will be abandoned. Only if the benefits are greater than the risks will the drug proceed to human clinical trials.

In clinical trials, a small number of people take various doses of a new drug and their health is monitored to determine whether the drug is safe to use and effective in treating disease. If the compound passes this test, it can be put on the market. Drugs for common conditions may be used by millions of people, including some who are very sick, some who are taking medicines for other health problems, and some who may not take the drug the way they should. Animal tests reduce the risk of dangerous side effects, but they cannot guarantee that new drugs will be safe for everyone who might use them.

Is research painful?

Minimizing pain and avoiding distress in research animals is an ethical, legal, and scientific imperative. Many experiments are painless. Others do involve procedures that can be painful, but most of the time drugs and other measures are used to relieve the animals' discomfort. The Animal Welfare Act and the Public Health Service Policy on Humane Care and Use of Laboratory Animals require researchers to relieve animals' pain unless doing so would interfere with the research, such as studies on pain relief itself.

If a procedure is likely to cause more than slight pain—like a needle stick—the research proposal must go through a special review by the institutional animal care and use committee. This committee makes certain that the experiment is needed to answer the scientific question and that the researcher does everything possible to minimize pain and stress for the animals. In addition to ethical considerations, pain and distress cause changes to the body that could interfere with the research. For this reason, minimizing pain and avoiding distress also contribute to sound science.

Improving Animal Welfare

In 1959, William Russell and Rex Burch published *The Principles of Humane Experimental Technique*. In it they suggested that researchers can make their experiments more humane by taking the following steps:

- ***Reduce the number of animals:*** Researchers should study the minimum number of animals needed to obtain statistically valid results.
- ***Refine the procedure:*** Researchers should improve research techniques to make them less painful or distressing to animals.
- ***Replace animals with non-animal methods:*** Whenever possible, researchers should answer scientific questions using non-animal methods such as computer models, cell cultures, or chemical tests.

Researchers practice ***reduction, refinement,*** and ***replacement*** as much as possible but sometimes there is no other way to answer a particular scientific question.

When it is necessary to obtain experimental data from living organisms, researchers minimize pain as much as they can and select the right species and minimum number of animals to get a scientifically valid answer.

INFORMATION SOURCES

See these websites for more information about animals in research:

American Physiological Society
http://www.the-aps.org/pa/policy/animals.htm

Kids4Research
http://www.kids4research.org

Animal Research Info
http://www.AnimalResearch.info

What a Year!
http://www.whatayear.org/

Americans for Medical Progress
http://www.amprogress.org

Foundation for Biomedical Research
http://www.fbresearch.org

States United for Biomedical Research
http://www.statesforbiomed.org

Centers for Disease Control and Prevention FAQ
http://www.cdc.gov/news/2006_11/animal_care/factsheet_ar_general.htm

Institute for Laboratory Animal Research
http://dels.nas.edu/ilar_n/ilarhome/

National Institutes of Health
http://science.education.nih.gov/animals

Center for Alternatives to Animal Testing
http://altweb.jhsph.edu/resources/education.html

Understanding Animal Research
http://www.understandinganimalresearch.org.uk/

THE AMERICAN PHYSIOLOGICAL SOCIETY
9650 Rockville Pike • Bethesda, MD 20814

The American Physiological Society (APS) was established in New York City in 1887. From 28 founders, the APS has grown to some 10,000 members. The APS sponsors scientific meetings and publishes journals. It also works to improve science education and public understanding of physiology.

Animal Research: Finding Cures, Saving Lives is available on the web at:
http://www.animalresearchcures.org

Questions People Ask About Animals in Research...With Answers From The American Physiological Society is available on the web at:
http://www.the-aps.org/animalresearch