California
Biomedical
Research
Association

P.O. Box 19340, Sacramento, California 95819-0340
Tel 916.558.1515 Fax 916.558.1523
E-mail: info@ca-biomed.org Website: www.ca-biomed.org

Fact Sheet:
Primates in Biomedical Research

Research with nonhuman primates plays an important role in the advancement of human *and* animal health. Primates share 98 percent of human genes. For this reason, nonhuman primates are critical to biomedical research targeting the causes, progression, prevention, and treatment of a wide variety of diseases. Furthermore, the benefits move in both directions – breakthroughs in human medicine are also used to treat diseases in other animals, including nonhuman primates.

Because nonhuman primates reflect the anatomical, physiological, and behavioral makeup of humans, they provide an indispensable, and currently *irreplaceable*, bridge between basic laboratory studies and clinical use. Much of what we know about the brain, heart disease, Alzheimer's, AIDS, viruses, hepatitis, and cancer has come from nonhuman primates.

How Many Nonhuman Primates Are Used?
It is important to stress that the majority of animals in biomedical research in the U.S. are rodents (95%). Currently, *less than one* percent (about 0.30%) of all animals needed for medical discovery in the U.S. are nonhuman primates, and approximately 30 different species are studied.

In general, the most common species studied are Old World monkeys like rhesus monkeys (Macaca mulatta), and cynomolgus (also known as crab-eating or long-tailed) monkeys (Macaca fascicularis). These animals are critically needed for vaccine testing, particularly for AIDS. Greater apes (chimpanzees, gorillas, etc.) are used very sparingly and only when the investigator can provide strong justification. Of course, in field and zoo settings, a variety of different species are studied.

Where Do These Nonhuman Primates Come From?
With few exceptions, nearly all of the nonhuman primates used for research are bred at the eight National Primate Research Centers (NPRCs) and other institutions in the U.S. Such facilities minimize the need for importing animals from the wild, and domestic breeding insures that animals do not possess pathogens (viruses, bacteria) that could adversely influence the outcome of research projects. While a limited number of animals are still imported from the wild, the overall number of primates imported to the U.S. has steadily declined since the 1950's. Typically, the U.S. imports 12,000 to 15,000 monkeys per year for a number of purposes, only one of which is research. Every effort is made to ensure that imported monkeys are not captured from the wild. Old World Primates come from Asia (China, India, Philippines) and Africa. New World Primates are found in South and Central America.

Does This Threaten Their Extinction in The Wild?
Today, the major threats to non-human primates in the wild are deforestation, land use, and development – not research. Specifically, human inhabitants are the greatest threat to these animals. Their villages and farms are encroaching on the forests and open lands. For this reason, some species of nonhuman primates in their natural habitats are classified as endangered. Using an endangered animal for research is strictly prohibited by law. Chimpanzees have not been imported into the U.S. for research purposes since the mid- 1970's, and Chimpanzees bred in captivity may in the future be the source for survival of some wild populations. Furthermore, primatologists and researchers work with governments and conservation organizations to see that all international trade in nonhuman primates follows regulations set forth in the Convention on International Trade in Endangered Species (CITES). Currently, more than 120 countries have signed this agreement.

Laws Governing Primates Use in Research
In general, there are four federal agencies that regulate the use of animals, including primates, in research.

One is the Public Health Service (PHS), which issues the *PHS Policy on Humane Care and Use of Laboratory Animals.* The recommendations in this policy statement have the force of law, under the Health Research Extension Act (PL99-158) passed in 1985. The Public Health Service Policy specifically regulates the care and use of all vertebrate animals used in research, testing, and education, giving mice, rats, and birds the same protections other vertebrate animals receive under the AWA. Among other things, this policy requires the existence of an Institutional Animal Care and Use Committee (IACUC) at each institution that conducts research with funds from federal sources. The IACUC is composed of individuals from the institution and the community, and they review (and must approve) all proposed research projects involving live vertebrates. The National Institutes of Health (NIH), which funds more than half of all medical research in the U.S., conducts unannounced inspections of facilities to ensure compliance with their regulations as well.

The Institute of Laboratory Animal Resources (ILAR) of the National Research Council, National Academy of Sciences writes the ILAR *Guide for the Care and Use of Laboratory Animals*, which is published by the National Academy Press. NIH funds ILAR to write the document. Investigators that receive funds from PHS (including NIH and the Centers for Disease Control and Prevention) for research involving live vertebrates, must adhere to these guidelines, which address the day-to-day aspects of caring for laboratory animals. In addition, all research facilities that receive federal funds (affecting almost all non-human primate work) are required to file an Assurance with the Office of Laboratory Animal Welfare (OLAW) of the National Institutes of Health. This Assurance is a legal commitment that the facility will comply with the NIH *Guide* and includes extensive descriptions of the institution's facilities, personnel, policies, equipment, etc., and in particular a description of its program of veterinary care. An approved Assurance is a prerequisite for the award of federal research funding. Non-compliance with the Assurance may result in disqualification of the facility to receive federal research funds, and withdrawal of funds already approved. There is even a possibility of prosecution under the Federal False Claims Act.

The USDA's Animal Plant and Health Inspection Service (APHIS) is responsible for enforcing the Animal Welfare Act, the second principal law governing the use of animals (Title 7, Sections 2131 et seq. of the U.S. Code, amended in 1985 by PL99-198). The Act was created in response to public concern about animal welfare, and covers species such as cats and dogs, as well as primates. The regulations created by the USDA to enforce the Animal Welfare Act do not cover the most common species of laboratory animals, rats (genus Rattus), and mice (genus Mus), nor do they cover agricultural uses of farm animals. The Animal Welfare Act requires that APHIS perform at least one compliance inspection per year on each research facility that uses animals in experimentation. USDA sets the same minimum for all regulated entities that use animals, including research facilities (i.e., hospitals, universities, diagnostic laboratories, and private firms in the pharmaceutical and biotechnology industries), dealers, exhibitors, and in-transit carriers (e.g., airlines). Compliance inspections are unannounced.

The Food and Drug Administration (FDA) has regulations pertaining to Good Laboratory Practices. These regulations address animal care issues and apply to safety studies of any food additive, drug, or medical device intended for humans that use animals, and require extremely detailed records of all aspects of study. FDA requires adherence to the ILAR Guide.

In addition, one independent, non federal organization that is involved in animal welfare in captivity is the American Association for the Accreditation of Laboratory Animal Care (AAALAC). Institutions voluntarily join AAALAC, which inspects facilities on a regular basis every three years. They then accredit those institutions that meet the highest standards for animal care. Institutions proudly display their accreditation by AAALAC.

The Institutional Animal Care and Use Committee (IACUC) at the institution must approve any experiment that a scientist proposes to conduct with monkeys where the scientist works. The scientist must describe in detail the specific procedures that he or she plans to use on the animals, such as any behavioral testing, surgical procedures, or experimental substances like drugs or vaccines that the animals might receive. There must be an explanation of whether any of the procedures are likely to cause the animal pain or distress, and if so, details must be presented describing all steps the scientist will take to minimize or eliminate pain or distress. The scientist must also provide a justification for why the proposed research must be conducted with monkeys rather than some other animal; whether there are any alternative ways that the scientist can find the answer to his or her question (for example, by studying cells rather than whole monkeys); and why the scientist needs to study the specific number of animals that he or she is proposing to study in the research. In addition, the scientist must indicate that the proposed research does not unnecessarily duplicate research that has already been conducted, and must describe the sources he or she used to determine that the study has not already been done. Finally, the scientist must list all personnel who will be involved in the project, and must be able to document the training that those individuals have had with respect to the procedures to be employed and the animals to be used. The IACUC must approve this proposal before the research can be begin.

The same principles apply to research on wild nonhuman primates in their natural habitat. The precise regulations governing research on wild primates vary from country to country, and it is the responsibility of the researcher to make sure all application procedures have been followed. Generally, such applications include a detailed description of the research, its possible consequences for the subjects, and likely benefits for the country involved. Through such fieldwork, primatologists help to educate people around the world about biology, wildlife conservation, and the importance of natural resources.

Why are nonhuman primates studied, and what kinds of research are conducted?
Human and nonhuman primates share physiological characteristics. For example, the way in which the brains of rhesus monkeys and humans are organized is similar. One brain area that has been studied extensively is the visual system. Neuroanatomical studies of the nonhuman primate brain have been extremely useful in helping us to understand how the human brain functions and how we see. In this way, nonhuman primates serve as models of particular processes that would be extremely difficult or impossible to study in humans.

Study of nonhuman primates has also contributed to our understanding of basic biological phenomena such as reproduction; to better understanding of diseases such as AIDS; and to the development of drugs, treatments, and vaccines for the promotion of better health for human and nonhuman primate alike. In fact, research conducted with nonhuman primates has contributed to Nobel-prize-winning research: development of yellow fever vaccine (1951); culturing of poliovirus that ultimately led to a polio vaccine (1954); and the significant discoveries in visual processing in the brain (1981).

While nonhuman primates comprise a *tiny* fraction of all research animals, they have played, and continue to play, a critical role in medical progress on a wide variety of diseases. Some specific examples follow.

Early 1900s
Components of blood and plasma discovered. Treatment of pellagra.

1920s
Ability to diagnose and treat typhoid fever.

1930s
Modern anesthesia and neuromuscular blocking agents. Mumps virus discovered.

1940s
Treatment of rheumatoid arthritis. Discovery of the Rh factor, blood-typing knowledge critical for safe blood transfusions.

1950s
Development of polio vaccine. Chlorpromazine and its tranquilizing derivatives. Cancer chemotherapy. Development of yellow fever vaccine.

1960s
Mapping of the heart's connections to arteries. Development of German measles vaccine. Therapeutic use of cortisone. Corneal transplants.

1970s
Treatment of leprosy. Procedures to restore blood supply in the brain. Interaction between tumor viruses and genetic material. Understanding of slow viruses, which linger in the nervous system.

1980s
Development of cyclosporine and anti-rejection drugs. Processing of visual information by the brain. Identification of psychophysiological co-factors in depression, anxiety, and phobias. Treatment of malnutrition caused by food aversion following chemotherapy. Treatment of congenital cataracts and "lazy eye" in children. First animal model for research on Parkinson's Disease, enabling doctors to more accurately research human Parkinson's Disease. Heart and lung transplant to treat cardiopulmonary hypertension. First Hepatitis B vaccine. Rhesus monkey model for AIDS used to establish the effectiveness of early administration of AZT in cases of diagnosed infection. Addition of taurine to infant formulas. An amino acid in breast milk, taurine is necessary for normal retinal development.

1990s
Estrogen discovered to control an enzyme key to making serotonin, the brain chemical that regulates mood. Represents first step to providing effective medications for depression at the end of the menstrual cycle, and postpartum and postmenopausal depression. Lead toxicity studies help U.S. fight childhood lead exposure. Ongoing development of a one-dose transplant drug to prevent organ rejection. First controlled study to reveal that even moderate levels of alcohol are dangerous in pregnancy. Breakthroughs in understanding the mechanisms of puberty and disorders of puberty. Primate embryonic stem cells studied extensively for the first time, advancing efforts to better understand reproduction and genetic disorders. Control of intimal hyperplasia. Parent to child lung transplants for cystic fibrosis. Monkey model developed for curing diabetes. Naturally regenerative mechanism discovered in the mature primate brain, spurring new research toward curing Alzheimer's, other degenerative brain disorders. Wild primate species help characterize emerging infectious diseases. Rhesus and cynomolgus monkey kidneys developed for use in diagnosing influenza. Development of anthrax vaccine.

2000s
Gene that boosts dopamine production and strengthens brain cells used to successfully treat monkeys showing symptoms of Parkinson's Disease, a neurodegenerative disorder. Monkey model developed to study the effects of malaria in pregnant women and their offspring. Cyclospora, a food-borne pathogen, is characterized in primates. Dietary restriction without malnutrition provides major health benefits and may extend maximum lifespan. Rhesus monkeys are now prime model for development of human immunodeficiency virus (HIV) treatments and potential vaccines. There are 14 licensed anti-viral drugs for treatment of HIV infection alone. Human embryonic stem cell work based on research in monkeys makes dramatic advances.

Acquired Immune Deficiency Syndrome (AIDS)
Researchers depend heavily on monkeys for the development of promising strategies to protect people from this disease. Vaccines containing various strains of a simian immunodeficiency virus (SIV), a closely related virus that follows a disease course similar to HIV, or a hybrid human/simian immunodeficiency virus (SHIV) are being tested in macaque monkeys, and several research groups have successfully vaccinated monkeys with viral preparations that reduce viral load and halt disease progression. If these results can be generalized to humans, the vaccines may be used to treat HIV-infected humans. Due to primate studies, significant strides have been made, especially in maternal transmission of HIV/AIDS to fetuses and infants.

Hepatitis B and C
Research with chimpanzees has virtually eradicated Hepatitis B and C infections acquired through blood transfusions. Commercially available Hepatitis B vaccines have prevented the development of cirrhosis and liver cancer in millions of people. Because no vaccine for hepatitis C infections is yet available, scientists continue to study the pathogenesis of this disease in chimpanzees to gain a better understanding of the infection process.

Malaria
Researchers are beginning to overcome some of the enormous obstacles in developing a vaccine against malaria, a disease that affects millions of people annually. New World monkeys and chimpanzees are the only species suitable for vaccine evaluation because they are susceptible to the same strains of the parasites that cause human malaria. A number of promising vaccines are being tested and have successfully stimulated protective responses in animals and may soon be ready for human trials.

Acute Respiratory Disease
Respiratory syncytial virus (RSV) can cause life-threatening respiratory infections in infants, young children, and the elderly. Since there is no effective therapy, a vaccine is a high medical priority in the U.S. Vaccines are being

tested for their ability to protect chimpanzees, the animal that is naturally infected by RSV and develops an illness with symptoms similar to those seen in humans.

Periodontal Disease
This infection of the tissue supporting the teeth is the most common cause of bone and tooth loss in humans and may be an important risk factor for cardiovascular disease. It is also a health problem for captive primates, making these species excellent models for studying the connection between chronic oral infections and systemic disease. Several groups of researchers have shown that immunizing monkeys with a vaccine containing a killed oral bacterium can stop the progress of infection and suppress bone loss.

Aging and Nutrition
Scientists are currently studying the effects of long-term calorie restriction (CR) on the biology of aging in macaque monkeys. They have learned that a reduction in calories over a period of several years lowers body temperature, slows metabolism, lessens the risk of cardiovascular disease, and reduces predisposition toward diabetes. Long-term studies of CR have increased the life span of monkeys.

Brain Biology
Because nonhuman primates share many of the same features of brain biology and structure with humans, they are extremely valuable models for studying normal brain function and brain-related diseases, including mental, neurological, and addictive disorders.

Alzheimer's Disease
The decline of memory and other mental functions in patients with Alzheimer's Disease is associated with the loss of or damage to cholinergic nerve cells that use the chemical acetylcholine to transmit messages to other cells in the brain. Scientists have shown that grafting genetically modified cells to produce nerve growth factors directly into the brains of macaque monkeys is a safe procedure that enhances the survival and function of the cholinergic nerve sells. Such studies are now being extended to humans in an attempt to slow the loss of memory in patients with this disease.

Parkinson's Disease
Parkinson's Disease is a slow progressive disease generally found in the aged. Recently, scientists have found a new method to deliver the gene that produces GLNF (a factor that protects brain cells) directly in the brains of monkeys. The treatments successfully prevented the progression and reversed the symptoms of the disease. Clinical testing to forestall human disease is under consideration.*

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* *Sources: United States Surgical Corps; Centers for Disease Control; Massachusetts Society for Medical Research, Inc.; National Center for Research Resources; National Primate Research Centers; National Institutes of Health; National Institute on Drug Abuse; American Physiological Society; Children with Diabetes; Time Magazine; Seattle Post-Intelligencer; Americans for Medical Progress; National Association for Biomedical Research.*