

## *The Essential Need for Animals in Medical Research*

### Introduction

While mice and rats are key models of research,<sup>1</sup> many other animal species have also contributed to dramatic advances in biology and medicine.

A review of the medical literature affirms that studies with other animals, mainly rabbits and guinea pigs, have also made enormous contributions to understanding the cause, treatment, and prevention of many complex human diseases.

A sampling of studies being conducted in species not commonly viewed as laboratory animals is included in this survey.

### Rabbits and Guinea Pigs

Research involving these species is integral to continued biomedical progress. Because the general physiology of their cells, tissues, and organs is similar to humans, these animals provide excellent models for many human diseases.

There is an urgent need to develop more efficacious vaccines or alternative vaccination regimens to achieve immunity in humans against virulent anthrax spores. Rabbits exposed to these spores develop a disease very similar to humans. A recent study has shown that rabbits immunized with a licensed vaccine preparation were protected against inhalation anthrax when challenged by aerosols containing lethal doses of spores.

Because anthrax inhalation studies cannot be conducted in humans, the rabbit model is crucial for evaluating the immune status of vaccinated humans.<sup>2</sup> Guinea pigs are also a useful model for testing the efficacy of promising anthrax vaccines.<sup>3</sup>

Rabbits have been and continue to be very important in the study of cardiovascular disease, particularly hypertension and atherosclerosis. When fed high cholesterol diets, they develop vascular plaques similar to those in humans. Studies in rabbits have shown that lipid-lowering treatments, such as the administration of statins, act directly on plaques and decrease inflammation. The use of these compounds in humans has led to a reduction in the incidence of stroke and cardiovascular mortality.<sup>4</sup>

Guinea pigs carry the majority of their plasma cholesterol in low density lipoprotein (LDL), making them useful models for the study of cholesterol and lipoprotein metabolism.<sup>5</sup>

### Woodchucks

Although vaccines and antiviral drugs that treat acute and chronic liver disease (hepatitis, cirrhosis, cancer) caused by hepatitis B virus (HBV) are available, they are not yet fully utilized by the public. Better therapies are needed for the estimated 1.2 million chronic carriers in the U.S. Woodchucks infected with woodchuck hepatitis virus (WHV), a virus closely related to HBV, also develop severe hepatitis and are at 100% risk for cancer. For this reason, they are an ideal model for the preclinical assessment of new drugs and new strategies for human immunotherapy.<sup>6</sup>

### Pigs

The pig has become an excellent model for evaluating ways to prevent restenosis, the renarrowing of an artery following balloon angioplasty. As a clinical alternative to dilation, heart specialists have begun implanting cardiac stents, expandable tiny mesh tubes, to prop open clogged arteries. Before starting clinical trials, the results from the porcine model demonstrated the potential therapeutic benefits of this device for the prevention and treatment of human coronary restenosis.<sup>7</sup>

The pig is also one of the best models for studying the healing process of skin wounds because the repair process is similar and the findings can easily and rapidly be applied to the human condition.<sup>8</sup>

### Sheep

Because of their anatomic similarities to humans, sheep are becoming popular as models for orthopedic research on diseases and injuries of the bones, joints, and muscles. They are frequently suitable alternatives to the use of dogs. During the last decade, sheep were used to study numerous musculoskeletal conditions, such as the repair of fractures, limb lengthening, and treatment of osteoarthritis and osteoporosis.<sup>9</sup> The sheep is also a valuable model for testing implanted mechanical valves to replace aortic valves (within the main artery of the body) and mitral valves (within the heart). Researchers have confidence that the ovine model provides data that have good predictive value for preclinical evaluation of these lifesaving devices.<sup>10</sup>

## Marine and Freshwater Animals (zebrafish, squid, sea snail)

Historically, fish models have played a significant role in assessing the risks associated with exposure to chemical contamination in aquatic environments.

Researchers rate zebrafish as one of the most promising animal models for studying early vertebrate development and gene function. The embryos are produced in high numbers, develop outside the mother, and, most importantly, are transparent. At certain stages they are remarkably similar to human embryos, possessing all sensory systems: taste, tactile, smell, balance, vision, as well as learning. By injecting pieces of DNA into the fish embryo, scientists can create mutant fish and identify the genes and their specific roles in controlling certain processes. Because the functions of hundreds of these genes are conserved among the different vertebrate groups, the information gained from zebrafish studies can provide invaluable insights into the genetic mechanisms that control development in humans.<sup>11</sup>

The squid, octopus, and sea snail are important models for neurobiological studies. The squid has some of the largest nerve cells found in nature. By comparison, mammalian nerve cells are small and difficult to study. Researchers using the giant axon of the squid have unlocked the secrets of how human brain cells work. For example, they discovered that nerve cells use electrochemical signals to transmit messages and that learning causes physical changes in the neurons.<sup>12</sup>

Sea snails (*Aplysia*) also have large and individual neurons linked to specific behaviors that can be tracked by placing electrodes into individual cells to measure electrical impulses conducted in the nervous system. Using this model, scientists have learned that the spaces at nerve cell endings, or synapses, adapt over time and play an important role in learning and memory.<sup>13</sup>

## Armadillo

Naturally occurring leprosy is found in wild armadillos. By studying the transmission of leprosy in this natural population, researchers will eventually learn how this ancient disease spreads among humans. Because it is still impossible to grow the leprosy bacillus in culture, armadillos are the only source of organisms for the preparation of vaccines.<sup>14</sup>

## Invertebrates (leeches)

The same leeches once used in the practice of bloodletting are being used to study memory and learning at the cellular level. The leech brain consists of 32 clumps of nerve cells along a spinal column. The simplicity of the leech's nervous system permits researchers to study the cellular basis of simple behavior. As reported recently, this animal shares with humans a binding protein that is a key component in memory.<sup>15</sup>

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