Animal Research Is Wasteful and Misleading

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The use of animals for research and testing is only one of many investigative techniques available. We believe that although animal experiments are sometimes intellectually seductive, they are poorly suited to addressing the urgent health problems of our era, such as heart disease, cancer, stroke, AIDS and birth defects. Even worse, animal experiments can mislead researchers or even contribute to illnesses or deaths by failing to predict the toxic effects of drugs. Fortunately, other, more reliable methods that represent a far better investment of research funds can be employed.

The process of scientific discovery often begins with unexpected observations that force researchers to reconsider existing theories and to conceive hypotheses that better explain their findings. Many of the apparent anomalies seen in animal experiments, however, merely reflect the unique biology of the species being studied, the unnatural means by which the disease was induced or the stressful environment of the laboratory. Such irregularities are irrelevant to human pathology, and testing hypotheses derived from these observations wastes considerable time and money.

The majority of animals in laboratories are used as so-called animal models: through genetic manipulation, surgical intervention or injection of foreign substances, researchers produce ailments in these animals that “model” human conditions. This research paradigm is fraught with difficulties, however. Evolutionary pressures have resulted in innumerable subtle, but significant, differences between species. Each species has multiple systems of organs—the cardiovascular and nervous systems, for example—that have complex interactions with one another. A stimulus applied to one particular organ system perturbs the animal’s overall physiological functioning in myriad ways that often cannot be predicted or fully understood. Such uncertainty severely underlines the extrapolation of animal data to other species, including humans.

Animal Tests Are Inapplicable

Important medical advances have been delayed because of misleading results derived from animal experiments. David Wiebers and his colleagues at the Mayo Clinic, writing in the journal Stroke in 1990, described a study showing that of the 25 compounds that reduced damage from ischemic stroke (caused by lack of blood flow to the brain) in rodents, cats and other animals, none proved efficacious in human trials. The researchers attributed the disappointing results to disparities between how strokes naturally occur in humans and how they were experimentally triggered in the animals. For instance, a healthy animal that experiences a sudden stroke does not undergo the slowly progressive arterial damage that usually plays a crucial role in human strokes.

During the 1920s and 1930s, studies on monkeys led to gross misconceptions that delayed the fight against poliomyelitis. These experiments indicated that the poliovirus infects mainly the nervous system; scientists later learned this was because the viral strains they had administered through the nose had artificially developed an affinity for brain tissue. The erroneous conclusion, which contradicted previous human studies demonstrating that the gastrointestinal system was the primary route of infection, resulted in misdirected preventive measures and delayed the development of a vaccine. Research with human cell cultures in 1949 first showed that the virus could be cultivated on nonneural tissues taken from the intestine and limbs. Yet in the early 1950s, cell cultures from monkeys rather than humans were used for vaccine production; as a result, millions of people were exposed to potentially harmful monkey viruses.

In a striking illustration of the inadequacy of animal research, scientists in the 1960s deduced from numerous animal experiments that inhaled tobacco smoke did not cause lung cancer (tar from the smoke painted on the skin of rodents did cause tumors to develop, but these results were deemed less relevant than the inhalation studies). For many years afterward, the tobacco lobby was able to use these studies to delay government warnings and to discourage physicians from intervening in their patients’ smoking habits.

Of course, human population studies provided inescapable evidence of the tobacco-cancer connection, and recent human DNA studies have identified tobacco’s “smoking gun,” showing how a derivative of the carcinogen benzo(a)-pyrene targets human genes, causing cancer. It turns out that cancer research is especially sensitive to differences in physiology between humans and other animals. Many animals, particularly rats
and mice, synthesize within their bodies approximately 100 times the recommended daily allowance for humans of vitamin C, which is believed to help the body ward off cancer.

The stress of handling, confinement and isolation alters an animal’s physiology and introduces yet another experimental variable that makes extrapolating results to humans even more difficult. Stress on animals in laboratories can increase susceptibility to infectious disease and certain tumors as well as influence levels of hormones and antibodies, which in turn can alter the functioning of various organs.

In addition to medical research, animals are also used in the laboratory to test the safety of drugs and other chemicals; again, these studies are confounded by the fact that tests on different species often provide conflicting results. For instance, in 1988 Lester Lave of Carnegie Mellon University reported in the journal Nature that dual experiments to test the carcinogenicity of 214 compounds on both rats and mice agreed with each other only 70 percent of the time. The correlation between rodents and humans could only be lower. David Salsburg of Pfizer Central Research has noted that of 19 chemicals known to cause cancer in humans when ingested, only seven caused cancer in mice and rats using the standards set by the National Cancer Institute.

Indeed, many substances that appeared safe in animal studies and received approval from the U.S. Food and Drug Administration for use in humans later proved dangerous to people. The drug milrinone, which raises cardiac output, increased survival of rats with artificially induced heart failure; humans with severe chronic heart failure taking this drug had a 30 percent increase in mortality. The antiviral drug fialuridine seemed safe in animal trials yet caused liver failure in seven of 15 humans taking the drug (five of these patients died as a result of the medication, and the other two received liver transplants). The commonly used painkiller zomepirac sodium was popular in the early 1980s, but after it was implicated in 14 deaths and hundreds of life-threatening allergic reactions, it was withdrawn from the market. The antidepressant nomifensine, which had minimal toxicity in rats, rabbits, dogs and monkeys, caused liver toxicity and anemia in humans—rare yet severe, and sometimes fatal, effects that forced the manufacturer to withdraw the product a few months after its introduction in 1985.

These frightening mistakes are not mere anecdotes. The U.S. General Accounting Office reviewed 198 of the 209 new drugs marketed between 1976 and 1985 and found that 52 percent had “serious postapproval risks” not predicted by animal tests or limited human trials. These risks were defined as adverse reactions that could lead to hospitalization, disability or death. As a result, these drugs had to be relabeled with new warnings or withdrawn from the market. And of course, it is impossible to estimate how many potentially useful drugs may have been needlessly abandoned because animal tests falsely suggested inefficacy or toxicity.

Better Methods

Researchers have better methods at their disposal. These techniques include epidemiological studies, clinical intervention trials, astute clinical observation aided by laboratory testing, human tissue and cell cultures, autopsy studies, endoscopic examination and biopsy, as well as new imaging methods. And the emerging science of molecular epidemiology, which relates genetic, metabolic and biochemical factors with epidemiological data on disease incidence, offers significant promise for identifying the causes of human disease.

Consider the success of research on atherosclerotic heart disease. Initial epidemiological investigations in humans—particularly the Framingham Heart Study, started in 1948—revealed the risk factors for heart disease, including high cholesterol levels, smoking and high blood pressure. Researchers then altered these factors in controlled human trials, such as the multicenter Lipid Research Clinics Trial, carried out in the 1970s and 1980s. These studies illustrated, among many other things, that every 1 percent drop in serum cholesterol levels led to at least a 2 percent drop in risk for heart disease. Autopsy results and chemical studies added further links between risk factors and disease, indicating that people consuming high-fat diets acquire arterial changes early in life. And studies of heart disease patients indicated that eating a low-fat vegetarian diet, getting regular mild exercise, quitting smoking and managing stress can reverse atherosclerotic blockages.

Similarly, human population studies of HIV infection elucidated how the virus was transmitted and guided intervention programs. In vitro studies using human cells and serum allowed researchers to identify the AIDS virus and determine how it causes disease. Investigators also used in vitro studies to assess the efficacy and safety of important new AIDS drugs such as AZT, 3TC and protease inhibitors. New leads, such as possible genetic and environmental factors that contribute to the disease or provide resistance to it, are also emerging from human studies.

Many animals have certainly been used in AIDS research, but without much in the way of tangible results. For instance, the widely reported monkey studies using the simian immunodeficiency virus (SIV) under unnatural conditions suggested that oral sex presented a transmission risk. Yet this study
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