INT. J. BIOL. BIOTECH., 3 (2): 243-247, 2006.

CONTROVERSIES IN USING ANIMAL MODELS FOR SCIENTIFIC STUDIES: A DIFFERENT PERSPECTIVE

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ABSTRACT

It is estimated that 50–100 million animals worldwide are used annually and subsequently killed in scientific procedures. The topic is controversial, with supporters and opponents arguing about ethical issues and whether using animal models is good or bad science. According to the U.S. Foundation for Biomedical Research (FBR), "animal research has played a vital role in virtually every major medical advancement of the last century for both human and animal health"and seven of the last ten Nobel Prizes for medicine have depended in part on animal research, though whether that aspect of the research was necessary is in question. It is now been voiced that use of other alternative techniques in place of animal models can be employed successfully that includes cell cultures, statistical interpretation of data and futuristic computer simulation models that could minimized the sufferings of animals. This paper deals with the both negative and positive aspects of animal models comparable to non animal studies and conclude that improvements in experimental methedology the suffering and pain of the animal can be reduced .

Key words: Controversies, animal models, LD_{50}, toxicity

INTRODUCTION

It is estimated that 50–100 million animals worldwide (1,2,3) are used annually and subsequently killed in scientific procedures, mostly in universities, medical schools, pharmaceutical companies, and commercial facilities that provide animal-testing services to industry. Testing is also carried out on farms, in defense-research establishments, and by public-health authorities, on a variety of species from fruit flies and mice to non-human primates (4).

The topic is controversial, with supporters and opponents arguing about ethical issues and whether using animal models is good or bad science. Animal research however, has played a vital role in virtually every major medical advance of the last century for both human and animal health. (5). The developments attained through the use of animal models include the development of penicillin (mice), organ transplant (dogs), and work on poliomyelitis that led to a vaccine (mice, monkeys) (9).

The moral basis of the pro-testing position was summarized by a British House of Lords inquiry in 2001–2: "The institution of morality, society, and law is founded on the belief that human beings are unique amongst animals," and are therefore morally entitled to use them for their own purposes. This belief is "combined with a further belief that there is a moral imperative ... to develop medical and veterinary science for the relief of suffering " (10). Some people also believe that animals may suffer less during experiments than human beings would, arguing that although all mammals have similar pain receptors and central nervous system pathways and may feel physical pain in the same way, non-human mammals suffer less because they have a reduced capacity to remember and to anticipate pain (11).

In the United States, animal testing is primarily regulated by the 1985 Animal Welfare Act, which is enforced by the Animal and Plant Health Inspection Service of the United States Department of Agriculture (USDA). It contains provisions to ensure animals used in research receive humane care and treatment. However mice, rats and birds are exempt, meaning over 95% of research animals in the USA are not covered by this legislation. (14,15).

Experiments on vertebrate animals in Europe are subject to the European Union's Directive 86/609/EEC on the protection of Animals used for Experimental and other Scientific purposes. however, there is considerable variation in the member countries choose to exercise the directive (compare, for example, legislation from Sweden , The Netherlands and Germany (16). In the United Kingdom, the 1986 Animals (Scientific Procedures) Act (17) requires experiments to be regulated by three licences: a project licence for the scientist in charge of the project, which details the numbers and types of animals to be used, the experiments to be performed, and the purpose of them; a licence for the institution to ensure it has the facilities and staff to provide proper care; and a personal licence for each scientist or technician who carries out any procedure. The experiments must use "the minimum number of animals, involve animals with the lowest degree of neurophysiological sensitivity, cause the least pain, suffering distress or lasting harm, and most likely to produce satisfactory results" (Section 5/5-b) (18). In France, present legislation (principally the decree of 19th October 1987) requires an institutional and project licence before vertebrate experimentation may be carried out. An institution must submit details of their facilities, the reason for

the use of animals and the species they house, after which a five-year licence may be granted following an inspection of the premises (19). The system in Japan is one of self regulation. Animal experiments are regulated by the one clause in the 2000 Law for the Human Treatment and Management of Animals, which requires those using animals to cause minimal distress and suffering. There are no inspections, and there is no reporting requirement for the numbers of animals used (20).

Unfortunitely the data about most of the developing countries pertaining to the subject is not avialable. Pakistani has no exception.

It is estimated that 100 million animals are experimented around the world every year, 10–11 million of them in the European Union and 1101958 in the United States in 2004. The Nuffield Council on Bioethics reports that "estimates of the total number of animals used annually in research around the world are difficult to obtain and range from between 50 to 100 million animals". Animals bred for research then killed as surplus, or used for breeding purposes, are not included in the figures.

Figures released by the British Home Office show that, in 2004, 2,854,944 procedures were carried out on 2,778,692 animals. The term "procedure" refers to an experiment, which might last several months or even years. The figures show that most animals are used in only one procedure: animals either die because of the experiment or are killed and dissected afterwards (21,22,23,24,25,26).

In most of the animals studies rats and mice are used in large proportion because they are small, cheap, easy to handle and care for, and can produce up to 100 babies in a year. Albino rabbits are used in eye irritancy tests because they have less tear flow than other animals. Beagles and non-human primates are used in toxicity tests, surgery, dental experiments, and brain research. In addition, baboons, macaques, marmosets, and chimpanzees are also used. The use of *Hominidae humans*, gorillas, chimpanzees, and orang utan is prohibited in Britain, but chimpanzees are still used in the U.S., with an estimated 1,300 in use at any given time, according to the Humane Society of the United States (27).

There are a range of scientific uses of animals, which can be split into three broad and at times overlapping categories. i. Advancing scientific knowledge, ii. Studying disease and developing medicines and iii.. Drug testing
Out of these LD 50 test is widely used in the third world countries (and in advanced nations)to elicite the toxic response. This concept was created by J.W. Trevan in 1927. The choice of the 50% mark avoids the potential for ambiguity of making measurements in the extremes

Some animal welfare groups (particularly those influenced by the animal research movement) object to the studies needed to calculate this figure. This is particularly the case where the substance is not particularly toxic and a large quantity of the material is ingested by the animals over a long period, in some cases causing slow, painful deaths. Another criticism of LD_{50} testing is that lethality in test animals does not always give an accurate indication of lethality in humans, because resistance varies from one species to another. As concern grows for the welfare for animals, and as alternatives become more sophisticated, the test is administered less frequently, though the collection of data already obtained make it useful. Estimated LD_{50} numbers can be compared to those older numbers obtained more traditionally.

DISCUSSION

Now after an elaborate overview review the two faces of a picture, a brighter side and dark aspect, an optimistic view and a pessimistic approach is presented and discussed.

Advocates of animal testing

Testing advocates argue that:
It would be unethical to test substances or drug with potentially adverse side-effects on human beings.
Controlled experiments involve introducing only one variable at a time, which is why animals are experimented on while confined inside a laboratory. Human beings could not be confined in this way.
There is no substitute for the living systems necessary to study interaction among cells, tissue, and organs. Animals are good surrogates because of their similarities to humans.
Animals have shorter life and reproductive spans, meaning that several generations can be studied in a relatively short time.
Animals can be bred especially for animal-testing purposes, meaning they arrive at the laboratory free from disease.
Humans in some parts of the world are healthier in large part due to advances in medical research derived from animal testing.

Animals receive more sophisticated medical care because of animal tests that have led to advances in veterinary medicine.
There have been several examples of substances causing death or injury to human beings because of inadequate animal testing (35).
Animal testing has helped to develop vaccines against diseases like rabies, polio, measles, mumps, rubella and TB
Antibiotics, HIV drugs, insulin and cancer treatments rely on animal tests. Other testing methods aren't advanced enough
Scientists claim there are no differences in lab animals and humans that cannot be factored into tests
Operations on animals helped to develop organ transplant and open-heart surgery techniques (36).

Opponents of animal testing

Opponents argue that:
The animal-testing industry is a multi-million dollar concern. Advocates of testing may argue that their interests are scientific, but they are just as often commercial.
Even with medical and non-commercial research, tests are often conducted to produce academic papers in order to acquire a Ph.D., academic tenure, or more funding, and not because the research is beneficial. (37)
The suffering of the animals is excessive in relation to whatever benefits may be reaped .
Animal-testing facilites are not properly regulated or inspected, and several undercover investigations by activist groups have uncovered evidence of animal abuse.
Animal testing is regarded by opponents as bad science because:
Animal models of disease are induced, and should not be compared to the same disease in humans. Parkinson's disease in humans cannot be reproduced by causing brain damage in an animal.
Many drugs have dangerous side-effects that were not predicted by animal models; a well-known example of this is Thalidomide.
Some drugs have different effects on human and non-human animals: aspirin, for example, is a teratogen in animals, but not in humans, and has beneficial effects on humans, such as stroke prevention, that are not reproduced in animals (38).
The conditions in which the tests are carried out may undermine the results, because of the stress the environment produces in the animals. It id believed that the laboratory environment and the experiments themselves are capable of affecting every organ and biochemical function in the body. "Noise, restraint, isolation, pain, psychological distress, overcrowding, regrouping, separation from mothers, sleeplessness, hypersexuality, surgery and anaesthesia can all increase mortality, contact sensitivity, tumour susceptibility and metastatic spread, as well as decrease viral resistance and immune response"(39).
Animal experiments can be misleading. An animal's response to a drug can be different to a human's
The stress that animals endure in labs can affect experiments, making the results meaningless
Animals are still used to test items like cleaning products, which benefit mankind less than medicines or surgery
Some opponents, particularly supporters of animal rights, argue further that, even if animal testing did reap benefits to human beings, these could not outweigh the suffering of the animals, and that human beings have no moral right to use individual animals in ways that do not benefit that individual.
On the basis of aurguments of the both groups following alternatives and solutions are recommended:

The 'Three Rs'

Replacement - use alternative methods, e.g. testing on cell cultures (*in vitro*)
Reduction - use statistics to reduce the number of animals that must be used for each experiment
Refinement - improve the experiment to reduce animal suffering

Paying for alternatives

Humanitarian organizations and governments have funded studies into alternative methods since the 1960s and spent millions of dollars for alternative methods.

Reducing deaths

In the past, the toxicity of a new substance was measured by an 'LD50' (lethal dose 50%) test. This test required up to 200 rats, dogs or other animals to be force-fed different amounts of the substance, to determine the dose that

would kill exactly half that group of animals. Recent changes in protocol have put a ban on the LD50 test, save in exceptional circumstances. In addition, the Organization for Economic Co-operation and Development says that if a substance kills the first three animals it is tested on, further trials are unnecessary.

By using statistics

A vaccine is only considered effective if at least 80% of the vaccinated animals survive after being exposed to a particular disease. However, the disease must also kill 80% of a control group not protected by the vaccine. Using statistical methods, Coenraad Hendriksen of the National Institute of Public and the Environment in the Netherlands has developed a method to test diphtheria and tetanus vaccines that only requires measuring the level of antibodies in an animal.

Apart from greatly reducing their suffering, it also uses half the number of animals. Other statistical techniques can use patient data to understand how a disease spreads, without testing it on animals.

Using fewer mammals

Horst Spielmann of ZEBET, Ref the German centre for animal testing alternatives, has surveyed decades of industry data on pesticides. He concluded that if mice and rats prove sensitive to a chemical, it does not have to undergo further tests on dogs. Spielmann Ref anticipates that 70% of dog tests can now be dispensed with.

There is a general effort by researchers to use lab animals that are less likely to suffer the sensations of pain or discomfort. In Canada, many studies have replaced mammals with fish, and now researchers are even trying to use bacteria in tests instead of rats.

Conclusion

Animal researchers say that it will be impossible to eliminate all animal tests. But most scientists accept that it is extremely important to minimize the suffering of laboratory animals, and to use as few animals as possible. After reviewing the data it can be concluded that the suffering and death of laboratory animals can be minimized more meaningfully just by improving the experimental methodologies.

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(*Accepted for publication March 2006*)