

## EDITORIAL

## USE OF ANIMALS IN MEDICAL RESEARCH

The last two decades has seen a fiery but yet unresolved debate on the value of using animals in medical and scientific research, drug testing and education. Proponents for the use of animals in research cite numerous instances why animals are necessary in the investigation of newly emergent diseases, and to elucidate mechanisms and novel therapies for diseases of old.

Historically, animal research has provided answers to many debilitating viral and bacterial diseases that have afflicted man, from clarifying concepts on transmission and pathogenesis of disease to the development of vaccines; fostered the introduction of new drugs (sulfonamides, penicillin); made possible the development of open-heart surgical procedures, organ transplantation and treatment of renal-failure. Extraction from animal tissues of new hormones (insulin) and drugs (heparin) has proven a boon to the therapy of many illnesses..and the list goes on. Animal activists on the other hand contend that animal research is wasteful and misleading and in turn cite instances when such experiments have failed to address the pertinent health problems of our era. They stress that the uniqueness of animal biology, the unphysiological means whereby disease is introduced in the test subjects and the stresses of the laboratory environment introduce irregularities that are irrelevant to human pathology and therefore that all such testing is a waste of time and money. These individuals go on to cite failed monkey experiments of the early 20s and 30s, which led to misconception on the natural biology of the polio virus, delaying preventive measures, the early development of a vaccine, and finally when vaccine was synthesised from virus cultured in monkey cells, it potentially exposed many humans to potentially harmful monkey viruses. They speak of failed and inconclusive early animal experiments which delayed the implementation of anti-tobacco measures and point out data originating from the U.S. General Accounting Office review which found 52% "serious postapproval risks" in 198 of 209 new drugs marketed between 1976 and 1985, which were not predicted by animal testing.

There are also other ethical considerations. Although there is still much disagreement among scientists in judging pain and suffering in the housing and use of research animals, among the present day challenges are to address and characterise these issues and developing techniques and methodologies that eliminate such suffering. In recent years too, we have come to appreciate that animals have tremendous complexities in life, communicative abilities, social structures and emotional repertoires. The Netherlands in 1996 passed into law that animals have "intrinsic value", are sentient beings and are entitled to the moral concerns of humans.

In the light of all this, most scientists are agreed that some form of cost-benefit analysis should be performed to ascertain if the costs of animal pain, distress and death are counterbalanced with the benefits of acquisition of new knowledge and the development of new medical therapies for humans.

World-wide, the numbers of animals being used in laboratory experiments is declining and in many countries in the West, the total figures have dropped by almost half since the 1970s. The work of animal-rights activists such as that of the Australian philosopher Peter Singer and ethologists Dian Fossey and Jane Goodall have certainly played a role in fuelling the passage of laws regulating animal experimentation. Nevertheless, there is also a definite change in the mentality of modern-day researchers, who growing up in a later era, are alive to these concerns, acknowledge the inherent moral dilemmas of animal experimentation and have also imbibed the concerns of British zoologist William M.S. Russell and microbiologist Rex L. Burch who put forth the "three Rs" in their book "The Principles of Humane Experimental Technique". The 3 Rs exhort animal researchers to : replace animal by *in vitro* methods wherever possible; reduce animal numbers by means of statistical techniques; refine experiments so that animals do not suffer. Although these principles of "replace, reduce and refine" were set forth in 1959, it has taken the better part of twenty years to be accepted in scientific circles.

Present day researchers have at their disposal a vast armamentarium of modern research tools which they should be encouraged to exploit. These include epidemiological studies and clinical intervention trials, careful clinical record-keeping and laboratory testing, *in vitro* testing on human and cell cultures, autopsy examinations, utilisation of microinvasive or non-invasive imaging studies and the use of molecular epidemiological studies. Data emerging from recent research trends in atherosclerosis and HIV research are eye-openers because these emphasise how much new information can be derived while eschewing experimental animal studies. After all, it must never be forgotten that animal "models" are, at best, analogous to human conditions, and no theory can be proved or refuted by analogy alone.

The scientific community is now witnessing changing trends in the sense that humane organizations and government agencies are now investing in and funding research in alternative methods although this is more evident in Europe than in the US. Since 1992, a body has been set up by the European Commission, the Centre for Validation of Alternative Methods, which has an annual operating budget of US \$9 million. Statistical sophistry is allowing the classical LD50 test for animal toxicity to be eliminated and replaced by protocols which call for reduction of the number of animals used from 200 to 20. The Organization for Economic Cooperation and Development requests that between 3 and 18 animals be used - if the substance being tested kills the first three, no further testing is required. Similar modification in the LD80 for vaccine testing are being proposed, to greatly reduce the number and suffering of animals used. The use of "data mining" techniques has yielded interesting new findings that allows further purification of animal experimentation methodologies. Horst Spielmann of ZEBET, the German centre for alternatives to animal testing, "mined" decades of accumulated data from industrial testing of pesticides and concluded that if mice and rats prove sensitive to a chemical, it does not have to be tested on dogs. Through the activities of ZEBET, production of monoclonal antibodies in tumour-carrying mice has reduced significantly in Europe, as alternative methods are explored. *In vitro* cell lines have

supplanted the use of animals in the production of many vaccines and hormones, the most telling success story being that of the production of the polio vaccine. Biomembranes such as Corrositex are now being used in place of the shaved skin of live rabbits for skin corrosivity testing. Cosmetic companies are also reducing animal testing, relying largely on using chemicals tested previously. In medical schools, alternative teaching tools are used, which include the use of multimedia and virtual reality to re-create clinical scenarios; the use of human cadavers to hone surgical training skills is also being actively advocated.

In the US, more than a third of the medical schools do not use animals in their regular curricula. Other changes include the mandatory requirement that all animal experimenters require specific training and licensure before being allowed to do animal related research work. In several medical schools, there is an added emphasis in undergraduate curricula for students to explore and think of experimental methods alternative to animal research.

The Animal Care and Use Committee (ACUC) of the Faculty of Medicine was formed in 1988 with a composition of 9 members and empowered with the following terms of reference: "approve the uses made of animal subjects in all animal research studies; to review all animal studies for appropriateness and quality of the animal models; critically evaluate for the humaneness and appropriateness of procedures and conditions surrounding the animal subjects before and throughout the study; evaluate the animal research facility at least annually and to recommend appropriate action to correct deficiencies noted." Although these terms were formulated to reflect the prevailing philosophies on animal care research of the late 80s, it is noteworthy that the Faculty ACUC has endeavoured to promote and practise the same principles which remain current even today.

The ACUC records show that since its inception, approval of animals for experimental use in the Faculty (and in some instances, the University) has gradually increased and seems to be attaining a plateau presently. In 1992, a single request from the Department of Anatomy was given approval by the Committee. By 1996, the number of

projects approved by the ACUC had risen to 25. Aside from the Faculty of Medicine, the Faculty of Dentistry, Department of Genetics and Cell Biology and IPT, as well as government agencies such as PORIM use the Central Animal Facility for research.

It is the present Faculty thinking that at least some kinds of animal research are worth doing as there is no other alternatives available, and the expected results of such animal studies are

conceivably beneficial to humans. But in turn, animal researchers must be painfully aware that since animals may be physically (and perhaps emotionally) such good models for human conditions, then a moral and ethical dilemma exists in using them. We must acknowledge the debt we owe our fellow creatures and support endeavours and measures to achieve the maximum possible gain in scientific knowledge with the least cost in numbers and suffering to the animals.

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