

Ethics And Animal Use In Biomedical Research

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1. INTRODUCTION

The recognition for humane and responsible biomedical research by scientists, professional societies, scientific organizations and governmental agencies have enabled a better understanding of the resources, support, ethics and aims in this area. Animal experiments remain as the foundation for biomedical research and are the best hope in reaching a solution to the problems that face both the animals themselves, and human beings. Finding the cause of a certain disease, its treatment and prevention require animal subjects either as a unique cell or the organism in its complete form. The aim is to find a cure for pain, disability, and functional disorder of a system or perhaps death. Denial of better quality and longer health for mankind and animals in the future would add up to the present problems, should we abandon research making use of laboratory animals. Public and scientific awareness must be encouraged by practical and effective information dissemination. The ethics, rules and regulations that involve animal research to obtain medical benefits and improvement to our lives should be available and enforced thoroughly both in research and in education. Every effort and precaution taken to avoid experimental animal suffering and inhumane practice or mistreatment is a must¹⁻¹⁶.

For animals, as well as for people, preventive medicine is the least expensive, yet the most effective way in reaching a huge population. It is through the techniques and products of biomedical research where preventive medicine has greatly benefited both animals and humans with

proper nourishment, sanitation, vaccination, and breeding methods. Medications and measures to prevent and treat infestations or infections such as parasites (hookworms, tapeworms, etc.) and microbes (cholera, rabies, hepatitis, smallpox, diphtheria, tetanus, whooping cough, etc.) developed through research have saved and are still saving millions. Striking similarities between human and animal physiologic systems place animals as very valuable and irreplaceable insights into the human system. Thus, animal models have been critical in understanding the basic biology of microorganisms, and recently in determining how the immune system and genomics and proteomics work. Animals have played a vital role in detecting desirable and unwanted features of newly developed vaccines. Strict regulations prevent vaccine from being used directly in humans until it passes tests for safety evaluations in research animals. Furthermore immunomodulation (control of the immune system) in humans is possible through determination of antigenicity, route of infection, the dose of vaccine required for optimal response, all of which are derived from animal models¹⁵⁻²¹.

Animal experiments constitute the foundation of biomedical research. Finding a cause of a certain disease, its prevention and treatment require animal subjects either as a unique cell or as the organism in its complete form. The most prestigious scientific award since 1901, the Nobel Prize, recognizes the outstanding achievements such as chemistry, medicine; all of which have used animals in research. The Guinea pig, hamster, rat, mouse, snake, reptiles, frog, toad, amphibians, chick, chicken, sea slug, crab, squid, fish, fruit-fly, bee, pigeon, birds, worms, rabbit, dog, cat, pig, sheep, cow, horse, chimpanzee, monkey, various animal cells are to name a few. Hence a layout of some biomedical research winning Nobel prizes awarded since 1901 and examples of animals used in the corresponding research is presented in the following table (Table 1) by the Foundation for Biomedical Research, Washington, D.C., USA.

Analgesia for laboratory research animals is the usual practice in surgical or traumatic experiments, whereas euthanasia is mostly used when a thorough examination of the animal's tissues are required. The purpose is to reduce or abolish pain or anxiety related suffering. Of utmost importance is not to affect the results of the experiment, by using such analgesic agents. The animal in pain will not feed or drink, but will lose weight. Furthermore, it will position itself in the cage in a strange manner and be unresponsive to external stimuli. Euthanasia is administered either by chemical means as overdose (lethal) analgesics or by physical means such as decapitation, cervical dislocation, liquid nitrogen freezing, microwave heat or excessive bleeding. Researchers, too, must take into consideration the dangers to themselves of various chemicals or physical agents used in such

experiments. Discarding the corpses of experimental animals must also follow well-established rules; for example: either being cremated or buried in limed ditches⁴.

*Table 1. Examples of animals used in biomedical research winning Nobel prizes since 1901*¹⁸

Year	Scientist/s	Animal/s	Contributions made to biomedical science
1901	von Behring	Guinea pig	development of diphtheria antiserum
1902	Ross	Pigeon	understanding of malaria cycle
1903	Pavlov	Dog	animal responses to various stimuli
1905	Koch	Cow, Sheep	studies of pathogenesis of tuberculosis
1906	Golgi, Cajal	Dog, Horse	characterization of central nervous system
1907	Laveran	Bird	protozoa as a cause of disease
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...			
1996	Doherty, Zinkernagel	Mouse	immune system detection of virus-infected cells
1997	Prusiner	Hamster, Mouse	discovery and characterization of prions
1998	Furchgott, Ignarro, Murad	Rabbit	NO, signalling in cardiovascular system
1999	Blobel	Various animal cells	proteins, intrinsic signalling for transport
2000	Carlsson, Greengard, Kandel	Mice, Guinea pigs, Sea slugs	signal transduction in the nervous system
2002	Brenner, Horvitz, Sulston	Roundworm	genetic regulation of organ development and programmed death.
2003	MacKinnon, Agre	Bacteria	discovery of potassium and water channels in the cell membrane

Rats and mice that are specially bred for laboratory account for 95% of the animals used in research. Most of the remaining animals are rabbits, dogs, cats, Guinea pigs, hamsters, piglets, sheep, horse, cattle, fish and insects. Non-human primates, dogs and cats only account for less than half a per cent (0.5%) of the animals used in biomedical research^{8, 9,20}. Since the subject is very important, many publications concerning the ethical use of laboratory animals in biomedical practice have been propagated during the last few decades. Some examples of textbooks published for animal experimentations are given in Table 2.

Table 2. Examples of textbooks concerning use and ethics on animal use in biomedicine

The Biology of The Laboratory Rabbit.	Eds: Weisbroth S., Flatt R., Kraus A., Academic Press, 1974, ISBN: 0-12-742150-5
The Laboratory Rat: Biology and Disease: Research Application, Vol 1-2	Eds: Baker H., Lindsey R., Weisbroth S., Academic Pres, 1979, ISBN: 0-12-074901-7 and 0-12-074902-5
Formulary For Laboratory Animals.	Eds: Hawk C.T., Leary S., Iowa State University Press, 1999, ISBN: 0-8138-2469-9

Humans depend on animals for energy, food, clothing and research, yet there should be more interest for the responsible use of animals in biomedical research. Hence, C. Everet Koop (Paediatric Surgeon, former US Surgeon General) has said: "Virtually every major medical advance for both humans and animals have been achieved through biomedical research by using animal models to study and find a cure for disease, and through animal testing to prove the safety and efficacy of a new treatment. Without the use of animals in research, continuation of medical milestones will be stifled"¹². The rationale underlying the use of animals in biomedical research is that a living organism provides an interactive, dynamic system that can be observed and manipulated experimentally in order to investigate mechanisms of normal function and of disease¹⁴. While the use of animal models is a common component, its role and its scientific and ethical justification are frequently not addressed in the education and training of junior researchers.

2. HOW ANIMAL RESEARCH BENEFIT ANIMALS

Vaccines for feline leukaemia, rabies, distemper and parvovirus are available only because of animal research. Treatments for heartworm, certain cancers, and hip dysplasia have also been developed using animals. Endangered species of animals have been preserved and increased in number with the knowledge and technique developed through animal research. Although benefits of biomedical research are usually described in terms of life and death for humans and animals, there are economic benefits as well: the government and citizens save in medical costs and lost wages for money spent on biomedical research. Every American dollar spent in applied research and clinical trials saves 8 dollars in the treatment costs (National Health Institutes, USA)¹².

Should difficult ethical judgments arise in using a certain animal for a specific research, these are to be faced with a proper logical and scientific approach if other animals and humans are to benefit from healthcare advances resulting from that experiment^{5, 17}.

Having served as the secretary for the Research Granting Committee in Health Sciences at The Scientific and Technical Research Council of Turkey (TUBITAK) for over six years (1994-2001), the author had some experience in many confrontations and disagreements among the scientists, institutions, hospitals, the universities and the international organizations involved in such biomedical research. World Health Organization (WHO) and United Nations Educational, Scientific and Cultural Organization (UNESCO) and other organizational bodies, such as research bodies and institutions, universities and medical research foundations including the European Medical Research Council (EMRC, a standing committee under the European Scientific Foundation (ESF) in Europe), National Institutes of Health (NIH, USA), and the Royal Society (UK), have all agreed to the importance of the results and the benefits we have all obtained from antibiotics and insulin to blood transfusions, solid organ transplantation and treatments of cancer or HIV, oral contraceptives and in-vitro fertilization to hormone replacement therapy. In short, practically every medical achievement that has been gained depends directly or indirectly on animal use in biomedical research¹⁵.

Biological weapons and security in laboratories need to be also addressed, since bacteria, viruses, prions, or microbial toxins can be misused or perhaps intentionally used against humans and animals. Hence, bio-terrorist activities are under close scrutiny, especially in the past few years. Guarding against such activity has intensified interest into and protection from smallpox, anthrax, plague, botulism, tularaemia, hemorrhagic fever viruses, and most recently SARS (Serious Adult Respiratory Syndrome, originating in China and South-East Asia). A threat to human and animal life, these stockpiles of lethal disease of mass destruction require a thorough understanding and control of such sites. Identification, preventive measures and developing vaccines against such attacks can only be achieved through scientific knowledge obtained with animal research^{16, 21}.

Women and nature having been exploited by the patriarchal system, have been taken into consideration by most philosophers following the recognition of environmental problems during the 1970s. A strong relationship between the oppression of females and degradation and destruction of nature exist, where in turn a feministic perspective can be helpful in fighting against or solving such aggression. Cultural and social *ecofeminism* has gained much stride towards a world that we all accept as our home, peacefully living with the nature surrounding us (*Francaise*

d'Eaubonne)²². One of the major revolutions of the history of civilization was realized by women, with the domestication of plants during the Neolithic age enabling mankind to switch from a parasitic to a productive economy (*Mother nature*). Yet, with the formation of towns and political organizations leading to a “man cult”, which in turn both animals and women became slaves of this patriarchal system²³.

Integration to the world involves commitment and adaptation to developments in knowledge, productivity, equality, freedom of belief and speech, just and judicial government, democracy, clarity, ability to justify and ethical values¹⁷. A brief history of rules and tendencies for animal experimentation is given in Table 3.

Table 3. History of rules and tendencies for animal experimentation

Laws of Khammurabi (Sumerians, 1750 BC)	point out the rights for individuals. But is well kept in the area of “eye for an eye” understanding
The Oath of Hippocrates (470 BC)	has led from euthanasia patients’ rights. Thus, the saying, “Trust in the doctor to honouring of the patient and his/her rights.”
St. Francesco d’Assisi	has further pointed out that, animals are considered as sibling creatures and that their welfare are left to humans
James Watt	as the father of the steam-engine has indirectly saved animals from labour
P.J.M. Flourens (Physiologist, France, 1840)	has used anaesthesia for animal experiments
John Hunter	is considered the father of experimental medicine and biology, transplantation
Alexis Carrel	has further added to animal experimentation by enabling vascular anastomosis
Arthur Schopenhauer (1777)	has summarized the humanistic approach to animals

3. QUERIES CONCERNING ANIMAL RESEARCH

Queries to be answered before embarking on animal experimentation are as follows:

- Are animals a source for spare parts for human beings?
- Is human health and long-life worth the effort spent for biomedical research applied on animals in spite of the suffering?

While one needs to be concerned about the above questions there are facts to be considered for ethical evaluation in animal experimentation. These are presented in Table 6.

Table 6. Facts to be considered for ethical evaluation in animal experimentation ^{1-3,5,8-14,18}

Computer technology has enabled chemical, biological, plant and animal models for experimentation.

As biomedical experiments benefited both man and the beast there has been more trust on animal research.

Benefit for the human society has become more and more apparent.

Hence, benefit for the animals / plants / other living creatures

Frankness and open-minded research developed into knowledge based research

Awareness of pain and death has become a worldwide trend.

And what we as humans owe to animals has become a worthy ethical topic.

What do we expect of a world where humans have no or little respect for others? Humans affect the balance of nature, cause global inequality and global warming. Unethical biomedical research during the second world war such as experimentation on Jews by the Nazi rule and the 1970 Tuskegee syphilis research in the USA led to the 1947 *Nuremberg bylaws* and 1964 *Helsinki Declaration*^{1,6,21-23}.

Views Concerning Animal Use in Biomedical Research²⁴

“The advancement of biological knowledge and the development of improved means for the protection of the health and the well-being both of man and of animals require recourse to experimentation on intact live animals on a wide variety of species”

1982 CIOMS (Council for International Organizations of Medical Sciences)

“Animals are essential for biomedical research. Animals offer the best hope of finding the cause, treatment, and prevention for many diseases that inflict pain, disability and death. The study of animals remains a necessary prelude to using human subjects. Our choice is clear: animals must continue to play a vital role in medical research. Future generations of humans and animals cannot be denied better health.”

American Academy of Paediatrics

“Animal use in biomedical research is essential for continued medical progress.”

41st World Medical Assembly, 1989, World Medical Association

The use of animals in biomedicine is a moral issue as well. People from religious centres and scientists as well have not yet resolved the unease of taking the life of animals in pursuit of scientific knowledge and better medical care. Broadly, all major religions believe that human life is more valuable than animal life, that humans have a God-given authority over animals, that humans may eat or use animals for work, that humans should not be cruel to animals and cause their pain or suffering, that humans should be kind to animals. And they all actively support the use of animals in biomedical research or are tolerant towards those who conduct such research with a high degree of concern for the welfare of the animals.

4. THEOLOGICAL ASPECTS OF ANIMAL RESEARCH

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Animal Research From the Point of View of Religions

“A man is worth many sparrows, but not one sparrow can die unnoticed in God’s World.”

Matthew 10 vv.29-31, New Testament Church of England

“Provided they remain within reasonable limits medical and scientific experiments on animals are morally acceptable since they may help to save human lives or advance therapy.”

Catholic Church

“A very good case can be made out for vivisection of animals provided safeguards are taken to reduce the pain to a minimum. Here benefits to medical progress are considerable and the price worth paying.”

Judaism

“Some research on animals may yet be justified, given the traditions of Islam. Basic and applied research in the biological and social sciences, for example, will be allowed, if the laboratory animals are not caused pain or disfigured, and if human beings and other animals would benefit because of the research.”

Islam

“ Actions shall be judged according to intention. Any kind of medical treatment of animals and experiments on them becomes ethical and legal or unethical and illegal according to the intention of the person who does it.”

Islam

“A human life is distinguished from animal life due to its heavy responsibilities...”

Hinduism and Sikhism

“I undertake the rule of training not to do any harm to any living (breathing) thing.”

Buddhism

5. ANIMAL RIGHTS AND BIOMEDICAL RESEARCH

To date an extra twenty years and nine months have been added to human life by conquests established through the use of animals in biomedical research. Yet a tragedy and a waste of resources have come into being by the combat of anti-vivisectionists who claim to protect animal rights. Since

Darwin's establishment of "the origin of species" (1859) two basic ideas confront each other for use of animals in biomedical research^{7,12-14,17}:

1. *anti vivisectionists*: animals have the same rights and privileges as humans and should never be used for research purposes.

2. *animal welfare advocates*: animal experimentation can be allowed under ethical principles.

Opponents point of view

"Even painless research is fascism, supremacist, because the act of confinement is traumatising in itself." "Six million Jews died in concentration camps, but six billion broiler chickens will die this year in slaughterhouses"

Ingrid Newkirk (President, PeTA, People for Ethical Treatment of Animals)

"The life of an ant and that of my child should be granted equal consideration"

Michael W. Fox (Advisor to the Humane Society of United States)

"Arson, property destruction, burglary and theft are acceptable crimes when used for the animal cause"

Alex Pacheco (People for Ethical Treatment of Animals, PeTA)

"It would be great if all the fast-food outlets, slaughterhouses, these laboratories and the banks who fund them exploded tomorrow"

Bruce Friedrich

"In a war you have to take up arms and people will get killed, and I can support that kind of action by petrol bombing and bombs under cars, and probably at a later stage, the shooting of vivisectionists on their doorsteps"

Tim Daley (Animal Liberation Front)

6. PHILOSOPHICAL UNDERSTANDING OF ANIMAL RESEARCH

Cartesian dualism and modern concepts in philosophy and social sciences about man, medicine and ethics²⁷.

Rene Descartes > Cartesian dualism:

Man is a natural being / Man is a rational and free-will being

Thus the tension between medicine/ ethics

In other words; fact/ value

Tension cannot be decreased without the support/coordination of medicine with philosophy and social sciences.

Bio security identifies the preventive measures to control harmful consequences of biotechnology and its products on human life². Basic and applied sciences, which concern the security and ethics, are given in Table 4.

Table 4. Basic and Applied Sciences which Concern the Security and Ethics

Basic sciences	Applied sciences
Chemistry	Medicine
Genetics	Agriculture
Biochemistry	Ecology
Microbiology	Food
Physiology	Bio quality
Computer sciences	Fermentation

7. THE PRINCIPLES OF HUMANE EXPERIMENTAL TECHNIQUE

Russell and Burch have formatted the principles of ethical use of animals in biomedical research shown in the following lines as the “three R’s”; replacement, reduction and refinement, which have been well accepted by the scientific community.

- Replacement;** use of lower animals with one of higher development
use of dummies, in-vitro or computer models
- Reduction;** use of least possible number of animals leading to
understandable results and knowledge
- Refinement;** minimization of suffering during experimentation

These enhance the use of individual molecules, mathematical and computerized models, cells, tissue cultures, invertebrates, indirect laboratory tests, in vitro tests, transgenic or chimeral animals, maximal use of researchers knowledge and skills, best possible Project suggestions and management... more respect for other living creatures. Hence, through these principles the number of animals used for biomedical research in the British Isles have dropped from 5.5 millions to 2.3 millions during 1973 - 1997.

Objectives of Institutional Animal Care and Use Committee are: (IACUC)^{8,9}:

- understanding the ethical pros and cons for use of animals in research
- information of resources and regulations regarding the care and use of animals
- experience in relating to cases drawn from biomedical engineering
- understanding and validating of animal models

Basic criteria for IACUC approval:^{8,9}

Research has the potential for new information
 teach skills or concepts that cannot be obtained using an alternative
 will generate knowledge that is scientifically and socially important
 is designed such that animals are treated humanely.

Any project using animals in research should⁷ have a rationale for using animals (benefits to be gained); a description of procedures involving animals, a research design; with observational checklists for determining endpoints, and reduce (minimize) the number of animals needed in research. Maximizing the data gained from an individual animal; avoiding the duplication of prior research unnecessarily, using sound statistical methods in design and analysis are solid principles to be followed in the ethical use of animals in biomedical research. Refined experimental procedures to minimize pain and distress, confining with the standards for acceptable means of euthanasia are also most important.

In conclusion, continued biological, biomedical, veterinary, medical or even forestry, marine, agricultural and horticultural progress in the world, in other words, life in a universal scale depends upon animal research, properly and ethically performed.

REFERENCES

1. Özgür, A., Animal use in scientific research and alternatives. *Bioethics Congress*, May 2003, Bursa, Turkey
2. Kaplan S., Çobanoğlu N., Bioethical approach to biotechnology: Bio security. *Bioethics Congress*, May 2003, Bursa, Turkey
3. Müftüoğlu, A., An enquiry on the philosophical foundations of the relation between medicine and ethics. *Bioethics Congress*, May 2003, Bursa, Turkey
4. Altuğ, T., Karaca, Ç., Bayrak, İ., Analgesia and euthanasia of animals in research. *Bioethics Congress*, May 2003, Bursa, Turkey
5. Yılmaz, A., Social, economical, environmental, ethical and political outcomes of biotechnology and genetic engineering. *Bioethics Congress*, May 2003, Bursa, Turkey
6. Aksoy, N., Edisan, Z., Çevik, E., Aksoy, Ş., Ethics in international research. *Bioethics Congress*, May 2003, Bursa, Turkey
7. Bird, S.J., *The ethics of using animals in research*. <http://www.onlineethics.org>
8. Americans for Medical Progress, *Animal research*. <http://www.amprogress.org>
9. OLAW (Office of Laboratory Animal Welfare): *Public Health Service Policy on Humane Care and Use of Laboratory Animals. Health Research Extension Act 01 1985*, NIH 2002
10. FBR (Foundation for Biomedical Research), <http://www.fbresearch.org>
11. ACLAM (American College of Laboratory Animal Medicine), <http://www.aclam.org>
12. The Foundation for Animal Use Education, *Animals in Biomedical Research*. <http://www.animaluse.org>
13. *Your child may have been saved through animal research*, American Academy of Pediatrics, 1987, <http://www.acadped.org>

14. *Do we care about research animals?* 2000. National Institutes of Health. Public Health Service: NIH Pub. No. 79-355.
15. Gökçora, İ.H., 2003, in *Periodical Publishing in Medical Sciences* (O. Yılmaz, ed) TÜBİTAK Pub. House, Ankara, pp 1-3
16. *Regulations concerning ethical committee on animal experiments*, 2003, Baskent University Press, Ankara, Turkey
17. Tansal, S., Türkiye Etik Değerler Merkezi (TEDMER) Vakfı: *For a better Turkey*, Yılmaz Basımevi, İstanbul, 2002
18. Nobel prizes: The payoff from animal research, Foundation for Medical Research: <http://www.fbresearch.org>
19. *Draft report on The Animal Protection Act and views of the Commission for Ecology of the Turkish Republic*, 1999, Turkish Grand National Parliament, Official Gazette, Ankara.
20. Sümbüloğlu, V., Geyik, P., Sümbüloğlu, K., Ethics for the use of statistics in research, 1999, in *Medical Ethics Research* (B. Arda, ed.), Öncü Pub., Ankara, p: 19-22
21. von Engelhardt D, 1997, *Ethik im Alltag der Medizin Spektrum der Disziplinen zwischen Forschung und Therapie*, Birkhauser Pub, Berlin (Turkish: Namal A: Tıbbın Gündelik Yaşamında Etik: Araştırmadan Terapiye Disiplinler Yelpazesi. Nobel Tıp Kitabevleri Ltd Sti, Ankara, 2000)
22. Egemen, M.N., Çobanoğlu, N., Ecofeminist approaches to bioethics, *Bioethics Congress*, May 2003, Bursa, Turkey
23. Başağaç, R.T., Özkul, T., The slaves of patriarchy – women and animals, *Bioethics Congress*, May 2003, Bursa, Turkey
24. What organizations, scientists, major religions, opponents say about animal research, Foundation for Medical Research, <http://www.fbresearch.org>
25. Rosner, F., 1986, *Modern medicine and Jewish ethics*. Ktav Pub House Inc., New York, pp 317-333
26. Our responsibility for the living environment, Church House Press, London, 1986, pp 29-32
27. Masri, B.A., Al-Hafiz, A., 1989, *Animals in Islam*. Athene Trust, London, p 17