

Animal Experimentation Historical Aspects, Ethical Principles and Procedures

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Abstract

The objective of this work is to present historical aspects of animal experimentation, as well as to show the ethical principles to be considered in any experiment and the procedural characteristics that all research involving non-human animals must follow. To this end, the information obtained was categorized into five sections: introduction to the topic, record of the use of animals as anatomical and physiological models, ethical principles to be considered in animal experimentation, procedures to be followed in all animal research, and the lack of ethical foundation for vivisection. Finally, conclusions are presented resulting from the analysis and reflection of the theoretical concepts found regarding ethics in experimentation with non-human animals, with the aim of informing the debate on this complex topic.

Key words: animal experimentation; vivisection; ethical principles; suffering; replacement

Introduction

Biomedical research has focused on the use of animals as experimental models, since the observation of their anatomy and physiological processes has provided answers to questions about human health. Humans are considered superior to living beings within the context of reductionist Cartesian philosophy, as they are seen as the only beings possessing both body and soul, a dualism that grants them superiority in the animal kingdom. Furthermore, they are the only beings capable of being aware of their suffering, according to René Desartes (1596-1650), a view supported by W. Harvey (1578-1657) in his description of blood circulation, as well as by Mateu Roger Orfila (1787-1853), a toxicologist, and by Claude Bernard (1813-1878), an expert in vivisection (the practice of vivisection on live animals) and a prominent pupil of Orfila [1-3].

The biology and physiology of the human body were only superficially understood before the 18th century and were steeped in popular and religious beliefs. However, knowledge of these aspects increased substantially from the first half of the 18th century onwards with the use of vivisection, which aimed to reveal blood flow and cardiovascular, respiratory, and gastrointestinal physiology, as well as the reaction to toxins, poisons, and plant extracts. Even then, there was concern about vivisection because it was a cruel procedure that disregarded animal suffering, its practice based on the mechanistic view of humans as superior to all other life forms on Earth, who had to be kept healthy and at their maximum capacity regardless of the environment [4, 5].

It can also be noted that there is a clear obstinacy in pursuing scientific advancement, as well as a disdain for the slight improvements in the treatment of laboratory animals, considered insufficient due to a supposedly superior morality. This has served as an insurmountable obstacle to the possibility of convergence on common ground, that is, on a science with ethics [6-8]. The objective of this paper is to reveal, through analysis, relevant aspects of bioethics in animals, categorized under the following subheadings: brief description of the record of the use of animals as anatomical and physiological models, ethical postulates to consider in laboratory animals, procedures in animal research, vivisection as a primitive tool without ethical foundations, and conclusions.

Brief Description of The Record of The Use of Animals as Anatomical and Physiological Models

It was in ancient Greece, some 2,400 years ago, that live animals were first used in experiments, as this did not pose any moral impediment. Later, in the Middle Ages, animal experimentation was justified by theologians of that era, among whom Saint Augustine of Hippo (4th century) and Thomas Aquinas (13th century) stand out. They pointed out that animals were created to help human beings and that it would only be sinful to mistreat other people's animals because they were someone else's property [5, 9, 10].

The transition from the Middle Ages to modernity, during the Renaissance between the 15th and 16th centuries, bolstered the use of animals in solving scientific problems due to the Catholic Church's opposition to the dissection of the human body, which at that time was

being illegally dissected in contravention of the civil and religious rules of the era. Consequently, vivisection was revived during this period based on the argument that human interests prevailed over animal suffering [5, 11].

The use of animal vivisection to compare them with human anatomy and physiology continued to be employed by physicians in the 19th century, generating formidable controversies between those who support and those who oppose this practice [10]. In this regard, in 1635, the first regulations for the use of animals were established in Ireland, focusing on the prohibition of skinning mammals and the protection of horses in agricultural and draft work, which would later lead to the prohibition of cruelty to creatures used by humans [5, 12]. In 1660, cockfighting, dogfighting, and bullfighting were common practices in Iberian cultures. A century later (1754), Jean-Jacques Rousseau argued that, as sentient beings, animals should be included in natural law despite not being rational; and Marie Arouet (pseudonym: Voltaire) (in 1764) criticized those who considered animals as machines devoid of understanding and feelings, and their subjection to vivisection to discover in them the same sensory organs as those who carried out the atrocious procedure [5, 12].

The United Kingdom was the first country in the world to enact legislation protecting animals, with its "Cruelty to Animals Act" of 1822 [13]. This was a trial run, because in 1876 the UK published the more specific "Cruelty to Animals Act," which included elements of scientific experimentation on animals. This law was replaced years later, specifically in 1911, by the "Animal Protection Act," which was more comprehensive and imposed harsher penalties for those who violated it [5].

The British Animal Cruelty Act was adopted in the United States due to the excessive increase in testing and technological inventions [14]. In 1920, John William Trevan (a British pharmacologist) made the first attempt, albeit indirect, to reduce the use of laboratory animals in experiments through his statistical standardization of toxicity studies of substances (expressed as median lethal dose, LD50) [15, 16]. A landmark event in 1950 was the proposal by William Moy Stratton Russell and Rex Leonard Burch of the "3Rs" principle: replacement, reduction, and refinement [15-17].

In 1975, the Australian philosopher and professor Peter Singer revived the principle of the "3Rs" with his book "Animal Liberation," which decisively contributed to the creation of ethical codes for animal management worldwide [18], to such an extent that in 1978, the United Nations Educational, Scientific and Cultural Organization (UNESCO) established the Universal Declaration of Animal Rights, which was adopted by the legislation of many countries [5, 19, 20].

Ethical Considerations for Animal Experimentation

Regarding the use of animals for experimentation and ensuring their best possible treatment, guidelines for action have been established dating back to 1831 by Marshall Hall, a British physiologist, who stated that: if observation allows the information to be obtained, experimentation should be avoided; the objectives must be clearly defined before conducting any experiment; unnecessary repetitions should be avoided; the least possible suffering should be inflicted on the animals; and it is essential to ensure conditions that guarantee clear results [21].

For animal experiments to be considered ethically and morally acceptable in 1950, as mentioned earlier, Russell and Burch, British scientists, in their book **Principles of Humane Experimental Technique**, postulated the Three Rs principle: replacement, reduction, and refinement. The first conditioned the use of the other two; that is, if it is not possible to replace animals with other experimental models, among which cell cultures are currently prominent, then the number of animals used must be reduced in a way that guarantees statistical significance and avoids animal suffering [22]. It is worth highlighting the important contribution of the humanities and social sciences to animal protection, particularly the impetus given to

the "3Rs" principle in the 1970s, which had previously been neglected by researchers [23, 24].

In research, the use of replacement models, in addition to minimizing animal suffering, contributes to the results in terms of consistency and accuracy (since it is not always possible to apply the conclusions obtained from animal experimentation to humans due to the differences between species and the uniqueness of each individual of the same species) and in reducing economic investment, since the findings can be achieved in less time, by skipping the formalities of authorization of the experiment by bioethics committees and in the maintenance of breeding facilities or animal facilities [6].

Procedures in Animal Research

All research involving laboratory animals (in basic research, for biomedical and pharmaceutical purposes, for industrial and commercial interests, for educational purposes, and in the military) must include a detailed and thorough protocol. This protocol must be approved by specialized bodies in the subject matter of the study and after a rigorous search for alternatives. Furthermore, it must guarantee compliance with ethical principles during the experimental phase and the review of results [25, 26].

In all research involving laboratory animals, strict adherence to ethical principles must be ensured. Moreover, it cannot be simply asserted, without an exhaustive search, that there are no alternative experimental models to animals. In this regard, the following are used as replacements: cell cultures, gene editing, three-dimensional models and tissue engineering, organoids, organs or bodies-on-a-chip, and even mathematical computational models, since they allow for good correlations [27-33]. It is understood from the foregoing that the use of animals for evaluating aspects that do not aim to solve health or environmental problems, including those related to cosmetic safety, is not currently ethically justified. In this regard, the European Union and countries such as Turkey, India, Taiwan, South Korea, New Zealand, and Guatemala have banned animal testing for cosmetic components [3].

The validation of alternative methods to animal experimentation is also crucial, to the point that official institutions exist in various regions of the world, such as Europe, to establish the reliability—that is, the intra- and inter-laboratory reproducibility—of the tests and to ensure the transferability of results, which are necessary to certify predictive capacity and scientific rigor [3].

Vivisection: A Primitive Tool Without Ethical Foundations

A profound understanding of the physiology and biology of living beings on Earth has led to the disuse of vivisection. It is no longer justified, especially given the current development and validation of new experimental models and the existence of perfectly designed study sequences, in their preclinical and clinical phases, based on cellular and protein/enzymatic tests (in vitro assays) and on animals (in vivo), including human volunteers in most cases, to verify the safety (acute, subacute, and chronic toxicity), pharmacokinetics, metabolism, and efficacy of drugs in healthy and sick individuals. This also applies to the study of the pathophysiology of diseases and harmful agents, as it would mitigate the negative effects that captivity (in animal facilities) produces on the physiology and behavior of animals, which are reflected in the deficient results obtained with the elements tested to solve the health problem in question [5].

In other words, the emergence of ex vivo methods allow for a drastic reduction in the use of mammals in preclinical laboratory tests, for example, of natural substances from plants, animals, microorganisms, semi-synthetic or synthetic drugs, and food additives. This respects the animal's right to exist without suffering, while also saving time, reducing labor, and achieving a good cost-benefit ratio. And, of course, it ensures animal welfare, a fact further supported by the artificial intelligence

involved in validating alternative experimental methods and detached from purely anthropocentric ethical principles [34-36].

Conclusions

Since antiquity, researchers, by virtue of being human, have believed they have the right to experiment on animals to solve the health problems afflicting the society to which they belong, to obtain quality food, and to ensure an optimal environment for their complete bio-psycho-social well-being. However, this position has been, and will surely continue to be, the subject of complex ethical debates, which have led over time to legal regulations with progressively increasing levels of animal protection. These regulations, however, are not always followed by all researchers.

The anatomical and physiological similarity between animals and humans was the argument used to justify vivisection. However, with the scientific and technological advancements achieved to date in the biological and biomedical sciences, the use of experimental animals has decreased, and their welfare has been promoted. Therefore, ensuring the absence of replacements based on spurious research and/or the difficulty in validating prospects is no longer a justification for their use. Likewise, good laboratory practices, with rigorously evaluated protocols, should be the defining principle of animal research when it is not truly possible to replace animals.

The scientific community is unfortunately plagued by ethical stances and assumptions that avoid research without suffering in non-human animals, despite the existence of legislation on the matter. Combating these circumstances must be the central focus of ethics committees, working towards the true construction of a theory of justice for both human and non-human animals. What is truly needed is the widespread development of empathy for a science free from animal suffering, a path that is not without theoretical and practical obstacles.

Declarations

Author Contributions

All authors have contributed equally.

Ethical approval and consent to participate

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Competing interests

The authors declare that they have no competing interests.

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