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Review Article

Ethical aspects of biomedical research in the context of progress in medicine

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ABSTRACT

Introduction: Among numerous branches of science, advances in biomedical research are perceived to be the most controversial. This relates to biomedical experiments which involve human and animal trials. This article attempts to outline both historical and current dilemmas in the field of biomedical sciences.
Aim: The aim of this study was to discuss ethical and moral issues connected with experiments involving animals and human beings. The authors aimed at presenting directions of development for new branches of medicine.
Materials and methods: This study presents a review of contemporary medical literature and legal regulations concerning experiments on animals and human beings.
Discussion: The issue and definition of bioethics, its historical evolution, as well as specificity of medical sciences, experimental control methods, current implementation of a new operative technique – fetal surgery – and legal regulations concerning the protection of animals used for experimental purposes are presented.
Conclusions: Experiments have always been a part of medical developments and it is unlikely that such would ever be abandoned. Over the years, not only the advancement of medical procedures, but also the efficacy of treatment has changed. Along with developments in medicine, the approach to medical experimentation on humans and animals has changed as well. Currently, medical experimentation has entered a new age which may be termed "humanitarian," "planned" or "aimed," which are all connected with devising well-accepted standards and appropriate legal regulations.

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1. Introduction

In the first part of this article the authors presented bioethics in the context of scientific experimentation and research, its history and the complexity of its financing. In the present article this discussion is continued, with special interest placed on the ethical aspects associated with the cloning of a human being, methods of controlling biomedical research, specificity of psychiatry in medical research and threats and benefits connected with the new branch of medicine – prenatal surgery.

2. Aim

The aim of this work is to present the ethical and moral aspects of biomedical research and progress in medicine.

3. Materials and methods

Authors performed a review of scientific literature and contemporary legal regulations concerning biomedical experiments.

4. Discussion

A special kind of control should be established with respect to biomedical research. The committee responsible for such a task should be fully independent of researchers and guarantee a multidirectional perspective concerning a given problem, in consequence of the multidisciplinary character of that team of experts – scientists and moral authorities – involved. Such a board would verify the bases of medical experimentation, its compatibility with the Declaration of Helsinki and national regulations. Members of the board would also verify in detail a patient's consent to the medical procedure that is to be undertaken, not only examining its authenticity, but also ensuring that the patient fully understands its content.

Control over research conducted on humans is exercised by Local Bioethics Boards elected in each Regional Medical Chamber or Medical University. These boards observe the regulations for accepting each research project according to the Declaration of Helsinki (1964), detailed at the Tokyo Conference in 1975. They act in compliance with national regulations. In Poland such regulations include, among others, the Medical Profession Act and the Ministry of Health ordinance on detailed regulations concerning the establishment, financing and functioning of bioethics committees. Standards of biomedical experiments are established in compliance with all legal regulations addressing this issue.[7,9,12,19,20,21,22,23,24,27,30,32]

Experiments on animals have always been and still are a driving force for progress in medicine as best exemplified by the first attempts concerning organ transplantation. Dehoux et al. mention the utilization of large animals, including the primates, in biomedical research in order to obtain data reproducible in humans.[5] Knight questions the benefits of including the primates in experimental research because of the neglectable impact of such data on the citation rate. Moreover, he states that conducting experimental work of questionable scientific value, burdened with high rate of moral doubts, proves a decline of science.[13]

Looking back, as in experimentation on humans, the first attempts involving animals were conducted in the absence of regulations which could prevent those animals from suffering. In 1978, during the UNESCO meeting in Paris, the Universal Declaration of Animal Rights was conceived. It is a set of regulations that oblige scientists, among others, to respect the dignity of animals; these regulations forbid killing animals for no justifiable reason, maltreating and subjecting them to acts of violence. When an animal must be killed, an appropriate method causing neither pain nor fear should be undertaken. No experiments connected with physical or mental suffering are allowed under the provisions of the European Council Directive 86/609/EEC. This Directive defines the types of animals which may be regarded as experimental (laboratory, bred animals), defines methods of humanitarian treatment, minimizes suffering by allowing a certain number of anesthetic drugs to be used, and establishes a proper control system over the experiments, protection of endangered species, decent conditions in breeding institutions placed in an official register.[31] Moreover, it allows only those killing methods regarded as humanitarian.[17,18] An unjustified act of killing an animal is regarded as a crime against life. In the light of Polish law, according to the Animal Protection Act[29] and the Act on experiments on animals,[28] experiments on animals are restricted only to those cases in which potential results are not obtainable by means of any other methods.

Local Ethics Committees, controlled by the National Ethics Committee, are responsible for controlling experiments conducted on animals.[31] They devise a list of institutions allowed to conduct experiments on animals, breed animals for the sake of experiments, and determine the register of animal species defined as "experimental." Moreover, they establish the rules of conducting research on animals. According to the experimental animals' register in Poland, the experimental species are mice, rats, guinea pigs, cats, Japanese quails, gerbils, field voles, red voles, and lab opossums.[14] The "scale of invasiveness of experiments on animals" defines the degree of invasiveness and thus constitutes one of the basic tools in the assessment of an experimental project by local ethics boards.[33] It is a five-point scale assessing not only the kind of procedure utilized, but also the involved species, the consequences of implementing a chosen procedure, the possibility of enforcing humanitarian methods of killing the animals and of minimizing their suffering. It begins with level 1 procedures (non-invasive), used mostly in behavioral studies, while level 3 procedures involve moderate suffering and stress – they cover most surgical procedures. Level X involves forbidden procedures, causing extreme stress or suffering, allowed only in extraordinary circumstances, having first obtained a positive opinion from the local ethics board.[2]

In Germany a specially designed, double control model was established in order to maximize the degree of transparency and ethics clearance of experiments on animals. This model

is applied not only by ethics boards, but also by the members of the German Animal Welfare Federation.[25]

It is important to note that the majority of the claims referring to breaking the law regulating animal rights do not involve the course of the experiment itself, but most often relate to the poor conditions in which animals are kept or to the conducting of experiments on homeless and stray animals such as cats and dogs.[2]

The following regulations established after the Nuremberg Court Statement of 1947 address the issues associated with medical experimentation: The Geneva Convention, Convention for the Protection of Human Rights and the Dignity of the Human Being with Regard to the Application of Biology and Medicine, and Convention on Human Rights and Biomedicine. These instruments, however, turned out to be insufficient as regards keeping pace with progress in medicine, especially a living organism cloning. On January 11, 1998, the European Convention on Bioethics was enriched with a "Supplementary Protocol to the Convention for the Protection of Human Rights and the Dignity of the Human Being with Regard to the Application of Biology and Medicine."

The success of medicine based on scientific research and biomedical experiments facilitates the implementation of the so-called "medical utilitarianism." It is, therefore, easier to objectify a human embryo than an adult human, especially if its creation has been denied all the mysticism and magic implied and is replaced by a lab tube and a laboratory room. In such an environment, it is easier to regard blastocyst not as an early stage of *Homo Sapiens* development, but as a group of cells that may be extracted in order to serve as "spare parts" for a mature "item".[1]

Besides a great interest in mediagenic phrases such as "cloning" (both therapeutic and reproductive), media representatives, lawyers, ethical authorities and Church representatives are particularly attracted to the following terms: "eugenics," "stem cells," "tissue and organ breeding," and "tissue engineering".[18] Governments that approved the European Convention on Bioethics were provided with a free choice in designing legal regulations concerning experiments on embryos and stem cells. The first model, based on the German one, implemented in Austria, Ireland, Luxemburg, Norway, Switzerland and Italy, either forbids one to undertake any experimentation on embryos, or allows such experiments if they are of benefit to the embryo itself.[2,18] The other solution, proposed in France, allows experiments on embryos only for the sake of high social interest (progress in medicine for disease eradication, facilitation of fertilization).[2,18] An additional criterion to determine the legitimacy of such experiments in the UK, Holland, Greece and Finland is the period of up to 14 days after fertilization.[2,18]

Issues connected with stem cells, tissue engineering and cloning are examples of conflict of interest between the imperative of progress in science and medicine and limitations associated with moral principles as well as doubts concerning the future effects of such actions.

Włodzimierz Korohoda's opinion as regards modern tissue and cellular biology appears interesting. He states that it is morally more unambiguous to use pluri- and multipotential cells instead of totipotential cells, because the first two types may be obtained from bone marrow, umbilical blood and even other tissues of a mature individual, unlike the latter ones that can be derived only from a human embryo. Moreover, pluri- and multipotential cells still exhibit the potential of differentiation to neurocytes, cardiomyocytes, myocytes or epithelial cells.[18]

It is important to highlight that stem cells in medicine *de novo* aroused a heated discussion about the beginning of life, thus transferring it to another dimension. The vast area of conflict of interest appeared among corporations seeking profits from new technologies, idealists hoping for the humankind salvation and philosophers, ethicists and moralists trying to control and supervise their actions.

As regards experiments on fetuses, two major options need to be analyzed. For histological and precise anatomical research it is necessary to work on fetuses obtained from spontaneous abortions, not burdened with congenital malformations. In such cases it is necessary to receive the approval from a Local Bioethics Board.[15,16,17] Another solution is to employ prenatal diagnostics. Along with the progress in medicine, ever more modern non-invasive methods of intrauterine fetal diagnostics are being implemented. They enable the detection of congenital malformations – both life-threatening and non-lethal – while not being burdened with the risk of fetus' damage. Along with the tendency to minimize the invasiveness of surgery, new horizons have appeared. It is now possible to conduct intrauterine surgeries during fetal life. Such procedures enable one to correct malformations without creating a scar and prevent a newborn from long and multistage reconstructive surgery in extrauterine life. From an ethical and moral point of view, such a procedure is sensible, when appropriate risk–benefit ratio is maintained – for both the fetus and the mother.[6,8,11,26]

Intrauterine surgery history began in 1918 when Mayer "transplanted" a guinea pig fetus from the uterine to the abdominal cavity. Next, fetal limb amputations, enucleation of the eye, and adrenalectomy were performed. In the 21st century, tissue engineering has been implemented to repair tissue defects. Modern fetal surgery procedures are allowed only in cases of proven lethal fetal malformations such as hydrocephalus or a posterior urethral valve. The first intrauterine surgery conducted on a human being was a fetal blood transfusion. The year 1981 is regarded to be the beginning of fetal surgery sensu stricto, when Harrison et al. performed the first open operation of bilateral hydronephrosis on a fetus.[10] Further operations included congenital diaphragmatic hernia, endoscopic discectomy, cleft lip reconstruction and myelomeningocele. Currently, indications to fetal surgery, including cleft lip and palate or gene therapy, are considered to spread.[29]

When discussing fetal surgery, one in fact talks about a new technique which is still in its experimental phase. Its bases are well-founded on experiments involving animals and this may serve as a good example of a legalization process concerning a new medical procedure, including any doubts associated with its moral character.[8]

The review of legal regulations addressing fetal surgery proposed by Doyal and Ward defines base-line restrictions, common for many countries (the UK, USA, Australia), for intrauterine surgery. The issues that are commonly applied include well-established experimental bases, pregnancy

termination time as independent of the researchers, minimal risk of the procedure for the fetus and mother, high sensitivity and specificity of prenatal diagnostic methods, maximal control of preterm labor being the most common and the most life-threatening complication of fetal surgery, employing an experienced and multidisciplinary team of experts, proven benefits of intrauterine surgery versus conventional surgery, informed consent provided by the mother and its specificity because it also is valid for the fetus, psychological support and surveillance of ethics boards.[8]

As previously mentioned, malformations detected *in utero* may be divided into two groups: lethal and non-life-threatening.[6] As long as intrauterine surgeries associated with the former group seem to be justified, keeping in mind all the expected threats for the fetus, when performing such procedures in the latter group of indications researchers face the dilemma between benefits obtained from a more effective treatment (practically scarless healing, no development of a potential impairment, avoiding long and multistage reconstructive surgery) and, on the other hand, potential fetal death or serious impairment as well as preterm labor. According to some authors, the risk of intrauterine surgery, including fetal death, approximates 50%.[8] A general rule is to implement the most secure existing surgical techniques, safe anesthetic techniques and – above all – precise prenatal diagnostics. It is also crucial to prove the therapeutic benefits associated with this kind of procedure.[6,8,11,26]

5. Conclusions

1. Experimentation has always accompanied medical progress.
2. Over the years, not only the complexity of medical knowledge and treatment efficacy has changed, but also the attitude to medical experiments.
3. As of 1947, medical experimentation takes into consideration ethical issues.
3. New branches of medicine, such as intrauterine surgery, should be developed under the strict supervision of bioethics authorities.

Conflict of interest

None declared.

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