Legal estimation of adverse effects of genome technologies applied to embryos

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Abstract. By manipulating the genome, it is possible to correct hereditary diseases in humans. Ensuring the birth of healthy children by diagnosing and selecting, for in vitro fertilization, an embryo that does not contain a pathogenic mutation is a serious prospect in modern genomic research. However, the legislative approaches of states towards this issue remain very ambiguous due to the complexity of the ethical and legal sides of this problem. We believe that a single consensus international position should be adopted on the issues of intervention in the human genome, otherwise permission to conduct in one country may lead to negative reactions in other states and lay criminal risks in this area.
Keywords: genetic research, genome, embryo, human genome editing, bioethics, ethics

1 Introduction

In 2019, it was reported that biologists applied to the Russian Ministry of Healthcare to approve a clinical research (trial) to edit the embryo of parents with hereditary deafness, having already found people to participate in the experiment [1]. Changes in the human genome may cure hereditary diseases. A genome editing experiment was planned to rid humans of hereditary diseases and, in the long term, to cure them by making it impossible for the patient's descendants to develop these diseases. Discussions about the possibility of embryo genetic editing research are taking place among clinical scientists around the world [2].

The discussion of embryo genetic editing research has mostly raised doubts about the feasibility of such procedures, but has also raised new and complex ethical, legal and social issues. Ethical issues are undoubtedly important and their resolution will determine the future of such technology [3].

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2 Materials and Methods

The materials for the work were the provisions of the Russian legislation, as well as normative-legal acts in force in the field of health care, and theoretical views of authors who have researched a similar topic. The reliability of the obtained results is provided by the study of legislative norms, as well as the use of modern methods of research method: logical, formal, legal, comparative-legal, system-structural and other methods of scientific cognition.

3 Results

Modern reproductive methods make it possible to detect genetic anomalies at the earliest stage of embryo development. There is no doubt that the idea of diagnosing and selecting embryos without pathogenic mutations for subsequent extracorporeal fertilization is promising. One should also consider the possibility of analyzing the embryo genome at the early stages of pregnancy and, if genetic defects are detected, giving parents the opportunity to decide whether to continue the pregnancy or terminate it. These reflections raise new and complex issues, both ethical [4-7] and social [8-10], and require the development of appropriate regulatory and technical mechanisms.

However, the state is taking measures in this direction as well, resulting in a dilemma about the need for such extraordinary measures. For example, by the Order of the Government of the Russian Federation No. 1510-r of June 9, 2022, starting from 2023 [11], "measures shall be implemented aimed at conducting expanded neonatal screening of newborns. Testing of newborns for hereditary diseases shall grow from 5 to 36 nosologies; in particular, hereditary metabolic diseases, primary immunodeficiency states and spinal muscular atrophy shall be included in the screening". The main objective of the program is diagnostics of hereditary diseases at early stages and implementation of an appropriate set of measures.

A committee established by the World Health Organization in 2019 took up the principles and oversight of human genome editing. Its decision was that it is currently unacceptable for anyone to pursue the clinical application of human embryo cells genome editing. The organization therefore called on states and their ethics committees to refrain from authorizing such clinical trials [12]. However, in 2021, the organization indicated in its report that such technology could be a cure for many diseases if it benefits many people rather than exacerbating inequalities among them [13].

In the international legal system, specific norms regulating experiments with the human genome are stipulated by the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine, adopted in 1997 [14]: Article 13 stipulates that interference with the human genome aimed at its modification may be carried out only for prophylactic, diagnostic or therapeutic purposes and only provided that it is not aimed at modifying the genome of the person's heirs. Article 14 prohibits the use of medically assisted reproduction technologies for the purpose of selecting the future child's sex, unless it is done in order to prevent the inheriting of a sex-linked disease. Notably, it is permissible to use assisted medical technologies to prevent the inheriting of a sex-linked disease.

The Convention addresses the possibility of interfering with the embryo's genome only in Article 18, which states that "if the law authorizes research on embryos in vitro, it shall also provide for appropriate protection of the embryo" [14]. In our opinion, this rule seems too general, leaving little specific guidance for states to regulate research. This may create uncertainty in how states should balance scientific development with protecting the future of humanity. Specifically, it is unclear how states should define protections for embryos in the context of such research and what protections should be considered adequate.

The current development of genome editing means that it is too early to talk about their clinical application. This requires comprehensive studies to investigate possible complications and predict the final effect. We believe that this is the correct decision that will not lead to negative consequences. Chinese scientists, He Jiankui and his two colleagues, became publicly known for conducting genetic research that resulted in the birth of two children with HIV immunity by editing the embryos' genome. Officially, such genetic experiments on human embryos are prohibited in China. Jiankui conducted his experiments with eight couples undergoing fertility treatment, where all men were HIV infected. The genetic changes were made during in vitro fertilization. The scientist was criminally prosecuted [15]. A lot of researchers condemned his work [16].

Researchers adhere to various concepts; some fully advocate the prohibition of such research [2] and others propose to legally allow experiments on embryos up to 14 days of their development [17]. According to A. A. Pestrikova, the issue that requires its own legal regulation "is the research with embryos at an early stage of development, especially regarding the acute problem of utilization of unused embryos, for example, in assisted reproductive methods, which can become the object of scientific research" [18].

4 Discussion

At the level of legal regulation, the following legal issues need to be resolved:

First, it is necessary to define the concept of "embryo", which is absent in the current legislation, and to consolidate its legal status. This will outline the unlawful acts that can be committed in relation to an embryo and increase its value and significance by establishing an effective legal protection regime. Notably, the term "embryo" is used in the current legislation, for example, Article 55 of the Federal Law No. 323-FZ of November 21, 2011 "On the bases of health protection of citizens in the Russian Federation" [19]. Recognition of its legal status will inevitably entail changes in the current criminal legislation designed to protect the most significant and important social relations, including those related to the editing of the embryo genome and encroachments on it. Current criminal-legal prohibitions do not contain norms protecting the fetal genome and prohibiting interference in it. Therefore, experts should formulate laws, regulations and guidelines to punish for genome editing and prevent such negative events in the future [20].

Secondly, given the future prospects, it seems important to speak about the possibility of allowing clinical trials related to embryo genome editing. However, we believe that such research should be conducted openly and be strictly regulated at the level of current legislation. It is worth reminding that the Russian legislation does not currently contain any prohibitions or authorizations for human embryo genome editing. In accordance with Article 37 of Federal Law No. 323-FZ of November 21, 2011 "On the bases of health protection of citizens in the Russian Federation" [19], medical care should be provided in compliance with the procedures for medical care, be based on clinical recommendations and take into account the medical care standards. To take into account the individual characteristics of the course of a patient's disease, a collegial decision is required, for example, at a meeting of a board of doctors or a medical commission. Consequently, a standard is needed to ensure that such a procedure is carried out in accordance with the law and to limit possible abuses and risks that may arise in this regard. It will also hold the health care provider accountable, including criminally liable, if necessary.

Thirdly, it is essential to consider the issue related to the definition of what the embryo genome editing activity will be – medical activity (medical assistance) or not? Based on the definitions of medical service and medical assistance, contained in Article 2 of Federal Law No. 323-FZ of November 21, 2011 "On the bases of health protection of citizens in the Russian Federation" [19], it remains unclear whether this type of activity will refer to medical

service, that is, prevention, diagnosis and treatment of diseases and medical rehabilitation. It seems that it will be necessary either to expand the concept of "medical service" in the current legislation, or to refer the activity of interference in the embryo genome to another type of activity, for example, genetic engineering or scientific research. At the moment, there is only a prohibition to use assisted reproductive technologies to choose the sex of a future child, except there is a possibility of inheriting sex-related diseases.

In addition, we believe it essential to distinguish between the purpose of genome editing – whether this manipulation will be used to prevent or treat diseases that endanger the life of a future child. On the other hand, it is well known that the line between treatment and improvement is blurred.

Fourthly, it is worth considering and introducing the mandatory obtaining of the patient's voluntary informed consent for medical intervention in the form of embryo genome editing. It is unclear how the voluntary informed consent may be expressed in this case, because it is not clear what negative consequences may result from the use of the new biomedical technology, what risks and threats may arise, and how effective and clinically proven it is.

Fifth, the subsequent approval of interventions into the human genome may raise a range of ethical issues related to programming the human genome to have certain aptitudes or skills, depriving the society of other talents that may suddenly become necessary. Not to mention the potential reduction in genetic diversity (because modifications can converge on a few preferred traits), since diversity is one of the tools by which evolution ensures that species thrive. The more types can be found in a population, the easier it is to face new environmental challenges, be it bacterial or viral threats or harsh climatic conditions.

5 Conclusions

One should support the authors' view that, as long as we cannot yet achieve the exact goal and do not know what side effects localized modification may cause, research should be restricted at the government level [2]. Any editing of human embryos may potentially spread to the entire species with unpredictable consequences.

We believe that a unified consensual international position should be adopted in the issues of interference in the human genome. Otherwise, authorization to conduct it in one country may entail negative reactions in other states and lay down criminal risks in this sphere.

Legislative regulation will undoubtedly have a decisive role in this issue, especially in the unforeseeable future. In our opinion, it may be justified to allow embryo genome editing (insertion) only in a few specific cases that involve a risk of death or extremely disabling life conditions.

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