

MATERIALS OF SCIENTIFIC-PRACTICAL CONFERENCE WITH INTERNATIONAL PARTICIPATION «THE INFLUENCE OF COLD ON THE HUMAN ORGANISM»

I. THE INFLUENCE OF COLD ON THE HUMAN AND ANIMAL ORGANISM (BIOCHEMICAL, IMMUNOLOGICAL AND GENETIC ASPECTS)

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THE ETHICS OF CARRYING OUT RESEARCHES ON LABORATORY ANIMALS

ABSTRACT

The basic ethical principles and rules of carrying out researches on laboratory animals are presented in the article. First of all, modern ethics of the humane treatment of animals should be based on correctly thoughtful design of an experiment to receive qualitative results. The science develops in the direction of minimization of using animals in experiments if there is an opportunity to receive similar results by alternative methods.

Keywords: bioethics, laboratory animals, clinical tests.

Historically in scientific researches a person always used different types of animals for studying of fundamental laws of life: anatomy, physiology, pathology. Animals are very convenient objects for experiments for imitation of biological conditions, human diseases, for development of scientific techniques, use as a training material etc. So, according to an ultimate goal, as models of a research insects (*Drosophila*), nematodes (*Caenorhabditiselegans*), fishes (*Daniorerio* or zebrafish), frogs (*Xenopus*) and many mammals as mice, rats, rabbits, dogs, cats, pigs and monkeys are used [5].

Conditioned reflex theory, established more than 100 years ago by I.P. Pavlov, is a fundamental theory in the history of physiology and psychology up to now. Of course, many operations performed by the scientist end deplorable for an experimented animal. In the parlance of Pavlov, when he cuts and destroys a live animal, he suppresses in himself bitter rebuke that breaks the art mechanism, but reminds himself to do it only in the interests of truth and for the sake of human benefits. Making the experiments, Pavlov did all surgical interventions only under anesthetic to prevent an animal additional suffering. The monument to a dog, established by Pavlov in St. Petersburg, also tells about the scientist's attitude to his little patients [3,4]. Nowadays, an interesting example of the experiments on dogs is the imitation model of Fallot's tetrad congenital heart disease (also known

as a blue baby syndrome) developed by Vivienne Thomas and Alfred Blalock. This model allowed developing a surgical method which salvages more than half a million children a year [15] these days.

Anyway, nearly 90% of the Nobel Prizes got by researchers in the opening in the field of physiology and medicine are deeply bound with the experiments on animals. Animals are peculiar victims of science, gratuitously and dumbly giving the lives on service to mankind. To the present, major bioethical discussions were held generally only about using human primates in experiments (a chimpanzee, etc.). After 2007 only the United States and Gabon continued to use a chimpanzee for researches, but in 2015 the United States made a statement that they won't finance any researches with participation of chimpanzees [5] any more. On the other hand, for example, the main problem with HIV infection is its increased tropism in human tissues complicating an animal HIV modeling. The virus isn't able to infect mice, rats, rabbits or macaques though it can be replicated in a chimpanzee. Find this way out using chimeric immunodeficient mice with the transplanted human cells and tissues. Progress in genetic technologies allows making a great number of experiments on transgene animals; there are created the whole pure line animals with prescribed properties of genes or, on the contrary, null mutant animals, so-called gene knockout animal models [9].

The fundamental ethical principles of work with laboratory animals should

be considered the principles entered by Russell and Bertsch [5,6]:

a) reduction - the greatest possible decrease of number of animals put to the necessary educational or scientific purposes;

b) refinement - improvement of the experimental techniques for depression (exception) a negative (painful, high-stress, etc.) influence on an animal;

c) replacement - elimination of animals from an experiment or a study if there is an opportunity to receive similar results by alternative methods [13,16].

Primarily, modern ethics of the humane attitude towards animals have to be based on correctly thoughtful design of an experiment to produce qualitative results and to exclude undesirable deviations. It is necessary to pay an attention to acceptance criteria (exclusion and inclusion criteria), required sampling size (the necessary quantity of animals) for ensuring the reproducible results [6,10].

Scientists notice that in basic biomedical researches large financial means are put and huge quantities of different types of animals are used, but when it comes to applied researches and introducing the results in practice many of the best research ideas promising translational effects fail. Especially, this includes translational researches in the field of aspects of human behavior where it cannot show any similarities between model of an animal and a human [6, 12] yet.

The right choice of species of a model

animal is of great importance for an ethical scientific experiment, for example, promising results on studying of type 2 diabetes mellitus were obtained on mice, because glucose exchange happens generally in myocytes and hepatocytes equally in all organisms including human [7].

Management of laboratory animals in an experimental room have a significant impact on the final results of the research. The housing conditions (temperature, humidity, light, food) is very important, an animal should have no stress. For example, in the research of studying of breast cancer on models of mice it was shown a tendency of tumor volume reduction of mice which lived in the improved conditions in contrast with mice kept in standard conditions where stress could enlarge inflammation of the mammary gland [11].

For a scientific experiment with use of animals it is ethically correct to calculate quantity of animals which should not be too little or too much. The amount of selection depends on four parameters: minimum expected difference; the calculated standard deviation; statistical significance; importance criterion. Before planning an experiment with animal models it is necessary to make meta-analysis of publications on the studied problem [6,8]. Advantages of meta-analysis over reviews of literature following:

- specifies that selection is more various than it was supposed, proceeding from a variety of samples;

- generalizes several researches;
- controls a variety between researches;

- can explain a variety between data;
- enlarges statistical power;
- works in the conditions of information overload (a large number of articles is published every year);

- generalizes several researches and therefore depends on separate finds less than individual researches;

- can notice systematic errors [8].

For the first time «Cruelty to Animal Act» was adopted by the British Parliament in 1849, he determined three main issues: 1. experiments on animals have to be made when there is an absolute need for knowledge useful to conservation or prolongation of life or relief of suffering of the person; 2. an animal has to be anesthetized; 3. animals have to be killed right after the experimental procedure if they were damaged or felt pains as a result of an experiment [2,5].

in 2010, at the initiative of the

international organization of the National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs) the management of ARRIVE (Animal Research: Reporting of In Vivo Experiments), approved by scientific magazines and the sponsor organizations, was framed. The ARRIVE contains the guides which were translated to several languages and has the check list of 20 points concerning such information as number and specific characteristics of the experimented animals (for example, types, gender, strain, genetic features), conditions of keeping, the description of experimental, statistical and analytical methods [5].

The ethical rules of work with animals applied in the Russian Federation are based on regulations of the Declaration of Helsinki and **References** in directives of the European Community (86/609 EU) [16] and also Rules of carrying out high-quality clinical tests in the Russian Federation (the order MZ USSR N 755 of 12.08.77 «About measures for further improvement of forms of work with use of «experimental animals»):

- Institutions can carry out work on animals if the following conditions are satisfied: a) having a vivarium (experimental biological clinic) equipped according to the sanitary requirements N 1045-73 from 06.04.73; b) having an experimental operation room (laboratory) with appropriate equipment; c) having staff providing care of animals.

- Housing conditions of an animal in a vivarium (clinic) have to provide a normal biological background and completely conform to the building code requirements.

- While planning studies or scientific experiments the species of the used animals, and quantity requested for obtaining reliable results have to be proved.

- All procedures on an animal which can cause severe pain or stress should be performed by adequate anesthesia (under local anesthesia or under narcosis), except the cases stipulated in the Appendix 3 to Order No. 755 of the Ministry of Health of USSR of 10.08.77.

- Use of an animal for morbid procedures more than once, except the animals used for experiment tests in a chronic series, is forbidden.

- Presence of a person responsible for acting a procedure and controlling adequacy of anesthesia and a condition of an animal is strictly necessary while carrying out the experiments and other procedures in the conditions of the

increased risk for animal life or while working with animals by unexperienced persons (for example, students).

- In the postoperative period an animal should receive the qualified care and adequate anesthesia.

- Upon completion of the educational or scientific manipulations on an animal leading to physiological dysfunctions and viability, the animal has to be killed with compliance of all humanity requirements.

- Euthanasia, i.e. humane killing of laboratory animals, should be performed by the responsible person or under his direct observation.

- An optimum and universal method of laboratory animal killing is an overdose - administration of an anesthetic in a lethal dose (x3 dosage for narcosis). Different possible ways of euthanasia of small and big animals are given in the Appendix 4 to Order No. 755 of the Ministry of Health of USSR [1, 2, 16].

Conclusion

Use of different types of animals in a scientific research allowed making an impressive progress in many spheres of human activity, prolonging thereby human life by that, having cured of serious diseases, prevented risks in use of new technologies, etc. Animals will always be test objects in experiments, it can't signify a consent or disagreement therefore only the scientist can take the responsibility for an ethical component of the researches to minimize an injury, to deal towards animals extremely humanely. The need for live objects of a research will increase in parallel with development of science, but also ethical demands to protocols of a research and design of an experiment by conducting ethical examination in committees on bioethics of different level will be tightened.

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The study was supported by Ministry of Education and Science of Russian Federation #6.1766.2017, FASO (BRK: 0556-2017-0003).

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