

ontology; event, involved in society. The term “bioethics” can preserve dichotomy, but can be interpreted as unity. However which experience in general does make it possible to speak about “unity”? Etymology does not solve else the question about experience where “essence” of such kind and the attempt to think unity rise, where the components of dichotomy become one.

Bios...Ethos, Life...Ethics. What is between them, connects and unites in one, though contradictory, but nevertheless the whole?

The answer is “simple”:- consciousness: consciousness corresponding ontologically to the existential experience of anthropoessential. Consciousness is ontological to the experience. The source of the problem of their connection and union in one whole- in phenomenological form, the name of which is bioethics is just in existential experience of anthropoessential. Bioethics is problematic phenomenological form; and the starting-point of this problem ontologically is in existential experience of anthropoessential. Point is ontological to experience. The talk is not about abstraction “bioethics”, not about bioethics in general, but about bioethics as the part of existential experience, about among-people-in-human-environment born phenomenon, that is about the phenomenon of the living world of anthropoessential. Bioethics is existentially-ontological phenomenon, inborn to the living world of anthropoessential.

In phenomenologo-existentially-ontological aspect the question arises: does bioethics essentially correlate with or existentially with the essence of anthropoessential? And first, and second. The essence of anthropoessential is existential, existence is social and bioethics, no matter how to define it, is “social phenomenon” [4]. Using language of phenomenological sociology one can say, that bioethics is existentially-essential form of social consciousness and at the same time ontologically problematic phenomenological form

**Conclusions.** In the living world of anthropoessential there is existentially united, though contradictory, continuum of event-bioethics. Bioethics takes place in event, event- in bioethics: they- collaborators. Their relations are asymmetric and tense, tension between them- motive power of their interaction.

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УДК 17+347.152

### PRINCIPLE “ETHICAL EQUALS PRECISE” AS BASIS FOR ETHOS OF BIOMEDICINE

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The principle of “ethical - means precise” suggests that only if ethically correct approaches to a living object are observed, it is possible to obtain accurate information about it. Previously, the problem of following ethical norms in biology has traditionally been examined in the context of the requirements of ethical committees on observance of certain formal rules for working with animals. In the present work, an attempt is made to justify the necessity of observing ethically adequate approaches to biological experiment as a necessary condition for obtaining accurate scientific information about a living object. Ethical approaches are considered ethical, which considers an animal in natural, natural conditions. This approach goes back to the ethics of naturalism, which means the return of remote monitoring of a living object as the basis for obtaining precise information about its structure and function.

**Keywords:** ethical equals precise, ethological approach, 3R principle, principle of additionality, non-invasive technologies, study of weak and superweak influences in biology

## ПРИНЦИП «ЭТИЧНОЕ – ЗНАЧИТ ТОЧНОЕ» КАК ОСНОВА ЭТОСА БИОМЕДИЦИНЫ

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Принцип «этичное – значит точное» предполагает, что только при соблюдении этически правильных подходов к живому объекту возможно получение точной информации о нем. Ранее, проблема следования этическим нормам в биологии традиционно рассматривается в контексте требований этических комитетов по соблюдению определенных формальных правил работы с животными. В настоящей работе предпринята попытка обоснования необходимости соблюдения этически адекватных подходов к биологическому эксперименту как необходимого условия получения точной научной информации о живом объекте. Этически адекватными предполагаются подходы этологии, которая рассматривает животное в естественных, природных условиях. Этот подход восходит к этике натуралистики, что означает возвращение дистанционного наблюдения за живым объектом как основание получения точной информации о его структуре и функции.

Ключевые слова: этически адекватные подходы, биологический эксперимент, научная информация, живой объект

When speaking about extensive use of bioethical concepts in experimental science we usually discuss the regulations of scientific research on vertebrates. This undoubtedly important aspect of scientific experiments in biology normally results just in observing so-called “protocols”. Apart from that the range of interest within biologists’ community in deep understanding of required ethics and, as a result, in compliance to these ethics, remains at the level of nominal perception of the problem. There are no reasonable grounds for the inner rejection of ethically non-appropriate experimental procedures. And this issue is not connected with the existence of an ethics committee in an institution and not with obtaining a certain permission from such a committee, in most cases a phantom one. No one could be happy with the obvious and inevitable necessity of using quite a number (in many cases a big number!) of vertebrates for biomedical research and especially in preclinical trials. Still there is no rational appreciation of the importance of compliance to certain ethics in biomedical research.

We suggest a turning point in biological experimental research for clear understanding of the importance of compliance to ethical procedures in experiments on living organisms can take place only when we realize that this is closely connected with reaching the research objectives. Firstly, we can speak of the case when obtaining precise research data is possible or not possible outside the observation of relevant ethical approaches.

In this article, we present a detailed structure of a leading principle of biological ethics – “ethical equals precise” [1,2]. In full it reads – “ethical knowledge is precise (knowledge)”, as we mean that compliance to ethical procedures in work with living organisms is necessary for obtaining precise scientific knowledge, which presents the aim of positivist science.

We show the place and volume of ethical component in modern biomedical research as essential part in obtaining a precise result. Thus, observation of ethical procedures in research work with animals stops being a moral imperative and becomes an obvious requirement for fair research practice. Then we could expect biologists and medical researchers to comprehensively, not formally, observe the requirements of ethical (humane) expertise of scientific research which bioethics is calling for [3,4].

### **1. Introduction. Issues of ethical conduct in biomedical research in the aspect of history of science.**

In the history of biological research has been inevitably connected with tragic circumstances – destruction of objects used for experiments. Nevertheless, until now this obvious fact has not been decently accompanied by ethical expertise. At the beginning of XXIst century only we see first publications devoted to negative psycho-emotional background for daily biological experiments and its influence on the emotional condition of researchers [1]. This negative phenomenon occurs in context of remarkable progress in modern biology and biomedicine, which meets the demands of modern society in new more effective targeted medicine. At the same time the society persistently demanding new medicine equally and more persistently criticizes the biomedical community for the “reverse side” of the progress in biomedicine – use of millions of vertebrates (rodents) in the process of creating new medicine. Omitting the obvious fact of double dealing here we still realise that the issue of use and destruction of animals in biomedical experiments by itself poses a challenge for biomedicine. Public criticism of biomedical research is a fact of life in western society as in European Community only the number of animals used for preclinical trials reaches 20 million subjects per year. This is one of major challenges for modern biomedicine.

In practice the so-called approach 3R (refine, reduce and replay) has been applied for quite a long time in biomedical experiments [5]. This approach specifies the

improvement of conditions for biological research including total usage of anesthetics when carrying out acute and subacute experiments – *refine*. Besides, efforts are made to minimize the number of animals used for experiments: firstly, new statistical verification methods on even smaller groups of animals are being developed – *reduce*. Third principle of good practice means replacement of vertebrates by cellular or molecule-based models or by invertebrates - *replace*. This approach, which appeared in the end of 50s of XXth century, significantly improved good practice in all the three lines of biomedical research. Still we do not see any progress in biologists' understanding that such bioethical principles are reasonable grounds for their good practice.

The position in seeing principles of good bioethical practice just as a nominal procedure of preparing reference notes and reports for ethics committees still dominates. Biologists refer to such procedures as “management imposed” requirements, which they observe anyway. Truly if we take the ethics committee requirements as formal procedures, many researchers see them as bureaucratic, not connected with real work and complicating the mode of carried research by excessive completion of research protocols.

In Russia, the issue of ethics control of biomedical research has its own distinctive history. We must admit that in Russian and Soviet society there has been a clear understanding of the use of superior vertebrates in experiments. I.P. Pavlov argued with representatives of the Society for protection of animals about their requirement for public participation (!) in biomedical research. In 1904 the representative of the headquarters of Russian Society for Patronage of animals Baroness von Meierdorf published a paper with the title “Vivisection as Outrageous and Useless Scientific Activity”. In result, a Committee on Vivisection was organized in Military Medical Academy. Professor I.P. Pavlov, future Nobel Prize laureate, expressed his own view of this issue and supported the rights of medical researchers to use vertebrates in experiments especially not connected with vivisection.

Professor Pavlov strongly opposed Baroness von Meierdorf's idea expressed in her paper that are experiments with animals counterproductive. Pavlov insisted that medical researchers are quite capable of estimating ethical risks in experiments with animals and

absolutely denied the possible participation of animal rights activists in biomedical experiments [6]. Nowadays this position can be viewed as accurate: discussions of biomedical experiments with the public is now part of modern biomedical research. Though, even today animal rights activists do not take part in carrying out biological experiments.

On the other hand, in Soviet Union biology as science concentrated on the study of fundamental laws of biology. Reaching the practical outcomes and application of research results was not a priority. The changes are taking only now which requires revision of stereotypes, in biomedical education as well.

At present, the system of bioethical protocols is applied to biomedical experiments on vertebrates. At the same time, we can observe quite a formalistic attitude of Russian researchers to the requirements of ethics control to experiments. There is no real comprehension of the importance of such protocols. This can be explained by not quite a responsible attitude to procedures and rules generally approved in Russian (Soviet) society.

It might also be explained by continuous lack of resources for carrying out research at higher standards, which the author of this article could witness in the times of Soviet science when starting his scientific work after graduating from the university. A typical situation, when an experiment was prepared was the following – according to the procedure, we need a certain chemical reagent, we do not have it, we replace it by an “analogue” with similar activity. The same situation could occur in other aspects of work, for example, choice of animals for experiments: we need linear mice but there is no financial resource for buying them and we take “ordinary” mice... As a result, majority of Russian techniques were quite authentic and did not allow for objective comparison of experiments results to ones obtained by colleagues from other countries.

On the other hand, this practice had not a negative meaning only. Using a new technique possesses a chance of obtaining completely new knowledge, which is positive. In fact, even when we just check the experiments results of colleagues from other countries and use “modified” techniques we get absolutely new information.

Nevertheless till a certain moment, when experiments were carried out at milli- and micromolar level to study “strong” impact on biological objects results in research protocols did not differ much from those obtained

in experiments when the authentic technique was used. At present biology studies weak and superweak impacts at nano and femto scale, which are basic levels for regulating biological processes. Observance or non-observance of standard procedures in this case can seriously affect the experiment protocol and result in lack of quality of the obtained research result. For example, when working with planarians in order to get reliable (repeated) results we had to create a whole new system of standard working procedures [7]. It allowed for obtaining pioneer results about the weak and superweak impact of chemical and physical factors on the process of planaria regeneration.

At present, many factors contribute to obtaining precise results – pure lines of animals, observance of standard conditions for keeping these animals during the experiment procedure, required feeding and qualified veterinarian support (including biological sampling and preparation of experimental models). It is highly important to realize that these procedures of planned experiments are crucial for adopting new ethics of good biological research. Apart from that, use of higher vertebrates for biological experiments requires a profound zoological and psychological study of their behavior. It specially concerns the work with vertebrates in conditions of their free behavior.

It seems that the experimental paradigm must correspond to ethologically verified ideas about the behavior of animals. Then there appear prerequisites for obtaining precise knowledge about a living object. To account for animals' behavior becomes crucial as only the conditions of free behavior can contribute to objective monitoring of any biological indicators of the animal's condition. Thus, the principle "ethical equals precise" is based on the ethological approach takes account of the specifics of animals' free behavior: ethics of biology comes up from the ethics of ethology.

#### **Major science objective and its application in modern biomedical research.**

Aim of science means obtaining a precise result verified by various procedures. At present the frameworks of biological experiment consists in carrying out a research of a biological model using a set of various techniques: molecular and genetic, biochemical, physiological, morphological. When results of using such complex research techniques coincide, this allows for verification or

non-verification of the suggested hypothesis. At the same time the type of interaction between a researcher and the object of research, type of intervention, the object condition and the conditions of experiments normally are not described in scientific papers. The complementarity principle firstly adopted in physics in order to estimate the degree of external interference into the object has not been considerably valued by biologists [8]. As biological research now operate at nanoscale we should realize that when we study weak and superweak impact on the object the risk of obtaining non-precise results increases considerably and greatly depends on the conditions of the object under research.

In biological research, such dependences can present a special value as a biologist deals with a living organism, which has a wide range of reactions when treated in different ways. The dependence of the quality of obtained results on conditions of study of live biological model used for experiment increases accordingly. Nowadays ethology as science of free behavior of animals adopts naturalistic approach when the research of an object is carried out distantly without interference in its behavior. At best, an ethologist studies an animal in its free behavior. During experiments, it is quite difficult, sometimes impossible, to observe such conditions as creating of biological model is often connected with a certain degree of interference (not only surgery). The best conditions for experiments would be conditions of free behavior. Here at least we can establish certain working standards for experiments with animals.

In the Institute of Theoretical and Experimental Biophysics RAS, A. Azarashvili, PhD in Biology, managed to carry out a research on rats in a mode when the rats left their cages without distress and allowed to be made an injection. That demonstrated an established trust between a researcher and the animals and the creation of favourable conditions for the objects. Such procedure is preferable both from scientific and ethics perspectives as animals stayed at comfortable conditions of free behavior [9]. In case of our experiments with planaria when creating their behavior reflex we minimized the external impact on objects to allow them to move freely on the experimental area. It was especially laborious and important when training the regenerating objects. Still we managed to create ethically accepted procedures when intact and regenerating objects were held in similar conditions [10].

Later this approach was applied to developing a method of intravital computer morphometry when regrowth of regenerating blastema was registered only in free movement of planaria in ocular view [7].

One of unique features of planaria biology is their ability to move to the head end of the body not only in intact, undamaged, condition but even after resection of the head end with central ganglion. A researcher gets an opportunity to register the dynamics of regeneration process in identical conditions (at disengaged, free, movement) during the whole time of the process and in the same group of planaria. Thus we can provide identical conditions for obtaining morphological data in the whole continuous process of regeneration. If we aim to get exact dimensions of an animal's body it would be better to provide such conditions when it will show its morphology by itself in free behavior. This way the researcher would be able to register its image in noninvasive way.

Thus, observing biological features of planaria we could provide identical conditions of registration of behavior and morphogenesis it being necessary for obtaining precise research results. Understanding of animal behavior complies to basic ethics requirements to research work and contributes to obtaining precise research results: here the principle "ethical equals precise" works. We must admit that both experiments – training behavior reflex and intravital registration of planaria regeneration – present an example of work with most complex objects in experimental biology.

When we analyse this experimental approach from ethics perspective, its humane expertise (B.G. Yudin and P.D. Tishensko term), we see that such precise results were obtained under conditions of disengaged observation specific to classical naturalism [2,7]. On the other hand, animals' rights for ethically appropriate treatment during experiment were observed. Owing to this we obtained most precise data about regeneration process and results concerning training behavior reflexes in a limited time scale of the experiment (we aimed at training a reflex of regenerating animals within one day of the experiment) [10]. Here the principle "ethical equals precise" is confirmed again.

**The peculiarity of the practice of biological research in the conditions of the digital revolution is the need for distant interaction**

Nowadays modern digital non-invasive methods of monitoring the condition of living organisms allow for complete compliance to ethical principles of naturalism: observation without interference into an object's structure. Thus, for the first time in 150 years we can "go round" the dominating principle of complementarity and can minimize the impact of such interference [8].

Issue of outer interference into experiment conditions was first raised in nuclear physics. The question whether we study the atom or the result our interference into it gave birth to complementarity principle [11]. Minuscule atom nuclei encounter in gigantic particle accelerators at great energy deposition, then their ray paths are registered. Naturally, scientists raised an urgent issue of conformity of obtained results with the aim of studying the delicate structure of an atom nucleus after such neglecting impact. It became obvious that the results obtained in such conditions could not be considered as precise. Simultaneously "area of application" of complementarity principle did not cover the wide area of classical physics where experiments were not carried out under conditions, which destroyed the object of research.

Quite on the opposite in experimental biology where any treatment of the object is *a priori*, it means nonreversible interference into a living organism structure and most often leads to fatal consequences. In fact, experimental biology always applied the complementarity principle as all experiments on creating biological models were connected with surgery. Only in the time of computer (digital) biology with application of non-invasive methods of research and observation, we can witness the decrease in use of the complementarity principle in biology. [1,11].

We should also distinguish the issue of validity and precision in scientific research, especially in neurobiology and animal behavior. Aiming at estimating cognitive functions scientists face the contradiction between *reliability* of knowledge and its *validity*. Reliability characterizes the repeatability of a certain method of registration and assessment of behavior reaction, validity shows degree of compliance of the parameter measured to the certain generalized image of the object [12]. Here we can again refer to comparisons between ethology approaches and research in the area of higher nervous activity. Where an ethologist studies the animal behavior in its natural environment researchers of higher nervous activity when applying methods for training

conditioned and even unconditioned reflexes use artificial signals. Thus, when analyzing reasons of failures in training conditioned reflexes with planaria we had to compare non-comparable modes of training used by various authors [10].

The issue of interaction and validity in studies of behavior is quite urgent nowadays. It is obvious that validity of ethological approaches is much higher than in classical techniques of training conditioned reflexes. This is directly connected with the major methodology principle of ethology – to study animal behavior in their natural environment. This is also ethically appropriate for interaction between a researcher and an object. Here we can provide the reliability of obtained results as an object is in natural environment and we observe standard conditions for work with a live object. In experiments on planaria it was necessary to be ultimately distant from applying invasive manipulations and provide standard working conditions used for studying behaviour and training conditioned reflexes [7,10].

Further development of methods of digital biology will contribute to decrease in degree of invasion into biological object and restrain the previously dominating complementarity principle in biology. This way biology returns to ethics of naturalists, ethics of observing an object in a new computer era [1]. This “new and old” ethics complies with the principle “ethical equals precise”.

#### **Conclusion. Ethics of biology: from emotional (ethical) to rational.**

We suggest that one of major reasons for “complicated” attitude of professional biological community to bioethics lies in its special attitude to the issue of interaction between a researcher and an object of research: “emotion” vs “ratio”. On one hand, everyone accepts 3R principles, which refer to application of advanced anesthesia techniques and new methods of research results analysis – adoption of these principles extends the opportunities for work with smaller groups of animals. On the other hand, we see lack of understanding that compliance to ethics of good laboratory practice is not so much a moral challenge but an obvious provision for good faith experiment.

We see compliance to ethics procedures for work with animals as basics for quality of obtained data. This way issue of ethics of experiment stops being a moral issue and becomes a feature of professional activity. This

reflects the main aim of bioethics – to bring “harmony” into the interaction between a researcher and an object of his research. Obtaining precise results is directly connected with developing non-invasive methods, which got promotion by extensive use of digital imaging. Progress in digital technologies for work with living organisms facilitates the process of obtaining ethically supported research results [2].

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## PRACTICAL BIOETHICS ПРАКТИЧЕСКАЯ БИОЭТИКА

УДК 17+347.152

### MEDICAL LAW, BIOETHICS AND MULTICULTURALISM: POINTS FOR CLOSE COOPERATION OF UNESCO AND WAML

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Medical Law and Bioethics are new scientific disciplines appeared in the end of the last century as response to the challenges and technological innovations coming to the human activities related with health and biology. To respond these challenges on the global level scientists and experts come together within different organizations on international level in attempt to find out possible suggestions and solutions, appropriate in the different parts of the world. World becomes smaller nowadays and international cooperation starts to play crucial role for future success. This increases role and importance of Multiculturalism as approach based on general and global human values with respect to the diverse cultural needs and particularities. World Association of Medical Law (WAML) was created in 1967 in Gent, Belgium with purpose to focus on multicultural issues in the field of Medical Law. UNESCO as one of the largest UN organizations is a key international organization in the field of science, education and culture, which declared Bioethics and Multiculturalism as own priorities. The first session of the General Conference of UNESCO took place in Paris in 1946. Despite WAML has indirect associate membership at UNESCO as non-governmental non-profit professional organization, in recent years cooperation of these two influential organizations has not been strongly seen. The 23<sup>rd</sup> WAML Congress in Baku, Azerbaijan in July 2017 was named “Medical Law, Bioethics and Multiculturalism” and brought together these international organizations.

**Keywords:** Medical Law, Health Law, Bioethics, Multiculturalism

### МЕДИЦИНСКОЕ ПРАВО, БИОЭТИКА И МУЛЬТИКУЛЬТУРАЛИЗМ КАК СФЕРЫ ТЕСНОГО СОТРУДНИЧЕСТВА ВАМЛ И ЮНЕСКО

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Медицинское право и биоэтика – это новые научные дисциплины, появившиеся в конце прошлого столетия как ответ на вызовы и технологические преобразования в сфере человеческой деятельности в областях медицины, здравоохранения и биологии. Для консолидации усилий ученых на глобальном уровне очень важным является совместное обсуждение актуальных проблем в рамках различных международных организаций в целях поиска общих решений и предложений, которые могли бы быть полезны в различных странах и во всем мире. Активное международное научное сотрудничество становится ключевым инструментом для успешного решения многих проблем в сегодняшнем быстро меняющемся мире, что актуализирует значение Мультикультурализма как платформы