The Physiologist’s Ethical Dilemmas

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Physiologists are bound to test their scientific theories in experiments on living matter and, ultimately, on living organisms—animals or humans. This confronts the physiologist with ethical dilemmas: can we engage in physiological experiments in the face of possibly harming the interests of living beings, or should we refrain from such studies, thus preventing the good that can be derived from scientific progress?

It is our business as physiologists to study life and the multitude of processes that make it happen, from the functioning of membrane channels, through the electrical activity and hemodynamics of the heart, to the integrative events in the brain. Our obligation is to study all of this with the approach of science, starting with a theory, leading to a hypothesis, which is tested by experiments whose results are analyzed, followed by a critique of the theory—and the game goes on. Most of this approach is common to all of science. But there is one significant difference: since our object is the understanding of life processes, the experimental tests of theories and hypotheses must be performed on living matter, from cells to whole organisms, even on humans.

This raises ethical issues—and presents us with ethical dilemmas—because such experiments must, in part, be performed on living animals or on humans. Good experiments are, by necessity, based on controlled interventions, on perturbing the normal functioning of the organism. This is also the case with the new physiological research strategy of functional genomics. Do we have the right to do such experiments, to interfere with the life of another creature, perhaps to cause suffering or even some risks? If so, how can this be justified and what are the conditions that must be fulfilled? The basic ethical dilemma we are facing is this: can we engage in the physiological experiments that our scientific interests impose in the face of possibly harming the interests of living beings, animals or humans, or should we refrain from such studies?

Clearly, these are very difficult questions, and they cannot be dealt with in any depth in this short note. I would therefore just like to make a few reflections that I consider central to the issue, discuss existing guidelines for this work, and direct you to further reading on this matter. A good start is a small booklet published a few years ago and based on a symposium organized by IUPS and UNESCO in Paris, entitled The Ethics of Life (10). Here fundamental questions relating to physiological research and its ethical justifications—and limitations—are discussed. It contains a chapter on the “Respect for life and the foundations of bioethics” and one on “Respect for life and the law of the living” that show the vast complexity of the ethical issues we need to consider. The book also features chapters on legal aspects of the question as well as some historic background on physiological experimentation on humans and animals, to some of which I shall refer later.

Respect for life: a guiding principle

One of the key ethical concepts pertinent to this discussion is “respect for life,” a principle first proposed and discussed extensively by Albert Schweitzer early in the 20th century (12). Schweitzer starts with a fundamental statement that immediately defines our challenge and our responsibility: “I am that which wants to live in the midst of life that wants to live.” The central issue here is the will to live, the striving for life, which is common to all living beings, animals and humans, and which we humans must respect in all life forms. For Schweitzer, ethics is “that I experience the need to respect the will to live equally as I do my own.” I personally cherish this principle because it calls on our direct personal responsibility toward other living beings, be they humans or animals. Because of this, I consider it much stronger than other statements that assign certain higher properties, such as (a poorly defined) dignity, to all living creatures.

The principle of respect for life is at the very basis of important ethical movements, such as the human rights movement that have developed since the Second World War in the interest of preventing future atrocities like those that occurred during the Nazi reign (13). The so-called Nuremberg Codex, formulated in 1947 by the court ruling about the scandalous human experiments by Nazi physicians, marked the beginning of a movement to regulate biomedical research involving human subjects. This led to two significant declarations of an ethical nature. On the one hand, the United Nations broadened the scope of the Codex in the Universal Declaration of Human Rights of 1948, stipulating that “everyone has the right to life, liberty, and the security of person,” which applies to all humans. On the other hand, the World Medical Association (WMA) refined the 10 theses of the Nuremberg Codex, and this resulted in the Declaration of Helsinki adopted by the 18th WMA General Assembly in 1964. This declaration set the universally accepted rules for research involving humans. It has undergone several revisions and was issued anew in October 2000 by the 52nd WMA General Assembly held in Edinburgh, Scotland (15).
The principle of respect for life also applies to animals, whose rights must be adequately protected. It is perhaps unfortunate that large international bodies such as the United Nations or WMA have not followed their declarations on human rights with similar statements on the relation of humans and animals and on animal rights. In the absence of such statements, animal rights activists and antivivisection movements have taken the stand that the protection of animal rights does not permit any experiments on animals. It cannot be as easy as that, however. First, we humans use animals for many purposes, such as for labor and for meat production. To use animals for biomedical research is then only a special variant of this relation of humans to animals. Second, if we are allowing research to be done on humans under certain conditions, it appears justified to permit it also for animals. However, it is ethically imperative that we set proper conditions for this work, ethical rules for animal experimentation that adhere to similar ethical standards to those for humans, as discussed below.

Thus respect for life is the guiding ethical principle for physiological research involving human subjects as well as for animal experiments in physiology. It helps us define the limits of what we can and should do, and it allows us to take responsibility for our acts. It may therefore lead us in resolving the dilemmas we are facing when engaging in experiments to test physiological theories. However, this principle is too general for immediate application, so we depend, in our everyday work, on guidance on the basis of a consensus on how respect for life translates into specific judgments and practices. Here we must clearly differentiate between experiments on humans and those on animals.

**Physiological research involving human subjects**

The Declaration of Helsinki, as well as the CIOMS Guidelines for Biomedical Research involving Human Subjects, were worked out and published, for the first time in 1982, by the Council for International Organizations of Medical Sciences (CIOMS) of the World Health Organization in Geneva, and most medical academies adhere to this guide. A thorough revision of these guidelines has been undertaken over the past several years, and a draft revision was recently been published, with extensive commentary, on the World Wide Web at www.cioms.ch (2).

These guidelines start by setting down the prerequisites of biomedical research: 1) the research must be justified, 2) there must be a detailed protocol, and 3) all proposals must be submitted for review and approval to an independent ethical and scientific review committee. The first two points appear self-evident, and the third I find most important because it allows us to share our concerns with peers and with people outside of the science enterprise, who may sometimes have a different, more detached view of the situation. The question of how to obtain and ascertain informed consent is dealt with in great detail, and, finally, some consideration is given to the question of equitable distribution of burdens and benefits resulting from such research.

On the whole, these ethical guidelines of CIOMS have already served a useful purpose. They have helped to formulate guidelines and legislation in different nations by setting a common ground of minimal standards for research involving human subjects and thus for research in human physiology.

**Physiological research involving animals**

The Declaration of Helsinki, as well as the CIOMS Guidelines on Research Involving Human Subjects, stipulate that some studies on humans can only be performed if preliminary animal experiments have shown their safety and efficacy. Physiology is not limited to serving medical research. As a basic biological science, it has the obligation to advance the understanding of life processes independent of any possible medical application. Such studies must involve animals lest they are not performed at all, another dilemma facing the physiologist.

The principle of respect for life and the ethical postulate that like should be treated equally require that we set rules for...
B. Committee on Ethics

The Committee on Ethics of IUPS is mandated to:

1) critically review and interpret these guidelines in view of their implementation in specific areas of physiological research;
2) serve as a body of reference and reflection to advise Council on the positions IUPS should take in these matters and for contributing to the further development of these guidelines accounting for the evolution of physiological research; and
3) develop means for disseminating knowledge of these guidelines within the physiological community worldwide, for example, by teaching or by preparing suitable texts with directives for the practical implementation of these guidelines in the different fields of physiology, thus also contributing to capacity building in the developing parts of the world.

Resolution of Council of IUPS

Concerning

Ethical Principles for Physiological Research on Humans and Animals

In order to serve the wellbeing of humans and animals by advancing knowledge on life processes, physiological research must depend on experiments using humans or animals. Even though many fundamental questions can be approached in model systems such as cell or tissue preparations the significance of such studies must ultimately be tested in relation to the whole organism. Such studies must, however, respect fundamental ethical principles that safeguard the integrity and safety of the subjects.

A. Ethical Guidelines for Physiological Research

In order to ensure similar ethical standards for physiological research on humans and on animals in all countries, IUPS declares the following international guidelines as binding for all research conducted by physiologists associated with IUPS and for all research presented and communicated at meetings under the auspices of IUPS:

1) The Ethical Guidelines for Biomedical Research Involving Human Subjects of the Council for International Organizations of Medical Sciences (CIOMS) of 1993, currently under revision; these are based on The Declaration of Helsinki of the World Medical Association (1964, revised 2000), which sets the basic rules for all research involving humans; and

2) The International Guiding Principles for Biomedical Research Involving Animals of CIOMS (1985), which are based on the principle of respect for life.

In all scientific meetings under the auspices of IUPS, strict adherence to these guidelines will be imposed.

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tional biomedical community and should therefore be applicable worldwide to ensure similar standards everywhere. They emphasize the need for animal research for the advancement of the biomedical sciences and thus also of physiology, but they strongly state that “the biomedical scientists should not lose sight of their moral obligation to have a humane regard for their animal subjects.” These principles are patterned on and linked to the guidelines for research involving human subjects, with obvious differences. They discuss questions of animal care and the possibilities and potentials of alternatives to animal experiments.

The physiologist’s dilemmas

As physiologists, we are faced with a series of dilemmas that each of us needs to resolve. The advancement of the understanding of life processes with which we are mandated depends crucially on testing theories of how things work by experiments in nature, and this means on living matter. Some have resolved the dilemma by limiting their experiments to small subunits such as ion channels, units that cannot “suffer.” But, in fact, the study of channel function depends on obtaining material from cells and organisms, particularly if one resorts to genomic manipulation of channel properties. Ultimately, the results of such studies make sense only when they are related to organismic function, and here experiments on humans or animals can hardly be avoided.

To ensure similar ethical standards for physiological research worldwide, the Council of IUPS, at its recent meeting in New Zealand, adopted a resolution that declares the two above-mentioned sets of guidelines from CIOMS as binding for all members of IUPS (see box on p. 45).

We must face it: the ethical dilemmas of the physiologist cannot be resolved. We must live with them. It is important, however, that we remain conscious of the ethical problems raised by physiological research involving humans or animals. But we must make every effort to reduce the number of animal or human experiments as well as their potential burden on the subjects to the minimum. We must accept that such research must be well justified and performed with concern and empathy. The best justification is, of course, that the study is done with high competence and that it provides a significant step forward in our understanding of life.

Further reading