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From Abuse to Protection. A Journey on the Path of Research Ethics Regulation - the Nuremberg Code and the Helsinki Declaration[1]

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[1]A shorter version of this paper was delivered as an oral presentation at the World LUMEN Congress 2016

Abstract: ***Research on human subjects has been essential for the progress of science and for improving people's lives. In time it was acknowledged that in order to provide benefit to people, research has to be conducted under strict rules which promote respect for the physical and psychical integrity of the research participants on one hand and respect for communities in which they belong on the other hand. In this paper the author explores the roots of the international regulation in the field of research ethics. In doing this the author analyzes the most important moments in the evolution of this field and discusses the emergence of two essential international ethical regulations, i.e. the Nuremberg Code and the Helsinki Declaration in the context of the abuses which shaped them, such as the experiments conducted in the Nazi concentration camps during the Second World War.***

Keywords: ***research, ethics, abuse, Nuremberg Code, Helsinki Declaration.***

Introduction

Research on human subjects has been present in the history of humankind since old ages and it has been essential for the progress of science and for improving people's lives. The importance of research on human subjects was acknowledged by ancient scholars such as Avicena (980-1037) who showed that "experimentation must be done on the human body, for testing a drug on a lion or a hourse might not prove anything about its effects in man". At the same time, respect for the human participants in research was acknowledged. For instance, Moses Maimonides (1135-1204) mentioned that research participants must be treated "as ends in themselves and

not as means for learning new truths" (1).

For a long time research on human subjects was an isolated and empirical activity, many physicians experimenting various treatments on themselves, their relatives or neighbors. Although in the 19th century the research on human subjects was supported by the scientists, the informed consent of the subjects was not considered an issue at that time.

At the beginning of the 20th century the necessity of establishing ethical limits to human experimentation was acknowledged. For instance, in 1907 William Osler showed that research on human subjects has to be conducted within a certain ethical framework, including prior experimentation on animals and the obligation of enrolling the subjects only with their informed consent. However, in the context of the rapid progress of science and medicine, some of the researchers considered the benefit of medical or scientific research to be more important than the welfare of the human participants and generated the grounds for unethical researches on human beings which marked the 20th century and eventually shaped the international regulation in this field (1, 2). The Nazi experiments were, probably, the ones which dramatically showed the consequences of using human beings as a means of science and of doing research outside an ethical framework.

The Nazi experiments and the emergence of the Nuremberg Code

In 1931, the German Health Council issued the "Guidelines for new types of therapeutic treatment and for undertaking scientific experiments on human beings", providing that it was the researchers' duty to follow the principles of medical ethics and to protect the human life and health through prior animal experimentation, thorough assessment of the risks and benefits and the informed consent of the participants. The Guidelines also granted special protection to vulnerable segments of the population such as: children, underage youth, persons "in a social position of need" or dying (3). However, during the Second World War, in the Nazi concentration camps many experiments were conducted on human beings, all of which had aberrant research hypothesis and design and did not respect any ethical standard. These experiments resulted in death or permanent impairment of the human subjects as the researchers made no attempt to minimize any possible risks. The research subjects were all in the vulnerable position of war prisoners, they were not

informed about the purpose and the procedures of the research, their consent was not sought at any moment and they did not have the chance to refuse participation in the research or to withdraw from it.

At the end of the Second World War, at Nuremberg, the International Military Tribunal created by the allied countries, judged the crimes against humanity and the war crimes committed by the Nazi. As part of the Nuremberg trial, an American Military Tribunal judged the Nazi physicians who were accused of having committed infamous experiments on human subjects. At the end of the trial, two American physicians- the neuropsychiatrist Leo Alexander, and the physiologist Andrew Ivy (4)- and Harold Sebring, one of the American judges (5), formulated ten principles which formed the Nuremberg Code. The Code was issued as part of the Court decision and it was the first international document which provided the ethical requirements for research on human subjects and aimed to protect the research participants and their rights. The Nuremberg Code combines the Hippocratic Oath with the protection of the human rights, focusing on the fundamental rights of the research participants and on the responsibilities of the researchers towards them (4). On one hand the provisions of the Code request the researchers to protect the participants and on the other hand they give the subjects the possibility to protect themselves (5, 6).

The Nuremberg Code promotes three principles which must be respected in research on human beings: respect to persons, beneficence and justice.

According to the stipulations of the Nuremberg Code, the research must have scientific value proved by an adequate design and supported by data obtained in prior experimentation on animals. The research must benefit society and can be conducted only by qualified researchers and only if there are no other means of obtaining the same results. Another concern of the Code is to ensure protection of the participants and the research can thus be carried out only if the expected benefits outweigh the risks. Additionally, the researcher has the obligation to stop the research if at any point the subjects' safety or freedoms are jeopardized. The research participants must give their informed consent before being enrolled in the research and they must have the possibility to withdraw from at any time, according to their needs or wish.

The Nuremberg Code has had no legal force (4) and it has not been

officially adopted by any country or important medical association in the world. However, it has been influential in terms of respect for human rights and medical ethics and has changed the way in which the physicians and the general public consider the proper conduct of research on human subjects.

The Nuremberg Code has not been exempt from criticism. Some authors showed that the Code was heavily inspired by the 1931 German Guidelines for Human Experimentation. The authors of the Code did not admit this relationship, maybe because the Nuremberg judges rejected the request made by the accused physicians to be judged according to the provisions of the 1931 Guidelines and decided to charge them for crimes against humanity (4).

The World Medical Association and the Helsinki Declaration

In 1946, 32 medical associations created the World Medical Association (WMA), which issued the Helsinki Declaration concerning research on human beings in 1964[1]. In contrast to the Nuremberg Code, the authorship of the initial text of the Declaration cannot be attributed to specific persons; it was the result of the common effort of national medical associations. The Helsinki Declaration was issued under the auspices of the WMA's Committee on Medical Ethics (7), being directed towards the physicians involved in research on human subjects (8).

The original version of the Helsinki Declaration has its origins in the provisions of the Nuremberg Code-ten out of twelve appear in the original version of the Helsinki Declaration. In contrast to the Nuremberg Code, which focuses on the human rights of the research participants, the Helsinki Declaration focuses on the obligations of the physician-researcher towards the research them (5). The original version of the Declaration was followed by many amendments, of different importance, which updated the provisions of the Declaration according to the progress of research on human subjects (9).

The Helsinki Declaration differentiates between therapeutic and non-therapeutic research, i.e. the clinical research with a main therapeutic purpose and the clinical research with purely scientific purpose and its provisions are shaped accordingly (9).

The general principles promoted by the Helsinki Declaration are: protection of health and wellbeing and rights of the research participants. The provisions of the Declaration are designed so that they ensure the protection of the research

participants before the beginning of the research, throughout the implementation of the research protocol and after its completion.

The protocol of the research must be carefully designed in order to provide the best results with the minimum risks or burdens to the participants. Therefore, the research must have scientific value and it has to be conducted according to the accepted scientific standards and with a clear and correct design. The evaluation of the risks/burdens and benefits of the research must be carefully considered before the beginning of the research. The risks of the research must also be monitored throughout the research so that the researcher can change the protocol or interrupt the study if the risks to the research participants become unacceptable (8).

The Declaration also refers to study methodology, especially to the placebo studies. The first reference to the placebo trials was made in a minor revision of the Declaration, in 1996[2] (9). Currently, according to the Helsinki Declaration, the placebo studies are allowed only if there are no medical interventions with proven efficacy as well as no additional risks of serious injury of the research participants. More so, according to the 2000 revision, the abuse of this research method must be avoided (8).

According to the Helsinki Declaration, the research participants can be enrolled only with their informed consent. The participants must be informed about: aims, methods, funding sources, possible conflict of interests, risks and benefits of the research and also their right to refuse participation or to withdraw at any moment during the research. In contrast to the Nuremberg Code, the Helsinki Declaration allows for the enrollment in research of the persons who are legally incapable, in certain circumstances and under strict rules[3]. Closely related to the provisions concerning the informed consent of the participants, the Declaration also refers to vulnerable groups which need special protection during research[4] (8).

The researchers also have the obligation to take all the necessary protection measures for the personal data and privacy of the research participants.

The 1975 amendment to the Helsinki Declaration provided a very important safeguard to the research participants by imposing the necessity of the evaluation of the research protocols by independent research ethics committees prior to the beginning of the research and of its on-going monitoring (9). This provision was also of great benefit to the field of research ethics by

increasing its visibility and importance among the scientists and general public (10).

The Declaration contains provisions referring to the post-trial obligations of the researchers. Thus, the Helsinki Declaration promotes the distributive justice in research, namely the equitable distribution of the risks/burdens and benefits of research and the post-trial access of the participants in need to the medical intervention identified during the research. Also, at the end of research, the researchers have the obligation to disseminate the results. However, according to the 1975 amendment, the results of the research which does not comply with the provisions of the Helsinki Declaration should not be published (8).

The Helsinki Declaration has had a prominent position as an international document which provides general principles of ethical guidance to the physicians involved in research on human subjects. The Helsinki Declaration was issued by the World Medical Association, the largest international group of physicians in the world, which have the necessary authority to issue opinions concerning the medical profession. This document contains general principles which are widely accepted and it has been regularly updated according to the progress in medical research due to its successive amendments. Therefore the Helsinki Declaration has been a source of inspiration for further international and national documents in the field of research ethics. It is also important to note that the ethical standards established by the Helsinki Declaration are considered as minimal requirements, so that any other international or national regulation should aim to at least a similar protection to research participants (9).

Conclusions

The roots of regulations in the field of research on human subjects are deeply embedded in abusive research. This field travelled a long way from abuses to protection of research participants and the lessons learnt by the researchers and the general public in time shaped research ethics into its current content. In this context, the Nuremberg Code and the Helsinki Declaration can be placed at the very origin of the present day international and national regulations as foundational and reference documents in this field.

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Notes

1. The launch of the Helsinki Declaration was announced by the British Medical Journal on July 18, 1964 (9)
2. ”In any medical study, every patient-including those of a control group, if any- should be assured of the best proven diagnostic and therapeutic method. This does not exclude the use of inert placebo in studies where no proven diagnostic or therapeutic method exists” (9).
3. For persons who are legally incapable the consent for their participation in research should be sought from their legal representatives. The person’s refuse to participate should be respected. Research on persons who are legally incapable can be done only if research is beneficial to the persons or to the group to which the persons. belong and only if research cannot be carried out with similar results on legally capable individuals.
4. Vulnerable subjects can be enrolled in research only if the research targets a health need or the group to which they belong, and the research cannot be conducted with similar results on non-vulnerable subjects.

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