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ETHIC

Ethics in medical research

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Medical research, as we know it, must be covered by strict ethical and moral principles, with total protection and respect for those who are the objects of the study. Unfortunately, it was not always like this, as we have seen at various times in history.

There are references to Herophilus of Macedonia (325 to 280 BC), a Greek physician who, together with Erasistratus, founded the Alexandria School of Medicine. He identified the cerebellum, differentiated nerves from tendons and also motor nerves from sensitive ones. Erasistratus (304-250 BC) discovered lung movements, the tricuspid valve and the prostate. Both used vivisection in criminals sentenced to death to carry out their studies.

Historical reports show that in 1559, in France, King Henry II, during a battle, was wounded in the eye by a spear. Doctors Vesalio and Paré were called by the queen to assist him. At the time, there was no X-ray apparatus and, to see the exact location of the spear, the doctors dissected the skull of criminals condemned to death, to try to figure out the spear's path.

In 1721, England, Doctor Charles Maitlandi, to study the evolution of smallpox, inoculated the virus in six prisoners, with the promise of freedom.

In the 20th century, in 1931, the German Ministry of Health launched a document on new therapies and experiments on human beings, based on the participant's will; the therapeutic test and the non-therapeutic test; the physician's responsibility as a researcher and the physician's responsibility as a care giver.

This did not prevent prisoners from becoming human guinea pigs during World War II, against their will, and from being subjected to the greatest atrocities, on the grounds that such conduct would supposedly help science and the Third Reich.

These abject and inhuman actions would lead, in 1940, to the creation of the Nuremberg Code of Ethics, with 10 Ethical Principles:

1. Obtain the participant's voluntary consent;
2. Produce advantageous results;
3. Be based on results of experimentation on animals and previous studies;
4. Avoid suffering and harm;
5. Be conducted by scientifically qualified people;
6. Be terminated if it is found that it may cause damage, disability or death;
7. It should not be done if there is a risk of death or permanent disability;
8. Have an acceptable risk degree and be limited by the importance of the problem intended to solve.
9. Protect the patient from any possibility of damage, disability or death;
10. Give the patient freedom to withdraw at any time during the study.

In 1964, the Helsinki Declaration listed topics to be respected throughout

Medical Research:

1. Be based on laboratory experiments, in vitro, on animals and on knowledge of scientific literature;
2. Have the research protocol approved by an independent committee;
3. Be conducted only by scientifically recognized persons;

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4. The risk to the participant should be proportional to the importance of the objective;
5. Have the risk assessment compared to the anticipated benefits, respecting and ensuring the participant's wellbeing.

In Brazil, it was only in the 90s, that ethics in research involving human beings became mandatory, and this was made clearer with Resolution 196/1996 of the National Health Council (CNS), which would regulate the functioning of the Ethics Committees in Research (CEP) and the National Commission for Ethics and Research (CONEP). We list here the main points of the document:

1. Subject's consent;
2. Ensuring the privacy of the subject's information;
3. Peer and community approval.

This resolution was replaced by 466/2012, from the same CNS, with ethical principles and scientific foundations much more present and explicit.

As we know today, the concern with ethical and moral principles in Science became more evident since the emergence of Bioethics, in the late 1960s, which, according to Berlinguer, is a philosophical discipline that connects science with life and morality.

And we cannot stop thinking and discussing Bioethics when we are faced with countless scientific advances that we know: the first heart transplant; the first baby conceived in a test tube; the HIV/AIDS epidemic; stem cell research; the cloning of Dolly, the sheep; brain death; euthanasia and the Karen Ann Quinlan case.

Karen Ann Quinlan (1954 - 1985) fell into a coma in 1975, progressing to a vegetative coma. Her parents asked the doctors to turn off the mechanical ventilator, which was not allowed by the court. After a legal fight, the parents, with the support of doctors, obtained permission to disconnect the device in 1976. Karen Ann survived until 1985. Her parents said, "We never asked for her death, simply asked that she be put back in a natural state so she could die in God's time." This case, until today, had an impact on bioethics, as it involves euthanasia, civil rights and legal custody of the patient, with repercussions in Medicine and Law.

We shall not forget one of the most emblematic, the Tuskegee case. This was the Study of Untreated Syphilis in Black Men, carried out by the US Public Health Service, in Tuskegee, Alabama, between 1932 and 1972. At the time, 600 men were selected, 399 with latent syphilis and 201 as a group control. There was no treatment for syphilis at the time, and the patients were given a placebo. In 1947, penicillin was discovered, which proved to be a treatment for syphilis and, even so, the placebo was maintained. In the 1960s, after a complaint by an employee of the Service itself, a committee was formed, and after analyzing the project, opted for its continuation, to follow the participants until their deaths, in order to perform necropsies and analyze the study data. In 1972, the press reported the fact and the population's reaction forced the research to end. Parts of the study had already been presented at conventions in the USA. At closure, 28 patients had died of the disease; another 100 patients had complications from the disease; at least 40 spouses had been infected; and 19 cases of congenital syphilis have been identified.

Today, there is no way to discuss Medical Research without referring to the Bioethical Principles of BENEFICENCE, NON-MALEFICENCE, AUTONOMY AND JUSTICE.

Let us assess the situation of a particular drug, which has been approved for human use, it is effective against certain disease (s), although it has potentially serious and rare side effects. We can use it if its results (benefit) justify the risk (cost). In this situation, we would be upholding BENEFICENCE.

If even the drug is not proven effective against any other pathology, its use should not be encouraged, as an eventual and improbable benefit would not justify the risk. In this situation, NON-MALEFICENCE should be our main concern.

In both cases and within ethical limits, we must respect the patient's will, who, after being informed and clarified about the possible risks and benefits involved, can make his/her own choice, asserting his/her AUTONOMY.

It should be noted that, when seeking authorization for research in human beings, the Code of Medical Ethics, in addition to requiring the consent of the object of the research (AUTONOMY), refers, when the patient is a minor, to the consent of the legal guardian and also the consent of the child or adolescent, thus recognizing that minors must have their autonomy recognized and respected within their capacity for discernment,.

Let us now analyze a study in which there is a need for a random distribution of participants in experimental and control groups (randomized and double blind), in which we guarantee that it is not possible, in principle, to establish advantages of one procedure over the other. If, during the development of the study, an evident advantage is detected, the study should be ended, from then on, the best treatment should be guaranteed to all participants, thus upholding the principles of JUSTICE and BENEFICENCE.

Likewise, if damage is detected during the study, it must be terminated, ensuring the health of the participants. JUSTICE and NON-MALEFICENCE.

Also in the name of JUSTICE, we must guarantee to all participants in any study, the possible benefits derived from it.

Let us see what the Code of Medical Ethics says about Research, which deals with the theme in some of its chapters and in many of its articles.

In Chapter I, Fundamental Principles, we see that (article V) "It is the physician's responsibility to continually improve his/her knowledge and use the best of scientific progress for the benefit of the patient and the society". BENEFICENCE; (article VI) "The doctor will keep absolute respect for the human

being and will always work for the patient's benefit, even after death. He/she will never use his/her knowledge to cause physical or moral suffering, to exterminate the human being or to allow and cover up attempts against a patient's dignity and integrity ". BENEFICENCE and NON-MALEFICENCE; (article XXIII) When involved in the production of scientific knowledge, the physician will act with impartiality, independence, truthfulness and honesty, with a view to the greatest benefit for patients and society". BENEFICENCE; (article XXIV) "Whenever participating in research involving human beings or any animal, the doctor will respect national ethical standards, as well as protect the vulnerability of the research subjects". JUSTICE.

We must remember that the doctor cannot be capitulated to any of the articles of the Fundamental Principles or be punished for disrespecting them. For that, it is necessary that these principles are present in the deontological articles, in which there is an obligation to do.

Chapter VII, Medical Teaching and Research, states that it is forbidden to the doctor (article 99) "Participate in any type of experience involving human beings for war, political, ethnic, eugenic or other purposes that violate human dignity". NO MALEFICENCE and JUSTICE; (article 100) "Failing to obtain approval of a protocol for conducting research on human beings, in accordance with current legislation." JUSTICE; (article101) "Failure to obtain from the patient or his legal representative the free and informed consent form for conducting research involving human beings, after due explanations about the nature and consequences of the study. § 1 In case the patient participating in the research is a child, adolescent, person with a mental disorder or illness, in a situation of reduced ability to discern, in addition to the consent of their legal guardian, their free and informed consent is necessary to the extent of their understanding. § 2 The access to medical records will be allowed to doctors, in retrospective studies with justified methodological issues and authorized by the Research Ethics Committee (CEP) or by the National Research Ethics Commission (Conep) ". AUTONOMY and JUSTICE; (article 102) "Stop using the correct therapy when its use is authorized in the country. Sole paragraph. The use of experimental therapy is permitted when accepted by competent agencies and with the consent of the patient or his legal representative, adequately clarified of the situation and the possible consequences ". AUTONOMY and JUSTICE; (article 103) "Conducting research in a community without first informing and clarifying it about the nature of the investigation and failing to meet the objective of protecting public health, respecting local characteristics and the relevant legislation". AUTONOMY, JUSTICE, BENEFICENCE; (article 104) "Failing to maintain professional and scientific independence from medical research funders, satisfying commercial interest or obtaining personal advantages". JUSTICE; (Article 105). "Conduct medical research on subjects who are directly or indirectly dependent on or subordinate to the researcher". JUSTICE; (article 106) "To maintain a link of any kind with medical research on human beings who use only placebo in the study, when there is an effective prophylactic or therapeutic method". BENEFICENCE, NOT MALEFICENCE and JUSTICE; (article 107) "Publish on the doctor's behalf scientific study in which he/she did not participate; attribute to himself/herself exclusive authorship of study carried out by his subordinates or other professionals, even when performed under his guidance, as well as omitting from the scientific paper the name of whoever participated in it ". JUSTICE; (article 108) "Using data, information or opinions not yet published, without reference to the author or without his written authorization". JUSTICE; (article 109) "Failing to ensure, when being a professor or author of scientific publications, the veracity, clarity and impartiality of the information presented, as well as failing to declare relations with the pharmaceutical industry, orthoses, prostheses, equipment, implants of any nature and others that may constitute conflicts of interest, albeit in potential ". JUSTICE.

It is essential that we keep in mind that the Physician, when participating in research, mainly involving human beings and/or other animals, must respect ethical and moral principles, always seeking benefits for human beings and for the society.