

Bioethics – a brief history: from the Nuremberg code (1947) to the Belmont report (1979)

Bioética – uma breve história: de Nuremberg (1947) a Belmont (1979)

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DOI: 10.5935/2238-3182.20140060

ABSTRACT

This study tells the story of Bioethics in the period between the Nuremberg Code (1947) and Belmont Report (1979). Bioethics is a word etymologically formed by two Greek etyma: bio (s) and ethike. A triple paternity and triple birth place was allocated to this neologism: Van Rensselaer Potter in Wisconsin; Shriver and Hellegers in Washington; and Fritz Jahr in Halle an der Saale (Germany). Potter was concerned, in principle, with the environment and sustainability of human life on the planet; the Washington group was mainly concerned with problems and ethical challenges imposed on Medicine by new technologies; and Fritz Jahr was concerned with ethical relations between human beings and animals and plants. Bioethics is born bringing into memory the inhuman experiments performed on vulnerable people during the World War II, and grows side by side with great scientific and technological development. That same technology that increases the potential of medicines brings serious moral challenges that the traditional Hippocratic ethics has difficulties to respond. All this is happening at the same time when people are fighting for more autonomy and rights. To reflect on this context and identify the best alternatives of conduct is one of the roles of Bioethics.

Key words: History of Medicine; Bioethics; Ethics.

RESUMO

Este estudo conta a história da Bioética no período compreendido entre o Código de Nuremberg (1947) e o Relatório Belmont (1979). Bioética é uma palavra etimologicamente formada por dois étimos gregos: bio(s) e ethike. A esse neologismo foi imputada uma tríplice paternidade e um triplo local de nascimento: Van Rensselaer Potter em Wisconsin; Shriver e Hellegers, em Washington; e Fritz Jahr, em Halle an der Saale (Alemanha). Potter se preocupava, em princípio, com o meio ambiente e a sustentabilidade da vida humana no planeta; o grupo de Washington, principalmente com os problemas e desafios éticos impostos à Medicina pelas novas tecnologias; e Fritz Jahr, com as relações éticas dos humanos com animais e plantas. A Bioética nasce trazendo na memória os experimentos desumanos realizados em pessoas vulneráveis durante a Segunda Guerra Mundial e cresce lado a lado com um grande desenvolvimento científico e tecnológico. Essa mesma tecnologia que aumenta as potencialidades da Medicina traz consigo sérios desafios de ordem moral que a ética hipocrática tradicional tem dificuldades de responder. Tudo isso acontecendo ao mesmo tempo em que pessoas lutam também por mais autonomia e direitos. Refletir sobre esse contexto e identificar as melhores alternativas de conduta é um dos papéis da Bioética.

Palavras-chave: História da Medicina; Bioética; Ética.

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Submitted: 2013/08/22
Approved: 2014/04/24

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INTRODUCTION

What is Bioethics? There is a phrase from Epictetus (55-135 AD), stoic philosopher who lived at the beginning of the Christian era, who says: “First learn the meaning of what you say, then say it”. However, there are terms that seem to be simple at first but when you want to define and use them, some disturbance arises. St. Augustine (354-430 AD) reported about it. Talking about time, he asks: “What is time? He reflects, is surprised and says: When no one asks me, I know it, but if I want to explain to who asks me, I do not know”.¹

But what is Bioethics? Let us face the challenge and try to answer. It seems logical to begin to investigate the etymology of the word. After all, Aranguren observes that the role of this subject is to recover the original meaning of words and rescue their true meaning, which may have been worn by its prolonged use over time.² The etymological study reveals that Bioethics is formed by two Greek etyma: bio(s) – initially used in the sense of human life and later, by extension, applied to all living beings; and ethike – meaning ethics. This second etyma (ethike) comes from the noun ηθος (eethos by transliteration, written with a double vowel or the Greek initial eta), whose first meaning, and original, was home. Over time, however, it transformed into εθος (ethos by transliteration, with single vowel or Greek initial épsilon), also changing meaning.^{2,3}

Weber and Perez Tamayo claim that Heidegger recovered the homeric and pre-philosophical meaning of ἦθος, showing that both in the Iliad and Odyssey, it was used to designate the “den” of animals, where they were safe from storms and predators. It was, therefore, their preferred habitat, where they felt safer. This was the oldest and most original meaning of the term: den, habitat, home.^{2,4} Over time, the term ἦθος will change. In Aeschylus, Thucydides and specially in Aristotle, a word a little different emerges – εθος (ethos), now no longer written with eta (or double vowel), but with epsilon (or simple vowel) and its meaning also changes. It stopped meaning den, habitat, or home and began to be habits or customs. It is in this meaning that it will be translated into Latin, when Cicero created the words mos, moris (mores in the plural) – becoming moral in Portuguese. “That part of Philosophy with regard to customs, which the Greeks call ethos, we call it – Dos Costumes. But it is appropriate that who wants to increase the vocabulary of the Latin language, call it moral” (Cicero, The Fact, 1.1).^{5,6}

Over time, the term εθος (ethos) will change again, written with a double vowel again – εθος (eethos) – and again, changing its meaning. Instead of going back to mean den or habitat, it will mean character (in the sense of our inner attitude towards life).

Therefore, there are three different meanings for the second etyma: den or habitat, habits or customs, and finally character. It is understandable, then, why so many people use the terms moral and ethical in an interchangeable way and with the same meaning. However, from the point of view of many philosophers, it is necessary to establish a distinction. Moral refers to the behavior according to customs and conventions accepted by people. Sánchez Vázquez defines it as:

*Moral is a system of norms, principles, and values by which mutual relations between individuals, or between them and the community, are regulated, so that these norms, with a historical and social character, are freely and consciously adhered by an inner conviction and not by a mechanical, external, or impersonal way.*⁷

On the other hand, ethics also called the moral philosophy, is concerned with the reflection and justification of principles that provide the basis of morality. It seeks to establish the reasons why an action is considered right or wrong; it is a rational study of human behavior from the point of view of moral duties and virtues. In short, ethics is the reflected moral. The Spanish philosopher Adela Cortina observes that ethics would be sterile if restricted only to the clarification and justification of moral. It is also necessary to apply its findings to the different spheres of social life.⁸ In the same line, the American Henry D. Thoreau says: “To be a philosopher is not merely to have subtle thoughts, nor even to found a school. To be a philosopher is to solve some of the problems of life, not in theory but in practice”.⁹

It is considered that the fundamental question to ethics is: how to live, detailing: what to do and why do it? The existence of three areas in its study is understood in this context: meta-ethics (or philosophical ethical), normative ethics, and applied ethics.

The meta-ethics studies the meaning of terms used in the ethical discourse. It relates to the concepts and theories used to think about actions and whether or not these ideas are appropriate and true.¹⁰ Here is the question: what is the source of ethics? What is the conceptual universe of ethics? How to know what is ethical?

The normative ethics seeks to guide towards what should be done, seeks to determine what action or rule is correct, seeking to be based in theories. And they are many. There are teleological theories that appeal to the consequences of actions, saying that an action is morally correct or not according to its consequences. Its best-known version is utilitarianism. There are also ethical theories that appeal to the intrinsic nature of the action and not its consequences. Norms and codes of professional behavior derive from them. It is also important to mention the theory of virtues, which seeks to determine the correctness of an action, asking if it would or not be practiced by a morally virtuous person. It is practically a reformulation of the question of “what should I do” to “what should I be”. Obviously, all these theories, originally proposed by Jeremy Bentham and John Stuart Mill, Immanuel Kant, and Aristotle have suffered reinterpretations to suit the new conditions imposed by society changes.¹¹

The applied ethics or practice uses normative ethics in conflict resolution. Here, it finally meets Bioethics. It is considered a form of applied ethics. In a circumscribed and still limited way, we can begin to understand it and define it as:

[...] a form of applied ethics that is concerned with solving problems related to life (bios). At the moment that human action gains the power to change life as if it is naturally given to us, this action on life falls within ethics – especially Bioethic.¹²

What gave birth to the neologism bioethics?

Van Rensselaer Potter, American biochemist and oncologist who worked at the Medical School from the University of Wisconsin, created the term Bioethics.¹³ It initially appeared in the article “Bioethics, the Science of Survival”, published in 1970 in the journal *Perspectives in Biology and Medicine* (1970; 14: 127-153), and later in his book *Bioethics: Bridge to the Future*, published in 1971.¹⁴ These are publications expressing great concerns from Potter: scientific knowledge growing exponentially without being accompanied by adequate consideration of its use and possible consequences for the survival of mankind. In the translation by Ferrer and Alvares, it can be read:

There are two cultures – sciences and humanities – they seem incapable of speaking with each other, and if this is part of the reason

for humanity’s future being uncertain, then we could possibly build a bridge to the future, building the Bioethics subject as the bridge between the two cultures. Ethical values cannot be separated from biological values. Humanity urgently needs a new wisdom to give an understanding of how to use knowledge for man’s survival and improved quality of life.¹⁵

For Potter, Bioethics then combines biological knowledge (bios) with a system of human values (ethics). Despite the idea’s initial amplitude, it walked preferably on a slope specially focused on the challenges imposed by new technologies and genetics, leading Potter to modify his original term and rename his position as global Bioethics.¹⁶

There is a second paternity, not by the originality of the term, but by the emphasis in a specific meaning. Bioethics as a more focused reflection on the analysis of problems related to the development of Biomedicine. It had also emerged in 1970 and independently in a conversation involving Sargent Shriver, Eunice Kennedy Shriver’s husband and Andrew Hellegers, a Dutch obstetrician among others, about the possibility of the Joseph P. Kennedy Jr. Foundation to sponsor an institute for the study of religious and ethical advances in biological sciences, in the University of Georgetown, by applying the reasoning of moral philosophy to medical dilemmas.¹⁷ From these conversations, they created in 1971, The Joseph and Rose Kennedy Institute for the Study of Human Reproduction and Bioethics, today known as the Kennedy Institute of Ethics.¹⁸ It is the first time the word bioethics would appear as the name of an institution.

The third source of the word bioethics, Halle an der Saale, Germany, appeared in a conference held in 1997 by Rolf Lothar, and has been gradually investigated.¹⁸⁻²⁰ In this case, the source that cites the word bioethics is an editorial in the *Kosmos* magazine from 1927.²¹ Its author is the German Fritz Jahr (1895-1953), philosopher, educator, and protestant church minister. The original article was translated into Portuguese under the title: “Bioethics – reviewing the ethical relationship between human beings and animals and plants” and it can be found in the annals of the VIII International Congress of Clinical Bioethics, held in May 2012 in the city of São Paulo.²² In an analogy to Kant, Fritz Jahr proposes a bioethical imperative: Respect every living being as a matter of principle and treat it whenever possible such as one. If Kant formulated his categorical imperative based on human

dignity, Fritz Jahr based his on compassion.¹⁹ Rincic and Muzur comment something apparently paradoxical, happening simultaneously: While Jahr advocates the extension of Kant's categorical imperative also for animals and plants, Nazism in Germany, restricted it to Aryans in detriment of the rest.¹⁸

In his book *The Birth of Bioethics*, Albert Jonsen believes that the neologism bioethics wins canonic status in 1974, when it is cataloged and placed as a point of entry in the American Library of Congress.¹⁷ The justification for this entry was the article *Bioethics as a Discipline*, by Daniel Callahan, published in 1973 in the first issue of the *Hastings Center Studies*.²³ Thus, the birth certificate of the word bioethics is officiated.

How and why did the bioethics emerge?

It can be said that bioethics has been molded in a major scientific and technological development with profound social, political, and cultural changes, together with a resounding progress, great abuses, especially in research involving humans.

At the end of the 40s, the Western world was still trying to recover from the nightmare of World War II, when the Nuremberg Tribunal, responsible for the trial of war criminals, brings out the monstrosity of some experiments, in the Nazi Germany, on vulnerable humans. More seriously, the perplexed humanity sees, sitting in the dock, 23 people accused of war crimes and against humanity, and among them 20 are doctors. Out of these 23, 16 are considered guilty, seven sentenced to death.^{24,25} This context shows that the professional ethics of doctors, charitable in principle, is not always trustworthy, nor the moral conscience of the researcher is sufficient as a safe limit for the control experimentation. The physician paternalism and supposed neutrality of science are simultaneously affected.

In August 1947, the same court releases their sentences and develops a historical document called the Nuremberg Code. In it, ethical recommendations are proposed to be observed in research involving human beings.²⁶ The first article provides that for human experimentation, the voluntary consent of those involved is imperative. In the following year, 1948, there was another historical document: the Universal Declaration of Men Rights²⁷, praising: "Art. 1st All men are born free and equal in dignity and rights. Art. 3rd. Everyone has the right to life, liberty, and personal safety." These documents apparently suggested tranquility

to society. The limits for scientific research on human beings seemed well established. Pure idealism. In the opaque atmosphere of the cold war, exceptions were made over what was recommended. The most obvious of them understood that the patient's consent would be unnecessary in cases of therapeutic experiments to benefit him. The transposition of the text into the practice was shown to be problematic, and the winding path, full of advances and retrocessions.

April 25, 1953 is an important date in the history of science. James D. Watson and Francis H. Crick publish in one page in the journal *Nature*, an article with the potential to unleash true biological revolution. "The molecular structure of nucleic acids".²⁸ It is believed that the key of the secret of life is found. It was hiding in the double helix that forms the DNA molecule. There, man could learn how organisms are formed and evolve, perhaps, the cause of possible evolutionary defects and even perhaps, through manipulation, the possibility of healing. It was a fascinating and frightening discovery at the same time. Fascinated by the immense open perspectives and frightening by awakening the recently convicted ghost of eugenics. Could men play God? Wouldn't it be a new fire of Prometheus, bringing a Pandora's Box afterward? Are there limits to science after all? A positivist idea hinted that science was neither good nor bad. Its use was important. Conversely, those would admit limits would have to define who should establish them and how. These were controversial and fundamental questions imposed. What is certain is that, pioneers Watson and Crick became famous. They were awarded the Nobel Prize in Physiology or Medicine in 1962 and celebrated by the Spanish surrealist artist Salvador Dali in 1963 (*Galacidalacidesoxyribonucleic acid*. Salvador Dalí, 1963). There were some people, however, questioning about the fairness as they had access to the X-ray diffraction data from Rosalind Franklin!

Still in the 50s, specifically in August, in the summer of 1952, Copenhagen was devastated by a polio outbreak. The only hope existed for a large number of patients with the paralytic respiratory form of the disease, was the so-called "iron lung" – a cylindrical tank where the patients were placed, with their head outside. This mechanism created a negative pressure around the patient's chest provoking passive inspiration and expiration. But it was a very limited technology, both from an operational point of view and its size and cost. When called to assist a young woman in a desperate situation with paralytic disease and se-

vere bronchospasm, the anesthesiologist Bjorn Ibsen decided, as a last resource, to anesthetize her, perform a tracheotomy and ventilate her with intermittent positive pressure through a rubber bag. The recovery of the young lady was surprising. Shortly after, more than a thousand Medicine and Dentistry students were called to work in shifts of six hours, ventilating patients with respiratory paralysis. So many lives were saved this way. In the next summer, when the polio epidemic arrived in Sweden, they already had a mechanical ventilator for the treatment of their patients.²⁹ The new equipment brought an effective solution, spurred the emergence of intensive care units, saved lives, but, it introduced new challenges of moral order. How should be the procedure in relation to an unrecoverable patient who can only survive by being connected to the equipment? Is it allowed to be turned off? When? How to decide? Who should do it? Such a challenge was proposed by Dr. Bruno Haid, an anesthesiologist from the University of Innsbruck, Austria, to a moral authority, the Pope Pius XII. In his reply, given in a speech on November 24, 1957, the pontiff introduced the idea of ordinary and extraordinary means.

(The natural reason and Christian moral)... usually requires the use of ordinary means (according to the circumstances of people, places, time, and culture), i.e., means that do not impose any extraordinary burden to self or to the other. A stricter obligation would be too burdensome for most men and would render the acquisition of the most important superior goods more difficult.³⁰

The 60s decade was an effervescent period in which freedom and self-assertion were sought. The political and sociocultural contexts were constantly boiling. There were increasingly inflamed movements for individual and collective civil rights. Models and authorities were challenged, questioned about the institutions of family, government, and church. There was a fight for many reasons and on many fronts: in defense of the rights of women, blacks, homosexuals, etc. In that decade, 1968 was emblematic. In Europe, there was the Prague spring, and the student revolts in Paris. In the USA, the Vietnam War was loudly questioned, and the assassination of Martin Luther King Jr reflected. The echoes of rebellion also echoed here. The radicalization of the student fight and military dictatorship was lived. Protests multiplied and also arrests and disappearances of activists. Mouths were gagged, and pages were censored. Even though, pro-

tests were heard even in popular music. The song of Geraldo Vandré, second in the Third National Festival of Songs in 1968 – Walking or not to say that I have not spoken of flowers – became the anthem of the civil resistance to the dictatorship. It was censored just because its chorus was considered an incitement to armed struggle. “Come, let’s go, because to wait is not to know. Those who know make the time and do not wait for things to happen.”

Medicine itself in the 60s has undergone great transformations. In the words of Stephen Toulmin, of an almost artisanal practice, based more on tradition than on knowledge, it became a scientific subject increasingly accurate and efficient. From generalist and home based, it became specialized and hospitalized. It brought undoubtedly great results in terms of combating diseases and increasing life expectancy, but, paradoxically, the doctor-patient relationship deteriorated. It gradually became less empathic and more distant, as if bringing the cool machine that increases professional accuracy anesthetized its sensitivity. The patient noticed that the humanitarian paternalism gradually faded. The area prepared by the Nuremberg for the autonomy of research subjects also became a fertile ground for the patient’s autonomy in the clinical practice. And he would claim it.

The freedom that was sought and longed for also had its eyes focused on the practical application of research results. Emblematic example: the pill. After tests in the late 50s, in communities from Puerto Rico and later in Mexico City and Haiti, in May 1960, the FDA approved the Enovid®, the first effective contraceptive pill,³¹ as a reliable and safe solution for good family planning. A big concern at the time that prompted the research from which it emerged was a possible overpopulation in certain regions of the planet. For the first time, a drug was marketed for continuous use by healthy and specially married people. At the same time, however, it was placed in the hands of this generation, who yearned for freedom, an instrument that would allow it the rejection of traditions, a challenge to institutions, as well as the redefinition of the women’s role. Sexuality was separated from reproduction. A freer and safer sexual behavior was possible, and objectives could be enjoyment and communication. Questions arose again, now mostly of religious and moral basis. From a moral point of view, is chemical contraception acceptable? If so, when? Will the decision be exclusive to women? And the husband or partner? Is there a role for the State in this context?

Will greater domain over the body and sexuality bring the risk of more promiscuity? Today, after 50 years of use, the strength of behavior tries to impose over the religious questioning. Science has developed a lot, and it has already put at the disposal of women a pill for emergency contraception. In our country, the so-called morning-after pill. However, the moral questioning remains: Is this a chemical abortion?

The society will also continue to be surprised with new slips, misunderstandings, and ambiguities in the medical practice involving not only research but also the clinical care. On March 9, 1960, in Seattle Washington, the nephrologist Belding H Scribner used for the first time, the cannula developed to connect a patient to the hemodialysis machine, opening, this way, the possibility of prolonged treatment for patients with chronic renal failure. It became possible to extend the life of chronic renal patients over long periods and even return them to an active life. However, the reality of the moment was awkward: many needed treatment and few could be assisted.³² Again the technology was imposing dilemmas to the health professional. How to select these few patients? With what criteria? In the first phase, patients had to meet criteria from clinical indication. From that point, the doctors delegated the decision to a committee of seven members in the community, people considered above any suspicion. Initially, a church minister, a lawyer, a housewife, an executive, a labor leader and two non-nephrologists doctors were involved. This committee, later known as the “God Squad,” established the criteria they thought relevant: age, race, marital status, number of dependents, income, education level, prior to community services, and future capabilities.³² The embryo of clinical bioethics committees was glimpsed here.

This selection context became public in a report by the journalist Shana Alexander, published in the *Life* magazine, November 11, 1962. The title of the article drew attention: “They decide who lives, who dies”. The subtitle, “Medical miracle puts moral burden on a small committee”.^{32,33} This was the longest article published in *Life* magazine so far. The main questions that emerged were: how to decide? Who should decide? What criteria to use?

Abdicating from its decision-making role, medical ethics lead to what was to be called “Strangers at the Bedside” – title of a book by David J. Rothman.³⁴ Professionals from other areas, mostly philosophers and theologians, felt that the selection process adopted was a serious ethical problem and needed an

in-depth analysis. The debate was opened to more people. The philosophical argument of social utility to theology contrasted the inherent dignity of the human person. It was the technological advance arousing more questions about life and death. Albert Jonsen, in his aforementioned *The Birth of Bioethics*, believes that it is the first big debate of the nascent bioethics.

Another big debate would soon follow. Henry Beecher, an anesthesiologist from Harvard Medical School, unhappy with the ethical aspects of some researches, elaborated an article criticizing them. This article was originally submitted to *The Journal of the American Medical Association (JAMA)*, but refused.³⁵ After a review, it was accepted by *The New England Journal of Medicine (NEJM)* and published as a special article entitled: *Ethics and Clinical Research*.³⁶ In it, the author cited 22 research papers published in important journals, such as *JAMA* and *NEJM*, conducted between 1948 and 1965 with flagrant ethical violations; 14 were conducted in university centers – all taking advantage of government resources or pharmaceutical companies, in which the subjects involved in the research always came from vulnerable populations (children, elderly, mentally retarded, etc.). It also highlighted the lack, in the research protocol, of the expressed consent from those involved. And this was already advocated since the Nuremberg Code established in 1947!

Similarly, the World Medical Association had been positioned, from the Declaration of Helsinki I, enacted in 1964. In it, the scenario of clinical research was detailed when combined with professional care. Beecher’s article brought embarrassment because it made clear that ethical violations were not things from the past or uniqueness of Nazism. The confidence in the ethics of doctors and scientists was undermined again. Among the 22 studies indicated by Beecher, two drew more attention: the first, an investigation on hepatitis conducted at Willowbrook State School, an institution that interned children with mental retardation; and the second, a study of immune response to the injection of live cancer cells conducted at the Jewish Chronic Disease Hospital (Brooklyn, New York), using chronic and debilitated patients.

The Willowbrook State School, located in Staten Island, New York, was an institution that received children with mental retardation. The hygienic limitations of hospitalized patients propitiated multiple possibilities of contamination, which ended up making the environment endemic for infectious hepatitis.

Most of the susceptible hospitalized patients were infected between 6 and 12 months after hospitalization. The research design was based on three objectives: “a) to describe the circumstances in which the disease occurs and the effect of gamma globulin reducing occurrence; b) try to induce a passive-active immunity by administering the virus to people protected by gamma globulin; c) to identify the excretion of virus during the disease incubation period”.³⁷ The criticism of the work was directed to the following aspects: a) the use of vulnerable patients (children with mental retardation); b) the purposeful infection of a group of children with the hepatitis virus ; c) the existence of biases in the consent form.

On April 10, 1971, the *Lancet* magazine published, in the session letter to the editor, a text by Stephen Goldby questioning the ethical aspect of this research and suggesting that it was performed simply to increase knowledge about the topic and not to benefit the research subjects.³⁸ Saul Krugman, the chief researcher, responded to these criticisms in the same magazine on May 8 justifying the experiment with the following arguments: a) all children who were hospitalized would be exposed to the same virus in natural conditions; b) children in the research were placed in special units, protected from other potential infections; c) they would probably have a subclinical infection and then would be immunized against that type of hepatitis; d) only children whose guardians had given their “informed consent” were included in the research.³⁹ There are today advocates and critics of the ethical position of these researchers.^{40,41,42} However, questions and technical justifications aside, the fact is that many saw the episode as an exploitation of the vulnerable. Another incentive for conformation to Bioethics.

The experiments performed at the Jewish Chronic Disease Hospital (JCDH), in Brooklyn New York, were also cited and criticized by Beecher. There was a team of researchers led by Chester M Southam, from the Sloan-Kettering Institute for Cancer Research, interested in the study of human immunity to cancer.^{43,44} Between February 1954 and July 1956 they conducted their first experiments in humans, including 14 patients with advanced cancer and incurable condition. They received an infusion of live cancer cells from a different type of cancer. The responses to these infusions were lumps in the infused region that grew for about four to six weeks and then regressed spontaneously and completely. Apparently, the experiment did not interfere with the evolution of these

patients. The procedure and also its reason would have been explained, and they had consented orally.

In a subsequent step, in May 1956, the same type of experiment was performed in healthy prisoners, at the Ohio State Penitentiary, who volunteered and gave their written consent.^{43,45} This was probably the first experiment with the injection of live cancer cells in healthy patients. The immune response was also the formation of nodules that regressed and disappeared spontaneously and in a much shorter time. These data suggest that patients with cancer lose their immunity to the disease. However, it was necessary to ensure that this phenomenon could not be attributed only to the weak state of the patient.

It was then necessary to investigate chronic and debilitated patients who were not suffering from cancer. Patients with these characteristics could be found at the JCDH. Chester M. Southam contacted Emanuel E. Mandel, clinical director of the hospital at the time, and he agreed with the performance of the research in his institution. They selected 22 patients between 43 and 83 years old, who received a subcutaneous infusion of live cancer cells in the anterior portion of the thigh.⁴⁶ Such experiments caused great discomfort within the institution. First, the appropriate acquisition of consent from the patients was questioned. Second, the word cancer had not been mentioned to the patients. They would simply have been informed that they would receive an infusion of certain types of cells. Three professionals left the institution in protest against this procedure.⁴⁷ When asked about the experiment, Chester M Southam and the hospital board argued that they were sure about being the safety of the procedure and that the word cancer, by its peculiar connotation would cause great anxiety among patients. They also claimed to have obtained oral consent from each of the participants. William A. Hyman, a lawyer and board member of the hospital, became aware of the situation and wanted to investigate it. Because access to the medical records from those patients was denied, he took the case to the Supreme Court of Brooklyn and gave it publicity. In an interview with the *Science* magazine in January 1964 he even claimed that the consent from the patients could not have been obtained by physical and mental inability in those involved, since many were senile, others speaking only Yiddish, and one was deaf.⁴³ Due to the judicial inquiry, this case has been in the media for a long time. The analogy with Nazi experiments became explicit, probably because

those involved in the research were vulnerable and from the Jewish race.

Another important episode in the configuration of bioethics happened outside the American scientific community. On December 3, 1967, Christiann Barnard, at the Groote Schur Hospital in Cape Town, South Africa, performed the first heart transplant. He removed the heart of Denise Darvall, 25 years old, victim of trampling, and implemented it in the terminal cardiac Louis Washkansky, 54 years old. The patient survived the procedure, and the surgery was considered a big success by the media.⁴⁸ Barnard became world known, being on the cover of the “Time” magazine. Again science and technology amazed and dazzled the universal community. However, unfortunately, the development of immunosuppressants did not work out along the surgical ability. Washkansky survived only 18 days and died of pneumonia.⁴⁹ Along with this fascination, new questions arose: how is it possible to remove a living heart from a dead person? When do you consider that someone is definitely dead? Is the death a moment or a process? As a process, is it possible to determine when it becomes irreversible?

The first response came in the very next year. The Journal of the American Medical Association, from August 5, 1968, published under the coordination of Henry Beecher: “A definition of irreversible coma: Report of the ad hoc committee at Harvard Medical School to examine the definition of brain death.”⁵⁰ Brain death criteria were developed, however without unanimity. And again, questions from multiple sources – scientific, religious, and cultural: is the conscious life the only life form? When the brain dies, does the person die too?

The criteria for brain death increased greatly with the potential of organ donors. Perhaps that was one of its main objectives. The saga of transplants started in 1954 with the first successful kidney transplant, quickly extending to other organs. Also on this aspect of technological advancement, another moral questioning was imposed on society: Who can be an organ donor? The donation should be voluntary or can it be presumed? Can it be paid in any way? May a prisoner have his sentence reduced when he offered himself as a donor? Can a child be a donor? Who will decide for the child? How to face the pregnancy of a child with the future goal of being a donor?

These questions transcended the hippocratic ethics and began to be reflected in the context of another knowledge. Bioethics was being gestated as a multidis-

ciplinary knowledge. In 1969, the philosopher Daniel Callahan and psychiatrist Willard Gaylin created in New York, a center for the reflection on these topics: Center for the Study of Value and the Sciences of Man, later known as The Hastings Center.^{51,52} In 1970, the American theologian Paul Ramsey (1913-1988) published an important text for bioethics: *The Patient as Person – Explorations in Medical Ethics*.⁴² Again, a layman reflected on topics such as the consent in human experimentation, the concept of death, care of the dying, organ donation, and patient selection before the allocation of scarce resources. He also reflected on the moral criteria that should guide the medical practice, placing emphasis on human dignity, which should be considered in every patient. In 1971, as seen before, an important center for bioethical reflection was created in Washington, The Joseph Kennedy and Rose Kennedy Institute for Human Reproduction and Bioethics, later known as The Kennedy Institute of Ethics.

However, the research that would mobilize not only the scientific community but the entire society and the American Congress was yet to be revealed: the “Tuskegee Study of untreated syphilis in black men.” It was a project developed by the Public Health Service of the United States, to know the natural history of non-treated syphilis.⁵³ The site of the study was Macon, a poor district in the rural area of Alabama State. At the end of 1920, Macon had approximately 27,000 inhabitants, 82% of African-American descent, 36% of them infected with syphilis.⁵⁴ At that time, the idea of racial Medicine was still influential, which conceived a different disease behavior according to the patient’s race.⁵⁵ In the case of syphilis, it was believed that the black race would have a more protracted evolution. Moreover, its treatment was uncomfortable and with questionable efficacy. Based on these ideas, the Public Health Service of the United States created a project that would allow knowing the natural history of untreated syphilis in black patients.

The Macon population seemed a unique opportunity for this observational study. It started in 1932, and the initial project was modified in the following year. It became an observational study of long duration in its final conception, with periodic clinical and laboratory evaluations, ending only with the death and autopsy of the patient. After examining more than 4,000 people from the Macon region, 399 patients were selected, 25 years old and older males. A total of 201 other non-infected people were included as a control group. The patients voluntarily participated

in the project; however, they had no clear idea of their role in it. To the eventual questioning about a possible disease, they received the answer that they had bad blood, a popular name for various types of involvements.^{56,57} Ernest Hendon, the last survivor in the study (died in 2004) remarked: “They said it was a study that would be good for us”.⁵⁸

Some stimuli were created to maintain the enrollment of the selected participants along with periodic clinical assistance, 25 dollars for every year participating in the program, and funeral assistance of 50 dollars. It is noted that the idea of rewarding participants already has a long history! There was still a community nurse, Eunice Rivers, who became an important link between the subjects and the research group. Her role in the project is highlighted in a film produced by HBO in 1997: *Miss Evers Boys*. Another “gift” given to the participants in the study was the release of any call to military service during World War II. In 1947, when the conflict ended, penicillin, highly effective in combating syphilis, became also widely available to the civilian population, but this treatment was refused to those involved in the study. In an attempt to rationalize the refusal, researchers argued that never again would be a population like that one for the study and, in addition, there would be a risk of severe reactions to penicillin in a population with syphilis with long duration. This understanding completely ignored the Declaration of Helsinki, adopted in 1964, to protect human rights in research subjects.

In 1968, Peter Buxton, interviewer and researcher on venereal diseases in the public health service of the United States, communicated his questions about the morality of the Tuskegee study in a letter to the Center for Disease Control. Nevertheless, the study continues. Later, in early 1972, he reported and showed some documents on the case to Edith Lederer, a friend and a reporter for the Associated Press. She sent them to her superior and asked to be on the case. However, Jean Heller was appointed, a reporter based in Washington and with free movement between government agencies. On July 26, 1972 the story was printed as the cover story in the *New York Times*. Other media immediately approached the subject.⁵⁹ The public impact of the report was significant. The Tuskegee Study was considered an outrage, a serious violation of civil rights and a big display of racism.

Big gaps in the morality of medical and scientific research were again exposed. The old confidence in the detachment of physicians and scientists led to

suspicion. It was the end of the moral immunity of researchers. The Department of Health, Education, and Welfare then instituted a panel to evaluate the study, which considered it unethical and recommended its ending. The US government, meanwhile, developed a plan of benefits for the project participants and their dependents in the form of financial compensation and health care. On May 16, 1997, President Bill Clinton invited the survivors of the study and their descendants to the White House and on behalf of the nation apologized to them. “What the United States government did was shameful. I apologize”.⁶⁰

At the time, there were seven survivors of the study group. Six attended the White House. In 2004, the last participant died. In response to the accusations and scandals involving biomedical research on human beings, the Executive and the US Congress established a national committee to define the ethical principles that should guide them – the “National Commission for the Protection of Human Beings in Biomedical and Behavioral Research”. It was also established the obligation of an institutional review board for all research projects to be funded by the State.

In January of 1973, it began bringing a judicial decision in a controversial issue until today in the bioethical discourse. The US Supreme Court decided in *Roe vs. Wade* case, the legality of abortion in the first trimester of pregnancy. Subsequently, the American Hospital Association adopted the Patients’ Bill of Rights, giving the patient the autonomy to take the final decision on the interventions that could be submitted, in opposition to the traditional paternalism of the hippocratic ethics. In October of the same year, it was published again at *The New England Journal of Medicine*, another paper showing that in a special care unit for children, among 299 consecutive deaths, 43 occurred because the decision to not implement treatment. This brought to light the ethical and moral dilemma in this kind of professional behavior.⁶¹

As if that were not enough, there was a new controversial case in 1976. Karen Ann Quinlan, diagnosed with persistent vegetative state, was maintained on assisted ventilation. Considering the irreversibility of the picture, the patient’s father asked the doctor in charge of the case for turning the respirator off. Faced with a refusal, the request is forwarded to the justice. The Supreme Court of New Jersey, based on the right to privacy and autonomy of individuals said: a) when the patient is unable to make decisions about their own treatment, someone may exercise this right on

their behalf – creating the figure of enduring mandate; b) patients have the right to refuse treatment, even if that refusal would lead them to death. It was also considered that decisions that may lead to the death of a mentally incompetent patient are best taken by the family with the support of their doctors and not by the court. This is the proposition of the Committee of Clinical Ethics. This case received considerable media coverage and contributed to the legalization of the so-called “living will”. Paradoxically, after the removal of the ventilator, the patient started spontaneously breathing, surviving for over 10 years in a persistent vegetative state.⁶²

While these cases happened, the “National Commission for the Protection of Human Beings in Biomedical and Behavioral Research” was working. After four years, it published a paper that was known as the Belmont Report – a historical and normative document for Bioethics.⁶³ Three basic guiding principles for research involving humans were elected: a) respect for people; b) beneficence; c) justice. The respect for people with two ethical assumptions: a) individuals should be treated as autonomous agents; b) those with reduced autonomy (vulnerable) have the right of protection. Thus, the informed consent was institutionalized. The beneficence, of hippocratic tradition, has also two additional rules: a) do no evil; b) provide the most benefits with the least possible damage. Justice requires care in selection and equity for subjects in research studies. Ethical standards that should guide the experimentation with human beings were elected.⁶³

While the Belmont Report was created, Warren Thomas Reich, one of the researchers from the Kennedy Institute of Ethics, coordinated the first edition of the Encyclopedia of Bioethics, which was published in 1978 in four volumes, containing 315 articles and contributions from 285 authors. This work has become a key reference on the subject of bioethics. New editions came in 1995 and 2004. In the first edition, bioethics was considered as “the systematic study of human behavior in the area of life sciences and health care while this behavior is examined based on principles and moral values”.⁶⁴

Would it be possible to extend the principles defined as foundations for research with human subjects, from the Belmont Report to clinical care? In response, the classic work of Beauchamp and Childress emerged – Principles of Biomedical Ethics – initially published in 1979 and now in its seventh edition.⁶⁵ In this text, the principle of respect for people was re-

placed by autonomy, and beneficence was divided into beneficence and non-maleficence. Thus, the following principles are consecrated: a) autonomy, privileging the patient’s decision; b) beneficence and non-maleficence, attributed to health professionals; c) and justice, specifically distributed and geared to health-care institutions and society in the treatment of issues relative to life and health of human beings. With the publication of Beauchamp and Childress, the “principlism” is consecrated as a method of reasoning and decision in Bioethics. Although hegemonic, it will be contested, and many other methods and theories will offset it. This discussion, however, is beyond the temporal context proposed in this historical review.

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