History of Bioethics: Crimes Against Humanity in Human-Subject Research

Amy Reese Hohmann

In Macon County, Alabama, a poor man received excellent medical care from a team at the university down the road. None of his friends in the county could afford to visit the doctor, and his friends were a little jealous because they wanted the same medical attention that this man received. A physician from the Tuskegee Institute had reached out to the man because the physician learned that the man had "bad blood" and wanted to treat him. The man received rides to and from the medical clinic, free medical exams, and free treatment for minor conditions not related to his bad blood. The medical team even told the man that there would be a burial stipend paid to his family. He was grateful for this treatment. As an illiterate sharecropper, he did not know much about all the tests they performed on him. He knew bad blood had been the cause of death of some of his family members in the past. He wanted to be treated for his bad blood so he could continue to work for his family, so he just did what the doctor told him to do.

In the previous article of this column, we discussed the history of ethics. This article focuses specifically on the history of bioethics. Bioethics is a subcategory of ethics that pertains particularly to the ethics of healthcare. According to the Hastings Center, one of the leading institutes in the field of bioethics, "bioethics is the interdisciplinary study of ethical issues arising in the life sciences, health care, and health and science policy."[1] Bioethics pertains to the ethical conundrums faced in healthcare and by healthcare professionals such as pharmacists.

Bioethics grew out of a sordid history.

The Ethically Speaking column is coordinated by Amy Reese Hohmann, PharmD, MBe, Desert Regional Medical Center, Palm Springs, California. amy.c.reese@gmail.com

The field gained recognition as atrocities were unveiled in human-subject research. The heinous crimes against humanity during research reared their ugly heads. Society acknowledged mistakes it made and learned from the past. In this article, we will explore the 2 main blunders in human-subject research, which made people realize the need for guidelines on how to conduct ethically appropriate research.

Nazi Experimentation During the Holocaust

One of these crimes against humanity was the experimentation on human subjects that occurred during the Nazi regime under the Holocaust. Nazi physicians experimented on prisoners without consent that was often painful and led to death. Because of the idea of racial superiority and racial hygiene, physicians justified their experimentation on the prisoners of the Holocaust. These prisoners experienced experiments testing the limits of what humans could handle, such as maximum survivable altitudes and treatments for hypothermia. The prisoners were also test subjects for immunizations for diseases such as malaria and infectious hepatitis.[2]

Once World War II ended in 1945,[3] the Allied powers (United States, Great Britain, France, and the Soviet Union) uncovered these horrendous experiments. The Allied powers formed the International Military Tribunal (IMT)[4] and held the Nazi leaders accountable. The Nazi leaders stood trial in Nuremberg, Germany, from 1945 through 1946 for crimes against humanity, war crimes, and conspiracy to commit crimes.[4] The Nuremberg Trial led to the development of the Nuremberg Code, as shown in Table 1. The Code created a foundation of requirements that must be met for human-subject experimentation to occur ethically.

Table 1. The Nuremberg Code[5]

1. The voluntary consent of the human subject is absolutely essential.
2. The experiment should be such as to yield fruitful results for the good of society.
3. The experiment should be so designed and based on the results of animal experimentation and a knowledge of the natural history of the disease.
4. The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.
5. No experiment should be conducted where there is an a priori reason to believe that death or disabling injury will occur.
6. The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment.
7. Proper preparations should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability, or death.
8. The experiment should be conducted only by scientifically qualified persons.
9. During the course of the experiment the human subject should be at liberty to bring the experiment to an end.
10. During the course of the experiment the scientist in charge must be prepared to terminate the experiment at any stage, if he has probable cause to believe, in the exercise of the good faith, superior skill and careful judgment required of him that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject.

The Untreated Syphilis Study at Tuskegee

The second main crime against humanity prompted the development of the formal field of bioethics. The Untreated Syphilis Study at Tuskegee was conducted by the U.S. Public Health Service through the Tuskegee Institute in Tuskegee, Alabama. It began in 1932 and continued until 1972, despite the Nuremberg Code's establishment in 1947.

The study included 600 Black men, 399 with and 201 without syphilis.[6] The purpose of the study, unbeknownst to the subjects, was to analyze the natural progression of the disease by withholding treatment. This purpose was not revealed to the subjects, many of whom were illiterate sharecroppers. They were being treated for "bad blood," which was a colloquialism for multiple ailments such as syphilis, anemia, and fatigue.[7] The subjects were given free medical care for conditions other than syphilis, treatment for minor conditions, rides to and from the clinics where the experimentation occurred, and a burial stipend.[7]

Penicillin was produced in sufficient quantities by 1943 and became the first-line treatment for syphilis by 1947,[8] but none of the men in the study received the antibiotic. The study was finally stopped after a news article written by Jean Heller in the Associated Press on July 25, 1972,[7] created a public uproar.

In response, the U.S. Assistant Secretary for Health and Scientific Affairs created an ad hoc advisory panel to determine how to proceed. By October 1972, the committee declared that the study was "ethically unjustified" and terminated it. A class-action lawsuit in 1973 awarded the men and their families $9 million.[7]

Development of the Field of Bioethics

From tragedy, hope arises.

The National Research Act was passed in 1974 to create the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research.[9] An Ethics Advisory Board, comprising experts in biomedical and behavioral research, was established to analyze ethical issues in research. This Advisory Board wrote *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research* as a result.[10] The report was published on September 30, 1978.[10]

Through the identification of 4 principles, the Belmont Report established standards for the ethical conduct of human-subject research and created a foundation of bioethics. The principles of bioethics are respect for persons, beneficence, nonmaleficence, and justice.[10] These fundamental principles (nominal ethics) are used to address ethical conundrums in research. Research ethicists assess potential studies through the lens of these principles to assess whether the research will be conducted ethically.

As pharmacists, it is important to understand the history of human-subject research. We must be careful when conducting research on patients and handling study data by adhering to the Nuremberg Code and the principles of the Belmont Report. We must have our research reviewed by an institutional review board, or IRB, to ensure that the research is conducted safely for the research subjects and appropriately from an ethical viewpoint. Both of the crimes against humanity discussed here are reasons that experimentation on prisoners is extremely limited. Research is vital to the growth of our field, but we must guarantee that we conduct our research ethically. No one should experience the egregious experimentation that people endured in the past.

In the next installment of this column, we will explore the 4 principles of bioethics in depth.

References

1. The Hastings Center. What is bioethics? The Hastings Center. Accessed June 11, 2024. www.thehastingscenter.org/what-is-bioethics

2. Holocaust Encyclopedia. Nazi medical experiments. United States Holocaust Memorial Museum. Updated Aug. 30, 2006. Accessed June 11, 2024. encyclopedia.ushmm.org/content/en/article/nazi-medical-experiments

3. U.S. Department of Defense. Victory in Europe day: time of celebration, reflection. U.S. Department of Defense. Accessed June 11, 2024. www.defense.gov/Multimedia/Experience/VE-Day

4. The National WWII Museum: New Orleans. The Nuremberg trials. Accessed June 11, 2024. www.nationalww2museum.org/war/topics/nuremberg-trials

5. The Office of Research Integrity. Nuremberg code: directives for human experimentation. ORI introduction to RCR: chapter 3. the protection of human subjects. U.S. Department of Health & Human Services. Accessed June 11, 2024. ori.hhs.gov/content/chapter-3-The-Protection-of-Human-Subjects-nuremberg-code-directives-human-experimentation

6. Centers for Disease Control and Prevention. The U.S. Public Health Service untreated syphilis study at Tuskegee. The untreated syphilis study at Tuskegee timeline. Centers for Disease Control and Prevention. Accessed June 11, 2024. www.cdc.gov/tuskegee/timeline.htm (2022, December 5).

7. National Center for Bioethics in Research and Health Care. About the USPHS syphilis study. Tuskegee University. Accessed June 11, 2024. www.tuskegee.edu/about-us/centers-of-excellence/bioethics-center/about-the-usphs-syphilis-study

8. Gaynes R. The discovery of penicillin—new insights after more than 75 years of clinical use. *Emerg Infect Dis.* 2017;23(5):849–853. doi: 10.3201/eid2305.161556. PMCID: PMC5403050

9. Centers for Disease Control and Prevention. The U.S. Public Health Service untreated syphilis study at Tuskegee. Research implications. Centers for Disease Control and Prevention. Accessed June 11, 2024. www.cdc.gov/tuskegee/after.htm#:~:text=After%20the%20U.S%20Public%20Health,of%20Biomedical%20and%20Behavioral%20Research

10. Office for Human Research Protections. The Belmont Report. U.S. Department of Health and Human Services. Updated June 7, 2024. Accessed June 11, 2024. www.hhs.gov/ohrp/regulations-and-policy/belmont-report/index.html