Ethics Review

Ethical Considerations of the Past & Present

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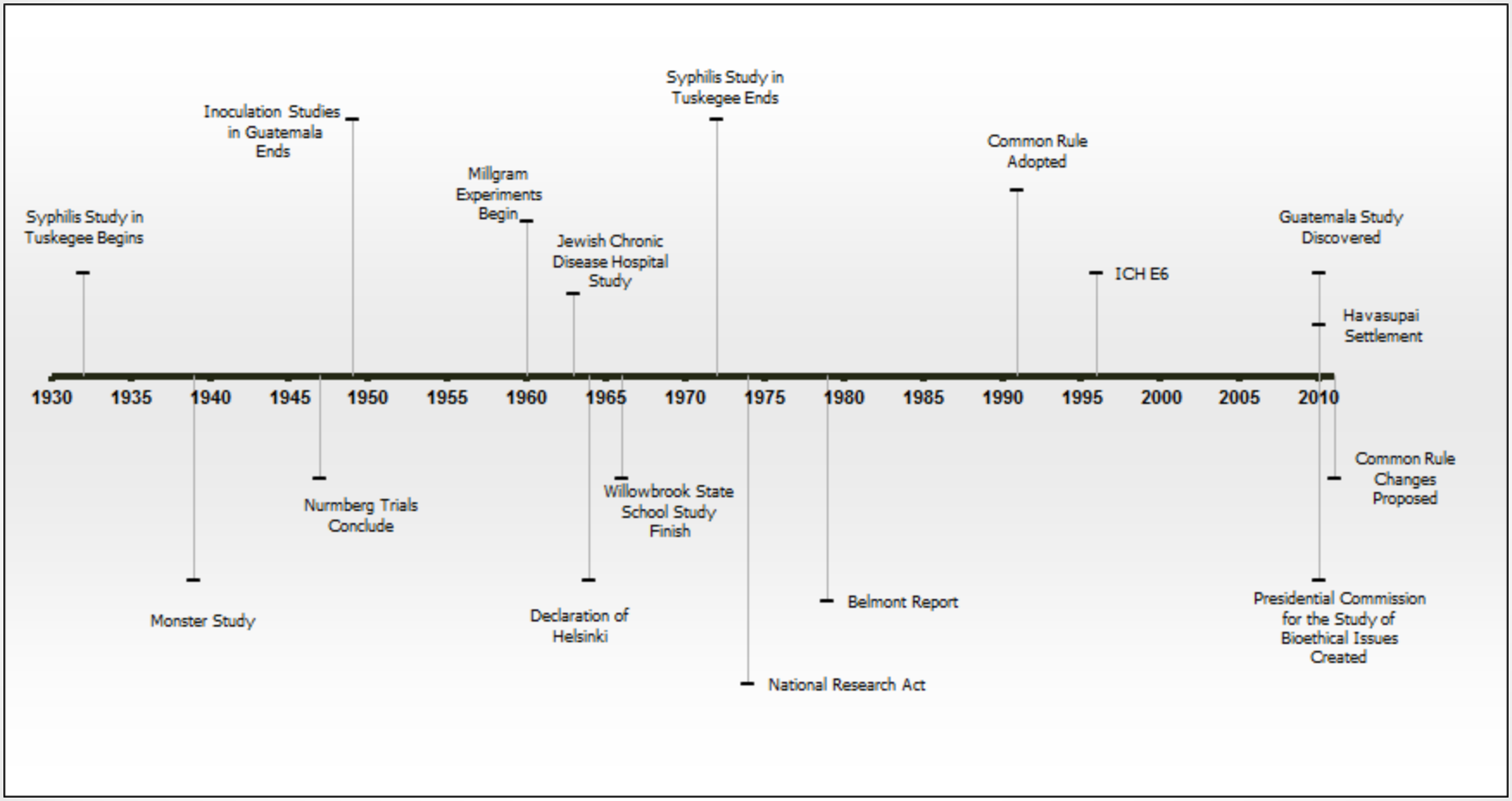
Research Ethics: Historical Events



Monster Study: 1939

- Termed the “Monster Study” by peers of the PI, Wendell Johnson from University of Iowa
- 22 orphaned children selected for this study on stuttering. Some who actually stuttered and some who did not.
- The investigators provided positive feedback to some of the subjects and negative feedback to others, depending upon whether they were included in the control or experimental group
- Many of the children with normal speech patterns suffered negative psychological effects, and some developed lifetime speech problems

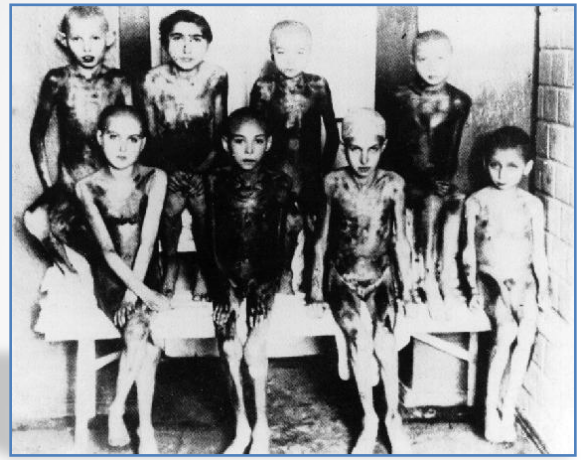
Nuremburg Trials: 1946 - 1947

- Trials at Nuremburg – series of military tribunals in response to WWII atrocities in the concentration camps
  - "Researchers" conducted cruel experiments on children & adults held in the camps with no informed consent

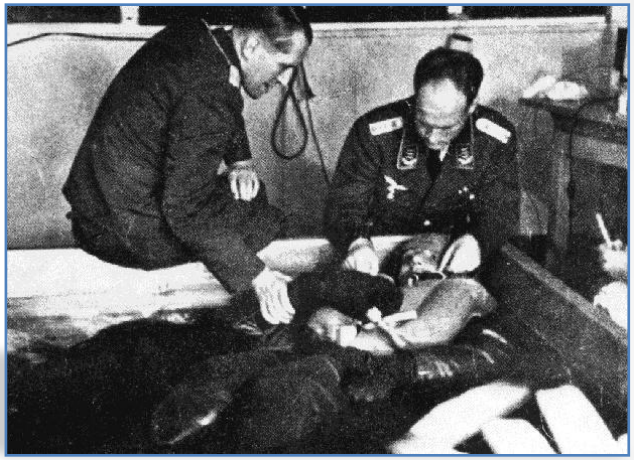
- Many defendants argued that the experiments were morally justified
  - Participants were going to die anyway
  - Sacrifice would provide scientific knowledge benefiting many

- 15 of the 25 defendants (20 MDs) were found guilty and 7 were sentenced to death

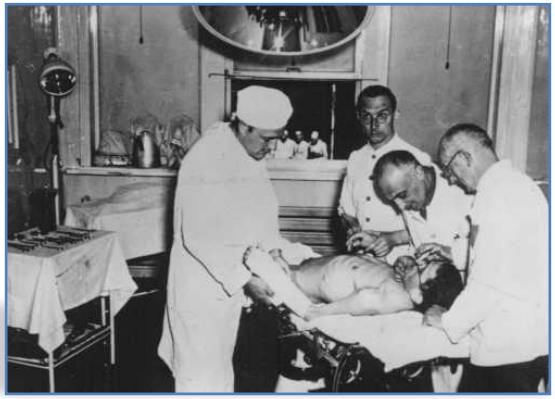
Nuremburg Photographs



Children of Auschwitz exposed to medical experiments during the Nazi regime



Cold Water experiments on Nazi prisoner



Medical personnel experiment on a prisoner at the Buchenwald concentration camp.

Nuremburg Code: 1947

- Developed as a direct result of the Nazi medical experiment atrocities committed during World War II that were revealed at the Nuremberg Trials.

- Makes clear that
  - The welfare and rights of human subjects must be protected
  - The research conducted must be sound and beneficial
  - The freedom of human subjects to participate or not is inviolable

Jewish Chronic Disease Hospital: 1963

- 22 elderly patients who were hospitalized in Brooklyn, New York due to a variety of chronic debilitating diseases were injected with live cancer cells
  - Intent to obtain information about the human immune system's response to cancer & transplant rejection process

- Researchers claimed oral consent was given but not documented
  - Patients were not told that they would receive cancer cells because the investigators believed this would frighten the patients unnecessarily

- Investigators defended the conduct of the study on the basis that they had good cause to predict that the cancer cells were going to be rejected

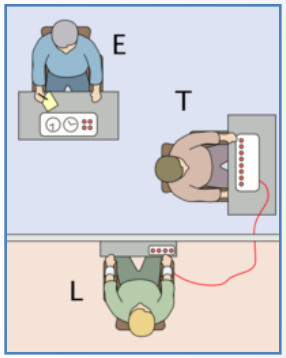
Willowbrook State School: 1963-1966

- Designed to gain an understanding of the natural history of infectious hepatitis and to test the effects of gamma globulin in preventing or ameliorating the disease
- Children subjects were deliberately infected with the hepatitis virus
  - Early subjects were fed extracts of stools from infected individuals and later subjects received injections of more purified virus preparations
  - Only children whose parents gave permission to participate in the research were admitted

- Investigators stated that the vast majority acquired hepatitis while at Willowbrook, and it would be better for them to be infected under carefully controlled research conditions

Milgram Experiments: 1960s

- Measured the willingness of subjects to obey an authority figure who instructed them to complete a task that conflicted with their conscience
  - Subject (T) instructed by the researcher (E) to give what subject believes are painful shocks to the learner-actor (L) when an incorrect answer is given
  - Subjects believed actual shocks were being given for incorrect responses



- Many subjects realized they were capable of committing acts of extreme violence against others

- Ethical questions raised due to the associated extreme emotional stress and insight into personal flaws inflicted upon the subjects

http://en.wikipedia.org/wiki/File:Milgram_Experiment_v2.png

Declaration of Helsinki: 1964

- Developed by the World Medical Association (WMA)
- Originally developed in 1964 in Helsinki Finland, and later amended six times, most recently in 2008.
- Statement of the ethical principles that should be followed in the conduct of medical research involving human subjects, including research on identifiable human material or identifiable data
- Addresses ethical review, risk/benefit considerations, research with vulnerable populations and other issues related to protecting the autonomy, rights and welfare of participants
- Served as a guide for establishing ethical committees in various countries to review research projects on humans

The Tearoom Study: 1965-1970

- Conducted by Laud Humphreys, a Ph.D. student studying stereotypical beliefs about men who committed impersonal sexual acts with one another in public restrooms.
- He gained the trust of individuals by posing as a voyeur and lookout.
- He secretly followed some men and recorded license numbers of their vehicles.
- A year later, Humphreys showed up at their private homes disguised and claiming to be a health service interviewer. He asked questions about their sexual orientation, marital status, race, job and other personal information.

The Tearoom Study, cont.

- The report had enough detail that the identities of some participants were obvious to them and their families.

- Issues:
  - Subjects were never consented
  - Invasion of privacy
  - Failure to protect against deductive disclosure of identity
  - Deception was used with no debriefing
  - There was a risk of societal harm and risk of civil or criminal liability (many of the men were married and these at the time, arrests for this behavior in public was more prevalent)

Tuskegee Syphilis Study: 1932 – 1972

- US Public Health Service Sponsored: “The Study of Untreated Syphilis in Negro Male”

- Subjects were disadvantaged, rural African-American men, several who were already infected and some who were not
  - Provided with free medical exams, free meals, and burial insurance, but were not told about their disease

- Infected men were denied treatment, although penicillin was accepted treatment in 1943, and PCN was available for syphilis treatment in 1952

National Research Act of 1974

- Created the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research

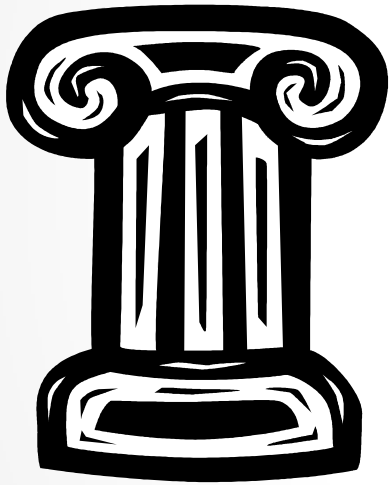
- Charge to the Commission:
  - Identify the basic ethical principles that should underlie the conduct of biomedical and behavioral research involving human subjects
  - Develop guidelines which should be followed to assure that such research is conducted in accordance with those principles

The Belmont Report: 1979

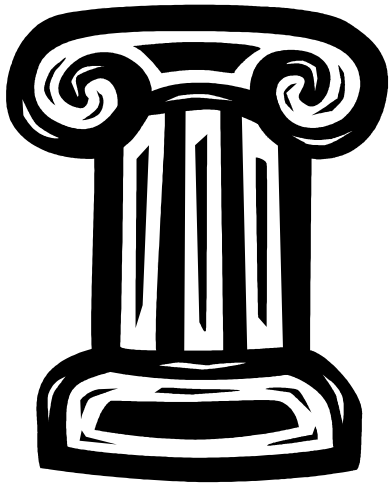
- Issued April 1979 by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research
- Made necessary due to a long history of various questions, concerns, difficulties and problems that arose in medical experimentation and other forms of research efforts involving the enrollment of human subjects
- Distinguished between medical practice (treatment) and research
- Established the responsibility of the investigator to submit research activity for review by an Institutional Review Board (IRB)

The Three Pillars of Belmont

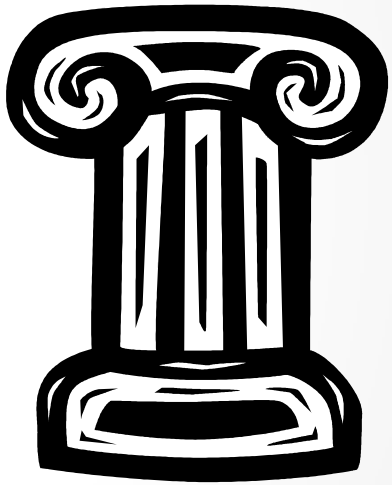
Respect for Persons



Beneficence



Justice



Respect for Persons

- The freedom and capacity of subjects must be protected
- Each subject is an autonomous agent, capable of making their own decisions, and not to be used as a means to an end
- Special measures must be taken to protect the rights and welfare of persons with diminished autonomy
- Informed consent is central to protecting the autonomy of human subjects

Beneficence

- Researchers have the obligation to secure the well-being of subjects
- Possible benefits must be maximized and possible harms must be minimized

Justice

- Researchers question who receives the benefits of research and who bears its burdens
- There must be fairness in the distribution of the risks and benefits of the research
- Each person must equally share in the distribution of risks/benefits according to individual need, individual effort, societal contribution, and merit

Common Rule: 1991

- 45CFR46, Subpart A
  - The Common Rule outlines the basic provisions for IRBs, informed consent, and Assurances of Compliance

- Codified in the regulations of 15 separate agencies (hence the name, "Common Rule")
  - Human subject research conducted or supported by each federal department/agency is governed by the regulations of that department/agency

International Conference on Harmonisation: 1996

- Established the ICH E6 Guidelines on Good Clinical Practice (GCP)
  - Designed as, “an international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects”
  - Generally agree with the Common Rule, but sometimes go farther

- ICH E6 contains 8 parts
  - Glossary, Principles of ICH E6, IRBs, Investigator, Sponsor, Protocol & Amendments, Investigators Brochure, Essential Documents

The Havasupai: 2010

- As part of a partnership with the tribe, Arizona State University (ASU) collected specimens for diabetes research in 1989.
- Researchers then used the samples, without complete consent, for unrelated studies on schizophrenia, migration and inbreeding- all taboo topics for the tribe
- In 2004, the Havasupai Tribe filed a lawsuit against Arizona Board of Regents and ASU researchers
- A settlement was reached in 2010:
  - $700,000
  - Medical care & educational services
  - Return of known remaining specimens

http://www.nytimes.com/2010/04/22/us/22dna.html

Guatemala Inoculation Studies: 1946-1948

- US Public Health Service Sexually Transmitted Diseases Study of 1946-1948
  - Conducted by the same PI as the syphilis studies in Tuskegee

- Intent was to discover new ways to prevent STDs
  - First experiments involved infecting female commercial sex workers with gonorrhea or syphilis, and then allowing them to have unprotected sex with soldiers or inmates
  - When few men became infected, research approach was changed to intentional infection of soldiers, prisoners and mental health patients

- ~1500 subjects involved
  - Governmental & Institutional officials were aware, but no subject consent obtained
  - Most, but not all, were treated for their infections

Presidential Commission for the Study of Bioethical Issues

- Advisory panel to the President that is comprised of the nation's leaders in medicine, science, ethics, religion, law and engineering. Seeks to identify and promote policies and practices that ensure scientific research, health care delivery

- In light of the 2010 discovery of the Inoculation Studies in Guatemala, President Obama requested that the Commission conduct an investigation into the specifics of this research and to assure that current rules for research would protect people from harm or unethical treatment, domestically and internationally.

Presidential Commission for the Study of Bioethical Issues

Presidential Commission for the Study of Bioethical Issues, cont.

- In response, the Commission created the International Research Panel, which was charged with conducting a full review of the currently established HSP regulations and companion international standards to determine whether they sufficiently protect the health and well being of research participants.

- In Sept. 2011 the commission released results of the Historical Investigation of the 1940s U.S. Public Service STD Studies in Guatemala

- In Dec. 2011, the Commission recommended 14 changes to current practices to better protect research subjects.

Presidential Commission for the Study of Bioethical Issues

Advanced Notice of Proposed Rulemaking

- Issued July 21, 2011
- The federal government is considering enhancements to the Common Rule
  - Data collection and security
  - Research classification
  - Modifications to informed consent documents & process
- Public comments were due by October 26, 2011, but no further information has been presented (as of Aug. 2013)

Other Professional Codes of Ethics

- Hippocratic Oath
- Government Agency Codes of Ethics
  - NIH, NSF, FDA, EPA, USDA

- Private Organization Codes of Ethics
  - Public Responsibility in Medicine & Research (PRIM&R)
  - American Psychological Association (APA)
  - Association for Clinical Research Professionals (ACRP)
  - International Committee of Medical Journal Editors
  - American Chemical Society
  - American Society for Clinical Laboratory Science
  - American Anthropologic Association
  - American Association of University Professors