Human Research Ethics

Research Skill II

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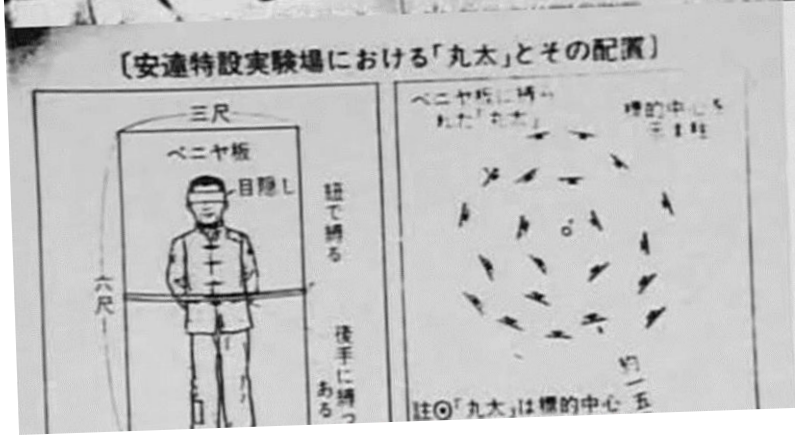
6 November 2020

Topics

- Unethical research in the past
- Important ethical principles
- Informed consent process
- Institutional review board (IRB)
- Research ethics, researchers perspective

The Monster Study (1939)


〔安達特設実験場における「丸太」とその配置〕
三尺
ベニヤ板
目隠し
縛る
後手に縛る
六尺
ベニヤ板に縛りた「丸太」
標的中心
註◎「丸太」は標的中心

UNIT 731

Nazi Experiments

Nuremberg code (1947)

- The Nuremberg Code was drafted at the end of the Doctor's trial following the Nazi Experiments during World War II in Nuremberg, Germany.
- Is considered to be the first research ethics guideline.

Courtroom at the Doctors' trial
en.wikipedia.org

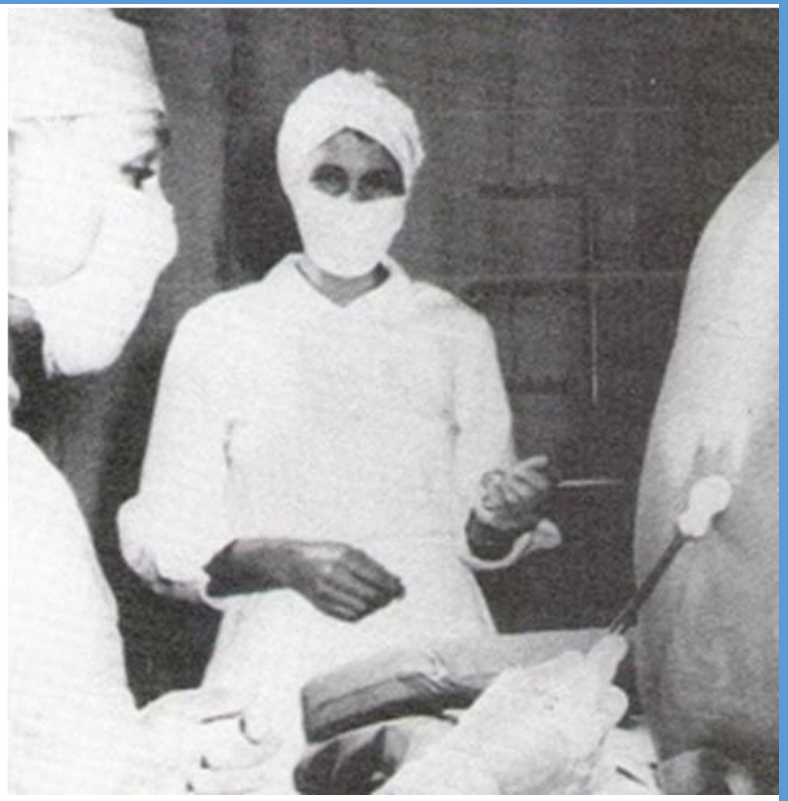
Nuremberg code (1947)

- Important points in Nuremberg code.
- Voluntary **consent of the human subject is absolutely essential**.
- The **experiment should be so designed and based on the results of animal experimentation…**
- 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.

Declaration of Helsinki (1964)

- A set of ethical principles regarding human experimentation developed for the medical community by the **World Medical Association**
- Important additions to Nuremberg code
  - The **well-being of the human subject should take precedence over the interests of science and society**
  - The study **protocol should be reviewed by an independent committee**.
  - Research **information must be disclosed to public**.
  - The **treatment should be compared with standard treatment** of that time.

Stanford prison experiment



Tuskegee syphilis study (1932-1972)

Belmont report (1979)

- A report prepared by the US National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research.
- 3 basic principles
  1. **Respect for Persons**
  2. **Beneficence**
  3. **Justice**

1. Respect for persons

- Individuals should be treated as autonomous agents.
- Individuals with diminished autonomy are entitled to protections
- Application: **Informed consent process**

Informed consent process

- **Information** - Does the consent form provide all the information necessary for the individual to make a reasoned decision?
- **Comprehension** - Is the consent form crafted in language understandable to the potential participant?
- **Voluntariness** - Does the consent form and clearly indicate that participation in the research is voluntary?

2. Beneficence

- Do not harm
- Maximum possible benefits, and minimize potential harms
- Application: **Risk/Benefits assessment**

3. Justice

- Fair distribution of burdens and benefits of research
- Application: **Proper selection of research participants**

International Conference on Harmonisation: Good Clinical Practice (ICH - GCP)

- The ICH-GCP is a harmonised standard that protects the rights, safety and welfare of human subjects, minimises human exposure to investigational products, improves quality of data, speeds up marketing of new drugs and decreases the cost to sponsors and to the public.
- The objective is to provide a unified standard for the European Union, Japan, and the United States to facilitate the mutual acceptance of clinical data by the regulatory authorities in these jurisdictions.

Institutional Review Board (IRB)

- IRB is an independent committee established to review and approve research involving human subjects.
- The purpose is to protect the rights and welfare of human research subjects.
- An IRB consists of at least five members, at least one scientist member and at least one member whose primary concerns are nonscientific.

IRB can have difference titles

- Institutional Review Board (IRB)
- Research Ethics Committee (REC)
- Independent Ethics Committee (IEC)
- Ethics Review Committee (ERC)
- Human Experimentation Committee (HEC)

Roles and authority of IRB

- Research involve human must be submitted to and be reviewed by an IRB.
- IRB review the proposal, informed consent form, and other documents according to the ethics principles.
- IRB has authority to approve or not approve, monitor the progress of research and stop the study.

Levels of IRB review

- Exempt review
- Expedite review
- Full board review

Responsibility of researchers to IRB

- Do not collect data before approval by IRB
- Conduct research as stated in the proposal
- Ask IRB for amendments if needed
- Submit progress report, usually once a year
- Request for extension if needed
- Report adverse events
- Report project closure

Personal bias

- Researchers must not have strong opinion, one way or another, toward the issue under study.
- Sources of personal bias:
  - Set target in mind that the outcome of the study must be as wanted
  - Strong beliefs related to traditions, morals, religions, etc.
- Impartiality could cause biases during research conduct, data analyses, or report writing.

Research ethics, researchers perspective

- Personal bias
- Qualifications
- Conflict of interest
- Publication and co-authorships
- Research misconducts

Personal bias

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Qualifications of the researchers

- Researchers must have sufficient scientific/clinical expertise on the issue under study, considering education and experiences.
- This is to assure:
  - quality of the research
  - safety of the participants
  - proper data analyses, discussion, and conclusion
- IRB will decide whether the research should be allowed to proceed by looking at investigators' CVs.

Conflict of interest

- In general, this refers to **'Financial conflict of interest'**.
- Significant Financial Interest directly affects, or could appear to affect, the professional judgment of a researcher when designing, conducting, or reporting research.
- Not consider guilty, except proved wrongdoing.
- What can be done?
  - Avoid potential financial conflict of interest
  - Disclose financial conflict of interest

among adults 70 years of age or older, without substantial safety concerns.

Supported by GlaxoSmithKline Biologicals.

Dr. Cunningham reports receiving consulting fees from Merck, BioCSL/Sequirus, and the GSK group of companies (GSK), all paid to his institution. Dr. Kovac, Dr. Campora, Ms. Vanden Abeele, Dr. Zahaf, and Dr. Oostvogels report being employees of GSK; Drs. Kovac, Zahaf, and Oostvogels also report holding stock in the company as part of their employee remuneration. Drs. Heineman, Lal, and Godeaux report being employees of and holding stock in GSK as part of their employee remuneration at the time of the study; Dr. Heineman is a current employee of Genocea Biosciences, Dr. Lal is a current employee of Pfizer, and Dr. Godeaux is a current employee of Crucell Holland. Dr. Chlibek reports receiving lecture fees

Publication and co-authorships

- Research must report research results to public.
- Submission of a manuscript to only one journal at a time.
- The authors have to
  - be responsible for the contents published
  - correct the errors once find out.
  - keep research and participants records for the time specified
  - qualify to be the authors
- Authors name lists have to rank appropriately.

Research misconducts

- Fabrication
- Falsification
- Plagiarism

Fabrication

- Making up data or results and recording or reporting them
- Example:
  - An interviewer fill the questionnaires without interview the subjects.
  - A study physician complete the case record forms without performing the physical examination.
  - A statistician adds a data point into the data set to get a significant statistical test.

Falsification

- Manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record
- Example:
  - Removing a data point from the data set.
  - Manipulate laboratory results
  - Change characteristics of potential participants so that they can be enrolled into the study

Plagiarism

- Appropriation of another person's ideas, processes, results, or words without giving appropriate credit
- Example:
  - Steal someone else's text
  - Publish the same results in multiple journals (self plagiarism)
  - A peer-reviewers copy the ideas of the papers under review without proper acknowledge.
- There are software to detect plagiarism, e.g. Turnitin