From Involuntary to Participatory: The Role of Humans in Research

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PERSONAL, PROFESSIONAL, PRACTICE

GOALS

1. Describe historical events that influenced the development of safety policies for subjects participating in research

2. Describe activities, and the reasoning behind engagement in those activities, by research teams to promote the safety and well-being of research subjects

3. Identify challenges to regulatory protections for humans in research.
CHALLENGE

Scientific knowledge is created by humans in an environment of inherent and accepted uncertainty.

• Scientific uncertainty
• Ethical uncertainty

Let’s think about the humans ...
RESEARCH ETHICS

1796 Cowpox human inoculations
1822 William Beaumont experiments
1932-1972 Tuskegee Syphilis study
1939-1945 Experimentation on Nazi prisoners
1942-1945 Manhattan Project ($2 billion to develop atomic bomb)
1944-1980s Radiation Research (and other research on human biology and physiology)
1947 Adoption of Nuremberg Code
1953 X-ray diffraction data used to discover the structure of DNA
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1950s-1963 CIA mind control research
1961-1962 Stanley Milgram "electric shock" experiments
1964 WMA Helsinki Declaration
1966 Henry Beecher NEJM article
1979 The National Commission releases the Belmont Report
1996 (Nicole) Wan Hoi-yan died at the University of Rochester
1999 Jessie Gelinger dies at the University of Pennsylvania
2003 The Havasupai Tribe approved “Banishment Order”
2017 US Department of Health and Human Services Final Rule on Common Rule
2017 San people of Southern Africa adopt a code
FIRST, PRINCIPLES

Autonomy
Beneficence
Non-Maleficence
Justice

Social and clinical value
Scientific validity
Fair subject selection
Favorable risk-benefit ratio
Independent review
Informed consent
Respect for potential and enrolled subjects
HUMAN RESEARCH?

What is the purpose of human research?
Why do we undertake research on humans?
What constitutes research?
On which humans do we conduct research?
Has our thinking about these questions changed over time? And if so, how?
OBSERVATION

Lithography depicting the inoculation of James Phipps
By Gaston Mélingue
(circa 1894)
EXPERIMENTATION

June 6, 1822
Beaumont tended gunshot wound on Alexis St. Martin

Beaumont and St. Martin

By Dean Cornewell, (circa 1938)
**WWII**

*President Franklin D. Roosevelt signing the Declaration of War against Japan*, December 8, 1941. 79-AR-82. National Archives Identifier: 520053

34,506,923 men registered for the U.S. draft

72,354 applied for conscientious objector (CO) status.
“I was young and I wanted to show that I was not a coward,” Neil Hartman.
Edward F. Adolph, Ph.D.

“Adolph's research interests at Rochester over a period of sixty-two years included investigations into the physiological regulation of size, body fluids and temperature, the physiology of man in the desert, physiological adaption, and the ontogeny of regulations.”

https://www.urmc.rochester.edu/libraries/miner/historical_services/archives/Faculty/adolph.cfm

“The research team was charged with determining water and food requirements, sweat rates, energy balance, heat tolerance, work capacity, and survival rates while soldiers were living and working under desert conditions.”

“Other studies considered how long men could survive without water under a variety of conditions, including men on life rafts at sea. A sobering result of some of these studies was a series of maps of the world’s oceans identifying estimated survival time for men on life rafts without water by season and location.”
URMC ROOFTOP EXPERIMENTS

https://www.urmc.rochester.edu/libraries/miner/historical_services/archives/Faculty/adolph.cfm
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Chapter 13: The Rochester Production Line

https://www.amazon.com/Plutonium-Files-Americas-Medical-Experiments/dp/0385319541
MANHATTAN ANNEX, 1943
1945 RADIATION EXPERIMENTS

Patients were injected with plutonium

- The selection of subjects is entirely up to the Rochester group. ... **It is of primary importance that the subjects have relatively normal kidney and liver function, as it is desirable to obtain a metabolic picture comparable to that of an active worker.** Undoubtedly the selection of subjects will be greatly influenced by what is available. The above points, however, should be kept in mind.

(Wright Langham, "Revised Plan of 'Product' Part of Rochester Experiment," ACHRE No. DOE-121294-D. p. 2) **Emphasis added.**

Some were injected with uranium

Some were given polonium
Amedio Lovecchio, HP1 (1878-1960)

“Lovecchio had two fig trees in his backyard. Each fall he bent the trees to the ground and buried them deep in the soil to protect them from the harsh winter. Each spring he gave the first fig to a pregnant daughter-in-law.”
“Your letter of February 27 regarding Hp 11 was startling, to say the least. . . . In case you should decide to do another terminal case, I suggest you use 50 micrograms instead of 5. This would permit the analysis of much smaller samples and would make my work considerably easier. I have just received word that Chicago is performing two terminal experiments using 95 micrograms each. **I feel reasonably certain there would be no harm in using larger amounts of material if you are sure the case is a terminal one.**”

[Wright Langham to Samuel Bassett, March 13, 1946, ACHRE No. DOE-121294-D.] **Emphasis added.**
“She [Dr. Waterhouse] believes that follow-up of these persons is an important project and is willing to cooperate to the fullest. She still sees two of the people on a regular basis and has contacted the physician who has been caring for the third patient known to be still living. She believes that all three persons would be agreeable to providing excretion samples and perhaps blood samples, but they are all quite old--in their middle or late 70's and cannot travel far. **More important, they do not know that they received any radioactive material.**”

[Patricia Durbin, December 9, 1971, ACHRE No. DOE-121294-D.]

**Emphasis added.**
DISTRESS

“Classification (prolonged) and the passage of many years before even classified publication of the findings led to his [Dr. Langham's] eventual responsibility for analysis and publication of the results. He is, I believe, distressed by this and other aspects of the study itself--particularly the fact that the injected people in the HP series were unaware that they were the subjects of an experiment.”

[Patricia Durbin, December 10, 1971, ACHRE No. DOE-121294-D.]
THE NUREMBERG CODE

1. The voluntary consent of the human subject is absolutely essential. This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, over-reaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved, as to enable him to make an understanding and enlightened decision. This latter element requires that, before the acceptance of an affirmative decision by the experimental subject, there should be made known to him the nature, duration, and purpose of the experiment; the method and means by which it is to be conducted; all inconveniences and hazards reasonably to be expected; and the effects upon his health or person, which may possibly come from his participation in the experiment.

The duty and responsibility for ascertaining the quality of the consent rests upon each individual who initiates, directs or engages in the experiment. It is a personal duty and responsibility which may not be delegated to another with impunity.

2. The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature.

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 or other problem under study, that the anticipated results will justify the performance of the experiment.

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; except, perhaps, in those experiments where the experimental physicians also serve as subjects.

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. The highest degree of skill and care should be required through all stages of the experiment of those who conduct or engage in the experiment.

9. During the course of the experiment, the human subject should be at liberty to bring the experiment to an end, if he has reached the physical or mental state, where continuation of the experiment seemed to him to be impossible.

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 judgement required of him, that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject.

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Duty of physician is to promote and safeguard health of the people.

It is the duty of the physician in medical research to protect the life, health, privacy, and dignity of the human subject.

The subjects must be volunteers and informed participants in the research project.
Respect for persons
Beneficence
Justice
(NICOLE) WAN HOI-YAN

19 years old

Sophomore at the University of Rochester

Studying to become a nurse

Volunteered (compensated $150)

Bronchoscopy: Tube inserted to collect lung cells performed under local anesthetic (Lidocaine)

“There is the question of when is a procedure more invasive than a 19-year-old should have the power to consent to. As a parent I wouldn't want my child to consent to this.” Dr. Debuono, NY State Health Commissioner
NEW YORK SEEKS TO TIGHTEN RULES ON MEDICAL RESEARCH

By ELISABETH ROSENTHAL  SEPT. 27, 1996

Prompted by the case of a healthy 19-year-old college student who died of a heart attack after volunteering for a medical research project, state health officials yesterday assailed the researchers and called for stricter state rules for such experiments.

After a four-month investigation, the state reported that the researchers at the University of Rochester Medical Center had violated their own guidelines by increasing the dose of an anesthetic for the student, Nicole Wan, who had agreed to participate for $150.

Health Commissioner Barbara A. DeBuono said Ms. Wan's death also raised a broader question of whether medical researchers in general paid enough attention to the potential risks faced by their volunteers.
The Research Subject

http://www.hpsnetwork.org
The Research Subjects
Research Participants

Guiding Principles for Community-Engaged Research

Long-term engagement
Mutual benefit
Mutual respect
Shared findings
Enhanced community capacity
Shared responsibility
Evidence-based
Collaborative from start to finish
Responsive to community priorities and perspectives
RESEARCH OBJECTIVES

Engaging more effectively with community organizations, agencies, and diverse population groups to identify research questions critical to the community and to improve methods to reflect community preferences;

Developing more effective strategies for recruitment and retention of participants in clinical studies;

Improving the dissemination of information from health promotion interventions and/or clinical trials to increase the community’s knowledge of health promotion and disease prevention.

https://www.urmc.rochester.edu/community-health/about-us.aspx
RISK ASSESSMENT

“Research that poses greater risk should receive more attention and deliberation than less risky research, and the degree and type of oversight should be commensurate with the level of risk.”

Department of Health and Human Services, 2015, p. 53941.
The Precautionary Principle & the Sanguinity Principle
SUMMARY

Slow **PROGRESS** over time

Even with good processes humans make mistakes

Requires exquisite attention to how individuals and teams make IRB/REC decisions
REFERENCES

E.D. Adolph Papers, Faculty Collection, URMC Miner Library Archives


Thank you.