

Research Ethics: History and Scandals

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Research Ethics: “Born in Scandal”

Some historical anecdotes

Edward Jenner,
(1749 – 1823)



Edward Jenner

- Discovered vaccination in 1796
- Saved countless lives
- During an epidemic he noticed that his patients who worked with cattle were immune to smallpox
- Inoculated 8-year old James Phipps with serum from cowpox sore
- Later inoculated the boy with serum from smallpox vesicle

Edward Jenner

- Could have been liable to murder charges if James died
- Research community felt more evidence was needed
- He recruited other children
- Even did a similar experiment on his 11 month old son

Jesse William Lazear,
(1866 - 1900)



Jesse William Lazear

- Demonstrated important characteristics of the transmission yellow fever
- “I think I am on the track of the real germ” – JWL wrote to his wife from Cuba
- Died 17 days later from Yellow Fever
- Investigations showed he inoculated himself for the experiments
- Other members of the team also had themselves inoculated as a precondition to joining

Yellow Fever

- 1897 Sanarelli claimed he isolated the organism
- To prove his claim he inoculated five men

William Osler

- 1898 - Osler condemns Sanarelli:

“To deliberately inject a poison
of known high degree of virulence
into a human being,
unless you obtain that man’s
sanction,
is not ridiculous,
it is criminal”

Yellow Fever

- Three years later Walter Reed was commissioned to study the epidemic in Cuba
- Laid down the condition about members serving as subjects; only adults to be recruited
- Drew up a contract – the first written consent form
- \$ 100 for participants and \$100 for those infected

Nazi Experiments 1939-1945

Over 7000 people in 70 experiments

200 physicians



Nazi experiments

- Intrauterine injection of silver nitrate during routine examination
- High altitude



Nazi experiments

- Poisons
- Sulphonamides
- Biological warfare experiments

The Nuremberg Code 1947



The Nuremberg Code

- The third part of the judgement
- 10 principles of ethical research

“the voluntary consent of the human subject
is absolutely essential”

Was it enough to stop
unethical experimentation?

Ethics and Clinical Research

Henry K. Beecher

New Engl J Med. 274 (1966)

Henry K Beecher

- Discussed 22 papers with questionable ethical backgrounds
- All conducted in reputable organizations by reputable researchers
- A landmark publication
- “thoughtlessness and carelessness”
- “NOT a wilful disregard for patient’s rights account for most of the cases”

Henry K Beecher

- Not to blame, but to draw attention
- The belief at the time was that adherence to Nuremberg was unnecessary for research in democracies
- Indispensable components =
informed consent + virtuous researcher

The Willowbrook Study

- Willowbrook school for children with mental and motor retardation
- Hepatitis virus was injected to children between 1963-1966 to learn the natural progress of infectious hepatitis
- The school was closed to new admissions during the trial
- Only parents who consented to have their children entered into the trial were allowed to register for admission
- It was known that children admitted to these facilities almost invariably developed Hepatitis

The Jewish Chronic Disease Hospital Study

- Live cancer cells were injected into patients in advanced states of cancer
- Results suggested that the defence mechanisms of those developing cancer may be impaired
- Live cancer cells injected into young healthy volunteers were promptly rejected
- Consent was said to have been obtained
- Probably obtained fraudulently

May 16, 1997



Tuskegee trial

President Clinton apologised from USA citizens because of Tuskegee trial

Tuskegee trial

- Started in 1932; ended 1972
- Study group of 400 men with syphilis; 200 healthy controls
- Offered free treatment
- Observation only, subjects not told
- Death rate x 2 in study group
- Penicillin available from 1952

Other Guidelines

- Declaration of Helsinki – 1964
- Belmont report – 1979
- CIOMS and WHO international guidelines – 1991 & 1993

"Death at the Hands of Science"

Ellen Roche, 24, died June 2001

Johns Hopkins University

Ellen Roche

- A study on inhaled hexamethonium in the treatment of asthma
- A 24 year old healthy volunteer
- Worked at Johns Hopkins
- Died despite vigorous treatment for pulmonary and renal failure
- JH accepted “institutional responsibility” for the death

Ellen Roche
External Review Report

- “Oversight and regulatory mechanisms at JH are a hindrance to research”
- Subtle coercion may have been used in recruitment
- IRBs (ERCs) were totally inadequate to deal with the number of projects
- PI was criticized for not sterilizing the drug
- FDA approval not sought
- The state temporarily stopped 2400 experiments being conducted at JH

Research is Big Money!!

Research is subcontracted to
companies

TGN 1214 Phase I Study

Contracted to PAREXEL by the
developers

- TGN 1412 designed to treat rheumatoid arthritis, leukaemia and multiple sclerosis
- A monoclonal antibody
- Six healthy volunteers developed multiple organ failure within hours of being administered the drug
- Required vigorous intensive care, and survived
- All six given the drug at the same time

Adherence to Ethical Principles by
Researchers: Experiences of a Sri Lankan
Biomedical Research Ethics Committee

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Experience in Sri Lanka

	2002	2003
Specified written consent would be sought	32%	46%
Verbal consent only	51%	32%
Applied after commencement	8%	16%
Recruitment by doctor providing care	14%	39%
Inadequate justification for study	53%	62%

Cautions for Sri Lanka

- Easy to get into 'scandals'
- Rigid review
- Adequate justification
- Beware doctors recruiting patients
- Application for clearance after commencement/completion
- **Training of ERC members**
- Lay members