Introduction & History of Research Ethics

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What is Bioethics?

- Bioethics is normative ethics applied to the practice of science and medicine
- It falls under the general group of applied & professional ethics
- A specific discipline that probes the reasoning behind our moral life within the context of the life sciences; how we decide what is morally right or wrong in bioscience

Development of Bioethics

Traceable to three different but interrelated events:

1. a set of unpleasant events ("scandals") in the history of biomedical research
2. advancement in medical technology
3. the civil rights movement

The Domain of Bioethics

- consists largely of health care, health policy & biological research
- political and economic forces that shape medicine & access to it
- societal issues addressed by bioethics involve access, allocation & distribution of health care resources
- new subjects arise from scientific advances, most recently in genetics, genomics, cloning, etc.

Research Ethics

- The analysis of ethical issues that are raised when people are involved as participants in research

- A subset of bioethics, concerned with responsible conduct of biomedical research in conformity to ethical norms

Research Ethics

- The goal of all medical research is to improve human well being

But:

- How can the rights of individual persons be reconciled with the demands of the scientific enterprise?
- Can such a laudable collective goal be pursued with full protection of the rights and dignity of individuals?

Research Ethics

Objectives

- Protection of human participants
- Conduct of research in a way that serves interests of individuals, groups and/or society as a whole
- Examining specific research activities and projects for ethical soundness, protection of confidentiality and the informed consent process

History of Research Ethics

- Though medical research has succeeded in increasing the well-being of much of the world, the successes were not without costs

- Many studies violated the rights & dignity of participants and, in some cases, cost them their health or even their lives

1st Century Experience

- *"it is not cruel to inflict on a few criminals sufferings which may benefit multitudes of innocent people through all centuries."*

  -Celsius, a 1st century Roman historian

1ST CENTURY EXPERIENCE

- This reflects an imbalance between the two goals of research: that of medical progress and the protection of the rights and welfare of human subjects.

- In the type of case cited above, a concern for medical progress is made to override the concern for human welfare and protection

History of Research Ethics

- Lind – conducted over a 6 year period in the 18th century
- In 1796, Edward Jenner conducted his famous chickenpox vaccination using children to include his own as well
- In 1900, U.S. surgeon general used 22 Spanish immigrant workers in Cuba to prove that mosquitoes transmitted yellow fever
  - He introduced use of healthy participants in research and use of written contract to confirm informed consent

History of Research Ethics

- Walter Reed's "Yellow Fever Board" sketched some guidelines for research ethics including
  - Self experimentation
  - Enrollment of only adults
  - Signed contract with sliding scale compensation

Nazi German War Experimentation

- high altitude (low pressure) experiments
- freezing experiments
- malarial experiments
- mustard gas experiments
- sulfanilamide experiments

Nazi German War Experimentation

- typhus experiments
- poison experiments
- human twin studies
- incendiary bomb experiments
- sterilization experiments

Nuremberg Code 1948

- In 1946, 23 Nazi defendants were tried for war crimes and crimes against humanity hence the Nuremberg Code
- Some components of the code are:
  - Requirement for voluntary participation in research
  - Informed consent
  - Favorable risk/benefit analysis
  - Right to withdraw without penalty

1950 Willowbrook Hepatitis Study

- Children and adolescents with disabilities were deliberately exposed to hepatitis virus in order to discover a way of preventing the disease
- New admission into the institution was closed
- Parents of children on the waiting list were written to inform them that their children could be placed on a research ward after which they could be transferred to the facility
- Researchers claimed they obtained consent from the parents and that various committees had reviewed and approved the study

1950 Willowbrook Hepatitis Study

- The researchers argued that almost all the children admitted into the facility developed hepatitis anyway, and this mitigated the deliberate exposure for the benefit of science
- Critics argued that because the participants were severely mentally retarded children whose parents wanted placement in one of few public institutions available rendered the consent invalid

Jewish Chronic Diseases Hospital Studies

- In July 1963, 2 physicians at the Brooklyn Jewish Chronic Disease Hospital injected ill elderly patients with live hepatic cancer cells without their informed consent to study "rejection of human cancer cells"
- Background studies suggested that such cells would be rejected by immune reaction leading to their rejection from the body

Jewish Chronic Diseases Hospital Studies

- It was then argued that the experiments presented no risk to the participants
- The researchers argued that informing participants about details of the research would have caused them needless psychological distress so failure to inform was based on the need to minimize distress

Jewish Chronic Diseases Hospital Studies

- The Governing Council of the University of the State of New York argued that while "*therapeutic privilege*" *may* justify non-disclosure in a physician-patient relation, same is not true of researcher-participant relationship
  - ✓ This case, among other things, highlighted the problem of conflicting loyalties for physician-researchers

Tuskegee

- Study initiated in 1932, Macon County, Alabama was:
  - ✓ Designed to take advantage of an epidemic of syphilis among the black population to study the natural history of syphilis
  - ✓ Over 400 sharecroppers were recruited
  - ✓ Neither they nor their partners were informed about the nature of the research or about their condition
  - ✓ When penicillin became available, they were not given an opportunity to use it; they were prevented from accessing it or obtaining information about it

Tuskegee

- Papers from the study were regularly published in medical journals and it did not evoke any ethical response
- In 1972, press reports finally prompted an investigation and stoppage of the study
- 74 of the original participants remained alive

Tuskegee

- Some saw no reason for the outrage after all, the study was not secret and was well known
- Others contented that the issues at stake were more about racism
- In the 70s participants were compensated and in 1997, the U.S. government apologized for the study

Pfizer Study in Northern Nigeria

- In 1996, during a large epidemic of CSM in Nigeria with 300,000 cases & 30,000 deaths, Pfizer, carried out a Phase II clinical trial of the safety & efficacy of Trovafloxacin in pediatric CSM
  - ✓ A randomized trial with 98 patients of trovafloxacin & 100 on I.V. ceftriaxone – the latter at doses subsequently shown to be lower than therapeutic
  - ✓ Case fatality was 6% for ceftriazone and 5% for trovafloxacin

Pfizer Study in Northern Nigeria

- Study raised several ethical questions including
  - Propriety of conducting such a trial in the middle of an epidemic usually known to have a high case fatality
  - Participants claimed they were not adequately informed that they were enrolling in a clinical trial;
    - ✓ about the risks
    - ✓ voluntariness
    - ✓ they did not provide informed consent

Nigeria's Response

- Increased awareness of clinical and research ethics
- Increased local and international training in research ethics
- Setting up of the National Health Research Ethics Committee
- Issuance of a standardized code for health research ethics
- Establishment and training of institutional health research ethics committees

Resources

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