BOSTON
MEDTECH
ADVISORS

More Experience ▸ Better Results

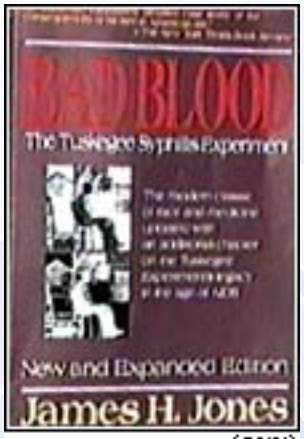
Ethics in Clinical Research

Zvi Ladin, Ph.D.

Historical Infamy

- Tuskegee syphilis study
  (1930s – 1972)
  - 399 black men signed with the US PHS for free medical service
  - Men were told they had ‘bad blood’
  - Disease followed without treatment
  - Penicillin – available since 1947
  - Outcome:
    - 28 men had died of syphilis
    - 100 others were dead of related complications
    - At least 40 wives had been infected
    - 19 children had contracted the disease at birth
  - Presidential apology (Clinton) - 1997

(Courtesy National Archives)



(CNN)

Ethics = Right vs. Wrong

- ***ethics*** *The rules or standards governing the conduct of a person or the conduct of the members of a profession.*

- Guiding Principles
  - Ethical goals
  - Protection of rights of human subjects
  - Unbiased research

- Underlying regulations
  - Declaration of Helsinki
  - US Food, Drugs and Cosmetics Law

- Open issues

Moral Compass

Guiding Principles – Research Goals

- Ethical Goals
  - Improving clinical outcome
    - Physiological processes
    - Pathological mechanisms
    - New treatment modalities
    - Better healthcare delivery
  - Risk of malevolent application
    - Clinician participation in the development of biological or chemical weapons – goal antithetical to the medical profession

Guiding Principles – Focus on the Patient

- Patient Consent
  - Understanding the patient's predicament
  - Relationship of trust
  - Full disclosure
    - Remuneration (clinician / patient)
    - Clinical alternatives

- Balancing potential future harm and benefit
  - Use of placebo
    - Even in the existence of accepted treatment

- Early termination of a clinical study

Guiding Principles – Unbiased Research

- Qualifications
  - Clinical
  - Research
  - Ethics
- Payments
  - Incremental costs of trial
    - To patient
    - To clinician
  - Remuneration commensurate with effort
  - Full disclosure

History of US Regulations

- 1947 – Nuremberg Code
- 1964 – Declaration of Helsinki

- June 16, 1966, NEJM – Henry Beecher, MD
  - Ethics and Clinical Research – 22 infamous examples
- 1960's – Patient consent added to FDC

- 1970's – IRB review of clinical protocols
  - 1972 – NIH established OPRR (Office for Protection from Research Risks)
  - Risks and benefits of research

- 1981 – FDA requires written patient consent

1998 OIG Report – Clinical Research's Shifting Environment

- Funding – from public to private
  - NIH → industry
- Nature – from single site to multi-center
  - Limited information to local IRB
- Size and numbers

1998 OIG Report – Revamping the IRB

- Overwhelmed Local IRB
  - Time and expertise limiting review
  - New ethical issues (e.g. genetic screening)
- Evaluating IRB Effectiveness
- Conflict of Interest Inside the IRB
  - Part of the organization that gains from research
- Limited Training of IRB Members and Researchers

Open Issues

- Clinician – Researcher and/or Physician
  - Separating consent from treatment
- International Studies
  - US IRB protocol approval (additional)
  - Consider local healthcare infrastructure
  - Patients' rights beyond study conclusion
- Data Safety Monitoring Boards
  - Adverse Events
    - Rate and severity
    - Relation to study
- Publication of Data from Unethical Studies

Quote of the Day

"An experiment is ethical or not at its inception; it does not become ethical *post hoc* – ends do not justify the means."

Ethics and Clinical Research,
Henry K. Beecher, *NEJM* 274[24]:1354-1360

References

- Helsinki Declaration – http://www.wma.net/e/policy/b3.htm
- AMA Code of Ethics – www.ama-assn.org
- National Institutes of Health Ethics Program - http://ethics.od.nih.gov/
- Good Clinical Practice in FDA-Regulated Clinical Trials - http://www.fda.gov/oc/gcp/default.htm
- Protection of human subjects – 21 CFR Part 50
- Ethics and Clinical Research. Henry K. Beecher. *NEJM* 274[24]:1354-1360, 1966
- Equipoise and the ethics of clinical research. B Freedman. *NEJM* 317[3]:141-145, 1987