ETHICS OF HUMAN SUBJECTS

RESEARCH

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UOB- March, 2007
Outline

• Historical aspects of codes of conduct in medical practice and research
• International Declarations & Guidelines
• Recent areas of controversy
• A way ahead (the context of research ethics in Lebanon)
WHY DOES RESEARCH EXIST?

To respond to human curiosity

- To understand and explain the natural processes
- To solve the challenges and threats that face Man
IMPACT OF RESEARCH ON HUMAN LIFE

→ A better knowledge and control of Nature
→ A better Quality of Life
→ Less diseases and death
→ Better management of Health Care
Ethical Medical Practice and Research

Human Rights & Humanity

Scientific & Technical Competence

Ethical design & conduct of research
“Morals do not forbid making experiments on one’s neighbor or one’s self. The principle of medical and surgical morality consist in never performing on man an experiment which might be harmful to him to any extent, even though the result might be highly advantageous to science, i.e., to the health of others” (1865).
Recognized that physicians appeared unwilling to concede the important distinction between the analytic power of observation and that of experiment.

“precise reasoning based on an idea born of observation and controlled by experiment”
Unethical Research

1. WARTIME RESEARCH

• World War II was a transforming event in the conduct of human subjects research.
• Transition from benefiting subjects to benefiting others
• Research agenda dictated by military need (e.g. malaria after Pearl Harbor – researchers infected residents of state hospitals and prisons)
• Use of vulnerable patients (mental patients, prisoners)
• Japanese use of Chinese residents and prisoners -
2. **NAZI DOCTORS IN WORLD WAR II**

   - Types of experiments:
     - Hypothermia experiments – subfreezing water immersion
     - Oxygen deprivation to learn about endurance
     - Deliberate injection by lethal organisms
     - Efficient sexual sterilization
     - Efficient death

   - Third Reich’s program for ‘racial hygiene’, purifying the German people by extermination and sterilization of groups
   - Nuremberg War Crime Trials, and the Nuremberg Code (1946)
International regulation of research

International Guidelines

- Nuremberg Code
- Helsinki Declaration
- CIOMS Guidelines
- International Conference on Harmonisation
- Council of Europe
- Nuffield Council
- UNAIDS
- NBAC Recommendations
- CIOMS revisions
- Nuffield Council Report
- USA (1947)
- WMA (1964, 2000)
- Europe (1996)
- Europe (1997)
- UK (1999)
- WHO (2000)
- USA (2001)
- Geneva (2002) draft
- April (2002)
Medical Ethics in Human Subjects
Research

• The Nuremberg Code included the concepts of informed concept, societal good, and volunteerism as the foundation of biomedical research.

• The Declaration of Helsinki in 1964 reemphasized the principle of informed consent for volunteers in biomedical research.
The Nuremberg Code (1947)

- Voluntary **informed consent** essential
- Research should be **beneficial**; Risk outweighed by benefit
- Based on **prior animal research**
- **Avoid suffering** of subjects - physical and mental
- No expectation of **death or disability**
- Subjects **protected by investigator** from any further injury that might occur
- Only **qualified individuals** should conduct research
- Subjects **may withdraw** at any time without loss of benefit
- **PI ready to withdraw subjects** who are experiencing excessive injury or harm
Declaration of Helsinki

World Medical Association 1964


- **Scientific basis** and rationale for research
- **Clear design** and performance
- Only by scientifically **qualified** and clinically **competent** person
- **Risk-benefit assessment**
- Safeguard **rights** and **privacy** of subject
- **Informed consent; freedom to withdraw**
- Informed consent **from guardian** if subject is incompetent.
- Research protocol must **declare compliance** with Helsinki, and discuss ethical issues.
Other Significant Documents


Ethical Principles in Human Subjects Research

Three basic ethical principles in human subjects research:

1. **RESPECT FOR PERSONS** – treat individuals as autonomous agents - protect those with limited autonomy. Informed consent by research subjects

2. **BENEFICENCE** (including **NON-MALEFICENCE**) – Make every effort to secure the well-being of people - Evaluation of risks and benefits for research subjects and others

3. **JUSTICE** – selection of research subjects - fair sharing of the burdens and the benefits of research.
1. Respect for Persons

INFORMED CONSENT

Respect for persons requires that subjects be able to choose what shall happen or not happen to them. This requirement is provided by the informed consent.

• Allow an informed voluntary decision on the part of the subject.

• Protect people with limited ability to make informed rational decisions: e.g. children, mentally retarded, stressed.

• Protect vulnerable people and those with limited autonomy: e.g. prisoners, students, employees, …

PRIVACY & CONFIDENTIALITY

• do not collect private information if you don’t need it & without permission; do not allow others to access private information.
Elements of Informed Consent (1)

COMPETENCE:

• Competence is a process,
• Three elements of competence:
  o Ability to communicate and understand relevant information about options
  o Ability to reason and deliberate about alternative options
  o Ability to evaluate options and their consequences by relating them to a stable set of values and goals
Elements of Informed Consent (2)

• **Information**: lists of items to be included, e.g., purpose, procedures, benefits, risks, alternatives, confidentiality …

• **Comprehension**: clarity; organization; time to consider and review; chance to ask questions. Special provision if comprehension is limited.

• **Voluntariness**: No coercion or undue influence. Chance to refuse or withdraw. Protect those with limited autonomy.
Ethical Principles in Human Subjects Research

Three basic ethical principles in human subjects research:

1. RESPECT FOR PERSONS – informed consent by research subjects

2. BENEFICENCE (including NON-MALEFICENCE) – evaluation of risks and benefits for research subjects and others

3. JUSTICE – selection of research subjects, and outcomes in the distribution of the benefits of research
2. Beneficence

Essence of Hippocratic tradition—“first do no harm”
Maximize benefits and minimize harm or risk

- Competent investigators
- Scientific and social value for the research
- Good research design
- What are the risks? Is risk/benefit analysis favorable? Can you change the design so as to minimize the risks?
- Continuous monitoring
2. **Beneficence (Contd)**

- **Risks Assessment:**
  - Risk of harm occurring to research subjects
  - Kinds of harm – physical pain or injury, psychological, social, economic, legal
  - Two key aspects of risk assessment:
    - Probability that harm may occur
    - Severity or magnitude of harm if it does occur

- **Benefits Assessment:**
  - Positive value related to health or welfare
  - for research subject, and others
    Payment for participation should not enter into risk/benefit assessment.
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3- Justice

• Who will receive the benefits of research and who will bear its burdens and risks?

  Fairness in Distribution

• Do procedures for selection of subjects and recruitment comply with this principle, or does the research target a particular group?

• Are the inclusion/exclusion criteria fair?, etc…Is this done on a rational and justifiable basis?

  (e.g. excluding women from drug studies because they may get pregnant, older people, children)
3- Justice (Contd)

New “international” injustice?

Research sponsored by the developed world in the developing world – what standards should prevail?
Ethical Standards – Whom Do They Serve?

- Medical Ethics – protects the patient
- Research Ethics – protects the study patient or subject, or the community
- Ethics of Scientific Practice – protects the “integrity” of the scientific process – Avoid scientific misconduct

The three are not always congruent
Why Does Scientific Misconduct Matter?

• Morally wrong
• Waste of resources
• Potentially harmful
• Erodes public confidence
• Endangers independence of science
Cardinal Sins of Ethical Conduct of Science

- Falsification
- Fabrication
- Plagiarism
- “Other serious deviations from accepted research practice”
Bias More Common Than Lying (bias=lying?)

• “Intended Effect” – likely to find the effect or outcome you “intend” to find

• Scientific measures to guard against bias – but hardly foolproof

• The essential element of scientific method is reproducibility
Ethical Norms - Authorship

• Sufficient participation in the work to take public responsibility for content

• Substantial contribution to:
  – Conception, design, analysis and/or interpretation,
  – Drafting or critically revising manuscript, and
  – Final approval of published version

• General supervision not sufficient
Social Pressures for Misconduct and Bias

“Publish or Perish”

- Publication and career advancement pressures
- Funding pressures
- Mentor pressures
- Unreasonable expectations
Create Social Conditions Favoring Ethical Behavior

- Mentor models good behavior
- Mentor spends time with trainee
- Mentor does not exert unreasonable pressure for productivity
- Promotion not based upon number of papers
- Contrary views more accepted
- Integrity needs to be nurtured
Ethical issues in international health research

• How ethical is it to undertake “new” research, when existing knowledge and interventions remain under-utilised?
• How can the ethical regulation of research reduce the equity gap?
• Reduce the dysfunction in public health?
The Problem is…

Less than 10% of global research funds are invested in 90% of the world’s health problems…now called the “10/90” gap in health research.

(Global Forum for Health Research, 1999)
The players in health research

Universities
- Public
- Private

Institutions

NGOs

Community (ies)

The State
Medical Research Councils
National Institutes
Ministry of Health

Are there intermediate steps?

Who bears the ethical burden of failure to support essential national health research?
A way ahead

• Developing Capacity in Health Research & Ethics
• Resource requirements to conduct and sustain ethical review
• Linkages and communication strategies
• Creation of novel training and learning opportunities
Function of the Ethical Review Committee

• “Ethical committees are responsible for acting in the full interest of potential research participants and concerned communities, taking into account the interests and needs of the researchers, and having due regard for the requirements of relevant regulatory agencies and applicable laws.”

WHO 2000
Ethical Review Requirements

• Independent
• Competent
  – Scientific aspects
  – Ethical aspects (comprehensive)
  – Public health and policy issues(?)
• Timely
ERC Role in Research Regulation

• National regulations may or may not provide a role for ERCs
• ERC approval may be required for some funding sources and not others
• ERC may be institutional or independent; even for-profit
• *Institutional* review may present conflict of Interest
ERC Independence

- Conflict of interest for committee members
- Freedom from pressures
  - Economic
  - Institutional
  - Political
Challenges to the ERC system (cont’d)

- No self-assessment of performance
- Conflict of interest
- Deficits in expertise (genetics, epidemiology, etc.)
Ethical Medical Practice and Research

Research on human subjects is necessary for the advancement of knowledge, science and treatments of disease.

The involvement of courageous people in such research has made possible major advances in science and medical treatment.

Such people deserve the highest standards which can be ensured by using good clinical practices and ethical treatment when conducting research.
Ethical Medical Practice and Research

Research is a privilege, not a right.

The well-being of the participant is paramount
Ethical Medical Practice and Research

- Human Rights & Humanity
- Scientific & Technical Competence
- Ethical design & conduct of research
If a health research system is the “brain” of a health system ..

.. then health research ethics represents its “conscience”!