



# The Ethics of Human Subject Research

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# Overview

1. Ancient History
2. Modern Research Ethics
3. Canada – Tri-Council Policy Statement (TCPS)
4. Internal Review
5. Moral Conscience/Consciousness

# Ancient Medicine

- ◆ Alexandrian physicians dissected and vivisected humans
- ◆ Herophilus and Erasistratus performed vivisections on criminals
- ◆ Aristotle: Best physicians are also natural philosophers

# Hippocratic Oath

I swear by the Apollo Physician and Asclepius and Hygieia and Panaceaia and all the gods and goddesses, making them my witnesses, that I will fulfill according to my ability and judgment this oath and this covenant:

To hold him who has taught me this art as equal to my parents and to live my life in partnership with him, and if he is in need of money to give him a share of mine, and to regard his offspring as equal to my brothers in male lineage and to teach them this art – if they desire to learn it – without fee and covenant; to give them a share of precepts and oral instruction and all the other learning to my sons and to the sons of him who has instructed me and to pupils who have signed the covenant and have taken an oath according to the medical law, but to no one else.

I will apply dietetic measures for the benefit of the sick and according to my ability and judgment; I will keep them from harm and injustice. I make a suggestion to this effect. Similarly I will not give to a woman an abortive remedy. In purity and holiness I will guard my life and my art.

I will not use the knife, not even on sufferers from stone, but will withdraw in favor of such men as are engaged in this work.

Whatever house I may visit, I will come for the benefit of the sick, remaining free of all intentional injustice, of all mischief and in particular of sexual relations with both female and male persons, be they free or slaves.

What I may see or hear in the course of the treatment of even outside of the treatment in regard to the life of men which on no account one must spread abroad, I will keep to myself holding such things shameful to be spoken about.

If I fulfil this oath and do not violate it, may it be granted to me to enjoy life and art, being honored with fame among all men for all time to come; if I transgress it and swear falsely, may the opposite of all this be my lot. [Translation, Ludwig Edelstein, Ancient Medicine]

# 19<sup>th</sup> Century Physiology

- ◆ “It is our duty and our right to perform an experiment on a man whether it can save his life, cure him, or gain him some personal benefit ... So, among the experiments that might be tried on man, those that can only harm are forbidden. Those that are innocent are permissible, and those that do good are obligatory.” [Claude Bernard, Experimental Medicine, 1865]

# German Code of Research Ethics

- ◆ Circular of the Reich Minister of the Interior: Guidelines for New Therapy and Human Experimentation (1931)
- ◆ Distinguished between therapeutic and non-therapeutic research
- ◆ “New therapy may be applied only if consent or proxy consent has been given in a clear and undebatable manner following appropriate information. New therapy may be introduced without consent only if it is urgently required and cannot be postponed because of the need to save life or present severe damage to health.” [Vollman & Winau, 1996]

# Medicine under the Third Reich

- ◆ Killing as “healing”
- ◆ Mass sterilization
- ◆ Euthanasia of the mentally ill and handicapped
- ◆ Research on concentration camp inmates

# Truth in Science?

“The search for truth, the search for new notions, has motivated scientists and doctors for centuries. Without it there would be no progress, no modern diagnostic and therapeutic knowledge and technique. However, in nineteenth-century science, this search became more and more a search for objective truths. The search for truth in medicine turned into destruction. It abandoned its purpose of healing the sick individual, of alleviating his suffering, and abandoned the Hippocratic *nil nocere* when experimentation was done for its own sake, for “superior” aims.” (Christian Pross, 1992, 39)

# Aberrations??

- ◆ Tuskegee Syphilis Study (1932-1972)
- ◆ Willowbrook Study (1956-1972)
- ◆ Jewish Chronic Hospital (1963)
- ◆ Cincinnati Radiation Experiments (1960-1972)
- ◆ Henry Beecher, “Ethics and Clinical Research,” *NEJM*, 16<sup>th</sup> June 1966

# The Nuremberg Code - 1947

- ◆ Voluntary Consent
- ◆ Social Utility
- ◆ Scientifically Sound
- ◆ Risk/Benefit Analysis
- ◆ Minimize Suffering and Injury

# Helsinki Declaration (1964)

- ◆ Benefit proportionate to risk
- ◆ Distinguishes therapeutic and non-therapeutic research
- ◆ Informed consent taken as far as possible.  
(Proxy consent)
- ◆ Responsibility remains with the clinical researcher

# 1979 Belmont Report (*Ethical Principles for the Protection of Human Subjects of Research*)

- ◆ Respect for persons requires respecting people's autonomy and protecting people with diminished autonomy;
- ◆ Beneficence requires minimizing harms and maximizing benefits;
- ◆ Justice requires fairness in the distribution of benefits and burdens of research



# Van Rensselaar Potter

## *Bioethics: Bridge to the Future*



- ◆ 1971
- ◆ “Biology combined with diverse humanistic knowledge forging a science that sets a system of medical and environmental priorities for acceptable survival.”

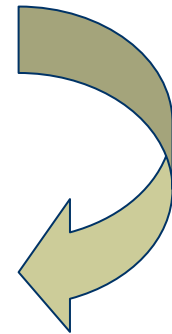
# Canada: Tri-Council Policy Statement

- ◆ Medical Research Council (MRC) – *Now CIHR*
- ◆ Social Sciences and Humanities Research Council (SSHRC)
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TCPS: Ethical Conduct  
for Research Involving  
Humans (1998)



# Tri-Council Policy Statement

- ◆ Replaces:

- 1) SSRC'S *Ethics Guidelines for Research with Human Subjects*
- 2) Former MRC's *Guidelines on Research Involving Humans*, and *Guidelines for Research on Somatic Cell Gene Therapy*

# TCPS: Context of the Ethics Framework

- ◆ A. The Need for Research
- ◆ B. A Moral Imperative: Respect for Human Dignity
- ◆ C. Guiding Ethical Principles\*
- ◆ D. A Subject-Centered Perspective
- ◆ E. Academic Freedom and Responsibilities
- ◆ Ethics and Law
- ◆ Putting Principles into Practice



# TCPS: Guiding Ethical Principles



- ◆ Respect for Human Dignity
- ◆ Respect for Vulnerable Persons
- ◆ Respect for Privacy & Confidentiality
- ◆ Respect for Justice and Inclusiveness
- ◆ Balancing Harms and Benefits (minimizing harm and maximizing Benefit)

# TCPS: Sections

- ◆ 1. Ethics Review\*
- ◆ 2. Informed Consent\*
- ◆ 3. Privacy & Confidentiality
- ◆ 4. Conflict of Interest
- ◆ 5. Inclusion
- ◆ 6. Aboriginal Peoples
- ◆ 7. Clinical Trials
- ◆ 8. Genetic Research
- ◆ 9. Gametes/Embryos/Foetuses
- ◆ 10. Human Tissue

# Informed Consent

- ◆ Article 2.1
- ◆ Prospective subjects need to give free and informed consent
- ◆ Refers to dialogue, information sharing and general process
- ◆ Voluntary – consent must be freely given and can be withdrawn at any time

# Exceptions to Consent

- ◆ i. Research involves no more than minimal risk
- ◆ ii. Waiver unlikely to have adverse affects
- ◆ iii. Research could not practicably be carried out otherwise
- ◆ iv. Provide additional pertinent information whenever possible
- ◆ v. waived or altered consent does not involve a therapeutic intervention

# Ethics Review

- ◆ TCPS expands on Belmont Report – autonomy, beneficence and justice
- ◆ Researchers no longer able to assess ethical acceptability of their own projects
- ◆ Research Ethics Boards (REB) authorized to review and approve research involving humans



## And ...



- ◆ Research involving human remains, cadavers, tissues, biological fluids, embryos or foetuses
- ◆ Research about a living individual involved in the public arena/artist if the subject is approached directly for interviews or for access to private papers

# Mandate of REB's

- ◆ Protection, safety and wellbeing of all human participants
- ◆ Ensured by review and evaluation of proposed and ongoing research
- ◆ Active promotion of ethical principles and regulations through education and training
- ◆ Authority to approve, reject, or require modifications of proposed research, or suspend ongoing research

# Ethical Criteria

- ◆ Risk/Benefit Ratio
- ◆ Maximize Benefit and Reduce Risk
- ◆ Refers to subjects, but also to those who might benefit from the research
- ◆ Requires scientific validity

# Local Institutions

- ◆ REBs function in accordance with the guidelines and directives set forth by various governmental bodies and funding agencies that are relevant to the types of research conducted within their institutions
- ◆ Although the administrative operation of each REB must conform to the normative framework as minimum requirements, REBs are free and encouraged to develop their own standard of operating procedures.
- ◆ McGill – 5 REBs + those at affiliated hospitals

# Death of a Human Subject at Johns Hopkins (2001)

- ◆ Ellen Roche
- ◆ Healthy Volunteer
- ◆ Independent IRB
- ◆ "There has got to be a cultural change here," Edward Miller
- ◆ "The idiosyncratic nature of the [Hopkins] IRB." Samuel Hellman
- ◆ "From our perspective, what we're not talking about is a change to a culture of compliance, though [compliance] is very important" Ruth Faden (Keiger and De Pasquale, 2002)

# Law Versus Ethics

- ◆ Questionable legal status of ethical codes
- ◆ REBs operate within the law
- ◆ “legal and ethical approaches to issues may lead to different conclusions. The law tends to compel obedience to behavioral norms. Ethics aim to promote high standards of behavior through an awareness of values, which may develop with practice and which may have to accommodate choice and liability to err. Further, though ethical approaches cannot preempt the application of the law, they may well affect its future development or deal with situations beyond the scope of the law.” (TCPS, p. I-8)

# Philosophical Approaches

- ◆ “REBs should be aware that there are a variety of philosophical approaches to ethical problems, and that debate between various schools of thought both informs ethical decisions and ensures an evolving context for ethical approaches. Some approaches are traditional, but others, such as feminist analysis, are centred on context, relationships of power and allocations of privilege that perpetuate disadvantage and inequality. Hence, the approach may help to correct the systemic exclusion of some groups from research.”

# Philosophical Approaches Contd.

- ◆ “Often, more than one principle will apply to a specific case. This is due in part to the diversity of research and in part to the range of fundamental values upon which the research ethics enterprise is founded. If the application of principles yields conflicts, then such conflicts properly demand probing ethical reflection and difficult value choices. Such choices and conflicts are inherent in the ethics review process. In their best uses, principles serve as short-hand reminders of more complex and context-specific moral reflection.”



# Moral Conscience/Consciousness



- ◆ In short there is no substitute for engaged moral reflection and a developed moral conscience!!!



# Acknowledgments



- ◆ Matt Hunt and Carolyn Ells

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