

The Impact of Abuse and Historical Perspective of Medical Ethics: A Moral Foundation for Human Research

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Background: Medical ethics play an increasingly important role in the practice of medicine and in medical research. Since the time of the Nuremberg trials, medical ethics has expanded and now it involves every aspect of medicine and research. There was no historical perspective of medical ethics in relation to medical and research abuse and to new development in the medical field.

Objective: A historical overview of the development of medical ethics, its response to recent medical advances and its relationship to the abuse of medical research.

Method: Electronic searches of the major databases and handsearching of relevant journals and publications to identify ethics guidelines appropriate for this study were conducted in March to May 2008. Guidelines were reviewed from Charles Babbage (1782-1871) till the advent of cloning. The dates of initiation of each guideline and the rationale for its development were recorded.

Result: Most of the medical ethic guidelines have evolved in response to the abuse of research, malpractice, and to discoveries or advances in medicine.

Overzealous physicians who were subservient to dictators or government of absolute power have contributed more than any other group to the abuse of research and consequently to the ethics. Next were those physicians who had little or no regard to patient or animal welfare.

Physicians and pharmaceutical companies who were driven by profit constitute the third group of abusers.

Scientific inaccuracy in publication, fraud, fabrication, falsification, plagiarism contributed to the abuse which sparked the development of ethical guidelines in research publication.

Conclusion: The majority of ethics guidelines have been developed in response to abuses in the practice of medicine, research, publication and recent advances in medicine.

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“Ethics is a system of morals, rules of behaviors, treatise on morals”. Rules and regulation of medical ethics were laid in the 20th century.

Medical ethics mainly have developed in response to inexcusable abuse of research by physicians and to scientific inaccuracy, fraud, fabrication, falsification, plagiarism and to recent advances in medicine.

Medical ethics are the moral values and rules applied to medical practice and medical research. Medical ethics has developed as an independent discipline taught in medical schools.

Medical ethics may be classified into three: 1) professional ethics, concerned with the conduct of the medical and nursing professionals. 2) bioethics is concerned with philosophy of science and the critique of biotechnology. 3) research ethics is group of guidelines concerned with research and the protection of the subjects or animals of research.

Medical ethics may be traced to Hippocratic Oath.. In the medieval and early modern period, medical ethics is indebted to Muslim physicians such as Ishaq bin Ali Rahawi (who wrote the *Conduct of a Physician*, the first book dedicated to medical ethics) and al-Razi (known as Rhazes in the West), Jewish thinkers such as Maimonides, Roman Catholic scholastic thinkers such as Thomas Aquinas, and the case-oriented analysis (casuistry) of Catholic moral theology. These intellectual traditions continue in Catholic, Islamic and Jewish medical ethics¹.

The aim of this review is to present a historical overview of the development of medical ethics, its response to recent medical advances and its relationship to the abuse of medical research.

METHOD

Electronic searches of the major databases and handsearching of relevant journals and publications to identify ethics guidelines appropriate for this study were conducted in March to May 2008. Guidelines were reviewed from Charles Babbage (1782-1871) till the advent of cloning. The dates of initiation of each guideline and the rationale for its development were recorded.

RESULT

Most of the medical ethic guidelines have evolved in response to the abuse of research, malpractice, and to discoveries or advances in medicine. It is impossible to mention all the abuses in research; therefore, I will mention only few, which had tremendous effect on development of medical ethics.

A. Ethical Guidelines in Response to Abuse of Research in Human and to Medical Advances

1. Nuremberg Doctors Trial of 1946

The trial was conducted for doctors who abused research. The reason for their studies: How would the German pilots survive adversities? For that purpose the victims were placed in vacuum chambers; the victims were immersed in ice water; the victims' wounds deliberately infected; the victims were exposed to chemical weapons and finally the victims were set on fire¹.

Fifteen of 23 doctors were found guilty; 7 were sentenced to death and the judgment included a set of standard known as the Nuremberg Code of 1947. The victims of the study mainly were Gypsies and Jews.

Following the trial, a set of research ethics principles for human experimentation was issued and coined as Nuremberg Code of 1947. Part of the code was informed consent. The code specify that human experimentation should be based on prior animal experimentation; anticipated scientific results should justify the experiment; only qualified scientists should conduct medical research; physical and mental suffering and injury should be avoided and there should be no expectation of death or disabling injury from the experiment².

2. Thalidomide Tragedy

This drug was introduced as a sedative in Europe and Middle East, it was given to pregnant women to alleviate the symptoms of hyperemesis gravidarum, and the outcome around the world was tragic resulting in limbless children. It was used in USA in "research" studies but no informed consent was taken, which led the FDA to require informed consent when studying experimental drugs³.

3. The Tuskegee Study

The study was designed to demonstrate the long-term effects of untreated syphilis – though it was known at that time. It was designed by an agency of the US Public Health Service (later was called centers for disease control and prevention "CDC").

Three hundred and ninety-nine syphilitic black males recruited for the study in 1932. The study was designed initially to last 6-8 months only, but the study continued for 40 years. No informed consent was taken, and instead, researchers told the men they were being treated for "bad blood".

In 1943, penicillin was accepted as treatment for syphilis, but the subjects were deferred from the draft to prevent treatment because treatment is a must before being drafted in the US army. The availability of penicillin was used to justify study as a "never-again" scientific opportunity.

The study was never hidden and papers were published in the medical journals. Only in 1972, newspaper stories (Associated Press) revealed the study, which led to compensation and apologies and it led to National Research Act of 1974, which required informed consent and the formation of Institutional Review Board (IRB). The study was described as "ethically unjustified"⁴.

4. Exposure to Radiation

In USA, 3000 military personnel were exposed to atomic radiation; 100 prisoners submitted to non-therapeutic testicular radiation and university subjects injected with plutonium. The previous studies led to the creation of the advisory Committee on Human Radiation. Experiments report in 1995 led to the creation of the National Bioethics Advisory Committee^{5,6}.

5. Mustard Gas and Lewisite [blister gas]

Approximately 60,000 military personnel were used as human subjects in the 1940s to test two chemical agents, mustard gas and lewisite [blister gas]. Most of these subjects were not informed of the nature of the experiments and never received medical follow-up after their participation in the research^{7,8}.

6. The Japanese “Unit 731”

The infamous Imperial Japanese army “Unit 731” conducted biological, chemical warfare research and frequently lethal pseudo-medical experiments – on thousands of prisoners and civilians,” including mass dissections of living humans during the Second Sino-Japanese War (1937–1945) and World War II.

In the autumn of 1945, MacArthur granted immunity to members of “Unit 731” in exchange for data of research on biological warfare^{9,10}.

7. Conducting Research in Developing Countries

Because of the abuse in conducting research in developing countries, the council for the international organization of medical sciences (1982) established the international ethics guidelines for biomedical research involving human subjects including a guide for researchers from more technologically advanced countries in conducting research in developing countries and it allows for cultural differences in ethical standards¹¹.

All the previous studies were performed by physicians.

In 1954, Dr. Joseph Fletcher wrote a book titled "Medicine and Morals", but the book fell on deaf ears. Joseph Fletcher was not alone in his trial, after 30 years (1981) I have written a booklet on proposed code of ethics of the Medical Profession and that one too, fell on deaf ears^{12,13}.

In 1960's Dr. Beecher of United States and Dr. Papworth of Great Britain exposed some of the bio-medical research abuses and because of that, the Medical Research Council drew up fundamental guidelines in research involving the human subjects¹⁴⁻¹⁸. 1960's were the birth of organ transplants and vast amount of abuses as well.

Declaration of Helsinki 1964

The most comprehensive rules of research were included in the “Declaration of Helsinki”, which was drafted by the World Medical Association and issued in 1964. It includes basic principles of research. Research was defined as “therapeutic” and “non-therapeutic”. In the declaration the consent issues was clarified¹⁹.

In the 70's patients were kept on life support systems for many years, and therefore the ethical question was raised: who is going to switch these machines off? Once they were put on. The definition of irreversible coma and death were debated²⁰⁻²².

In 1979, the Royal College of Physicians pioneered a research ethics committee, which was established in the hospitals, universities and all medical research centers in UK²³.

In 1979, the National commission for the protection of human subjects of biomedical and behavioral research wrote the Belmont report. The report is the cornerstone statement of ethical principles. The Belmont report specified the Institutional Review Board (IRB) composition of experts and community representatives.

The purpose of the IRB is to review research and determine if the rights and welfare of human subjects are adequately protected. The IRB can approve, require modification or disapprove all research activities. A researcher must report injuries to subjects, and the IRB must report to appropriate agencies. It is a continuing review process based upon progress reports²⁴.

The Belmont report defined the elements of informed consent:

Informed consent shall be documented by the use of a written consent form approved by the IRB and signed by the subject or the subject's legally authorized representative. A copy shall be given to the person signing the form.

Mrs. Margaret Wigley in United Kingdom, a lady, 83 years old, who had surgery for cancer of the bowel, was entered into randomized controlled trial. She was given fluorouracil without her knowledge or consent, after one month she died due to bone marrow depression caused by the fluorouracil²⁵.

The Belmont Report Contains the Ethical Principles of Research

1. Basic Principles
2. Respect for persons

Individuals should be treated as autonomous agents. Vulnerable groups are entitled to an increased protection. Vulnerable groups include: Children, pregnant women, mentally deranged, minority, patients with dementia and prisoners. Children cannot give consent. Parents or guardians provide permission.

Informed consent is an information exchange that takes place between the subject and the investigator, before, during and after the study. Information should include the research procedures, the purpose, risk and anticipated benefits, alternative procedures, the opportunity to ask questions and withdraw at any time should be granted. Comprehension means that the information cannot be presented too rapidly and allowing time for consideration and the subject to ask questions.

Participation in the study should be voluntary and free of coercion (a threat of harm to gain compliance) and free of undue influence (an offer of an excessive, unwarranted or improper award or other benefit to obtain agreement).

3. Beneficence or kindness that is to make effort to secure the well-being of the subject. First, do no harm and second maximize possible benefits and minimize risks. The researcher must consider not only psychological or physical injury, but social, legal and financial disadvantages. Issues of non-paternity and genetics should be considered.

4. Justice requires inclusion of diverse groups (women, minorities, and children).

In 1980's, prenatal diagnoses and genetic screening were developed with it few ethical dilemmas surfaced, such as genetic mismatch marriage and termination of pregnancy based on prenatal diagnosis²⁶. Genetic mapping was fraught with scare of unwanted knowledge and discoveries²⁷⁻²⁹.

In the 1980's, Several Important Development Affected the Advance of Medical Ethics

1. The patient's charter was established by the UK Association of Community Health Councils. In 1982, Infant Bio-ethics Committee was established in United States as a result of the baby Doe controversy and the Down's syndrome Murder in UK; the committee is responsible for any research on severely deformed children and when to withhold treatment to these infants. The guidelines are controversial in that it dictates what must be done for a child, regardless of the wishes of the guardians³⁰⁻³³.

2. Test-Tube Babies, or better termed Assisted Human Reproduction was developed. In United Kingdom, they had to rush Surrogacy Arrangement Act in 1985 and because of these developments the World Medical Association and WHO have advised every country to have a National Ethical Committee^{34,35}.

3. AIDS was discovered in 1983, accompanied with a scare, which became global; therefore, the question was raised: should we screen the population which might violate the civil liberties? More over, if we do not violate civil liberties, how much public health problem we are creating as doctors? Are we giving enough information to the public about the incidence and spread of AIDS in the community and, if not, is it ethical?³⁶

B. Ethical Guidelines in Response to the Abuse of Animals in Research

“Moral issues are the privilege of an existence above mere survival. Remember not only you have rights animals do also have rights”.

The researcher must obtain the approval of the Institution Animal Care and Use Committee (IACUC). The researcher should use appropriate species lawfully acquired. Avoid or minimize discomfort, distress and pain to the animal during surgical procedures, use of behavioral techniques, use of neuromuscular blocking agents and physical restraints.

Appropriate sedation, analgesia or anesthesia should be used and end-point of the experiment should be established. Qualified and experienced scientist should conduct the experiments on animals; under graduate student are not allowed. Non-animal method like

audiovisual, tissue culture sometimes could replace the use of animals. Replication and duplication of experiment should be kept to minimum.

Food, water and sleep deprivation should be kept to minimum. Avoid significant environmental alteration. The Animal should be returned to his normal habitat after completing the experiment. If euthanasia is necessary, it should be painless³⁷.

C. Ethical Guidelines in Response to Authors Abuse of Medical Ethics in Research

The ethical aspect of research publication has been highlighted especially in the New England Journal of Medicine and in the British Medical Journal because of several fraudulent papers and fake statistics. Therefore, the ethical aspect of research publication has been discussed extensively in the European Association of Science Editors, Council of Biology in USA, IFSEA (International Federation of Scientific Editors' Associations) and WAME (World Association of Medical Editors). It was agreed that the editors should make sure that a research to be published complies with acceptable ethical standard in its method of collection and analysis of data³⁸.

Fraud and Scientific Inaccuracy

Many papers have been retracted for reason either fraud or scientific inaccuracy. The institutes involved were Harvard, Yale and Emroy Universities³⁹⁻⁴³.

Properly conducted research should have approval of the institution, informed consent, proper treatment of laboratory animals and protection of confidentiality.

Should an unethical research be given a chance to be published? Most of the editors in reputable journals agree that it should not be, yet some get published. A research paper, on *Pseudomonas* Vaccine which was used in the prevention of infection in a severely burned patient, published in the Lancet, the trial was performed in New Delhi with the involvement of British Doctors and no proper consent was taken. The other study is the folic acid trial in the prevention of neural tube defects in a new born performed in United Kingdom; it was published in the British Medical Journal without proper informed-consent being obtained^{44,45}.

Ethical responsibility of author is honest behavior in designing, conducting and writing the research. This involves all the names on the paper.

Ethical Responsibility of Co-authors

They must be involved in literature search, study design, data gathering, data analysis, the writing of the study and final approval of the version to be published.

Who is an author? According to Vancouver Group Positive Author, authorship credit should be based only on substantial contributions to: conception and design or analysis and interpretation of data, drafting the article or revising it critically for important intellectual content and final approval of the version to be published. Conditions 1, 2 and 3 must all be met.

Scientific dishonesty was not something new; Charles Babbage (1782-1871) defined it as:

- A. Trimming: Smoothing of irregularities to make the data look extremely accurate and precise.
- B. Cooking: Retaining only those results that fit the theory and discarding others.
- C. Forging: Inventing some or all of the research data that are reported, and even reporting experiments that were never performed⁴⁶.

Because of the pressure of publication for promotion, gift authorship has become common practice. In study by Pignatelli et al, he found that 59% of the respondents had been a recipient of gift authorship⁴⁷.

A consultant who forged the signatures of two colleagues and falsely claimed authorship of research in which he had played no part was suspended for three months by the General Medical Council⁴⁸.

A consultant surgeon in England was found guilty of serious professional misconduct. He was suspended by the General Medical Council for publishing an article in *Gut in December 1990 that contained information which "was deliberately falsified"*⁴⁹.

A consultant obstetrician has been suspended from duty at St George's Hospital in south London after an inquiry into the scientific validity of two research papers⁵⁰.

In the 70's, most of the Western and American Medical Schools started to teach ethics. Unfortunately, no information is available about teaching Medical Ethics in the Middle East Medical Colleges.

In the 70's more than 20 centers of bio-medical ethics have been established in Western Europe and the same number in Unites States. Unfortunately, there is no information about the availability of any centre in the Middle East which deals with Medical or Bio-medical Ethics¹⁷.

The birth of the lamb Dolly at Roslin institute in Scotland in 1996 was a major development in biological science and was a major development in biomedical ethics. Some scientists and some laboratories announced their intentions to clone human being. Many governments have to rush laws prohibiting human cloning. Medical societies and religious groups around the World issued their ethical guidelines. Many have reaffirmed that cloning of human individuals is ethically unacceptable and contrary .to human dignity and integrity^{51,52,53}.

“When a doctor does go wrong he is the first of the criminals. He has the nerve and he has the knowledge. Palmer and Pritchard were among the heads of their profession”.
Sir Arthur Conan Doyle known as “Sherlock Holmes”

Finally, it is extremely beneficial to read the World Medical Association (WMA) declarations in the practice of medicine and ethical Standard.

1. Declaration of Geneva deals with the duties of physician in general (1948, 1968, 1983, 1994)

2. International Code of Medical Ethics (1949, 1968, 1983)
3. Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects 1964 to 2002
4. Declaration of Oslo on Therapeutic Abortion (1970, 1983)
5. Declaration of Tokyo: Guidelines for Medical Doctors Concerning Torture 1975
6. Declaration of Lisbon on the Rights of the Patient (1981, 1995)
7. Declaration of Venice on Terminal Illness (1983)
8. Declaration of Madrid on Professional Autonomy and Self-Regulation (1987)
9. Declaration of Hong Kong on the Abuse of the Elderly (1989, 1990)
10. Declaration of Hamburg Concerning Support for Medical Doctors Refusing to Participate in, or to Condone, the Use of Torture or Other Forms of Cruel, Inhuman or Degrading Treatment (1997)
11. Declaration of Ottawa on the Right of the Child to Health Care (1998)
12. Declaration on Ethical Considerations Regarding Health Databases (2000)
13. Declaration of Washington on Biological Weapons (2002)

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