

18.1. BIOETHICS

18.1.1. Basic Concepts

The discipline dealing with the ethical implications of biological research and applications especially in medicine. Bioethics includes the study of what is right and wrong in new discoveries and techniques in biology, such as genetic engineering and the transplantation of organs."

The term Bioethics (*Greek bios, life; ethos, behavior*) was coined in 1926 by Fritz Jahr, who anticipated many of the arguments and discussions now current in biological research involving animals. Many religious communities have their own histories of inquiry into bio-ethical issues and have developed rules and guidelines on how to deal with these issues from within the viewpoint of their respective faiths.

Bioethics is the study of ethical, social, and legal issues that arise in biomedicine and biomedical research. Bioethics includes **medical ethics**, which focuses on issues in health care; **research ethics**, which focuses issues in the conduct of research; **environmental ethics**, which focuses on issues pertaining to the relationship between human activities and the environment; and **public health ethics**, which addresses ethical issues in public health.

18.1.2. History

Bioethics as a distinct field of academic study has existed only since the early 1960s, and its history can be traced back to a cluster of scientific and cultural developments in the United States during that decade. The catalysts for the creation of this interdisciplinary field were the extraordinary advances in American medicine during this period coupled simultaneously with radical cultural changes. Organ transplantation, kidney dialysis, respirators, and intensive care units (ICUs) made possible a level of medical care never before attainable, but these breakthroughs also raised daunting ethical dilemmas the public had never previously been forced to face, such as when to initiate admission to an ICU or when treatments such as dialysis could be withdrawn.

Outline of Major Events

1947: Nuremberg Doctors' Trial and the Nuremberg Code

1948: Universal Declaration of Human Rights adopted by the UN.

1951: Clinical trial of oral contraceptives begun

1953: Elucidation of the double helical structure of DNA

- 1954: Salk Polio Vaccine trials
- 1960: Contraceptive Pill approved by FDA
- 1960: Invention of the Scribner shunt
- 1961: Convening of the Seattle Admission's and Policy Committee
- 1961: Publication of Rachel Carson's Silent Spring
- 1961: Revelation of the side effects of Thalidomide
- 1962: Kefauver-Harris amendments to the Food, Drugs and Cosmetics Act of 1938
- 1964: Declaration of Helsinki published by the World Health Organisation
- 1965: Medicare Act
- 1965: Griswold *versus* Connecticut legalizes access to contraception by married couples
- 1966: Publication of Henry K. Beecher's 'Ethics and Clinical Research' in the NEJM
- 1967: First heart transplant
- 1968: Harvard Committee's report 'Definition of Irreversible Coma'
- 1972: Revelation of the Tuskegee Syphilis Experiment
- 1973: American Hospital Association adopts a Patients' Bill of Rights
- 1973: Roe *versus* Wade decision
- 1975: Asilomar meeting on recombinant DNA technology
- 1976: Karen Quinlan decision
- 1976: Founding of Genentech
- 1978: Publication of the Belmont Report
- 1978: Declaration of Alma Ata
- 1980: Diamond vs. Chakravarty case
- 1981: First reported cases of G.R.I.D., later named AIDS
- 1984: John Moore case
- 1987: Founding of ACTUP
- 1988: Eli Lilly release Prozac
- 1994: Oregon Death with Dignity Act
- 1997: Birth of 'Dolly', the cloned sheep
- 2000: Publication of the rough draft of the Human Genome
- 2001: Terri Schiavo case
- 2001: George W. Bush announces stem cell policy
- 2006: Launching of No Lie MRI
- 2007: Sperm sorting offered by clinic in Virginia
- 2008: Health care access on the agenda for the election

18.1.3. Principles

The Four-Principle Approach: One of the most important approaches in bioethics or medical ethics is the four-principle approach developed by Tom Beauchamp and James Childress (1978, latest edition 2009). Since then they have continually refined their approach and integrated the points of criticism raised by their opponents, most notably Gert et al. (1990).

Four commonly accepted principles of health care ethics, excerpted from Beauchamp and Childress (2008), include the:

- 1) Principle of respect for autonomy,
- 2) Principle of nonmaleficence,
- 3) Principle of beneficence, and
- 4) Principle of justice.

18.1.3.1. Principle of Respect for Autonomy

Any notion of moral decision-making assumes that rational agents are involved in making informed and voluntary decisions. In health care decisions, our respect for the autonomy of the patient would, in common parlance, imply that the patient has the capacity to act intentionally, with understanding, and without controlling influences that would mitigate against a free and voluntary act. This principle is the basis for the practice of "informed consent" in the physician/patient transaction regarding health care. (See also Informed Consent.)

18.1.3.2. Principle of Non-maleficence

The principle of non-maleficence requires of us that we not intentionally create a harm or injury to the patient, either through acts of commission or omission. In common language, we consider it negligent if one imposes a careless or unreasonable risk of harm upon another. Providing a proper standard of care that avoids or minimizes the risk of harm is supported not only by our commonly held moral convictions, but by the laws of society as well (see Law and Medical Ethics). This principle affirms the need for medical competence. It is clear that medical mistakes may occur; however, this principle articulates a fundamental commitment on the part of health care professionals to protect their patients from harm.

18.1.3.3. Principle of Beneficence

The ordinary meaning of this principle is that health care providers have a duty to be of a benefit to the patient, as well as to take positive steps to prevent and to remove harm from the patient. These duties are viewed as rational and self-evident and are widely accepted as the proper goals of medicine. This principle is at the very heart of health care implying that a suffering supplicant (the patient) can enter into a relationship with one whom society has licensed as competent to provide medical care, trusting that the physician's chief objective is to help. The goal of providing benefit can be applied both to individual patients, and to the good of society as a whole. For example, the good health of a particular patient is an appropriate goal of medicine, and the prevention of disease through research and the employment of vaccines is the same goal expanded to the population at large.

It is sometimes held that non-maleficence is a constant duty, that is, one ought never to harm another individual, whereas beneficence is a limited duty. A physician has a duty to seek the benefit of any or all of her patients, however, a physician may also choose whom to admit into his or her practice, and does not have a strict duty to benefit patients not acknowledged in the panel. This duty becomes complex if two patients appeal for treatment at the same moment. Some criteria of urgency of need might be used, or some principle of first come first served, to decide who should be helped at the moment.

18.1.3.4. Principle of Justice

Justice in health care is usually defined as a form of fairness, or as Aristotle once said, "giving to each that which is his due." This implies the fair distribution of goods in society and requires that we look at the role of entitlement. The question of distributive justice also seems to hinge on the fact that some goods and services are in short supply, there is not enough to go around, thus some fair means of allocating scarce resources must be determined.

It is generally held that persons who are equals should qualify for equal treatment. This is borne out in the application of Medicare, which is available to all persons over the age of 65 years. This category of persons is equal with respect to this one factor, their age, but the criteria chosen says nothing about need or other noteworthy factors about the persons in this category. In fact, our society uses a variety of factors as criteria for distributive justice, including the following:

- 1) To each person an equal share
- 2) To each person according to need
- 3) To each person according to effort
- 4) To each person according to contribution
- 5) To each person according to merit
- 6) To each person according to free-market exchanges

18.2. ICMR'S NATIONAL ETHICAL GUIDELINES FOR BIOMEDICAL AND HEALTH RESEARCH INVOLVING HUMAN PARTICIPANTS

18.2.1. Introduction

The Indian Council of Medical Research (ICMR), New Delhi, the apex body in India for the formulation, coordination and promotion of biomedical research, is one of the oldest medical research bodies in the world.

The Indian Council of Medical Research (ICMR) issued the Policy Statement on Ethical Considerations Involved in Research on Human Subjects in 1980. Due to rapid advances in biomedical science and technology, new ethical dimensions emerged which necessitated further updation of these guidelines. Subsequently the Ethical Guidelines for Biomedical Research on Human Subjects was released in 2000, followed by the revised Ethical Guidelines for Biomedical Research on Human Participants in 2006.

18.2.2. Salient Features

- 1) To guide biomedical and health research and ensure protection of the general public in the conduct of biomedical and health research, ICMR has developed two national guidelines, **National Ethical Guidelines for Biomedical and Health Research involving Human Participants, 2017** and **National Ethical Guidelines for Biomedical Research Involving Children.**

- 2) A number of dissemination activities are being developed in order to raise awareness among all the stakeholders, including physicians, researchers, ethics committee members, students, nurses, and biomedical research academics.
- 3) The ICMR, which is the leading organisation for biomedical and health research, not only encourages and funds research but also ensure safety of participants to prevent exploitation and to protect their rights, welfare, and safety.
- 4) Most of the medical colleges and universities do not include ethics in their regular curricula, thus neither medical students nor non-medical students or researchers are aware of the standards. Since 1980, ICMR is leading in this area by developing and periodically revising guidelines for the country. National Ethical Guidelines for Biomedical and Health Research to be undertaken both on general populations and on guidelines specifically for children were created in response to the evolving ethical issues.
- 5) All biomedical and health research across the country, including clinical, research, basic sciences, epidemiological, socio-behavioural, and public health research, as well as studies involving data or samples, is covered by the guidelines. The guidelines would be extremely beneficial in sustaining principles of bioethics and providing protection to patients and research volunteers.
- 6) The guidelines are a landmark document for being thorough and user-friendly while addressing a variety of topics. They have been revised and harmonised with national and international requirements.

18.2.3. Guidelines of ICMR

There are 12 sections of the guidelines aiming on various research fields and the accompanying ethical requirements.

18.2.3.1. Statement of General Principles [Section 1]

General Principles

Any research involving human subjects must adhere to the following principles:

- 1) **Principles of Essentiality:** All biomedical research involving human subjects should be absolutely necessary after carefully considering all available options in the interests of knowledge advancement and human welfare.
- 2) **Principles of Voluntariness, Informed Consent and Community Agreement:** The concept of voluntariness and informed consent shall apply to the community as a whole and to each individual member who is subject of research.
- 3) **Principles of Non-exploitation:** Research subjects should be properly informed of any hazards associated with the research, regardless of their socio-economic status or level of education.
- 4) **Principle of Social Responsibility:** The research should be designed and carried out in a way that avoids creating or expanding social and historical divisions and interrupting societal harmony in community relationships.

- 5) **Principles of Ensuring Privacy and Confidentiality:** Records identifying human research subjects should be kept confidential and should not be shared unless there are valid scientific and legal reasons to do so.
- 6) **Principles of Risk Minimisation:** Care and caution should be taken to ensure that research subjects are exposed to a minimum amount of risk or are not exposed to any irreversible consequences.
- 7) **Principles of Professional Competence:** Only qualified and competent individuals should be allowed to conduct the research.
- 8) **Principles of the Maximisation of Benefit:** The research should be carried out for the benefit of all human being and for the improvement of society.
- 9) **Principles of Institutional Arrangements:** All institutional arrangements related to research that are necessary to be made should be conducted in a standard and transparent manner and records should be properly maintained and conserved.
- 10) **Principles of Transparency and Accountability:** The research should be conducted in a fair, honest, impartial, and transparent manner and the records and data are maintained for a reasonable amount of time.
- 11) **Principles of Totality of Responsibility:** Monitoring, continuous reviewing, and corrective action should be taken at all stages of research by all research volunteers who are involved directly and indirectly.
- 12) **Principles of Compliance:** All research volunteers who are involved directly and indirectly should adhere strictly to the established rules, guidelines, norms and directions.

18.2.3.2. General Ethical Issues [Section 2]

- 1) **Compensation for Participation:** Participants may be paid for the inconvenience and time spent, and should be reimbursed for expenses incurred, in connection with their participation in research. They may also receive free medical services.
- 2) **Conflict of Interest:** It is a set of conditions in which professional judgment concerning a primary interest like patient's welfare or the validity of research tends to be or appears to be unduly influenced by a secondary interest like non-financial (personal, academic or political) or financial gain.
- 3) **Selection of Special Groups as Research Participants:** Pregnant or nursing women should in no circumstances be the participant of any research unless the research carries no more than minimal risk to the foetus or nursing infant and the object of the research is to obtain new knowledge about the foetus, pregnancy and lactation.

Children will not be involved in research that could be carried out equally well with adults. A parent or legal guardian of each child has given proxy consent. Effort may be made to ensure that individuals or communities invited for research be selected in such a way that the burdens and benefits of the research are equally distributed.

- 4) **Essential Information on Confidentiality for Prospective Research Participants:** The investigator must safeguard the confidentiality of research data, which might lead to the identification of the individual participants.
- 5) **Compensation for Accidental Injury:** Research participants who suffer physical injury as a result of their participation are entitled to financial or other assistance to compensate them equitably for any temporary or permanent impairment or disability. In case of death, their dependents are entitled to material compensation.
- 6) **Post-trial Access:** The Declaration of the WMA in 2004 reaffirmed "its position that it is necessary during the study planning process to identify post-trial access by study participants to prophylactic, diagnostic and therapeutic procedures identified as beneficial in the study or access to other appropriate care. Post-trial access arrangements or other care must be described in the study protocol so the ethical review committee may consider such arrangements during its review."
- 7) **International Collaboration/Assistance in Bio-medical/Health Research:** Especially since the 1960s, the scope of international co-operation and collaboration assumed such proportions as to have exploitative connotations with commercial and human dimensions. Different levels of development in terms of infrastructure, expertise, social and cultural perceptions, laws relating to intellectual property rights etc., necessitate an ethical framework to guide such collaboration.
- 8) **Researcher's Relations with the Media and Publication Practices:** Researchers have a responsibility to make sure that the public is accurately informed about results without raising false hopes or expectations. Researchers should take care to avoid talking with journalists or reporters about preliminary findings as seemingly promising research that subsequently cannot be validated or could lead to misconcepts if reported prematurely. Investigator's publication plans should not threaten the privacy or confidentiality of participants.

18.2.3.3. Responsible Conduct of Research [Section 3]

The guidelines for the first time addressed issues in subject fields where little guidance is available, such as ethical research practises, public health research, socio-behavioural research, conducting research during humanitarian emergencies or natural disasters, dealing with vulnerable populations, conducting collaborative research, stored samples, biological materials, biobanking, and datasets.

18.2.3.4. Ethical Review Procedures [Section 4]

To protect the welfare and rights of the participants, it is mandatory that all proposals on biomedical research involving human subjects be approved by a properly constituted Institutional Ethics Committee (IEC), also known as an Institutional Review Board (IRB), Ethics Review Board (ERB), or Research Ethics Board (REB) in other countries. These committees are commended with not only the first examination of the planned research protocols prior to the start of the projects but also the continuing responsibility of regular monitoring of the approved programmes to ensure that the ethics are followed throughout the project's duration.

18.2.3.5. **Informed Consent Process [Section 5]**

For all biomedical research involving human participants, the investigator must obtain the informed consent of the prospective participant or in the case of an individual who is not capable of giving informed consent, the consent of a legal guardian. Informed consent protects the individual's freedom of choice and respect for individual's autonomy and is given voluntarily to participate in research or not.

The informed consent should be brief in content highlighting that it is given of free will or voluntarily after understanding the implications of risks and benefits. Assurance is given that confidentiality would be maintained and all the investigations/ interventions would be carried out only after consent is obtained. When the written consent as signature or thumb impression is not possible due to sensitive nature of the project or the participant is unable to write, then verbal consent can be taken after ensuring its documentation by an unrelated witness.

18.2.3.6. **Vulnerability [Section 6]**

Vulnerability has been precisely described since there was a lack of clarity regarding the topic. The additional protections needed as well as the duties of the sponsors, ethical committee members, and researchers have been described.

The rights and interests of vulnerable populations, such as those who are socially and economically disadvantaged, orphans, abandoned people, children, women in special circumstances, people with neurological or mental disabilities, LGBT people, people affected by humanitarian emergencies and disasters, etc., cannot be protected by them. The revised guidelines provide precise directions and guidance to the researchers during planning and carrying out a research on such particular populations with the highest ethical standards.

18.2.3.7. **Clinical Trials of Drugs and Other Interventions [Section 7]**

A clinical trial is a research or investigation in which individuals or groups of individuals are prospectively assigned to one or more health-related interventions to assess the impact on health outcomes.

The intervention could involve the use of drugs, vaccines, biosimilars, biologics, phytopharmaceuticals, radiopharmaceuticals, diagnostic agents, socio-behavioural interventions, technologies, devices, surgical procedures, or traditional medical systems, etc.

Clinical trials that seek regulatory approval for marketing should be carried out as per the Drugs and Cosmetics Act and Rules, and any relevant recent amendments. If a clinical trial needs regulatory approval, the investigator should ensure that the trial adhere to all the guidelines of the Central Drug Standards and Control Organization (CDSCO) notification and to any relevant recent amendments.

After carefully evaluating the advantages, disadvantages, and other ethical considerations, an EC must approve such investigations. The licencing authority should then be notified as per the established protocols.

18.2.3.8. Public Health Research [Section 8]

This section contains the ethical issues associated with the research carried out in public health setting, like implementation research, disease registries, data analysis, epidemiological surveys, surveillance programmes, data and programme evaluations, demonstration projects, community trials, etc. An EC will decide whether a given protocol relates to public health practice or research while examining a public health research, due to the challenges in clear description of limitations between practice and research requiring ethical oversight and governance of public health information.

18.2.3.9. Social and Behavioural Sciences Research for Health [Section 9]

This section comprises of the new technology-based research ethics, such as those involving genetic studies, CRISPR technology, etc. There is insufficient knowledge regarding the requirements of research related to public health, so particular guidance has been provided to meet the many ethical issues related to social and behavioural sciences research as well as public health research. It also includes research using traditional medicine.

18.2.3.10. Human Genetics Testing and Research [Section 10]

This section defines the Ethical, Legal, and Social Issues (ELSI) that ensures constant, timely monitoring and thoughtful responses to the newly developing ethical issues relating to human genetic testing and research.

18.2.3.11. Biological Materials, Biobanking and Datasets [Section 11]

This section assist most of the researchers involved in collecting, analysing, or storing biological materials, biospecimens, or samples, including biological fluids like blood, dried blood spots, body fluids, urine, tissues, organs, cord blood, oocytes, sperm, or embryos.

A repository or biobank refers to an organised collection of resources which can be used to recover human biological material and data for research purposes. Bio resources are a protocol-based prospective collection of biospecimens, left-over samples from clinical investigations or research proposals, biopsy materials, surgical or autopsy specimens or tissues, embryos or foetuses, cell lines, or waste materials, like abandoned organs or tissues. There are three parts to repository activities, i.e., collection of biospecimens and/or data; storing biospecimens and data along with its management; and retrieving and disbursement to researchers. The biological materials could be preserved for forensic, research, or for Assisted Reproductive Technology (ART) purposes.

Dataset is referred to an organised collection of data and information maintained in physical, electronic, or digital form and suitable for use in biomedical and health research. In addition to biospecimen data found in biobanks, there are additional repositories including illness registries, health surveys, disease monitoring, census data, and even individual health records kept in healthcare settings that contain huge information for future research.

18.2.3.12. Research during Humanitarian Emergencies and Disasters [Section 12]

This is a new section containing revised guidelines and certain recommendations for how to conduct research in times of disaster and humanitarian emergencies. A humanitarian emergency or disaster is an event, or set of event, that poses a serious risk to the health, safety, security, or general well-being of a community or a great population, typically over a vast geographic area. Humanitarian emergencies and disasters are defined in these standards to include both man-made and natural events, some of which happen frequently.

The effect of the emergency on perceptions of ethical questions, changed or increased vulnerabilities, provider-patient and researcher-participant interactions, issues related to the integrity of studies, and ethical review procedures should all be carefully considered.

Another key challenge is creating or adopting creative relevant research that is based on quickly changing scientific and ethical uncertainty and is expected to produce results that are scientifically valid. Other difficulties include insufficient of time to plan a study and absence of infrastructure facilities and resources to carry it out in a disrupted physical-socio-cultural environment.

The involvement of ECs in these situations is crucial for examining the emergency situation protocols (s). Other aspects that should be considered about and planned for include responsiveness to the situation, monitoring, training, and preventing increased risk of violence.

18.3. EXERCISE

18.3.1. Multiple Choice Questions

- 1) The term bioethics was coined by _____
 - a) Dr. Van Renssler Potter II
 - b) Fritz Jahr
 - c) Enrico Fermi
 - d) Wilhelm Conrad Röntgen
- 2) In which year was the first reported cases of G.R.I.D.?
 - a) 1881
 - b) 1971
 - c) 1989
 - d) 1981
- 3) Which of the following section ensures constant, timely monitoring and thoughtful responses to the newly developing ethical issues relating to human genetic testing and research?
 - a) Biological materials, biobanking and datasets [Section 11]
 - b) Human genetics testing and research [Section 10]
 - c) Social and behavioural sciences research for health [Section 9]
 - d) Research during humanitarian emergencies and disasters [Section 12]
- 4) First heart was transplanted in the year _____
 - a) 1977
 - b) 1957
 - d) 1967