

# Informed consent

In the last half century, informed consent has become a central tenet of all research involving human subjects. However, even after the worldwide adoption of regulations aimed at ensuring the protection of subjects, some abuses continue. The installation of oversight bodies, such as institutional review boards, has prevented the bulk of deliberate mistreatment; however, unintentional coercion is still a problem. Informed consent is not limited to obtaining a signature on a consent form, but a process of decision making designed to protect the rights of patients and subjects. It is a constant, ongoing exchange of information between researcher and subject. Although research is invaluable to the advancement of medicine and transplantation, researchers have the responsibility to protect their subjects' rights and autonomy. This paper provides an overview of informed consent, principles behind the process, and implications of current regulations to assist readers in their endeavor for sound and ethical research. (*Progress in Transplantation*. 2005;15:371-378)

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## Notice to CE enrollees:

A closed-book, multiple-choice examination following this article tests your ability to accomplish the following objectives:

1. Discuss the informed consent process
2. Identify key principles of informed consent
3. Describe strategies to promote informed consent

**I**nformed consent is a fundamental aspect of the principles that govern the practice of both clinical medicine and healthcare research in the United States. A patient should give consent for participation in a clinical study only after he or she achieves an understanding of the relevant medical facts and the risks involved. Requiring informed consent enables the medical community to achieve a balance between allowing patients to exercise their autonomy and protecting them from undue harm. However, only recently has the assurance of proper information and consent been regarded as an essential aspect of our culture. In the early part of the 20th century, informed consent was virtually nonexistent. This is not surprising; human subject research was not a common practice in this country until the mid 20th century and the little clinical research that was performed was completely unregulated. In addition, the ethics pertaining to the general practice of medicine were only loosely defined until recently. Two different events were largely responsible for the development of informed consent in the last half century. The first was

a conscious redefinition of the ethical code governing clinical medical practice and the second was the discovery of the appalling injustices inflicted on human subjects and the candid disclosure of these events by the news media. In this paper, we aim to convey the importance of informed consent through an explanation of the development and principles of informed consent, as well as highlight aspects of the informed consent process pertinent to the conduct of research and the field of transplantation.

## Background

The Nuremberg Code,<sup>1</sup> written in 1949, was among the earliest doctrines of research ethics and the first to achieve widespread acceptance. The code was written by the judges who tried and condemned Nazi physicians for the murder and torture of individuals in concentration camps under the guise of science. The experiments involved torture, barbarity, and sadism unparalleled in the history of medical research, except for Japanese World War II experiments, with no intention of benefit to the subjects.<sup>2</sup> Much of the focus of the trial was on ethical conduct for human research. The judges not only found the defendants guilty, but also established a brief code composed of 10 principles intended to guide the practice of ethical human subject research.<sup>2</sup> The first of these principles mandated obtaining voluntary and informed consent from legally competent individuals prior to research. The principles addressed the responsibilities of the researcher to conduct responsible research and protect his or her subjects; there must

be evidence of reasonable potential benefit to society from the proposed research as well as an attempt to protect subjects from unnecessary and extreme harm.<sup>1</sup>

The Nuremberg Code was revolutionary; however, it was brief and did not sufficiently address all major concerns. Shortly after this code was established, the World Medical Association (WMA) also attempted to regulate research activities and define ethical research practice. In 1964, the WMA adopted the Declaration of Helsinki.<sup>3</sup> This declaration is similar to The Nuremberg Code, with 2 significant areas of expansion. First, the Declaration of Helsinki draws the distinction between therapeutic and nontherapeutic research. Therapeutic research includes a patient care component whereas nontherapeutic research is done with the expectation that there will be no direct benefit to the subjects. The Nuremberg Code mandates obtaining consent from competent individuals, whereas the Declaration of Helsinki recognizes that vulnerable populations need special attention.<sup>3</sup> The populations fall into 2 categories, vulnerable populations and those who cannot give consent for themselves. For individuals considered legally incompetent, such as a minor or a mentally disabled individual, research is prohibited unless the guardian grants consent; no research should be conducted on such individuals unless it cannot be conducted through other means. Whenever possible, the researcher must obtain assent from the incompetent individual as well as consent from his or her guardian.

Despite the advances made in response to the Nuremberg Code and the Declaration of Helsinki, some research involving human subjects continued to show little or no regard for the recently established principles. Perhaps influenced by the creation of these codes, individuals like Henry Beecher began to expose scientists conducting unethical research. In a series of publications in the second half the century, Beecher brought to light the injustices being committed against research subjects across the United States. One of the earliest of these controversial cases was a study conducted by Dr Southam in the Jewish Chronic Disease Hospital.<sup>4</sup> In an attempt to study the reasons cancer patients reject cancer transplants, Dr Southam injected 22 unknowing patients with live cancer cells. The subjects were not asked for their consent to participate in a research study, nor were they aware they had been injected with cancer cells. Another infamous experiment was conducted on children at the Willowbrook State School for mentally disabled children. Saul Krugman led an experiment on hepatitis by admitting children into a special ward of the crowded facility if their parents consented and allowed them to be used as research subjects. The investigators not only coerced the parents into signing consent, but also gave them the misimpression that the study involved giving their

children a hepatitis vaccine while the children were, in fact, injected with the virus.

Arguably, the most notorious experiment in American history is the Tuskegee Syphilis Experiment, which began in 1932 and continued for the next 40 years. Researchers sponsored by the Public Health Service attempted to study the course of syphilis in the human body by observing 400 African American men who were recruited under the pretense of receiving special treatment for no charge. In fact, patients were subjected to painful procedures but never provided with appropriate medication. The men were prevented from participating in campaigns to eradicate venereal disease that came to their home county. When penicillin, the first real cure for syphilis, was discovered in the 1940s, the Tuskegee men were denied the medication. Investigators contacted local physicians requesting that they not provide subjects with lifesaving treatments should they request it. The experiment exploited African Americans of low socioeconomic status by enrolling them in an experiment without obtaining proper consent and putting the subjects at high risk with no potential for individual benefit.

The horrors of the Tuskegee affair astonished the public when a public health official, Peter Buxtun, expressed his concerns to the media and the experiment made the front page of major newspapers across the country in July 1972.<sup>5</sup> Two years later, Congress passed the National Research Act, which established the National Committee for the Protection of Human Subjects of Biomedical and Behavioral Research. The committee was responsible for establishing guidelines for the ethical conduct of research. On April 18, 1979, the committee released the Belmont Report detailing "ethical principles and guidelines for the protection of human subjects of research."<sup>6</sup> This report was not proposed as law, but it was used as a recommendation to the Department of Health, Education, and Welfare to be adopted and legislated after review.

The Belmont Report consists of 3 sections. The first provides a clear distinction between research and practice. According to the committee, research is designed to test a hypothesis, permit conclusions to be drawn, and consequently to develop or contribute to generalizable knowledge.<sup>6</sup> The second section of the report describes the basic ethical principles that ought to guide human subject research: autonomy (respect for persons), beneficence (an obligation to maximize possible benefits and minimize possible harm), and justice (providing equitable care). The third section of the report details 3 primary ways in which these ethical principles ought to be implemented in practice: the first of these is through informed consent. The report also outlines the essential components of informed consent as information, comprehension, and volition.<sup>6</sup> According to this report, any research protocol in which

subjects are not fully informed about the experiment or are not given the opportunity to participate voluntarily and free from coercion, as occurred in the cases mentioned above, is considered unethical research.

The Belmont Report was created as a recommendation; therefore, the proposed principles were not mandatory or enforceable by a governing body. In 1974, the Department of Health and Human Services codified the principles into Federal Regulations in what is commonly referred to as the Common Rule, The Code of Federal Regulations (CFR), Title 45 Part 46.<sup>7</sup> This document is the federal policy that governs research activity and ensures that human subjects participating in research are afforded certain rights protected by the development of institutional review boards (IRBs), informed consent protocols, and regulations for research involving vulnerable populations.

The Health Insurance Portability and Accountability Act (HIPAA), enacted by Congress in 1996, was designed to save money for healthcare businesses by encouraging electronic transactions, but also mandated increased protection for the security of the information. In November 1999, the Department of Health and Human Services fully enacted the nation's most recent patient protection legislation, the HIPAA Privacy Rule.<sup>8</sup> The Privacy Rule was designed to safeguard the confidentiality of identifiable health information, known as protected health information (PHI). Measures were put in place to regulate the way PHI can be used or disclosed by any organization covered by HIPAA. The Privacy Rule grants individual patients and research subjects rights to their own medical information and prevents such information from being disclosed without the permission of the individual.<sup>9</sup> For research requiring withholding information from a subject or requiring disclosure of PHI, a statement explaining the breach of HIPAA should be included in the informed consent.

## Ethics

Informed consent is a major component of clinical and research ethics. Four of the major principles guiding contemporary medical ethics are autonomy, nonmaleficence, beneficence, and justice.<sup>10</sup> These principles, as outlined below, guide the need for informed consent in both scenarios; however, there is a fundamental difference in the informed consent for clinical care and participation in research. The intent of a clinical treatment is to provide the patient with an intervention having direct benefit for the patient. Although there is a need to understand the risk/benefit ratio, the patient is consenting to an intervention in which his or her individual care and benefit are the primary goals. The primary goal of research, however, is to answer a clinical question and gain generalizable knowledge; the range of risks and benefits is often

unknown.<sup>6,11</sup> Direct benefit to subjects through participation in research is not guaranteed, nor are interventions conducted with this goal in mind. This distinction may be difficult for patients to understand, strengthening the need for thorough informed consent.

These 4 principles serve as guidelines for ethically appropriate conduct in the biomedical realm. In general, autonomy refers to the expectation that all patients should have the ability and the right to make informed, independent choices about their medical care, including participation in research studies. The informed consent process should thoroughly explain the research protocol and the implications of participation for the subject in order to allow the potential subject to decide whether to participate. According to the principles of nonmaleficence and beneficence, which are reiterated in the Hippocratic Oath, patients must not only be protected against intentional harm by the physician but also must benefit in some way from an intervention. As the extent of the risks and benefits of research are generally unknown, there must be a balance between these 3 principles. A clear explanation of the potential risks and benefits is an essential component of informed consent and must be provided to an individual before enrollment in a research study. The principle of justice asserts that all people should have equal access to medical treatment.<sup>10</sup> This includes equal opportunity to participate in medical research; researchers cannot exclude potential subjects without specific cause.<sup>11</sup>

Proper informed consent includes the assurance that people understand they are protected by these governing principles of healthcare. Historically, these 4 principles of biomedical ethics served as the precedent for establishing informed consent regulations to ensure ethical treatment of subjects and are still considered today in the revision and execution of such regulations. Informed consent implies that potential subjects understand they are agreeing to participate in a research that may not afford them any direct medical benefit. Subjects should also understand the differences between the research protocol and the standard level of care they would receive should they choose not to participate. The subject's decision should be free from coercion; the subject must not feel extreme pressure to participate from those requesting his or her participation and must be protected from the potential pressure to participate that a patient might feel on the basis of desperation arising from their personal circumstances.<sup>10</sup> Additional details on what constitutes informed consent and subject populations that are considered particularly vulnerable to coercion will be detailed later in this article.

## Current Regulations

Standards for informed consent are set forth in the CFR. Section 45 CFR 46.116 outlines the process for

obtaining informed consent, and section 45 CFR 46.117 describes how informed consent must be documented. In addition, the IRB is responsible for ensuring that research is carried out in accordance with the CFR.<sup>7</sup> The IRB can provide a researcher with detailed guidelines for writing consent forms and for the process of obtaining informed consent from subjects. In some cases, IRBs provide a checklist of elements to be included in consent forms. The pertinent sections of the CFR can be found at the following Web site: [www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm). Both the relevant sections of the CFR and all the material provided by the IRB must be read to ensure that the research is in regulatory compliance.

## Obtaining Consent

### When to Obtain Consent

Informed consent is an ongoing process that requires updating the subjects as the protocol changes. However, the researcher must obtain initial consent before beginning research. A subject should not enroll in a study until he or she has been fully informed about the risks and benefits and is able to make an informed decision to participate.<sup>12</sup>

### How to Obtain Consent

The best way to obtain consent is to review the elements of the consent form with each subject. Each element should receive a clear and detailed explanation. The subjects should also be asked to answer questions to demonstrate their understanding. Most participants will not possess the same medical vocabulary and knowledge that a researcher does; therefore, elements should have nontechnical explanations. The subjects should also understand that all their questions deserve answers, and any necessary explanation should be provided in as much detail as necessary to ensure a comprehensive understanding. If they feel rushed, participants most likely will not ask all their questions.<sup>12</sup>

Verbal consent may be permissible for potential subjects who cannot read the consent form. For this purpose, the subject or the subject's representative must sign a short version of the consent form and a summary of what is to be said to the subject or representative. A witness must sign both documents. Copies of the documents should be provided to the subject or his or her representative.<sup>12</sup>

In cases in which the subject cannot read the consent form because English is not the native language, the consent form should be translated into a language comprehensible to the subject. If this is not an option, verbal consent may also be an option. In this case, the witness must speak English as well as the subject's language. If a translator is present, the translator may serve as a witness. When a consent form is drafted in

a language other than English, an English translation of all consent materials must be submitted to the IRB for review as well.<sup>12</sup> It is important to remember that IRB regulations vary by state; thus researchers must refer to their IRB for specific instructions.

### Who Obtains Consent

It is vital that consent discussions and interactions between patients and research professionals not include participation on the part of the patients' primary care physicians. Physician involvement can easily cause confusion between research and treatment, and may affect a patient's ability to give an appropriate informed consent. Therefore, all steps of the consent process must be kept separate from primary care and treatment, as well as from the people involved in primary care and treatment.<sup>12</sup>

## Writing a Consent Form

### Readability

All subjects must sign a consent form before participation in the research study. The purpose of the consent form is to ensure that each subject has adequate knowledge of the study before making his or her decision to participate.<sup>12</sup> This also provides opportunity for individuals to ask questions and choose whether to consent or decline to participate in the research. For these reasons, it is extremely important to write consent forms at a level that is comprehensible to all potential subjects. Never overestimate how much a subject is capable of understanding. Although the forms may seem oversimplified, this is the only way to ensure that those with no medical knowledge will understand the forms. Consent forms should be written at or below the eighth grade reading level. In addition, it is best to write consent forms in the second person ("you"), and they should not include phrases such as "I understand..." which may be unintentionally coercive.<sup>13</sup>

### Research Procedures and Requirements

Every consent form must clearly state that the study involves research and must contain a comprehensive explanation of any procedures that are experimental, as opposed to the usual types of procedures patients encounter in visiting their physicians. After reading the consent form, subjects should understand how participation in this study will differ from the medical treatment they would receive if they were not involved in the research. This includes a disclosure of appropriate alternative procedures or any other courses of treatment that might be advantageous to the subjects.<sup>13</sup>

The subjects must also have a definitive understanding of what participation entails. The consent form must state the purpose of the research, an overview of the protocol, and an explanation of why the individu-

als are being asked to participate. Information should also include the anticipated duration, number of other participants, and any other logistical details that may influence their decision. This includes, but is not limited to, any financial burdens, travel, or temporary relocation that may be required because of participation in the research.<sup>13</sup>

#### Declaration of Risks and Potential Benefits

All potential risks to the subjects must be clearly explained before they are asked to sign a consent form. The consent form must include a description of any foreseeable risks or discomforts to the subjects. In addition, if appropriate, the form should include a statement informing participants that the particular treatment or procedure may involve currently unforeseeable risks. It is the investigator's responsibility to ensure that the subjects understand the risks of their participation and have ample opportunity to ask questions before making a decision. Except in extenuating circumstances, subjects should be given a copy of the consent form and time to consult with other family or community members before agreeing to participate in a study.<sup>12</sup>

The subjects must also understand what will happen in the case of an adverse event or an unexpected negative outcome. Consent forms should provide information regarding who subjects should contact if they experience an adverse event or perceive that they are being harmed because of their participation. For research involving more than minimal risk, the consent form should include an explanation of the following: whether any compensation or medical treatment is available if injury occurs, what such compensation or treatment consists of, and where further information can be obtained.<sup>13</sup>

To make a truly informed decision, the subjects must be aware of the risks as well as any potential benefits to themselves or to others that may reasonably be expected from the research. However, caution must be used when describing the benefits to avoid using language that may be embellishing or could lead the subjects to perceive an inflated probability of individual benefits. The consent form should not be written in such a way as to influence the consent decision. If the subjects will not receive any individual benefit because of their participation, as in a phase I clinical trial, this must be expressed clearly in the consent form. In addition, for research involving blinded randomization trials, the subjects must be informed that they may not receive the intervention and clearly comprehend the impact this will have on their treatment.<sup>12</sup>

#### Declaration of Participant Rights

Human research subjects are entitled to certain rights and should be made fully aware of these rights.

Every consent form must include language stating that participation in the research is voluntary. Forms should also state that refusal to participate or discontinuing participation will involve no penalty or loss of benefits, and that subjects can continue to receive the standard level of care. If there are any known consequences resulting from a subject's decision to withdraw from the study, it should be stated both in the consent document and in the procedures for orderly termination of participation in the research. In addition, if there are any anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent, they should be included in the consent form. The extent to which personal subject information will remain confidential and the exact circumstances under which patient confidentiality may be breached should be stated clearly. The subjects should know whom to contact with any questions regarding the research or their rights as research subjects. It may also be appropriate to inform subjects that they will be notified of any significant new findings developed during the course of the research that may relate to their willingness to continue participation.<sup>12</sup>

Although there are mandatory components of a consent form, forms are mostly evaluated at the discretion of the primary investigator and IRB. The guiding principle when writing a consent form is to include all information that may reasonably influence a person's decision to participate in the research. Further, the information should be construed in such a way that is comprehensible and unbiased, so that each research subject chooses to participate in an informed and voluntary manner.<sup>13</sup>

#### Vulnerable Populations

Several groups of people are considered particularly vulnerable as research subjects. These groups include prisoners, pregnant women, minors, and individuals with diminished mental capacity. Members of these groups are at increased risk of coercion because of an inability to give voluntary, informed consent and, therefore, require special protections throughout the course of the research, including the informed consent process. Children and individuals with diminished capacity may not have the ability to comprehend all the information necessary to make an informed decision. Other vulnerable populations may feel compelled to participate due to their socioeconomic status, which may prevent an individual from understanding participation as voluntary. As all populations are potentially subject to the need for transplantation, it is conceivable that a research protocol in the field of transplantation including transplantable organs, immunosuppressant therapies, and surgical techniques, may involve one or more of the following pop-

ulations. When formulating a research project, it is necessary to be conscious of the potential subjects and any special considerations they may need.<sup>12</sup>

### Prisoners

Historically, inmates in the prison system were considered an ideal population for human subject research. They had a highly regulated and standardized lifestyle, diet, and schedule, and were viewed as an eager research population. However, under current regulations, prisoners are considered highly vulnerable because of a lack of control over their environment. Prisoners may be used as research subjects; however, specific safeguards must be implemented if prisoners are to participate. The IRB must first be notified, and a specific prisoner representative must be selected and written into the protocol. The informed consent document must also assure the prisoner that participation will have no effect on prisoner status such as parole considerations. Additionally, if the subjects face, or believe they face, any threat or punishment from their institution if they choose not to participate, the IRB must be consulted immediately.<sup>12</sup>

### Those With Diminished Mental Capacity and Incompetence

There are particular regulations in obtaining informed consent from individuals with diminished mental capacity. Consent may be given on behalf of the subjects by proxy decision makers, but research has shown that proxy decision makers often misrepresent the best interests of a patient.<sup>12</sup> The accepted standard for proxy decision makers involves determining what is in the best interest of the individual with diminished mental capacity as well as what the wishes of the individual with diminished mental capacity are. This standard is especially difficult to uphold when asking for consent for a research study in which there is no anticipated benefit to the individual subjects. However, when using subjects with cognitive impairments, it is of primary importance to demonstrate how the subject's ability to give informed consent will be determined. It is also necessary to determine to what extent the patient's cognitive function is impaired and to document all potential sources of cognitive incompetence.<sup>12</sup>

### Children

Decision-making capacity depends on maturity, which varies child by child. In most states, the legal age for decision making is 18 years. However, some children are capable of decision making as early as age 14, whereas others may not be ready to make decisions until age 20. It is common practice to require the "assent" of children under the age of 18 years in addition to consent by the legal guardian. Assent does not

necessarily imply a fully informed understanding of the proposed research; however, it affords the child an opportunity to oppose his or her participation. If the child will not assent, he or she should not be used as a research subject. In most cases, children above age 14 should be actively involved in the consent process.<sup>12</sup> Laws regarding emancipated minors may vary by state; it is important to consult with the local IRB if planning research involving children.

### Pregnant Women and Fetuses

Subpart B of the CFR is dedicated to pregnant women and fetuses.<sup>7</sup> Because fetal development is easily disturbed by outside influences, pregnant women must be given careful consideration before being included in any type of research. Subpart B outlines the various issues that researchers must address in deciding to include pregnant women in their studies. When using pregnant individuals in a research design, consent must be obtained from both the pregnant woman and the father of the child, if feasible.<sup>12</sup>

### Severe Illness

The impact of severe illness on ability to provide informed consent has not been addressed adequately in the literature<sup>11</sup>; however, illness is an important consideration when enrolling patients in clinical trials. A patient's illness and the psychological response to the illness may affect his or her ability to comprehend and retain information, impeding on his or her capacity for informed consent.<sup>11</sup> Therapeutic misconception is of particular concern in these patients; this refers to a failure to appreciate that the research is not therapy and may not be in the best medical interest of the patient. Subjects tend to believe that they will gain direct health benefit from participation and/or do not accurately understand the potential harm of participation. Studies have shown that the sickest patients have a higher propensity for a therapeutic misconception.<sup>14</sup> Illness may cause a different perspective of risks and benefits. Ill patients may feel that they have little or no treatment option other than participation.<sup>11</sup> These factors may seriously undermine the informed consent of a subject suffering from a serious illness.

Transplant patients, especially those awaiting a transplant, often suffer from severe illness. Many transplant patients suffer from long-term and potentially life-threatening diseases and therefore may be at an increased risk of misconceiving research as treatment. This strengthens the importance of clear and accurate explanation of the risks and benefits of participation including those that are unknown, the difference between the research protocol and standard treatment, and the distinction between the goals of research and therapy when conducting research on this population.<sup>14</sup>

## Waivers and Alterations

In the following circumstances, informed consent may be waived or altered by the IRB: if the research involves no more than minimal risk (as perceived by healthcare professionals) to the subjects; if waiving or altering informed consent will not have a negative impact on the rights and welfare of the subjects; if the research could not be carried out in a practical manner without the waiver or alteration; or if the subjects will be provided with additional relevant information after participation in the study. In addition, the IRB may alter or waive consent if the study involves state or federal review processes. The informed consent requirement can only be waived by the IRB; if the investigator is considering not using a consent procedure, approval must be obtained from the IRB before initiating research.<sup>15</sup>

## Conclusion

Informed consent has been widely accepted as a tenet of ethical research practice. However, a number of barriers exist that impede the plausibility of a truly informed and voluntary consent. Finances may serve as an incentive for participation, especially for patients without insurance or of low socioeconomic class. The patient-physician relationship may limit a patient's ability to refuse participation and may lead the patient to the conclusion that participation is in his or her medical best interest. Likewise, a patient's medical condition may increase his or her propensity to misunderstand the risks and benefits causing a therapeutic misconception. It is likely that a transplant patient considering involvement in research faces one or all of these barriers. This is not to say that participation of these subjects is unethical, but heightens the need for researchers to provide potential subjects with thorough and accurate information. In addition, it is imperative that informed consent is understood as a process through which human subjects are afforded with the right to make informed and autonomous decisions.

The practice and ethics of healthcare are culturally mediated. Perceptions of medicine and the role of healthcare providers and patients vary across cultures. Members of other cultures may not value the principle most valued by Americans, namely autonomy, which guides the ethical and legal practice of medicine. However, as evidenced in the Nuremberg Code and

the Declaration of Helsinki the ethical obligations of researchers to conduct sound and ethical research and the human right to for protection from undue harm and involuntary participation in research is universal.

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**CE Test** Test ID 4000-J42: Informed Consent

**Learning objectives:** 1. Discuss the informed consent process 2. Identify key principles of informed consent 3. Describe strategies to promote informed consent

**1. When was human subject research established as a common process?**

- a. Early 19th century
- b. Mid 19th century
- c. Early 20th century
- d. Mid 20th century

**2. Which of the following best describes the benefit of the informed consent process?**

- a. It ensures that a signature appears on the consent form.
- b. It promotes patient understanding of tests and procedures.
- c. It protects the rights of patients.
- d. It allows surrogate consent.

**3. A patient should give consent to participate in a clinical study based on which of the following indications?**

- a. A substantial direct benefit can be obtained.
- b. The honorarium is of a sufficient amount.
- c. Assignment to the active treatment group.
- d. Understanding of the medical facts and risks involved.

**4. Which of the following was the earliest doctrine of research ethics relating to research?**

- a. Nuremberg Code
- b. Declaration of Helsinki
- c. Belmont Report
- d. Institutional review board doctrine

**5. Which of the following details the ethical principles and guidelines for the ethical conduct of research?**

- a. Nuremberg Code
- b. Declaration of Helsinki
- c. Belmont Report
- d. Institutional review board doctrine

**6. Which of the following ethical principles focuses on respect for persons?**

- a. Nonmaleficence
- b. Autonomy
- c. Beneficence
- d. Justice

**7. Which of the following ethical principles asserts that all persons should have equal access to medical treatment?**

- a. Nonmaleficence
- b. Autonomy
- c. Beneficence
- d. Justice

**8. Which of the following is an essential component of the informed consent process?**

- a. Written consent rather than verbal consent must be obtained.
- b. Risks and benefits must be explained.
- c. Actual cost of participation and treatment must be disclosed.
- d. Investigators' contact information must be provided.

**9. In what year was the Code of Federal Regulations established?**

- a. 1970
- b. 1974
- c. 1979
- d. 1982

**10. When was the Health Insurance Portability and Accountability Act enacted?**

- a. 1992
- b. 1996
- c. 1999
- d. 2000

**11. For research involving more than minimal risk, which of the following is not required on the consent form?**

- a. Whether compensation or medical treatment is available if injury occurs
- b. What the treatment consists of
- c. The cost of treatment
- d. Where further information can be obtained

**12. In which way does the Declaration of Helsinki expand the premises of the Nuremberg Code?**

- a. It highlights the responsibility of the researcher to conduct responsible research.
- b. It mandated obtaining voluntary informed consent from legally competent individuals before research.
- c. It established that there must be evidence of reasonable potential benefit to society from the proposed research.
- d. It drew the distinction between therapeutic and nontherapeutic research.

**13. What section of the Code of Federal Regulations outlines standards for informed consent?**

- a. 45 CFR 46.116
- b. 45 CFR 46.117
- c. 45 CFR 46.118
- d. 45 CFR 46.119

**14. Which of the following describes the best way to obtain informed consent?**

- a. Provide a written copy of the consent form to the subject
- b. Review elements of the consent form with subject
- c. Ask the subject to explain the study in their own words
- d. Explain the study to both the subject and a family member

Test answers: Mark only one box for your answer to each question. You may photocopy this form.

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