Translational Ethics

A Perspective for the New Millennium

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Modern medical care is increasingly dependent on the application of science to clinical practice, which occurs through clinical or translational research. We propose the concept of translational ethics, which incorporates the contributions of research codes of ethics that involve the protection of human subjects into the ethics of clinical practice. The modern research environment, which has contributed the scientific tools of modern medicine, has also framed the ethical environment in which medicine is practiced. The single most important contribution of research codes for protection of human research subjects to clinical practice is the doctrine of informed consent. Translational ethics, based on autonomy and informed consent, progresses beyond the narrow interpretation of those 2 concepts. It requires consensual understanding of a spectrum of clinical interventions that are increasingly complicated. Translational ethics helps navigate the ethical ramifications of technological and scientific advances that will increasingly challenge the corporate-oriented health system in the new millennium.

The Nuremberg Code

The Nuremberg Trials (1946-1947), were held in Nuremberg, Germany, after World War II to prosecute Nazi officials for a variety of war crimes. The second Nuremberg Trial, the so-called Doctor's Trial, concluded after 7 months of testimony on August 19, 1947. Twenty-three physicians and health officials were charged with crimes involving experiments on human subjects, mostly prisoners. Nine of the defendants were sentenced to long prison terms, 7 were sentenced to death by hanging, and 7 were acquitted. The Nuremberg Code, which came from the trial, established consent as the first and most important principle.

After the Nuremberg trials, in 1947, 10 principles of conduct expected of physicians in the conduct of research on human subjects were described in the Nuremberg Code on the Ethics of Human Research: voluntary consent; an expected beneficial outcome; prior experimentation on animals; avoidance of unnecessary pain and horror; avoidance of risk or disablement; risk taking not to exceed expected advantages; protection against the possibility, however slight, of injury, disablement, or death; scientifically and technically qualified experimenters; the subject’s freedom to retract consent; and the experimenter’s obligation to stop the experiment (Table 1).

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The Nuremberg Code on the Ethics of Human Research and the eventual Human Rights Movement were strongly influenced by the Chief of Counsel for War Crimes, Brigadier General Telford Taylor (1908-1998), the principal prosecutor (Figure 1). In his opening statement at the second Nuremberg trial, Taylor held physician behavior to a higher standard than the behavior of the general citizenry. He opined that the fatal experiments on human subjects were especially evil since they were performed by physicians who pledged by the Hippocratic oath to do no harm. Much of the legal foundation for the Human Rights Movement, especially as it has influenced medical ethics, is due to Taylor. His affirmation of the principle of self-determination is the starting point in medical decision making and represents the evolution and amalgamation of other ethical concepts, such as human rights and autonomy, into medical ethics and practice.

Arising from revulsion to the experiments conducted by Nazi physicians during World War II, the Nuremberg Code assimilated the legal and ethical conclusions of the deliberations of the Nuremberg trials. It exerted seemingly little impact on research practices until an adaptation of it was applied by decree of the US secretary of defense in 1953 to policy governing scientific investigation involving human subjects. It was 1954 before the World Medical Organization addressed the issue of experimentation involving human subjects, which had been the original setting and stimulus from which the Nuremberg codes were written.

Similarly, in the period immediately following the publication of the Nuremberg Code, from 1947 to 1975, national and international medical organizations demonstrated relatively little interest in applying its principles to research. Two updates to medical ethics in the post–World War II period that did reflect some influence of the Nuremberg Code were the Declaration of Geneva and the International Code of Medical Ethics.

In 1948, the World Medical Organization, 2 years old at the time, formulated the Declaration of Geneva, an ethical code written in English and French. It was based on the Hippocratic oath but contained some elements of the Nuremberg Code. It was directed toward physician professionalism rather than toward experimentation on human subjects, which had been the focus of the Nuremberg trials and the Nuremberg Code. The Declaration of Geneva was formulated with the belief that professional ethical codes and guidelines were needed because of the participation of Nazi physicians in the implementation of state policy.

In 1949, the International Code of Medical Ethics was developed. Directed toward clinical practice while retaining the ethical orientation of the Hippocratic oath,
it also was influenced by the Nuremberg Code. This code stated that a physician shall act only in the patient’s interest when providing medical care that might have the effect of weakening the physical and mental condition of the patient.

After 1975, a renewed interest in the Nuremberg Code occurred, and more of the code’s content became apparent in medical codes and practice. The Declaration of Helsinki of 1975 found its way into modern medical ethics by stressing the Nuremberg concepts related to scientific standards governing proper research.

In the United States, an important turning point in congressional regulation of clinical research occurred with the National Research Act of 1974 because it resulted in the formation of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. This commission produced the Belmont Report, a highly influential embodiment of research ethics involving human subjects that laid the foundation for many of the changes in federal regulations that took effect in the 1980s and remain in effect today. A study of informed consent performed by the commission noted, “The most complete and authoritative statement of the law of informed consent to human experimentation is the Nuremberg Code.”

The modern institutional review board resulted from the Belmont Report. Recently, a renewed focus by the Office for Protection Against Research Risk (OPPARR) on protection of human subjects has occurred. Subsequently, the office, with newly elevated stature, moved from its historical home at the National Institutes of Health, Bethesda, Md, to a separate agency.

The first and most important principle of the Nuremberg Code, informed consent, has become the cornerstone for the ethical practice of medicine and for the conduct of research involving human subjects. In research and the clinical setting, the goal is a relation of shared information and trust between physician and patient. Translational ethics, like translational research, uses the research codes for protection of human subjects as behavior norms for clinical practice. Other important concepts of translational ethics include autonomy and the capacity to withdraw from treatment or from the research protocol.

The mission of research differs from the mission of clinical medicine. Research aims to gain new knowledge, while clinical medicine strives to benefit the individual patient at hand. An elaborate process has been designed to protect human subjects involved in clinical trials beyond that which applies to patients under the care of physicians. In both instances, the doctrine of informed consent provides a “golden rule” to address the challenges of the clinical, scientific, and corporate changes transforming medicine.

Philosophers have long attempted to reconcile scientific and ethical thought. Ethics is as old as human thought, the moral and intellectual base being grounded in ancient cultures. In the western world, the work of Plato and Aristotle blended with the medieval church and its great thinkers to form the basis of modern thought. The ancient and medieval worlds combined the concepts of Aristotle and Saint Thomas Aquinas to explain science and the universe. When physics appeared, traditional explanations were adapted and the belief emerged that the world through faith serves human purposes. As noted by Randall, the balance of science and ethics is constantly changing, “Modern medicine is science, while medieval medicine was less powerful but more important, ethics.”

Expressed as a code, ethics implies morality. The code, spoken or unspoken, is modified and influenced by social change but retains a constant force. Professional codes are an evolutionary amalgam of ethical theory, etiquette, law, and professional socialization. They are influenced by religion, social mores, corporate culture, and the societies in which they are practiced. Because medical ethics involves a relation between laypeople and health professionals, the foundation must be built on loyalty, fidelity, respect, and trust (Figure 2).

Ethics is defined as the disciplined study of morality. Morality comprises good and bad character, right and wrong behavior. Ethics identifies the characteristics of virtues and vices and analyzes issues about right and wrong actions to develop arguments about which actions are ethically defensible and which actions are ethically indefensible. Ethics refers not only to the rules, customs, and beliefs of a society but also to its scholarly effort to articulate and analyze those rules, customs, and beliefs.
The word ethics is used in many ways. It may designate the moral beliefs and behaviors of individuals, the rules devised to prevent political conflict of interest, the customs of a society, or, as stated in the Oxford English Dictionary, “the department of study concerned with the principles of human duty.” Medical ethics, a specialty of ethics that is more than 25 centuries old, is rooted in the works of the ancient philosophers and expressed, in part, in the Hippocratic Corpus. Medical ethics deals with the morality of medicine. Its central concept is that the physician serves as the moral fiduciary of the patient.

While medical ethics has often included bioethical concepts, bioethics developed as its own separate subspecialty following World War II. Maturing in the turbulence of the 1960s and Vatican II, bioethics is defined as “the systematic study of the moral dimensions—including moral vision, decisions, conduct and policies—of the life sciences and health care, employing a variety of ethical methodologies in an interdisciplinary setting.” Some have credited the new field of bioethics to the founding of the United Nations in 1945. Its charter, declarations, and works incorporated codes to protect individuals. Like the Nuremberg Code, these United Nations’ codes were reactions to the Axis governments that had subjected citizens to state tyranny that involved the use of unwilling human subjects for research and that practiced the euthanatization of “undesirable” citizens.

The committee that crafted the United Nations’ Universal Declaration of Human Rights was chaired by Eleanor Roosevelt (Figure 3). In a sense, the declaration is analogous to the addition of the Bill of Rights to the Constitution of the United States, since it was to be attached to the United Nations charter. Endorsed by the General Assembly of the United Nations with no dissenting vote on December 10, 1948, the declaration defines responsibilities and features of health care that, when absent, violate human rights.

The Universal Declaration of Human Rights consists of 4 tenets: (1) the basic right to human dignity; (2) civil and political rights; (3) economic, social, and cultural rights; and (4) solidarity rights. Human dignity, emphasized in article 1, is a historical right derived from many religions, philosophies, and traditions, including Judaism-Christianity, the Koran, and the Tal- mud. It is the most ancient of the ethical tenets and includes the right to basic health care.

The second tenet, known as civil and political rights, emphasized primarily in articles 2 through 21, refers to the liberty to pursue human dignity against the abuse of political authority. These concepts were originated by theorists during the Enlightenment and have also been embodied in the Declaration of Independence, the US constitutional amendments, and the Bill of Rights. Known as first-generation or negative rights, they limit and restrict government and include the freedoms of speech, the press, and religion.

Second-generation rights, called positive rights, are those that hold the government responsible for the provision of societal needs such as health care, education, employment, and protection for aged and vulnerable populations. Found primarily in articles 22 through 27, these rights are largely an outgrowth of the industrial world of the 18th and 19th centuries and have philosophical advocates such as Karl Marx (1818-1883) and Thomas Paine (1737-1809).

Solidarity rights, articles 28 through 30, represent the last crucial notion in the United Nations’ declaration. These address the failure of domestic sovereignty that was prevalent during the last part of the 20th century when pollution, environmental protection, war, and international distributive justice came to the forefront. International cooperation to distribute food, meet basic needs, and provide for justice on a global scale illustrates applications of solidarity rights.
Contemporary emphasis is placed on the interdependence of all 4 tenets of human rights. Capitalist-oriented countries emphasize the first-generation rights that limit government; socialist countries emphasize second-generation, or positive, rights; and solidarity rights are most applicable to the poorest countries of the world. Most developed countries have accepted the concept that health care is a human right.11

The United Nations impacted medical practice by expanding the Human Rights Movement to embrace health care. For the evolving ethics of medicine, the Human Rights Movement broadened and defined the essential human right to health care. In several recent statements12 acknowledging the 50th anniversary of the Universal Declaration of Human Rights, the director-general of the World Health Organization, Gro Harlem Brundtland, MD, expressed this sentiment:

Health security is a notion which encompasses many of the rights enlisted in the Declaration. It means universal access to adequate health care, access to education and information, the right to food in sufficient quantity and of good quality, but also the right to decent housing and to live and work in an environment where known health risks are controlled.13(p3)

She articulated a commitment to a renewed focus on the relation between the political and legal links between health and human rights and acknowledged the challenge of the men and women who drafted the Universal Declaration of Human Rights, the challenge to secure human rights for all people and to provide universal access to health care.15

INFORMED CONSENT

The evolution of informed consent and its application to medical care redefined the essence of the physician-patient relationship. Consistent with Hippocratic tradition, the physician alone used to decide what was best for the patient.

This notion of consent being in the hands of the physician and not the patient has radically changed over time. Through the influence of the Nuremberg Code and the Human Rights Movement, patient care is based on mutual consensus and informed consent (Table 2). This evolution in the physician-patient relationship can also be seen in various other contractual and human relations characteristic of the late 20th century.

Paternalism, the traditional Hippocratic approach, contained the concept of primum non nocere (first, do no harm), which continues to govern the physician’s approach to the patient. It also recognized that there is a point beyond which aggressive maintenance of life provides no benefit and serves only to prolong dying and increase suffering. Hippocrates himself emphasized, “Do not seek to cure patients who are overwhelmed by disease” (Figure 4).15(p33)

Informed consent includes a strong emphasis on patient autonomy that replaces all forms of Hippocratic paternalism for competent patients and provides the patient the right to refuse or withdraw from treatment. In the past, the image of the wise, trusted, adored, and

Table 2. General Principles of Informed Consent*

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<th>1. Decision-making capacity</th>
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<td>The patient must have the ability to make an informed decision. The term competence is often used to denote decision-making capacity, but because competence is also a legal concept, decision-making capacity is the preferred ethical term. There are a number of abilities that make up decision-making capacity. The patient must be able to understand the reason for the intervention, the purpose of the intervention, and the benefits and risks of the proposed intervention. The patient must also be able to understand the implications of not intervening or of choosing an alternative intervention. The patient must be able to make a reasoned decision, a decision that is based on his or her values. Patients are entitled to make decisions that others would consider unwise.</td>
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<th>2. Disclosure</th>
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<td>The patient needs to be provided information about the proposed intervention, including the expected benefits, risks, and financial costs. The patient also needs to be informed about the benefits, risks, and costs of alternative interventions as well as of no intervention. The patient should be told all information that would be material or significant to the patient’s decision.</td>
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<th>3. Understanding</th>
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<td>In addition to having decision-making capacity, the patient needs to actually understand the information that has been disclosed. The physician may need to discuss the issues with the patient more than once.</td>
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<th>4. Voluntariness</th>
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<td>The patient’s consent must be given freely without being obtained through coercion or manipulation.</td>
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<th>5. Authorization</th>
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<td>The patient must actually assent to the proposed intervention. Consent should not be considered implicit in a general consent to treatment for an intervention that poses significant medical or social risks to the patient or when the patient may have other reasons for refusing the intervention.</td>
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*From the American Medical Association.14

Figure 4. Hippocrates. Although little is known of the life of Hippocrates, the “father of medicine,” he was born around 460 BC on the Isle of Cos in Asia Minor. His philosophy of medicine, the Hippocratic Corpus, divorced medicine from superstition and described a code of etiquette among physicians. It described the primary responsibility of the physician to the patient and to do no harm. Photograph provided courtesy of the Harvey Cushing/John Hay Whitney Medical Library, Yale University, New Haven, Conn.
beneficent physician predominated. The new ethos is
medicine as an enterprise pursued within a pluralistic,
secular society in which physicians and patients may be
moral strangers. This ethos makes patient autonomy and
informed consent necessities since no longer can any-
one speak for the patient but the patient.\textsuperscript{15}\textsuperscript{(p10)} The deci-
sions of the American courts recognize informed con-
sent and \textit{res ipsa loquitur} (the thing speaks for itself) as
2 favorite plaintiff tactics in courtroom strategy.

The doctrine of informed consent consists in legal
terms of instructing the patient regarding (1) the diag-
nosis for which intervention is proposed, (2) the recom-
mended intervention with attendant risks and benefits,
(3) the anticipated results or prognosis if no interven-
tion is attempted, and (4) any significant alternatives
and their attendant risks and benefits.

Therapeutic exceptions to informed consent cover
situations when (1) interventions need to be provided
immediately to prevent serious harm or death (the emer-
gency exception), (2) the patient voluntarily gives up the
right to be informed (the waiver exception), (3) the phy-
sician has sufficient reason to believe that disclosure would
result in physical or psychological harm to the patient
(the therapeutic privilege exception), and (4) the pa-
tient is deemed incompetent.\textsuperscript{15}\textsuperscript{(p36)} The freedom of self-
determination is emphasized; a person is free to make
many decisions, even unwise ones, without competence
being questioned unless sufficient reasons to the
contrary are identified.\textsuperscript{15}\textsuperscript{(p12-15)}

In the past, therapeutic exception existed under the
concept of usual and customary practice. The legal ori-
gin is concern for the bodily integrity of the individual.
If self-determination is not allowed and informed con-
sent is absent, intervention could be considered battery
or unauthorized touching. In practice, battery is seldom
used as a medicolegal charge.

Research ethics that address autonomy also trans-
late to medical practice. Research practices in the Jew-
ish Clinic Disease Hospital, Willowbrook, Staten
Island, NY, led to patient exploitation when develop-
mentally disabled patients were intentionally infected
with hepatitis, as did the Tuskegee syphilis exper-
iment when patients were left untreated for research
purposes. Issues of autonomy have been associated
with hepatitis, as did the Tuskegee syphilis exper-
iment when patients were left untreated for research
purposes. Issues of autonomy have been associated
2 significant court decisions having to do with
reproductive biology: \textit{Eisenstadt v Beard} [405 US 438,
92 SCt 1029 (1972)] determined that the distribution of
contraceptives to unmarried persons was per-
missible; and \textit{Roe v Wade} [410 US 113, 93 SCt 705
(1973)] determined that patients’ rights take prece-
dence.

American courts began to reference the Nurem-
berg Code in the 1980s. Most cases of medical ethics trans-
lated to law involved reproductive rights or issues of pa-
tient autonomy in hospital care for individuals unable
to give informed consent. The President’s Commission
for the Study of Ethical Problems in Medicine and
Biomedical and Behavioral Research was authorized
in 1978. Its first working meeting was held on May 13, 1980.
The Nuremberg Code was cited in \textit{Whitlock v Duke Uni-
versity} [637 FSupp 1463 (MDNC 1986)], a tort action
suit for inadequate disclosure to the research subject.

In 1987, the supreme court case \textit{United States v Stanley
[107 SCt 3054 (1987)]} referenced the Nuremberg Code. James
Stanley was a soldier who had been secretly ad-
ministered lysergide (LSD).

**TRANSLATIONAL ETHICS**

Translational ethics is based on autonomy and in-
formed consent but progresses beyond the narrow inter-
pretation of those 2 concepts. It requires consensual
understanding of a spectrum of clinical interventions that
are increasingly complicated. The complexity of mod-
ern medical science increases the difficulty of obtaining
and providing informed consent because many of the situa-
tions confronted are new to the experience of patient
and physician.

The corporate-oriented health system is chal-
cenged by new technology and its ethical ramifications.
Several contemporary clinical topics reside on the fringe
of ethics and law. Technological and scientific advances
pose unfamiliar challenges that strain professional ethi-
cal codes and that may pose different resolutions in a cor-
porate vs a professional culture. Among these topics are
transplantation, reproductive rights, genetic testing, clon-
ing, euthanasia, and physician-assisted suicide.

Transplantation ethics did not exist before the tech-
nology of transplantation and organ donation. The ethi-
cal and legal dimensions of transplantation have be-
come increasingly codified in law. The Seattle, Wash,
group on selection of transplant recipients was formed
in the 1960s. Two years after Medicare became law to
provide health insurance for the elderly, it was ex-
panded to include any patient with end-stage renal dis-
ee. The patients with end-stage renal disease thus be-
came the first population group with a specific disease
to be government funded for health care with no age limi-
tations. In England, the Human Organs Transplant Act
of 1989 prohibited commercial dealings in human or-
gans. A recent report\textsuperscript{16} of the Institute of Medicine of the
National Academy of Sciences responded to ethical con-
cerns regarding fairness in the distribution of organs. It
is likely that law will be codified to follow these ethical
considerations.

The Genome Project, which is well advanced, al-
ows uncommon monogenic diseases to be predicted and
thereby raises ethical questions of yet unknown dimen-
sions. The complexities in these cases of assuring in-
formed consent and consensual planning between pa-
tient and physician are extensive. Screening for Hun-
tington chorea exemplifies the almost unlimited poten-
tial for genetic screening of the population. The genetic
test for familial adenomyositis polyposis, which can pre-
dictably detect a family that will develop colon cancer
by the sixth decade of life, invokes such issues as
how widely to screen, how to fund screening, and how
the families identified will be assisted in using the in-
formation from the screening to make autonomous
decisions.\textsuperscript{17}

Reproductive rights evoke complicated cultural, ethi-
cal, and legal conflicts involving religion, politics, and
sometimes violence.\textsuperscript{18} The legal resolution to abortion re-
 mains inconclusive, having resorted to privacy issues co-
ered by Roe v Wade in 1976. Human cloning research, or its application, has abruptly surfaced new ethical issues that legislators have rushed to proscribe by law. Since Scottish scientists announced the birth of a lamb named Dolly that was cloned by combining the nucleus of an adult mammary egg and an enucleated sheep egg, people have been concerned about visions of human cloning factories. Most European countries have banned human cloning research, and such a ban is being discussed in the United States by the Presidential Council on Medical Ethics. The ethical debates surrounding reproductive technology bring to mind Aldous Huxley’s 1932 novel, Brave New World, in which all newborns are produced in state hatcheries.

One of the most immediate and complicated subjects facing medical ethics deals with end-of-life issues and specifically with the question of entitlement as a constitutional right in cases of euthanasia or physician-assisted suicide. Unfortunately, these issues are most commonly encountered in the vulnerable and elderly populations, often the same populations receiving the end-of-life care that is increasingly being implicated as a source of rising health care costs.

In the Netherlands, physician-assisted suicide and euthanasia represent 2.3% and 0.4% of all deaths, respectively. In the United States, the states of Oregon and Washington legally permit physician-assisted suicide. Nevertheless, the US Supreme Court in Washington v Glucksberg [521 US 702, 117 SCt 2258 (1997)] and in Vacco v Quill [65 USLW 3218 (US Oct 1, 1996) (No. 95-1858)] rejected the premise of a constitutional right to physician-assisted suicide. The court in the Vacco v Quill [80 F3d 716 (2d Cir 1996), cert granted] case opted for liberalizing the laws governing the prescription of narcotics for terminally ill patients. The Cruzan v Missouri Department of Health [497 US 261, 110 SCt 2841 (1990)] case involved a patient in a vegetative state whose parents petitioned the hospital to discontinue artificial hydration and nutrition. The court ruled otherwise.

With increasingly complex technologies available and anticipated, the concept of translational ethics embodied in the doctrine of informed consent takes on new importance. In addition to providing routine education and information to patients about medical alternatives, the new health care order calls for an initial and ongoing educational dialogue that will require new competencies of physicians and other health care providers.

Reconciling medical ethics, business ethics, professional ethics, and human rights with the physician’s fundamental fiduciary responsibility to the patient in the context of a secular, libertarian tradition will demand a fundamental reorientation. In the context of balancing Hippocratic medicine (doctor-patient) with the corporate dominance of health care in its current state of development, the patient’s rights of autonomy and informed consent must dominate.

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