INFORMED CONSENT AS RELATED TO CLINICAL INVESTIGATION AND PRACTICE*

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The concept of informed consent by the patient for diagnostic, therapeutic and experimental procedures has been in general use in western medicine as a guide with regard to new and unusual treatments for some centuries (1), although it rested on a predominantly informal base until the 1940s. The perversion of clinical experimentation and euthanasia by the Nazis, all too clearly revealed by the Nuremberg trials (2, 3) led to widespread recognition that medical tradition was not enough to protect the interests of the patient. The ethical problems involved in clinical experimentation have not yet, however, been translated into sharply defined rules of law. The Nuremberg Code made a very important step in the right direction (4). This placement of responsibility on the physician was further elaborated in a statement accepted by the British Medical Association in 1963 (4) which suggested full explanation of procedures to the patient, and free consent by the patient, "preferably in writing." Professor Plante (4a) has suggested that informed consent is not basically new, but its current use "in discussion of the liability of a physician to his patient" has led to confusion, and he stresses that the physician is obligated not to mislead the patient.

Clinical research and even day by day medical practice have been increasingly constrained in recent years by governmental regulation (for example, see the application forms for support of research involving clinical investigation by the National Institutes of Health), and legislation, fortunately intended to be directed toward the welfare of the patient. Much of the governmental regulation has been tempered by provision for peer-review of contemplated procedures.

Emergency procedures in the hospital have always been carried out as deemed necessary by the doctor for preservation of life on all types of patients regardless of consent.

At least as far back as 1920 the Massachusetts General and other hospitals required written authorization by responsible parties for operations on minors and mental incompetents. There have been since serious discussions by the staffs and administrations of many hospitals regarding such written consent for adults, and many decided, as did the Massachusetts General, not to require such permission. At the present time there is wide variation as to whether written permission is required for operation in hospital on competent adults. However, surgeons and internists routinely discuss with their patients the problems and benefits of major procedures. Even when consent forms have been used, at times patients have stated that they did not understand what they had signed.

For a time a few years ago concern for the patient's rights had gone so far that it was legally hazardous for a physician to provide even emergency roadside aid to an unconscious patient still at the scene of an accident. This situation was so obviously against the public interest that it has been relieved to a considerable degree by passage of the so-called good samaritan laws.

There are two sets of medical circumstances where informed consent may be entirely or largely disregarded by Government in the interest of the population as a whole. One is restriction of motion by quarantine to prevent spread of an outbreak of infectious disease, the other is

mass vaccination to control epidemics. In both these procedures exceptions to them may seriously compromise the effective application of the required measures and hence the rights of the individual must be subject to the interests of the community as a whole.

At times procedures such as blood transfusions have been deemed so necessary that the objections of individual recipients or their guardians, even though based on religious doctrine, have been overridden by court order. A significant extension of this principle has been presented by a recent court decision (5) to order blood transfusions for a minor setting aside the objections of his mother, a Jehovah's Witness. In this case the decision was incident not to life-saving surgery but to cosmetic surgery to correct a longstanding facial deformity of the child.

In one regard at least clinical investigation of the efficacy of new drugs has been hampered by the informed consent requirement, since unbiased "double blind" experiments, in which neither patient nor doctor are prejudiced by knowledge of whether drug or placebo has been given, are no longer feasible. This is regrettable because the mere mention of possible unfavorable symptoms related to administration of a compound or a surgical procedure may well be enough to cause these symptoms in suggestible patients. Courts have recognized this problem and in the case of the usual doctor-patient relationship have tended to absolve the doctor from blame if he acted in the best interests of the patient. ("The doctor's primary duty is to do what is best for the patient. Any conflict between this duty and that of a frightening disclosure ordinarily should be resolved in favor of the primary duty.") (5a) Equally well there may be an opposite effect with the

positive suggestion of curative powers since this will in itself often cause the patient to feel better.

However, these regulatory handicaps are better than uncontrolled or misdirected experimentation (2, 3). Medical ethics have provided a generally sound guide in the past, but with changing doctor-patient relationships and changing social pressures appear no longer totally adequate. Informed consent now is routinely required for clinical investigation in hospitals and institutions, and special committees are set up to control such procedures. While these indeed handicap clinical experimentation and cause delays, these effects are probably without too great social cost for the protection afforded.

I have seen two medical miracles, both performed without informed consent and under circumstances where had today's standards of treatment held the drugs, not yet governmentally approved, could not have been given and the patients would have died. The first, a moribund diabetic, too weak to even lift a finger, received insulin, the first used in the United States, and ten days later was carrying trays for other patients. The second miracle was the case of a delirious sailor, the victim of virulent gonococcal septicemia and panophthalmitis, who was cured within hours by the injection of the then but little-tried and crude penicillin.

In contrast, a highly successful example of regulation of new methods of diagnosis and treatment was provided by the United States Atomic Energy Commission when it made available at greatly reduced costs or free radioactive isotopes to aid in the diagnosis and treatment of certain diseases, notably cancer. These isotopes were made available only under clearly defined rules which insured the safety not only of

the patients themselves but those in contact with them. The phenomenal success of these new and potent agents was due in large part to the wise and effective regulation controlling the provision and utilization of these materials.

A quite different situation from the doctor-patient relationship develops in the use of volunteers in the trial of new drugs and procedures. Here there is not only the problem of informed consent but also, depending on the relationship of investigator and subject, a probability of implied coercion. For example, a medical student is relatively unlikely to refuse to be a subject in an investigation planned by one of his professors. A prisoner is hardly a free agent in volunteering for a project of scientific interest, particularly when rewards may be a factor in influencing his volunteering.

A very special case is that of the enthusiastic volunteer who is so engrossed in his project that he experiments upon himself without proper safeguard or in spite of sound advice against the procedure. I have come in contact with varying degrees of this attitude ranging from the enthusiastic physiologists who took unfully long chances in attempting to determine the body's reaction to sudden changes in atmospheric pressure or acceleration forces to the Japanese radiologist suffering from leukemia induced by excessive exposure to the radiation with which he had worked because he felt it improper to protect himself while other Japanese were risking themselves on the battlefield.

Still a different set of circumstances results when certain elective procedures, usually surgical, are requested. These are cosmetic or mutilating operations, and although they are eagerly sought by the

patient for some specific gain, there is nonetheless a burden of disclosure of possible detrimental results placed on the surgeon. Thus, an aging woman wishes to have her face lifted, a budding actress desires to have the size of her breasts increased by injection, or an anxious man who wishes a vasectomy to assure his becoming sterile. Even these simple and eagerly sought procedures have their risks which should be fully explained. For example, vasectomy has long been thought to be a safe and effective means of male sterilization, but Marshall and Lyons (6) have reported cases of sperm reappearance in the ejaculate some weeks (2 to 17) after vasectomy, and spontaneous recanalization (7) of the vas is a possibility. Effective vasectomy itself is reported to have a three percent psychosexual casualty rate (8), and much higher rates of psychological complications have been reported (9).

Even the simplest of medical procedures carry potential of harm. I have estimated a rate of occurrence of serious human error which seems to run around one in 15,000 for almost any medical procedure whether it be as simple as a blood transfusion or as complex as a prolonged general anesthesia.

Rarely is informed consent considered of moment in abortion, as the act is usually eagerly sought by the pregnant woman and often all too eagerly afforded by the abortionist, whether motivated by principle or greed. The inevitable risks and the contraindications tend to be glossed over. Major segments of society, oriented toward control of population growth or women's liberation emphasize the advantages of abortion and do not point out the possible untoward complications. As the pregnancy progresses, the more serious the risks of intervention

because (10). Likewise, the longer the pregnancy the greater is the investment of the maternal organism in the developing embryo and the greater is its potential value. While the risk of a properly performed early abortion is slight it is nonetheless real, and it is essential that the risks should be properly presented. Perhaps the most difficult cases involving informed consent for abortion are those in which there is fear that the fetus has been damaged and may develop into a seriously-deformed child, as, for example, the result of intrauterine exposure to rubella infection or to a large dose (100 rads or over) of ionizing radiation. Here the chances of the birth of a badly damaged infant must be discussed with the parents. Stewart (11, 12) has presented evidence, suggestive but not conclusive, although supported by some other studies (13), that intrauterine exposure to doses of radiation received by the fetus in the course of diagnostic x-radiation of the mother may lead to an increased likelihood of leukemia and other tumors in the child as it develops. However, even if proved correct, the risk is still slight, in the range of one in 25,000 (11).

Those horrified by exposure of an ovum or conceptus to slight doses of ionizing radiation should remember that not too many years ago Kaplan (14) made some women fertile who had previously been sterile by mild x-ray treatment of their ovaries without bad effects on the resulting children, a technique now generally regarded as unacceptable because of the risk of harm to the remaining ova.

The advances of cytogenetics are permitting sharper judgments as to the need for abortion in certain inherited diseases, as, for example,

the recognition of fetuses doomed to Tay-Sachs disease through biopsy of the amniotic membrane.

The majority of infants born of women exposed while pregnant to atomic bomb radiation at Hiroshima and Nagasaki showed no detectible harm (15), although some instances of microcephaly were encountered in those more heavily irradiated. Also, the first generation born to parents exposed there to atomic irradiation showed no increase in inherited abnormalities (16). The second generation is now being studied.

In considering this question of informed consent, one is led to weigh the complex and apparently changing attitudes of our society toward another potential burden of the medical profession, euthanasia. This act, though now generally abhorred, has been commonplace in many societies less affluent than ours where the survival of the family or tribe was threatened by the societal burden of the unfit. You may recall the grim humor in the Indian story of three men and a basket. After famine had gripped a village for some time the father began to rummage among the rafters, and his son asked him what he was looking for. He replied, "I am looking for the basket to take your grandfather to the river to drown him." "All right," the son replied, "but be sure to bring the basket back." In these instances the old or hopelessly ill or injured individuals were aware of the social customs and exigencies and accepted death docilely with implied consent, or even as in the case of old Eskimos walked out alone into the polar cold.

Under the influence of Judeo-Christian and Buddhist ethics, society has frowned on euthanasia and instead has tended to venerate age,

though this latter custom has been abrogated by much of today's youth. In the days before printing, photography and electronic communication, the elders were the main repository of knowledge, and hence the chief source of advice (witness Nestor in the Trojan War), experience and tradition. The aged are no longer necessary for this function in our modern society.

Our present American society has varying views on death as evidenced by a symposium on "The Power to Die" in the current ROTARIAN magazine (17) diversely considered by Toynbee, Bradbury, Vonnegut and Mitford, each a spokesman for quite different segments of the population.

Our emotions are aroused by the pathetic plight of those individuals mechanically or chemically sustained merely to give electronic recordings of heart beat or respiration. For such euthanasia has much to offer.

Frequently, the putative beneficiary of euthanasia is incompetent or comatose. Here the question of informed consent can enter into the picture only as to relatives whose interest may not be neutral. Consequently, if the procedure is to be condoned, some other guidelines for its application must be available (18). The key may lie in the motivation of the act: euthanasia for the convenience of relatives or society as a whole is murder, witness the almost universal execration of the Nazis for their slaughter of the mentally ill (2); euthanasia for the benefit of the hopeless moribund individual, particularly if maintained "alive" by artificial means, is accepted by many. As Morison (19) points out, death is often not easily definable but tends to blur into a continuum with life during some stages of senescence (20).

Thus far, the best rule to follow is that the hopelessly ill, suffering or moribund patient need not be kept alive by active intervention solely because a flicker of heart beat or of brain waves can be traced but rather that reasonable and ordinary means of treatment suffice (21).

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