Human Experimentation: New York Verdict Affirms Patient's Rights

New York, N.Y. Two years ago this month, New York City's yellow and not-so-yellow journalists had a feast with the disclosure that, as part of a research project, live cancer cells were being injected into hospitalized patients under circumstances in which the nature of their consent to the proceedings was exceedingly ambiguous (*Science*, 7 February 1964). A number of circumstances made the case particularly newsworthy. The patients in question were 22 seriously ailing and debilitated inhabitants of a relatively obscure Brooklyn institution, the Jewish Chronic Disease Hospital (JCDH). The research in question, studies in cancer immunology, was generally rated within the scientific community as among the most significant of all lines of research on malignant diseases. And both the researcher in question, Chester Southam, and his institution, Sloan-Kettering, held unassailable positions in the forefront of American medical science.

After considerable time the sensational charges and accusations of "Nazi tactics" disappeared from the headlines, although an article on the case, entitled "How doctors use patients as guinea pigs," appeared in a national women's magazine as recently as last fall. But in the labyrinths of New York State's administrative machinery, under the direction of a unit of the department of education known as the Division of Professional Conduct, the case was being subjected to intensive review. Last month the Regents of the University of the State of New York, acting under their responsibility for licensing the medical profession, issued their verdict.* Southam and Emanuel Mandel, medical director of the Chronic Disease Hospital, were found guilty of "unprofessional conduct" and of "fraud and deceit in the practice of medicine." Their licenses were suspended for 1 year, although execution of the sentences has been stayed. The men will be on probation, but allowed to practice.

In the course of their review, the Regents and the medical grievance committee which advised them explored many questions of serious importance to the entire medical research community. On two key questions—when is consent "informed," and how far may the physician exercise his physician's authority when he is acting in the role of experimenter—the Regents have developed definitions which, while not legal precedents (except perhaps in New York), represent a major attempt to put some precision into the vague ethical concepts now governing experimentation with human subjects.

Some of the arguments raised by the defense lawyers are also important, for they suggest that Southam and Mandel were stumbling through a signless desert and that, if they lost their way, they did no more than other researchers have done before them or than, in the absence of clearer standards, researchers will continue to do after them.

Finally, the fact of the proceedings is in itself significant, confirming what the large-scale publicity itself hinted—that the question of medical experimentation is already outside the house of science. The Regents' decision is an affirmation that there is a public interest to be protected in the field of medical research; it is an omen that the public may begin to set the rules. (The body of the Regents' decision is given on pages 664–665.)

The nondisputed facts in the case are these: Southam's work involved the injection of tissue-cultured cancer cells into human subjects and measurement of the speed with which the injected substance was rejected by the body. Earlier phases of the work had established that healthy persons would reject the tissue culture in 4 to 6 weeks, and that individuals already ill with advanced cancer would reject them in a longer period, ranging from 6 weeks to several months. To test the hypothesis that the slower rate of rejection in the cancer patients was in fact attributable to their cancer and not to the general debility that accompanies any chronic illness, it was necessary to perform the experiment on patients severely ill with nonmalignant diseases. A chronic-disease hospital was a logical place to look for patients with the required characteristics. Southam approached Mandel, who agreed to the collaboration, and, in July 1963, 22 patients (including three cancer patients used as controls) were subjected to the experiment. The patients were asked by Mandel, Southam, and their assistants if they would consent to an injection which was described as a test to discover their resistance or immunity to disease. They were told that a lump would form, and that in a few weeks it would go away. They were not told in plain language that the procedure was a research project unrelated to medical treatment of their own condition. And they were not told that the substance to be injected consisted of live cancer cells. The record indicates that all the patients approached agreed to the injection and, further, that none suffered any ill effects other than the transient discomfort of the injection and the nodule it produced.

Motivations

Both men had reasons for acting as they did. Their thinking is extensively set out in the records of the administrative hearings, and their views were restated in interviews with *Science* last week.

Southam's practices, developed in the earlier experimentation on cancer patients at Memorial and James Ewing hospitals in New York, rested on the conviction that the procedure involved no risk of transplanting cancer to the experimental subjects. "I saw no reason why we should use [the word *cancer*] because it is not pertinent to the phenomenon which is going to follow," he told the hearing board. "We are not doing something which is going to induce cancer. We are not going to do something which is going to cause them any harm. . . . We are going to observe the growth and rejection of these transplanted cancer cells. The fact then that they are cancer cells does not mean that there is any risk of cancer to this patient." In addition, Southam believes that the word *cancer* "has a tremendous

* The Board of Regents consists of 15 individuals elected by joint resolution of the two houses of New York's legislature for terms of 15 years. The Regents have jurisdiction over all education in the state, public and private, and over all licensed professions excluding the law. The three Regents most intimately involved in this decision were the three members of a special committee on discipline: Joseph W. McGovern, a lawyer; Joseph T. King, a lawyer; and Carl H. Pforzheimer, Jr., an investment banker. The remaining Regents, who concurred in the decision, are drawn from a variety of business and professional interests, including law, banking, education, and philanthropy.

Human Experimentation—The Regent's Decision:

We are of the opinion that there are certain basic ethical standards concerning consent to human experimentation which were involved in this experiment and which were violated by the respondents. When a patient engages a physician or enters a hospital he may reasonably be deemed to have consented to such treatment as his physician or the hospital staff, in the exercise of their professional judgment, deem proper. Consent to normal diagnostic tests might similarly be presumed. Even so, doctors and hospitals as a matter of routine obtain formal written consents before surgery, and in a number of other instances, and whether or not a specific consent is required for a specific act must be decided on the facts of the particular case.

No one contends that these 22 patients, by merely being in the hospital, had volunteered their bodies for any purpose other than treatment of their condition. These injections were made as a part of a cancer research project. The incidental and remote possibility, urged by Dr. Mandel, that the research might have been beneficial to a patient is clearly insufficient to bring these injections within the area of procedures for which a consent could be implied. Actual consent was required.

What form such an actual consent must take is a matter of applying common sense to the particular facts of the case. No consent is valid unless it is made by a person with legal and mental capacity to make it, and is based on a disclosure of all material facts. Any fact which might influence the giving or withholding of consent is material. A patient has the right to know he is being asked to volunteer and to refuse to participate in an experiment for any reason, intelligent or otherwise, well-informed or prejudiced. A physician has no right to withhold from a prospective volunteer any fact which he knows may influence the decision. It is the volunteer's decision to make, and the physician may not take it away from him by the manner in which he asks the question or explains or fails to explain the circumstances. There is evidenced in the record in this proceeding an attitude on the part of some physicians that they can go ahead and do anything which they conclude is good for the patient, or which is of benefit experimentally or educationally and is not harmful to the patient, and that the patient's consent is an empty formality. With this we cannot agree.

In his testimony . . . Dr. Mandel took the position that he regards these experiments as beneficial to the patients both because the experiment might result in a diagnosis of an advanced cancer which had not been discovered by the hospital, and also because the participation in the experiment would result in extra medical attention to the patients involved and possibly other patients in the hospital.

The record indicates that the only additional medical care any of these patients received as a result of this experiment was that the injections were made and they were occasionally checked thereafter as to the progress of the growth and disappearance of the nodule. The inference that participation in the experiment benefited the patients because of such additional medical care is without foundation in the record. Since the purpose of the experiment was to obtain verification of Dr. Southam's hypothesis that diseased patients would reject the implant in the same manner as healthy patients and that their rejection would not be delayed as was that of patients suffering from an advanced cancer, it is somewhat inconsistent for Dr. Mandel to say before the experiment was completed that he authorized it as a diagnostic measure. In any event, it was clearly not treatment, not experimental ther-

emotive value, disvalue, to everybody. . . . What the ordinary patient, what the nonmedical person, and even many doctors . . . whose knowledge of the basic science behind transplantation is not great—to them the use of a cancer cell might imply a risk that it will grow and produce cancer, and the fear that this word strikes in people is very great." The suggestion was raised in the hearing that, having recognized the emotional impact of the word *cancer*, the doctors avoided it through fear that its use would discourage consent and thus hinder the research. But Southam sees his action as an act of professional judgment and solicitude, based on an unwillingness to scare or arouse the patients when such fright was not in fact relevant to the objective situation. And he believes that his formula gave the patients all the information they needed to make an intelligent decision about participation.

On the basic question of the type of explanation to be given to the patients, Mandel followed, and endorsed, the practice described to him by Southam. But many factors influenced Mandel's agreement to the project. A relative newcomer to the Chronic Disease Hospital, he was alarmed by what seemed to him disastrously insufficient medical attention to the long-term, chronically ill patients. "I could tell you stories which would curdle your blood," he told *Science* last week, and he did. The experiment involved a number of visits to the patients by the JCDH resident working with Southam to check on the development and regression of the nodules, and Mandel believed that the added attention would improve their care. He saw some hope of using the injections as a diagnostic device, to discover undetected cancer in patients hospitalized for other illnesses. And he looked forward to the possibility of a more prolonged collaboration with the Sloan-Kettering, which would contribute to upgrading his own institution.

Within the hospital, Mandel's decision to permit the experiment to proceed became the focus of an intense disagreement which led to a battle with one of the hospital's directors over the confidentiality of patients' records and to the resignation of several staff physicians. The bad feeling between Mandel and the physicians, whether it preceded the Sloan-Kettering issue, as Mandel contends, or was the result of it, as the physicians imply, seriously impeded the efforts of the examining committees to evaluate one of the ugliest charges in the case—that the patients used were in such a debilitated physical and mental state that they were incapable of giving informed consent. Almost every patient became the subject of conflicting testimony from the opposing sides. In his report to the Regents, a physician mem-

"Some Physicians Believe . . . the Patient's Consent Is an Empty Formality"

apy, and not a diagnostic test which would reasonably be given to these particular patients. Nevertheless, from the manner in which they were asked for their consent and from the statement made to them that this was a test to determine their immunity or resistance to disease, the patients could naturally assume that it was being given to help in the diagnosis or treatment of their condition. They were not clearly and unequivocally asked if they wanted to volunteer to participate in an extraneous research project.

There is one point which is undisputed, namely, that the patients were not told that the cells to be injected were live cancer cells. From the respondents' standpoint this was not considered to be an important fact. They regarded the experiment as medically harmless. There was not appreciable danger of any harmful effects to the patients as a result of the injection of these cancer cells. It is not uncommon for a doctor to refrain from telling his patient that he had cancer where the physician in his professional judgment concludes that such a disclosure would be harmful to the patient. The respondents testified that they felt that telling these patients that the material did consist of live cancer cells would upset them and was immaterial to their consent. They overlooked the key fact that so far as this particular experiment was concerned, there was not the usual doctor-patient relationship and, therefore, no basis for the exercise of their usual professional judgment applicable to patient care. No person can be said to have volunteered for an experiment unless he has first understood what he was volunteering for. Any matter which might influence him in giving or withholding his consent is material. Deliberate nondisclosure of the material fact is no different from deliberate misrepresentation of such a fact. The respondents maintain that they did not withhold the fact that these were cancer cells because they thought that some of the patients might have refused to consent to the injection of live cancer cells into their bodies. This was, however, a possibility and a decision that had to be made by the patients and not for them. Accordingly, the alleged oral consents that they obtained after deliberately withholding this information were not informed consents and were, for this reason, fraudulently obtained.

Although there is conflicting testimony and evidence in this point, it is our opinion that some of these patients were in such a physical and mental condition that they were incapable of understanding the nature of this experiment or of giving an informed consent thereto. . . . We note that in no case were any relatives of any of these patients told about the experiment nor were any of these patients asked if they wished to think the matter over or discuss it with their relatives. It is noteworthy that one of these same patients was operated on two days after the injections and that prior to making the operation, which was a part of the patient's treatment, the hospital obtained two separate written consents each signed by both the patient and a relative. If there was any doubt at all concerning a patient's ability to fully comprehend and consent to this experiment, it was the duty of the physicians involved to resolve that doubt before proceeding further. . . . We do not say that it is necessary in all cases of human experimentation to obtain consents from relatives or to obtain written consents, but certainly upon the fact of this case and in view of the fact that the patients were debilitated, the performance of this experiment on the basis of alleged oral consents from these particular patients falls short of the ethical standards of the medical profession.

ber of the medical grievance committee which conducted the bulk of the hearings summarized descriptions of patients that had been supplied by the physicians who resigned. Patient No. 26 is fairly typical: "Suffering from advanced Paget's disease, with overgrowth of bone, pressing on the brain. This patient was suffering from severe deafness, blindness, mental condition." Another patient was described as suffering from "Parkinson's disease, lung abscess, was running and falling, speech was unintelligible." A chart stated that the patient "was misunderstood by the orderly, drools, and tries to avoid speech." Another patient, a 75-year-old man described as senile, was diagnosed as "impaired mentally, with easy crying and laughing, tendency to repeat the same sentence several times. Also it is difficult to obtain the patient's attention." In all these cases, Mandel and the resident, supported by Southam, testified basically that, if you knew the patients (as the resident did), it was possible to communicate adequately with them and that they had an alert appreciation of what was going on.

Although the Regents were unable to come to a definitive conclusion about the alertness of all the patients, they did find that at least "some . . . were incapable of understanding the nature of this experiment or of giving informed consent thereto." While agreeing with Southam's contention that he was not responsible for the internal practices of the Chronic Disease Hospital, the Regents argued that he had a clear responsibility nonetheless: "As a physician in charge of the experiment, it was his duty to pay enough attention to what was going on to make sure that he was dealing with persons capable of being volunteers and sufficiently informed to consent to the use of their bodies for the experiment and not merely with people who were too confused or too sick or too resigned to object to the injection." Southam believes, the Regents continued, that "it is important to make it clear to the patients that what is being done is an experiment and is not for the treatment or diagnosis of their own condition, yet he was present, this was not adequately done, and he did not complain. A physician may not shirk his ethical responsibility or violate basic human rights so easily." As for Mandel, the Regents concluded that although he had, legitimately, delegated responsibility for the actual conduct of the experiment to a resident, he was nonetheless "directly responsible for the determination of the procedure followed" in the selection of patients and the explanations he permitted them to be offered. In addition to the substantive arguments, lawyers for Mandel and Southam raised two technical points of some in-

terest. First, they claimed that, because "no clear-cut medical or professional standards were in force or were violated" by the two physicians, the attempt to find them guilty had an ex post facto quality. They also argued that the charges did not accurately fit the case. Testimony was introduced from well-known cancer and other professional researchers, including I. S. Ravdin, vice president for medical affairs of the University of Pennsylvania, and George E. Moore, director of Roswell Park Memorial Institute, to the effect that Southam's practices did not differ dramatically from those of other researchers. "If the whole profession is doing it," one of the lawyers remarked in an interview, "how can you call it 'unprofessional conduct' "? The lawyers also argued that the "fraud and deceit" charge was more appropriate to low-brow scoundrels, such as physicians who cheat on insurance, supply illegal narcotics, or practice medicine without a license, than to their respectable and well-intentioned clients.

Voice of the Public

To all arguments of humane motivations, extenuating circumstance, conflicting testimony, or legal ambiguities, the final answer of the Regents was very simple: It is no excuse. There was never any disagreement on the principle that patients should not be used in experiments unrelated to treatment unless they have given informed consent. But in the Regents' decision, two refinements of that principle are heavily stressed. The first is that it is the patient, and not the physician, who has the right to decide what factors are or are not relevant to his consent, regardless of the rationality of his assessment. "Any fact which might influence the giving or witholding of consent is material," the Regents said. "A patient has the right to know he is being asked to volunteer and to refuse to participate in an experiment for any reason, intelligent or otherwise, well-informed or prejudiced. A physician has no right to withhold from a prospective volunteer any fact which he knows may influence the decision. It is the volunteer's decision to make, and the physician may not take it away from him by the manner in which he asks the question or explains or fails to explain the circumstances. There is evidenced in the record . . . an attitude on the part of some physicians that they can go ahead and do anything which they conclude is good for the patient, or which is of benefit experimentally or educationally and is not harmful to the patient, and that the patient's consent is an empty formality. With this we cannot agree."

The second principle stressed by the Regents is that the physician, when he is acting as experimenter, has no claim to the doctor-patient relationship that, in a therapeutic situation, would give him the generally acknowledged right to withold information if he judged it in the best interest of the patient. In the absence of a doctor-patient relationship, the Regents said, "there is no basis for the exercise of their usual professional judgement applicable to patient care." Southam, in an interview, disagreed. "An experimental relation has some elements of a therapeutic relationship," he said last week. "The patients still think of you as a doctor, and I react to them as a doctor, and want to avoid frightening them unnecessarily." Mandel takes a similar position. In a letter to the editor of a medical affairs newspaper he stated: "In accordance with the age-old motto—primum non nocere—it would seem that consideration of the patient's well-being may, at times, supersede the requirement for disclosure of facts if such facts lack pertinence and may cause psychologic harm." But on this point, the Regents are clear: "No person can be said to have volunteered for an experiment unless he had first understood what he was volunteering for. Any matter which might influence him in giving or withholding his consent is material. Deliberate nondisclosure of the material fact is no different from deliberate misrepresentation of such a fact."

In closing their case, and acknowledging that the penalties imposed were severe—they might have just authorized a censure and reprimand—the Regents were pointed and succinct: "We trust that this measure of discipline will serve as a stern warning that zeal for research must not be carried to the point where it violates the basic rights and immunities of a human person."

What the impact of the case will be is by no means clear. The Regents' decision outlines clear rules for a very narrow situation and attempts to set out some broad principles as well. But it is by no means binding, and it by no means covers the variety of situations with which researchers seeking to use human subjects are faced. The question is, What will cover these situations? Codes and declarations, of which there are already several, are too general to offer specific guidance. Researchers and patients alike are too vulnerable to await a slow case-by-case accretion of specific rulings. One alternative is the development within each hospital or research institution of "ethical review committees" that could define the consent-and-disclosure requirements for each proposed experiment and see that they were adhered to. In theory, this is already taking place. During the Southam-Mandel hearings, the state attempted to prove that Southam, a recipient of an NIH grant, had violated regulations of the Public Health Service. In fact, the regulations in question govern only the normal volunteer program of the NIH Clinical Center in Bethesda. The PHS response to an inquiry from New York's Attorney General made clear that the rules were not generally applicable and stated that, "in supporting extramural clinical investigations, it is the position of the Public Health Service that proper ethical and moral standards are more effectively safeguarded by the processes of review and criticism by an investigator's peers than by regulation."

That is the theory, but the trouble is, it is not yet being done. And, given the tremendous growth and variety of medical research involving human beings, if it is not done by the scientific community, someone else will start to do it. The New York Regents may be only the beginning.—ELINOR LANGER

Manpower: Output of Scientists and Engineers May Exceed Goals Set by White House Committee

Supply-and-demand studies about manpower in science and engineering involve many imponderables and uncertainties, but current forecasts for the production of well-trained people in these fields are encouraging to those who have feared shortages. Indeed, the outlook is remarkably good in view of the concern that was being expressed a few years ago.

In January 1962 the late President Kennedy spoke of the "inadequacy" of the supply of scientists and engineers and asked his Science Advisory Committee (PSAC) to review the problem and report on possible remedial action. The PSAC panel which undertook the study, one chaired by Edwin R. Gilliland, professor of chemical engineering at M.I.T., focused its attention on the need for more productive graduate programs in three areas—engineering,