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A social problem is defined in part by he concern it arouses, and this one has clearly aroused concern. Members of the medical profession itself led the way, with increasing numbers of journal articles, books and seminars on the issues. The public has become aroused, largely through popular accounts of dramatic incidents—genuine scandals in certain cases—involving the violation of the dignity and rights of patients. And the Federal Government has moved to protect human subjects, potential or actual. Beginning in 1966 the National Institutes of Health, the Food and Drug Administration and the Department of Health, Education, and Welfare have issued increasingly detailed regulations governing experimentation with human subjects in projects they support, which means in most of the biomedical research done in the country. In 1974 a National Commission for the Protection of Human Subjects of

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Biomedical and Behavioral Research was established to advise the Department of Health, Education, and Welfare, and it is to be replaced by a long-term National Advisory Council that is to deal with the same issues.

The regulations, commissions and councils and the very fact of interference in medical activities by outsiders are viewed by many investigators as being onerous and even dangerous. On the other hand, many outsiders believe far more social control is required. The debate on the issue has been conducted without much reference to objective evidence. In 1970 our Research Group on Human Experimentation undertook two studies of investigators' attitudes and practices. On the basis of our results I would argue that there is indeed inadequate ethical concern among biomedical investigators, that it is reflected in excessively risky procedures and that better internal and external controls are essential.

There are two major reasons for the general recognition that experimentation with humans is a subject for concern, one of which I alluded to at the outset: the increased power, scope and funding of biomedical research. The other reason is a change in values: increased emphasis on equality, participation and the challenging of arbitrary authority.

It is easy to forget how new scientific medicine is. The revolutionary advances based on knowledge of physiology and biochemistry have come in the past 40 years, and they came from research. The basic work could be done with test-tube preparations and laboratory animals, but eventually human subjects had to be involved. Man is "the final test site," as Henry K. Beecher, a pioneer among physicians concerned about the ethics of research, once put it. Unfortunately there are no statistics on the number of people who are subjects in medical experiments or even on how many projects involve human subjects; the National Institutes of Health keeps records according to area of research (a disease or a physiological process, for example) rather than according to species of experimental subject; the NIH can say only that recently about a third of the projects it approves involve human subjects. It is clear, however, that the number of human subjects is larger than it used to be and that

some small but significant minority of those subjects are involved in risky experiments. If more people have been put at more risk, then there is a rational basis for concern about the satisfactory balancing of risks and benefits, about adequate protection from unnecessary risk and about some groups being put at more risk than other groups.

Over and beyond this utilitarian basis for the new social concern with medical experimentation is the value factor, which arises from recent social changes. All over the world individuals have been demanding more equality of treatment and the right to be informed about and to participate in decisions affecting them and have been challenging the right of experts to make those decisions unilaterally. People who define themselves as being unequal, underprivileged or exploited are demanding better treatment and better protection, whether it is underdeveloped countries as against developed ones, blacks as against white, women as against men, young as against old, patients as against doctors—or subjects as against investigators. This moral revolution of rising value-expectations has combined with the revolution in medicine to focus attention on the ethics of experimentation with human subjects.

Public awareness of the problem is too much the result of headlined scandals, but the scandals do illustrate some of the possible abuses. In the 1960s two respected cancer investigators who were studying the immune response to malignancies injected live cancer cells into a number of geriatric patients at the Jewish Hospital and Medical Center of Brooklyn without first obtaining the patients' informed consent. A few years later a leading virologist conducted an experiment at Willowbrook, a New York State institution for the severely retarded. Reasoning that a serious liver infection, hepatitis, was in effect endemic in the hospital anyway, he deliberately exposed some children to hepatitis virus in an attempt to achieve controlled conditions for testing a vaccine. The accusation was that the children's parents were not given enough information on which to base informed consent, and that in some cases consent was given perfunctorily by administrators of the institution.

More recently there was the exposure by the press of the ongoing syphilis experiment in Tuskegee, Ala. Since the 1930s a group of black subjects with syphilis had been kept under observation in an effort to study the course of the disease. That was not considered wrong in the 1930s, when the known treatments for the disease were only marginally effective, but by 1945 penicillin had become available as a safe and extremely effective cure for syphilis. Yet somehow the experiment was continued, and presumably some men died of the disease who could have been cured.

How significant are such scandals? We do not know, because no one has been doing the kind of social bookkeeping about numbers of subjects, degree of risk, adequacy of consent and efficacy of protective mechanisms that would yield an overall view of experimentation with human beings and that might contradict the more extreme allegations of abuse elicited by the publicized scandals. In the absence of such intensive record keeping it remains for social research to fill the gap by sampling the total range of experimentation with human subjects. To that end our group conducted first a national mail survey of nearly 300 biomedical research institutions and then an intensive interview study of 350 individual investigators at two institutions.

Our national survey questionnaire was answered by 293 teaching and nonteaching hospitals and other research institutions that, our analysis showed, constituted a nationally representative sample of all such institutions. Those who filled out the questionnaire were generally themselves active researchers and members of their institution's review committee, set up to pass on research proposals. We asked the investigators to give us their response to six simulated proposals such as those that might come before a review committee. The proposals were detailed research protocols designed to measure the degree of the investigators' concern about informed consent and their willingness to approve of studies involving various levels of risk. We could be confident that the protocols were "hypothetical-actual" rather than "hypothetical-fantastic" because we constructed them with careful attention to the research literature, checked them

45. A researcher plans to study bone metabolism in children suffering from a serious bone disease. He intends to determine the degree of appropriation of calcium into the bone by using radioactive calcium. In order to make an adequate comparison, he intends to use some healthy children as controls, and he plans to obtain the consent of the parents of both groups of children after explaining to them the nature and purposes of the investigation and the short and long-term risks to their children. Evidence from animals and earlier studies in humans indicates that the size of the radioactive dose to be administered here would only very slightly (say, by 5-10 chances in a million) increase the probability of the subjects involved contracting leukemia or experiencing other problems in the long run. While there are no definitive data as yet on the incidence of leukemia in children, a number of doctors and statistical sources indicate that the rate is about 250/million in persons under 18 years of age. Assume for the purpose of this question that the incidence of the bone disease being discussed is about the same as that for leukemia in children under 18 years of age. The investigation, if successful, would add greatly to medical knowledge regarding this particular bone disease, but the administration of the radioactive calcium would not be of immediate therapeutic benefit for either group of children. The results of the investigation may, however, eventually benefit the group of children suffering from the bone disease. Please assume for the purposes of this question that there is no other method that would produce the data the researcher desires. The researcher is known to be highly competent in this area.

45A. Hypothetically assuming that you constitute an institutional review "committee of one," and that the proposed investigation has never been done before, please check the lowest probability that you would consider acceptable for your approval of the proposed investigation. (Check only one)

( ) 1. If the chances are 1 in 10 that the investigation will lead to an important medical discovery.

( ) 2. If the chances are 3 in 10 that the investigation will lead to an important medical discovery.

( ) 3. If the chances are 5 in 10 that the investigation will lead to an important medical discovery.

( ) 4. If the chances are 7 in 10 that the investigation will lead to an important medical discovery.

( ) 5. If the chances are 9 in 10 that the investigation will lead to an important medical discovery.

( ) 6. Place a check here if you feel that, as the proposal stands, the researcher should not attempt the investigation, no matter what the probability that an important medical discovery will result. (IF YOU CHECKED HERE, please explain): _____

45B. Which of the above responses comes closest to what you feel the existing institutional review committee in your institution would make? ____ (Please write in the number of the response.)

45C. Which of the above responses comes closest to what you feel the majority of the researchers in your institution would make, acting in their role as researcher rather than as a "committee of one"? ____ (Please write in the number of the response.)

HYPOTHETICAL EXPERIMENT described here was one of six experiments submitted to investigators and administrators in hospitals and other research centers in a mailed questionnaire. In each case respondents were asked whether, under specified conditions, they would approve of the experiment. This proposal involved giving radioactive calcium to children with a bone disease and to a control group and measuring its uptake by bone.

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with specialists and pretested them with a dozen chiefs of research at medical centers, who found them to be convincingly real.

44. It has been shown that the thymus has an important bearing on the development and maintenance of immunity. For this reason the researcher proposes an investigation to determine the effect of thymus removal on the survival of tissue transplants, a very timely and important problem. In a sample of children and adolescents admitted for surgery to correct congenital heart lesions, he would randomly select an experimental group for thymectomy. Though the thymectomy will prolong the heart surgery by a few minutes, there is otherwise extremely little additional surgical risk from this procedure. At the conclusion of each heart operation, a full-thickness skin graft, approximately one cm. in diameter and obtained from an unrelated adult donor, would be sutured in place on the chest wall of both the experimental and control groups. He would then compare the survival of the skin grafts in each of the groups. It has been shown in a number of investigations of neonatal rats and other animals that those whose thymus had been removed were much less likely to reject skin grafts. The possible long-term immunological problems that might result are as yet not completely known, but a number of studies in animals indicate significant immunological deficiencies after thymectomy. Studies done in humans with myasthenia gravis, some of whom had undergone thymectomy, have not definitively demonstrated that the immunological abnormalities discovered in these patients were the result of thymectomies. To quote one authority: "There were no immunologic abnormalities that could be attributed to the effect of thymectomy per se."

The research will result in no therapeutic benefits for the patients involved. The researcher plans to obtain the consent of his potential patient-volunteers and/or their parents after explaining the procedures involved in the investigation as well as the possible short-term surgical and long-term immunological hazards for the subjects.

REMOVAL OF THYMUS GLAND during heart surgery was the experimental procedure proposed in another protocol in the questionnaire. Respondents were asked if they would approve of the experiment, given various probabilities that it would show thymectomy "considerably increases the probability of tissue-transplant survival in children and adolescents."

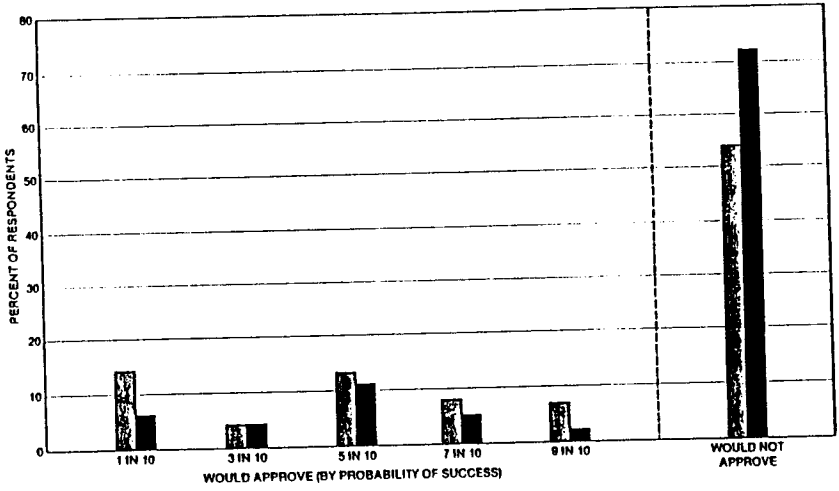
One protocol described a study of chromosome breakage in users of hallucinogenic drugs; blood samples (for chromosomes) and urine samples (for evidence of drug use) were to be taken, at no risk but also without notification of the experimental purpose, from students routinely visiting the university health center. Another protocol proposed that the thymus gland, which is a component of the immune system, be removed unnecessarily from a random sample of children undergoing heart surgery; the objective was to learn the effect of the thymectomy on the survival of an experimental skin graft made at the same time. The other protocols dealt with a random test of alternative treatments for a congenital heart defect in children; with an evaluation of the efficacy of a new drug for severe depression (placebos were given to some patients); with a study of lung function in patients kept under unnecessarily prolonged anesthesia after undergoing a routine hernia repair, and with an investigation of the effect of radioactive calcium on bone metabolism in children [*see illustrations on these two pages*].

The answers to the thymectomy, anesthesia and radioactive-calcium protocols in particular gave us measures of the respondents' attitudes toward the balancing of risks and benefits. A clear pattern emerged. In the case of the high risk thymectomy, for example, 72 percent of the respondents said the project should not be approved no matter how high the probability was that it would establish the efficacy of thymectomy in promoting transplant survival. On the other hand, 28 percent of the respondents said they would approve the experiment; 6 percent said they would approve it even if the chance of significant results was no better than one in 19 [*see illustration on page*]. Similarly, 54 percent were against doing the calcium study at all—but 14 percent said they would approve it even if the odds were only one in 10 that it would lead to an important medical discovery. Our basic finding was that whereas the majority of the investigators were what we called "strict" with regard to balancing risks against benefits, a significant minority were "permissive," that is, they were much willing to accept an unsatisfactory risk-benefit ratio.

The same general pattern of a strict majority and a permissive minority emerged from our second study, in which we interviewed 350 investigators actively engaged in research with human subjects. The investigators were at institutions to which we gave the synthetic names University Hospital and Research Center and Community and Teaching Hospital. the institutions were picked (by a technique known as cluster analysis) as being representative of two kinds of medical center that do considerable amounts of research. The interviewees told us about 424 different studies involving human subjects, and for each study they estimated the risk for subjects, the potential benefit for subjects, the potential benefit for future patients and the potential scientific importance of the study. It was reassuring to find that the investigators considered that only 56 percent of the clinical investigations graded for risk and benefits involved any risk for the subjects. We went on, however, to cross-tabulate the estimated risks and benefits [*see illustration on opposite page*], and we concluded that in 18 percent of the studies the risk was not adequately counterbalanced by the benefits. We called those studies the "less favorable" ones, and we proceeded to classify them further according to their potential benefits for other patients or for medical science. Even when these compensating justifications were taken into account, tabulation revealed a "least favorable" category of studies in which the poor immediate risk-benefit ratio was not compensated for by possible future benefits. These "least favorable" investigations constituted 8 percent of the investigations in our analysis.

The concept of informed consent is a troublesome one. the investigator wants to have enough subjects and is afraid of scaring them off. Patients are likely to be concerned about their own condition, may feel powerless with respect to the physician or hospital and often have difficulty understanding medical language or concepts. Even established medical procedures can have somewhat unpredictable consequences, so that physicians feel there is a limit to how completely "informed" a patient can be. The fact remains that regulations of Government funding agencies and most institutions now require that the human subject of an experiment (or his guardian, in the case of small children and mentally incompetent patients)

understand that something is being done (or some treatment is being withheld) for reasons other than immediate therapeutic ones; the subject or guardian must be informed of any risks and must give consent voluntarily.



REACTION OF RESPONDENTS to the two hypothetical-experiment questions illustrated on the preceding two pages is shown: the calcium study (*light gray bars*) and the experimental removal of the thymus gland for a skin-transplant study (*dark gray*). "As the proposal stands," 54 percent of the respondents would refuse to approve the calcium study and 72 percent would refuse to approve the thymectomy, regardless of the probability of success. Substantial minorities were much more "permissive," however.

With regard to informed consent, our questionnaires and interviews again revealed a minority with "permissive" views and practices, although that minority was smaller than it was for unfavorable risk-benefit ratios. For example, 23 percent of the questionnaire respondents said they would approve the chromosome-break proposal, which presented the informed-consent issue clearly and in effect by itself. The situation was more complex in the heart-defect protocol. Here other dubious elements competed with the fact that the investigator would not inform the parents that his decision whether or not to operate would be a random one, not based on therapeutic considerations. Only 12 percent of our respondents said they would approve of the study without requiring any revisions, but only 65 percent specifically mentioned the lack of informed consent as a problem.

The best available research evidence on informed consent comes from a study conducted by Bradford H. Gray, who was then a graduate student at Yale University, at a distinguished university hospital and research center (not the one in our interview study). With the consent of the responsible investigator, Gray interviewed 51 women who were the subjects in a study of the effects of a new labor-inducing drug. Although the women had signed a consent form, often in the hectic course of the admitting procedure or in the labor room itself, 20 of them (39 percent) learned only from Gray's interview, which was held after the drug infusion had been started or even after the delivery, that they were the subjects of research. Among those who did know, most of them did not understand at least one aspect of the study: that there might be hazards, that it was a double-blind experiment, that they would be subjected to special monitoring and test procedures or that they were not required to participate; four of the women said they would have refused to participate if they had known there was any choice. Many of the women had been referred for the study by their private physician, but instead of being informed that an experimental drug was to be administered they were told that it would be a "new" drug; they trusted their doctor and assumed that "new" meant "better."

How does it happen that the treatment of human subjects is sometimes less than ethical, even in some of the most respected university-hospital centers? We think the abuses can be traced to defects in the training of physicians and in the screening and monitoring of research by review committees, and also to a fundamental tension between investigation and therapy. We have data bearing on each of these causative factors.

THERAPEUTIC BENEFIT FOR SUBJECTS	RISK		
	NONE	VERY LITTLE	SOME, MODERATE OR LARGE
MINOR, LITTLE OR NONE	11	14	2
SOME	14	12	2
GREAT	10	19	7

RISKS AND BENEFITS were cross-tabulated for some 400 current research projects reported by investigators in two hospitals. Studies falling on or below the diagonal were considered to have risks for subjects that were more or less counterbalanced by benefits for subjects. (In 9 percent of the studies respondents reported no risk and were not asked about benefits.) Studies above the diagonal (*colored boxes*) were classified as "less favorable" for their subjects: they contained risks for subjects and, according to the investigators, offered relatively low benefits. These cases, 18 percent of the total, were further sub-divided (in a table not reproduced here) according to benefit for others or for science. Studies that were low in those justifications (8 percent of total) were called "least favorable."

It is in medical school that the profession's central and most serious concerns are presumably given time and place and that its basic knowledge and values are instilled. Yet the evidence from our interviews shows that there is not much training in research ethics in medical school. Of the more than 300 investigators who responded to questions in this area, only 13 percent reported they had been exposed in medical school to part of a course, a seminar or even a single lecture devoted to the ethical issues involved in experimentation with human subjects; only one respondent said he had taken an entire course dealing with the issues. Another 13 percent reported that the subject had come to their attention when, as students, they did practice procedures on one another; for 24 percent it was in the course of experiments with animals; 34 percent remembered discussion of ethical issues in specific research projects. One or more of these learning experiences were reported by 43 percent of the respondents—but the remaining 57 percent reported not a single such experience. The figures were about the same whether the investigators were graduates of elite U.S. medical schools, other U.S. schools or foreign schools. The figures were a little better, however, for those who had graduated since 1950 than for older investigators.

What little ethics training there is apparently not very effective: the investigators who reported having learned something about research ethics were only slightly less permissive in response to protocols presenting the risk-benefit issue than those who reported no such experiences. It would appear that both the amount and the quality of medical-school training in the ethics of research could be improved. In this connection it is worth remembering that the many physicians who are not engaged in investigation at all also need some background in experimentation ethics, if only so they can evaluate requests that they direct their patients toward a colleague's research project.

Scientific "peer review" is a keystone of scientific inquiry, operating implicitly in many ways and explicitly in the case of professional journals, grant-awarding committees and many institutional reviewing boards such as the "tissue committees" that assess the results of surgery in hospitals. Ethical peer review of

experimentation with human beings should be the counterpart of scientific peer review, but until the mid-1960s such activity received limited support among biomedical researchers. Even after 1966, when the NIH mandated ethical peer review for all its grantees, effective review did not become universal. Our questionnaire went to hospitals and other research centers that had filed with the NIH formal assurances that the required institutional review committee had been established but 10 percent of the respondents said their institution's committee reviewed only proposals for outside funds and 5 percent reported that only formal proposals to the NIH were reviewed. The two institutions in our interview study were among the 85 percent that stated they were reviewing all research proposals, and yet 8 percent of our interviewees volunteered the information that at least one of their own investigations with human subjects had not been reviewed.

How effective are the review committees in handling the protocols that do come before them? Our questionnaire respondents told us that in 34 percent of the institutions the committees had never required any revisions, rejected any proposals or had any proposals withdrawn in anticipation of rejection for ethical reasons; 31 percent reported revisions, 32 percent outright rejections and 19 percent withdrawals. Either some of these committees have very few ethical problems coming before them or they are ineffective. Gray's study in an institution with an active and strong committee suggests that they are ineffective rather than underworked. The committee whose performance he examined found relatively few proposals that did not need some kind of modification, and he thinks "a record of few actions by committees is an indication that their members are indifferent or that their standards are loose."

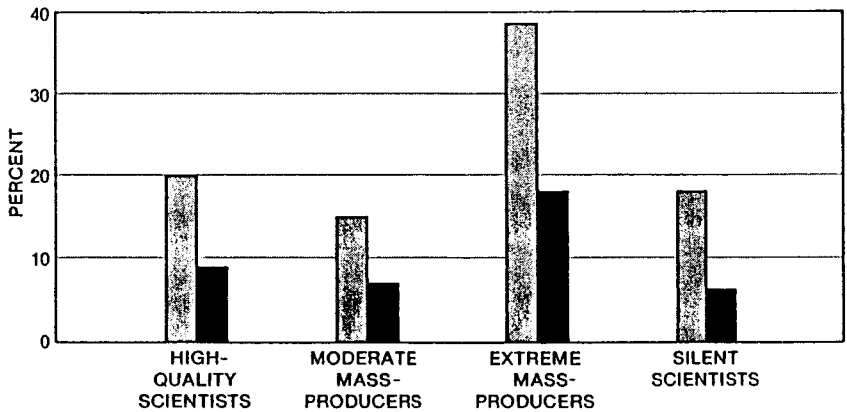
The peer-review groups seemed weak in other ways. In some institutions there was no face-to-face discussion among the reviewers. Only 22 percent of the committees had members from outside the institution, something that was then recommended and has since been mandated by the Department of Health, Education, and Welfare. In practically none of the institutions was there continuous monitoring of studies that were approved, although this was even then required by Government regulations. In general ethical peer review is hampered

by the fact that each committee operates in isolation and must consider every new issue on its own and without benefit of precedent. A case-reporting system, such as operates in the law, would make that unnecessary and would promote both equity among institutions and high standards. The major weakness in the system is the lack of keen interest in and support of the review committees on the part of most working biomedical investigators. Research is their business; research is their mission and predominant interest, not applied ethics or active advocacy of patients' rights.

Most biomedical investigators are, however, interested in taking care of patients and making them well. As a result medical institutions and individual investigators operate today with two powerful sets of values and goals. On the one hand there is the pursuit and advancement of scientific knowledge. On the other there is the provision of humane and effective therapy for patients. Through a broad range of complex interactions these two sets of values and goals are harmonious, even complementary and mutually reinforcing. Occasionally, however, scientific research and humane therapy can be in conflict. When that happens, there is sometimes a tendency to choose the pursuit of knowledge at the expense of the ethical treatment of patients. An irreducible minimum of conflict may be inevitable. The ethical task now is to come as close as possible to that minimum—and to resolve unavoidable conflict in favor of humane therapy.

There is evidence that the enhanced excitement attending scientific achievement and the rewards bestowed on it in recent decades have skewed the decision-making process in many cases of conflict. As our data show, the medical schools have been largely indifferent to training their students in the ethics of research. Moreover, their record in peer review has been inferior to that of other institutions. Answers to our questionnaire showed they were less likely than other research centers to have set up a review committee before the NIH required one, less likely to have one that met the first NIH guidelines in 1966, less likely to have a committee that reviews all clinical research and less likely to include on their committee medical or nonmedical members from outside the

institution. Medical schools, the Association of American Medical Colleges and professional associations of clinical investigators have been much quicker to seek research funds or to protest funding cuts than to organize seriously for the purpose of studying the ethics of research and main policy in that area.



PRESSURE TO PRODUCE leads to "permissiveness." Investigators were classed as "high-quality scientists" (most cited), "moderate mass-producers" (many papers, few citations), "extreme mass-producers" (many papers, no citations) or "silent scientists" (few papers and citations). Extreme mass-producers were twice as likely as high-quality scientists to have a role in one of the less favorable (*light gray*) or least favorable (*dark gray*) studies.

The same emphasis on the pursuit of knowledge rather than on ethics is apparent among individual biomedical investigators. Ethical concern for the subjects of their research is not a major factor when they select their collaborators; at least it is not often mentioned as a characteristic they look for in collaborators. Scientific ability is a major concern. when we asked our 350 interview subjects, "What three characteristics do you most want to know about another researcher before entering into a collaborative relationships with him?" 86 percent of the respondents mentioned scientific ability, 45 percent mentioned motivation to work hard and 43 percent mentioned personality. Only 6 percent of them listed anything we could classify as "ethical concern for research subjects."

The tension between investigation and ethical concern is perhaps best illustrated by indications that the struggle for scientific priority and recognition exerts pressure on ethical considerations. Our data show that the social structure of competition and reward is one of the sources of permissive behavior in experimentation with human subjects; the relatively unsuccessful scientist, striving for recognition, was most likely to be permissive both in his approval of hypothetical protocols and in his own investigative work. We divided our respondents into four categories based on the number of papers they had published and the number of times their work had been cited by other workers; the frequency of citation has been known to be a good measure of scientific excellence. We called the most-cited investigators the "high quality" scientists and those who had published a great deal but were never cited the "extreme mass-producer" scientists. It was the extreme mass-producers who were most often engaged in investigations with less favorable risk-benefit ratios, who approved of the protocols with poorer risk-benefit ratios and who least often expressed awareness of the importance of consent. Caught up in the socially structured competitive system of science, unsuccessful in it but still pursuing the prize of peer recognition, they appear to be more likely to overvalue scientific work as against humane therapy.

It is not only the mass-producers, contending for recognition among peers in their discipline, who are apt to be more permissive.

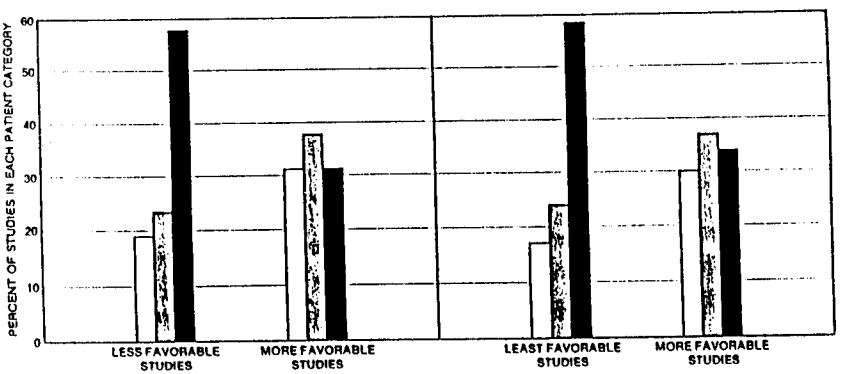
We also weighed the rank achieved by each worker within his own institution against various measures of his effectiveness compared with that of his colleagues. We found that the "underrewarded" investigators tended to be the more permissive. There is also a quite different kind of medical investigator who we think is likely to be pushed toward permissive practices by scientific competition: some of the professionally esteemed, highly successful medical scientists who are engaged in intense competition for priority and recognition in well-publicized areas of research. There are not many of those people, and they did not emerge in our sample, although some workers who refused to be interviewed may belong in that category. In the absence of real data we can only point to such evidence as published discussions concerning the worldwide heart-transplant competition of a few years ago, which raised questions about the premature exposure of human subjects to what were then stiff experimental procedures.

Given the fact that there are ethical defects in current medical-research standards and practices, do the resulting abuses strike particularly, as is often alleged, at certain social groups: at the poor, at children and at institutionalized patients (prisoners in particular?).

The evidence from our interviews with 350 investigators indicates that the poorer patients in hospitals are indeed at a disadvantage as subjects of research. For each of the 424 studies our respondents reported, they told us whether fewer than 50 percent, between 50 and 75 percent or more than 75 percent of the subjects were ward or clinic patients (as opposed to patients in private or semiprivate rooms and under the care of their own physician). We found first of all that ward and clinic patients were more likely to be subjects of experiments. Moreover, when we examined the cases we had previously identified as having "less favorable" and "least favorable" risk-benefit ratios, we found that both categories were almost twice as likely to involve subjects more than three quarters of whom were ward and clinic patients as the studies with the more favorable ratios were.

The ward and clinic patients are, of course, vulnerable to that kind of discrimination. They can most readily be channeled into an experimental group by admitting physicians and clerks without interference from a personal physician. They tend to be less

knowledgeable about hospitals, more readily intimidated and less likely to understand what they are told about an experimental project, and therefore less likely to be able to withhold their consent or to give genuinely informed consent. In sum, they are the least likely to be able to protect themselves.



DIFFERENTIAL TREATMENT of various patient categories is evident when studies identified as having the less favorable or the least favorable risk-benefit ratrios were classified according to whether fewer than 50 percent of their subjects were ward or clinic patients (*white bars*), between 50 and 75 percent were (*light gray*) or more than 75 percent were (*dark gray*). The less favorable studies were almost twice as likely to have subjects a large majority of whom were ward or clinic patients (*dark gray bars*) as the more favorable studies (*left*). About the same thing was true of studies that had been identified as having least favorable ratios (*right*).

Many institutionalized patients are poor and perhaps incompetent, and they may feel completely dependent on the institution's administrators and physicians. Prisoners are a special case: they are institutionalized in an implicitly coercive situation, so that genuinely informed consent may be a logical impossibility. On the other hand, a prison population is by definition a good source of experimental and control subjects living under controllable conditions, and there have been instances where prison studies have been conducted humanely, with good scientific results and apparently with good effect on the prisoners' morale. Experimentation with prisoners is nevertheless subject to grave abuses. Last summer the head of the Food and Drug Administration told a Senate committee that a review of experimentation in 10 prisons revealed abuses ranging from unprofessional supervision of drug tests to inadequate medical care and follow-up treatment.

Children constitute still another special group. Small children cannot give consent for their own participation in experiments; older children, who could, are often not asked. As the Willowbrook incident demonstrated, parents are not always adequately protective of their children's interests. In the case of institutionalized patients, prisoners and children, new regulations of the Department of Health, Education, and Welfare call for special protective committees and procedures. these will only be effective, however, in a context of better ethical training for investigators and more effective peer review.

The ethical problems that attend medical research with human subjects are representative of an entire class of problems created by the impact of professionals and professional power on the general public and on public policy. In the area of research with human subjects the medical investigators are not alone; there is a tendency in other fields too for humane concerns to be left at the laboratory door. Psychologists and sociologists have often been accused of circumventing the requirement for consent and of applying unethical manipulative techniques in their investigations of human behavior, and neither profession has welcomed scrutiny from outsiders or restrictive regulation. The issue goes beyond research ethics,

however. Many professions now command knowledge that has great potential usefulness for human welfare but bestows power that can be abused. Because professional power is largely based on knowledge that has not yet diffused to the general public it must to a considerable degree be self-regulated, but because professional power is of such major public consequence it must also be subject to significant public control. The medical-research profession does not have a proud record of self-regulation or acceptance of public controls.