Book Reviews

Risks and Benefits

Research on Human Subjects. Problems of Social Control in Medical Experimentation. BERNARD BARBER, JOHN J. LALLY, JULIA LOUGHLIN MAKARUSHKA, and DANIEL SULLIVAN. Russell Sage Foundation, New York, 1973. viii, 264 pp. $10.50.

Richard Titmuss has suggested the "gift transaction" as the appropriate concept for understanding such behavior as voluntary blood donation and serving as a subject for research and teaching. He notes that "If old age pensioners with chronic bronchitis put to themselves the Hobbesian question —why should men do other than to act to their own immediate advantage? —they might start charging for the gifts they make which are more likely to benefit future cohorts of chronic bronchitics" (*1*). What is extraordinary about medical teaching and research is that such gifts have come to be taken for granted, the expectation being that patients will give of themselves for the sake of research, the training of physicians, and the betterment of mankind. It is only in recent years that problems of social control in medical experimentation have emerged in the public's consciousness. Public outcries over the thalidomide tragedy and a highly publicized research project in a New York hospital in which live cancer cells were injected into geriatric patients without "informed consent" resulted, in 1966, in a regulation requiring that all biomedical research supported by the National Institutes of Health in which human subjects were to be used receive a special peer review. The requirements have since become more stringent and have been extended to all research on human subjects supported by any agency of the Department of Health, Education, and Welfare.

Although public interest focused on human experimentation because of such documented abuses as failure to obtain informed consent and exposure of patients to serious risk without commensurate benefits, the issues involved are more complex and extend into larger questions relating to medical education, medical practice, public regulation of foods and drugs, and the balancing of competing ends. While it may not be in the immediate interest of the patient to serve as a research subject or as "teaching material," it is in the interests of patients in the aggregate that physicians be well trained and experienced and that the medical sciences advance. Thus, the rules developed in seeking the gift of participation from patients and in defining the conditions of acceptance have the greatest bearing on medicine as an effective as well as a humane profession.

This book reports on two studies that sought to bring a sociological perspective to the practices and attitudes of biomedical researchers and to the problem of regulating their use of human subjects. In the first study data were obtained from 293 researchers in a large number of centers carrying on biomedical research with human subjects; 87 percent of these respondents were members of institutional committees that conducted reviews of such research. The second study focuses on two institutions, one a university hospital and research center, the other a community teaching hospital with no medical school affiliation; there data were obtained from 387 investigators that encompassed 424 research projects in which human subjects were used. The major variables of concern were developed from responses to hypothetical research proposals involving problems of informed consent and dangers to subjects. These are supplemented in the second study by analysis of ongoing projects. Two indices are developed—one taking into account the reported risk and expected therapeutic benefit to the subjects, the other contrasting the risk to the subject with all possible benefits that might accrue to other patients and the development of knowledge.

Establishing ethical guidelines is an uncertain process subject to much disagreement. Given the probability that the respondents projected themselves and their institutions in the best possible light, and leaving room for errors in their understanding and interpretation of the hypothetical materials, the authors make a convincing case that their estimates of "permissiveness" among researchers in applying risk-to-benefit considerations are not excessive. They find that, although the majority of the respondents were sensitive to issues of informed voluntary consent and expressed unwillingness to take undue risks, as many as one-third were not particularly attuned to these issues in hypothetical situations, and some were actually doing studies involving unfavorable risk-benefit ratios. For example, 23 percent would allow samples of blood and urine to be taken without informed consent from students visiting a student health service, and 28 percent would approve thymectomy of children and adolescents undergoing surgery for correction of heart lesions, as part of an important immunological study, despite the fact that this would involve high risks to the subjects without therapeutic benefits.

In examining the problem of social control of experimentation, the authors draw heavily on the literature in the sociology of science, which gives considerable attention to competition and the reward structure of research activity. Much of the analysis is an attempt to demonstrate, from data about the respondents' careers, that more insensitive use of human subjects is a result of relative failure in competition for professional status. The authors argue that it is mainly the scientists who publish many papers but are rarely cited, or who have high standing in the scientific community but do less well in their local institutional settings, who are most likely to abuse human subjects. Although the data suggest such a pattern, the relationships are neither particularly large nor fully convincing. The samples are too small for the study of such complex interactions and the data are not always consistent. And causal sequences are not so clear as the argument sometimes implies. But the analysis is provocative and the hypotheses deserve further study.

The analysis further documents the well-known fact—which is worthy of continued repetition—that medical schools are quite successful in instilling research values but give insufficient at-

tention to humane care. As Freidson found for associates in group practice (*2*), these authors find that collaborators in research tend to be more like each other in their ethical orientations than they are like other researchers, and it is suggested that such patterns of assortative collaboration may contribute to permissiveness in the use of subjects.

The authors find that private patients are used more in studies in which subjects are likely to receive some benefit than when that is not the case. Of the studies involving less favorable risk-benefit ratios for subjects, 58 percent drew more than three-quarters of their subjects from ward or clinic patients; of studies with more favorable risk-benefit ratios, only 31 percent used that many ward or clinic patients.

Some attempt is made to evaluate the effectiveness of mandated peer review. The authors note some development in the efficacy of institutional committees. Although this analysis is suggestive, the indicators of efficacy are ambiguous, and the quality of reporting is sufficiently suspect to make one doubt that the analysis goes deep enough. Thirty-four percent of respondents reported that their committees had required no revisions of research proposals, had rejected none, and had had no withdrawals. Another 31 percent had required revisions in one or more proposals but had rejected none. Although the existence of these committees may affect anticipatory behavior and make moral concerns more salient, serious evaluation of their effectiveness will require audit studies of the proposals they review. There is also indication that some investigators bypass ethical review either by not seeking federal funds for particular projects or by carrying out informal research within the context of broader investigations. Eight percent of the respondents in the two-institution study volunteered the information that they were carrying out research on human subjects which was not reviewed. We are still a long way from knowing the magnitude of ethical problems in human research, particularly in nonfunded projects, the frequency with which patients are billed for procedures that are carried out solely for research purposes, the extent to which actual practices conform to research protocols, the amount of exaggeration and deception used in obtaining consent, and a host of important related issues. Moreover, problems in the use of human subjects in research are just the tip of the iceberg of problems characterizing common clinical practices in teaching institutions. Neglect of informed consent for diagnostic and treatment procedures, the use of expensive and dangerous diagnostic procedures of little value in treatment, differential treatment on public and private units, and unethical behavior in obtaining autopsy permissions, organ donations, and the like are just a few.

In choosing the sociology-of-science perspective, this study limited to some extent its potential for exploring in greater depth the resolution of conflicting interests in human experimentation. Neither in the choice of hypothetical instances nor in their analysis is attention given to the possible situation where regulations governing the use of human subjects are so stringent that they make it virtually impossible to carry out certain types of research. Institutional representatives can protect themselves by taking no risks at all, but it is not apparent that this is in the service of the public. It is not insignificant that one of the best-known writers on ethical problems and standards in research on human subjects also wrote: "Scores of practitioners treating hundreds of cases over years of time may eventually prove a given procedure valuable or worthless. But why perform scores or hundreds of such operations with a definite death rate when, say, a comparison of 25 exposures of the suspected area, with nothing else done, and 25 exposures plus the new surgical procedure, would make clear the desirability or the uselessness of proceedings?" (*3*). I doubt that such an experiment would be allowed in most institutions today. I have serious reservations about this particular proposal, but there are certainly circumstances that require controlled clinical trials involving risks (*4*).

Although no researcher has the right to assume that patients are willing to take risks for the sake of mankind, the fact is that many patients are prepared to make such gifts. When they are asked to make altruistic choices, patients must be provided with full and objective information about what is being asked of them; and the request for consent should not be stated as an expectation which they will find difficult to refuse. The concepts of informed consent and freedom from excessive psychological pressure raise serious questions about the use of involuntary patients and those who are not competent for one reason or another to give consent, and every researcher who uses human subjects should be willing to apply the test used by a respondent in deciding a hypothetical situation in which normal control children were to be given radioactive calcium in a study of bone metabolism. He said, "I hate to be personal about it, but it seems to me that I will not allow my own children to be used as controls, and other children are as precious to their parents as mine are to me." His judgment may have been right or wrong, and reasonable men may differ, but his criterion was unimpeachable.

This book is clearly a landmark in opening an essential area of inquiry for the public and for the scientific community. But although I endorse such policy recommendations made by the authors as the reviewing of all research in institutions using human subjects, better continuing review in the course of a project, more subspecialization in review committees, and representation on such committees of informed nonscientists, I think a more direct approach than theirs is needed to the balancing of long- and short-term ends. Resolution of the problems in human experimentation must be viewed as just part of the larger task of weighing the conditions of technological progress against those of humane health care.

Biomedical research involving risks to human subjects will and should continue, and some patients will be injured. Although a prudent society does everything it can to limit unnecessary risk, a humane society insures that those who suffer injury on behalf of others receive compensation. While we continue searching for the appropriate balance between risks and protections, we might also devise a humane system of compensation to deal with the inevitable.

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References

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3. H. Beecher, "Surgery as a Placebo," *J. Amer. Med. Ass.* **176**, 1106 (1961).
4. A. L. Cochrane, *Effectiveness and Efficiency* (Nuffield Provincial Hospital Trust, London, 1972), pp. 45–66.