Letters

Experimentation: Rights and Risks

Wolfensberger, in writing on "Ethical issues in research with human subjects" (6 Jan., p. 47), seems to be concerned mostly with possible distress or damage to the psyche. In laboratories of applied physiology, hazardous experiments involving physical stress—acceleration, high and low pressure, extreme heat and cold, and vibration—are fairly common. Hazardous experiments involve risk of injury and would presumably fall in Wolfensberger's research category 3, with yielding of right (v). Informed consent would be desirable, but to be fully informed a subject would have to have academic training the same and experience as extensive as that of the experimenter. In my laboratory, and in many others, it is the rule that the experimenter goes first, followed by his colleagues; then, if more subjects are needed, the technicians act as subjects in experiments they have helped to operate. If, finally, outsiders are required to provide a large number of subjects, there is a body of experience available.

This practice may help to explain why there is a tradition, never explicitly stated but generally observed, that the responsible investigator is the first to experience the whole range of stress. He takes pride in being able to say that he has been the first to be exposed to 300°C, the first to test new equipment in a parachute jump from 40,000 feet (12,192 meters), or the first to dive to 1000 feet (304.8 meters) in a pressure chamber. Often, only one or a few experiments are necessary. The investigator is in the best position to assess the risk and to test his assessment.

In defining risk, the critical element is the degree of uncertainty involved. Incentive pay for hazardous duty is warranted if there is no precedent, or if the (small) risk of irreversible injury is unavoidable by known protective measures or safety procedures. To avoid the suggestion of possible negligence or malpractice, the experimenter employs as much care, as much selection and training of the subject, as much on-line monitoring and medical supervision as is used by any one of his colleagues. Some experimenters carry sizable liability insurance to protect themselves and their institutions, and to benefit the subject if harm comes.

Hazardous experiments are necessary to extend such contemporary frontiers as undersea exploration and space flight. These experiments are done only when necessary; they are done deliberately, using the best available protection for the subject.

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In categorizing research as level 1 (experimental activities and procedures employed but not consciously recognized or formally labeled as research), level 2 (activity identified and conceptualized as research involving manipulation of subjects but characterized more by unnaturalness than by inherent danger), and level 3 (research clearly risky to the subject), and by turning his attention mainly to the problems and ethics of informed consent for research at levels 2 and 3, Wolfensberger also draws considerable attention to the whole question of consent for level-1 research. He suggested that much of the clinical management of human beings falls into this category of activity, that almost every time a physician prescribes a course of action for a patient, he is conducting an experiment of a sort on a subject.

Data cited by Martin L. Gross in *The Doctors* (Random House, New York, 1966) suggests that level-1 research produces substantially more avoidable damage to individuals than does research at levels 2 and 3, if only because so much more level-1 research is conducted. Wolfensberger's guidelines state that "no consent for level-1 research should be required . . . to use a procedure . . . primarily for treating a person therapeutically *if* (i) the procedure is considered justifiable and appropriate by qualified peers, and (ii) a consent (to treatment) appropriate to the occasion and to the risk inherent in the procedure has been obtained." Earlier he states that "in the past . . . researchers muddled along in the belief or hope that procedures or conventions either in common use or approved by their peers were proper and ethical." This muddling along is apparently no longer acceptable for the relatively harmless level-2 research and the somewhat more dangerous level-3 effort, but is still adequate for the (I contend) much more damaging level-1 variety.

Any contention that a patient ought to be fully informed about the benefits, risks, and alternatives, and give formal informed consent prior to *each* and *every* therapeutic or diagnostic measure taken is dismissed as, for example, unnecessary, bad for the doctor-patient relationship, or too time-consuming. Stripped of its nonessentials, the total argument against truly informed consent for level-1 experimentation seems to be that "father knows best."

Without making judgment, let me say that the attitudes and concerns of society at present regarding individual rights are such that informed consent inevitably will be required, not only for level-2 and -3 research, but also for all of the much more common level-1 variety. If it will provide any solace to the physician, he will be joined in his dilemma by attorneys, managers, social workers, union leaders, salesmen, and indeed, anyone who engages in human-management enterprise.

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. . . I should like to stress how much medical science, and thus the human society as a whole, has benefited from investigations carried out on volunteers, deliberately infected with malaria, with the aim of assessing the value of various new drugs.

First of all it must be stated that no animal, with the exception of apes and monkeys, could be infected with human malaria parasites. Various experimental models on birds and rodents are

useful only for preliminary screening of potentially valuable antimalarials. . . . The decisive evaluation of drugs for the prevention and treatment of human malaria can be done only on man. For a number of years studies of antimalarial drugs were based upon the results of treatment of cases of malaria seen in hospitals. These observations were useful but the variability of the clinical response to natural malaria infections limited their scientific value and much difficulty has been experienced in the interpretation of data from different countries.

In 1942–43 when the acute shortage of quinine showed the vital need to develop new synthetic drugs, a number of experimental studies were carried out on human volunteers in Britain and the United States. The most famous of these experiments were those by Fairley in Australia on approximately 1000 army volunteers deliberately infected with malaria. This work was taken up in the United States by two outstanding malaria research projects that started in 1944 and still continue. One was set up at the Federal Penitentiary at Atlanta (*1*), the other in the Illinois State Penitentiary near Chicago (*2*). The stated objective of both projects was to assess the value of promising drugs for the prevention of sporozoite-induced malaria and for the clinical and radical cure of established infections. Those who are acquainted not only with the rules governing the acceptance of the service of volunteers in these two research units, but also with the way the medical and ethical principles are adhered to, can bear testimony to the fact that the health, the dignity, and the freedom of choice of these subjects are protected.

The World Health Organization expressed its appreciation of these studies in terms that are not often used in sober scientific reports (*3*):

> . . . At the present time, human malaria research centres employing non-immune volunteers exist only in the U.S.A. The amount and quality of scientific data obtained in these centres on the characteristics of drug-resistant strains of malaria parasites and on their response to drugs is invaluable, and . . . medical science owes an immense debt of gratitude to the administrators of these institutions, to the research workers concerned, and above all to the courage and devotion of the volunteers.
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> . . . It seems that straightforward, well-planned and perfectly executed investigations such as those at Atlanta and Stateville on fully informed, healthy human volunteers are ethically and professionally more justifiable than some trials done on hospital patients without their knowledge or consent.

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References

1. G. R. Coatney, W. C. Cooper, D. S. Ruhe, *Amer. J. Hyg.* **47**, 113 (1948).
2. A. S. Alving, B. Craige, Jr., T. N. Pullman, C. M. Whorton, R. Jones, Jr., L. Eichelberger, *J. Clin. Invest.* **27**, part 2, p. 2 (1948).
3. *World Health Organ. Tech. Rep. Ser.* **296** (1965).

In response to Webb's comments, I have come to the conclusion that no meaningful distinction can be drawn between the experimenter's volunteering for risky research (self-experimentation), and the use of well-informed and highly willing volunteers in general. The crucial issue is not whether the volunteer is the researcher, his research assistant, or a man off the street. The crucial question (and this also applies to Bruce-Chwatt's comments) is: Are there ethical or moral limits of risky research even with fully informed and highly willing subjects? Our Judeo-Christian value system condemns suicide as well as certain types of self-mutilation and risk-taking, and our society has embodied some of these moral precepts into law. I am not sure at what point volunteer research would cross a line into legally or morally proscribed territory, but I feel that in our society, with the values that prevail, there is such a line. If this premise is accepted, it then follows that use of volunteers (no matter who they are, or how well-informed or willing), does not *ipso facto* provide license for risky experimentation. While insurance protection for both researcher and subject is a good idea, I cannot see how incentives such as hazardous duty pay affect the issue of limits to ethically permissible research with volunteers.

There are two minor points on which Webb apparently misread my paper: I fully intended to equate considerations of physical and psychological risk; and I specifically and strongly argued against the notion that informing should include all details or full understanding of the experiment. Only essential elements, such as the types of rights and risks involved, were proposed as indispensable to an informed consent.

The issue raised by Stucki can probably be resolved by drawing a clear distinction between (i) experimentation designed primarily for the benefit of an individual in a human management situation, whether generalizable knowledge does or does not result from such an experiment; and (ii) experimentation not designed for the benefit of the subject, even though some advantages may (or may not) accrue to him. For the latter type of research on level 1, consent may be meaningless, as no rights may be involved; infeasible, as in studies of traffic flow; or outright undesirable, as in research use of national census data which U.S. residents must provide by law, whether they like it or not. However, I have the impression that Stucki is mostly concerned with the former (clinical management) experimentation. Here, I would agree that those playing human management roles need to learn to better recognize the tentative or unvalidated elements of their practice. They should make greater efforts to inform their clients, or clients' responsible agents, of the risks of treatment or management alternatives, and of the degree to which such alternatives are believed to be valid. An informed consent to submit to such treatments should, indeed, be obtained, but such a treatment consent should be clearly distinguished from a research consent where subject benefits are not primary.

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Military and Academe

Nelson's article on the new chancellor at Pitt has caused me some wonder (News and Comment, 3 Feb., p. 540). Would the same people who were "aghast" at the prospect of having a military officer as chancellor have considered a petition against a lawyer, a Negro, or a New Frontiersman *before* determining his academic qualifications? As a friend and colleague for some 5 years, I know that Posvar and his wife will be a welcome addition to the Pitt scene. I am very sure that if the stigma of serving one's country in uniform for 20 years proves too much for the Pitt faculty, there are other universities who can find a place for him, and for a few more like him who are approaching eligibility for retirement.

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