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STANFORD UNIVERSITY SCHOOL OF MEDICINE
Department of Genetics

Honorable Edward Kennedy
United States Senate
Washington, D.C. 20510

Dear Senator Kennedy,

I very much appreciate your letter of November 15th which gives an immensely broader perspective on your inquiry about problems of medical ethics than has been conveyed by newspaper accounts so far. I am particularly gratified that you place considerable emphasis on the dangers of creating a "therapeutic vacuum". To lump Dr. Hodgman's study with the Tuskegee program on syphilis does risk producing exactly that outcome. The dilemma of course is how to sustain the socially invaluable momentum of clinical research and at the same time to protect individual patients from exploitation, and in turn how to do this without transforming medicine and medical research into adversary processes which are unavoidable in politics and in litigation. I see many difficulties. A system that is so rigorous that it provides perfect and absolute insurance against any conceivable abuse will have to go even beyond the rights of due process, availability of counsel, and so on that today imperfectly guarantee such protections to alleged criminals. On the other hand, I am quite aware of the need for well understood formal procedures. A system that would allow a Joan Hodgman to conduct her medically invaluable and ethically defensible experiments with a minimum of objective oversight is also open to a level of abuse that should be forefended by more than Dr. Hodgman's personal stance of ethical responsibility. Others, if allowed to function in an equally unregulated environment might well reach a far less denfensible balancing of social and individual needs.

Furthermore, I certainly do not place an absolute value on social requirements for medical advance. We have only to look at the example of the "Doctors of Infamy" during the Nazi regime, and to note the medical profession's reaction to that history, to see that we will not tolerate the unwilling sacrifice of a single life in an experiment for the prospective benefit even of thousands of others. I do not believe that you would disagree with very much of what I have just written.

I do not believe, however, that there are such easy answers as "a retrospective collection of the Los Angeles County Hospital experience with chloramphenicol". If we were to place such reliance on uncontrolled studies we would have no basis for criticism of a great many of the drugs that have recently been judged to be totally ineffective and indeed there is great disparity of clinical impressions with respect to the safety of chloramphenicol. Many physicians persist in using it percisely because their own, uncontrolled, clinical experience with it has been very good, and it is only the careful accumulation of data with this drug, on a large scale, that has revealed its toxicity for adults, at a level of about 1 per 30,000 treatments in unambiguous fashion. To hinder prosepctive

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"experiments" in favor of retrospective judgements is in effect to insist that we collect data in a purposely obscured fashion. Indeed if a group of patients is treated with the reasonable expectation that the data on them will be used for such collations would not this bring the anticipated study within the legal framework of an experiment! The eventual effect of overly rigorous policing will be to obscure more and more the collection of comparative data. After all, very few experiences in medical care ar not, in the long run, experiments. Distinctions can indeed be drawn between those measures that, in good conscience, are intended to be for the benefit of the patient, and those that to various degrees are either neutral or do bear some degree of perceived risk. With respect to the latter there of course can be no question about the essentiality of constructive consent, and I am told that the word "informed" is superfluous since consent can hardly be meaningful without a requisite degree of information.

Many studies have however shown that the technical content of a medical treatment or experiment is rather fleeting in the minds of a significant number of patients -- we have only to look at the statistics on non-compliance in following medical advice to get a picture of the problem. I know then that many of my colleagues more actively involved in clinical work are quite skeptical about the utility of the rather legalistic approach to "informed consent" which may tend to obscure rather than clarify the risks that may be inherent in any procedure, be it therapeutic or experimental or both. As this is also all too familiar a reaction on the part of any group facing regulation you may be entitled to some skepticism about the validity of the complaint. As long as there remains any significant stratification of income or of privilege within the nation, it may be difficult to argue that any but the most highly educated and privileged patients are capable of making a voluntary decision that would expose them to any tangible risk in the light of the potentiality of coercion and other pressures in a status-polarized context. In that effect of pushing this argument to its extreme, however, will be to deny any opportunity for exercise of altruistic impulses, or merely group-oriented self-interest, to any but the "upper crust". Perhaps the deeper message is that the contemporary context of class conflict must be radically ameliorated before we can get much further on with our highest aspirations in education, science or health. But then we are in the dilemma of the French Revolution which "had no need for servance" like Lavoisier!
savants

After rereading your letter I do not believe I can have added much to your perception of the complexity of the problem you are addressing.

May I take the occasion, however, to bring your attention to a study in which informed consent was neither sought nor would it have been feasible. At first glance one might argue that the aims of this experiment, to facilitate a higher level of maternal attachment to their babies, are a no-risk proposition and from the standpoint of the infants this is probably true. I wonder, however, whether the Women's Liberation Movement would take quite the same view of a process that might be regarded as playing into the traditional subjugation of women by manipulating their feelings. In this case we can also ask what constitutes the experiment? Has it been the traditional practice of separating women from their babies or is it the rediscovery of leaving them together! Further, if one takes as critical a

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view of this experiment as would be consistent with many demands for tightening up on the regulation of experimentations, one must eventually ask why "experiments" are singled out for such special attention when many other forms of manipulation and exploitation go unhindered as part and parcel of everyday life, sometimes involving identical procedures.

In my own view the recent crystallization of procedures concerning human experiments, especially the establishment of critical review boards at the various institutions, have gone a long way towards meeting the practical needs for a more highly scrutinized system. In particular they also contribute to what I regard as the principal abuse of human subjects, namely to involve them in s study which is scientifically faulted owing to lack of proper experimental design or other faults in the technique.

There are comparable paradoxes in an analysis of medical educational policy. On the one hand there is indeed a demand to simplify and accelerate medical training in order to respond to community needs. On the other hand many of the errors in clinical judgement, for example in failing to maintain a sufficiently skeptical attitude towards new drug advertising, are not likely to be repaired by even less rigorous scientific training of prospective physicians. The gross over-prescription of many drugs is after all almost entirely in the province of the frontline deliverer of health care whose numbers need to be augmented. From the vantage point of the medical school its seems at least as important to find ways to encourage more consistent patterns of postgraduate re-education to maintain the quality of medical care as it is to multiply the numbers of providers.

Thank you for the opportunity to share these thoughts with you.

Sincerely yours,

Joshua Lederberg
Professor of Genetics

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encl: Klaus,M. et al., 1972
NEJM 286: 460 (Mar.2)