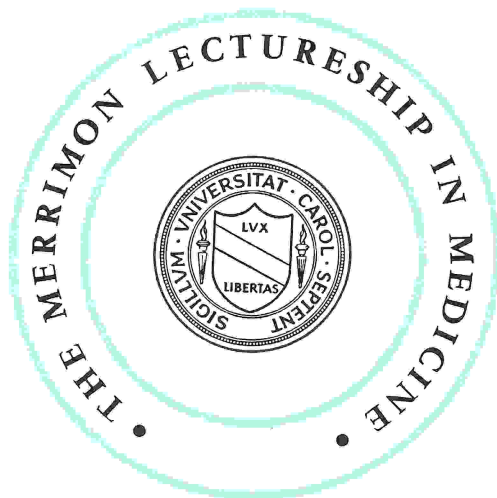


THE SCHOOL OF MEDICINE  
OF  
THE UNIVERSITY OF NORTH CAROLINA AT CHAPEL HILL



MERRIMON LECTURE

*by*

RENÉE C. FOX, Ph.D

*October twenty-fifth, Nineteen Hundred and Seventy-nine*

# THE MERRIMON LECTURE

## **Vision and Reality** **The Evolution of Medical Uncertainty**

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Annenberg Professor of The Social Sciences  
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THE SCHOOL OF MEDICINE  
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1979

## THE MERRIMON LECTURESHIP IN MEDICINE

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**RENÉE C. FOX, Ph.D.**



RENÉE C. FOX was born and reared in New York City, where she attended a public primary school (P.S. 9) and secondary school (Julia Richman High School). A *summa cum laude* graduate of Smith College, Northampton, Massachusetts (1949), she earned her Ph.D. in sociology in 1954 from Radcliffe College, Harvard University, where she studied in the Department of Social Relations as a student of Talcott Parsons.

Before going to the University of Pennsylvania in 1969, Dr. Fox was a member of the Columbia University Bureau of Applied Social Research (1953-1958); taught for twelve years at Barnard College (1955-1967); and then spent two years as a Visiting Lecturer in the Department of Social Relations at Harvard University (1967-1969). She is now Professor of Sociology in the Department of Sociology at the University of Pennsylvania, in the Departments of Psychiatry and Medicine in the Medical School, and in the School of Nursing. In 1978, she was awarded an interdisciplinary Chair, and became the Annenberg Professor of the Social Sciences.

Dr. Fox has lectured in colleges, universities, and medical schools throughout the country. In addition, in the capacity of Visiting Professor, she has taught in a number of universities outside the United States: the Université Officielle du Congo, Sir George Williams University in Canada, and the Katholieke Universiteit Leuven and the Université de Liège in Belgium.

Renée Fox's major teaching and research interests—sociology of medicine, medical research, and medical education—have led her to make first-hand studies in Continental Europe and Central Africa, as well as in the United States. She has conducted wide-ranging sociological research in Belgium for twenty years, and in Zaire during 1962-1967.

Dr. Fox is the author of four books: *Experiment Perilous*, *The Emerging Physician* (with Willy De Craemer), *The Courage to Fail* (with Judith P. Swazey), and *Essays in Medical Sociology*. She has also published numerous scholarly articles.

Dr. Fox has held positions in many professional associations and on a number of boards. In addition, she has served in various editorial capacities. At the present time, she is Vice-President-Elect of the American Sociological Association, a Board member of the American Association for the Advancement of Science, a member of the Council of the Institute of Medicine, Secretary of the Institute for Intercultural Studies, and Associate Editor of the journal, *Social Science and Medicine*. She has been appointed very recently to the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research.

She has received a number of honorary degrees: a Master of Arts from the University of Pennsylvania (1971); a Doctor of Science degree from the Medical College of Pennsylvania (1974); a Doctor of Humane Letters degree from Smith College (1975); a Doctor of Science degree from St. Joseph's College in Philadelphia (1978); and a *Doctor Honoris Causa* from the Katholieke Universiteit Leuven in Belgium (1978). She is a member of the American Academy of Arts and Sciences and the Institute of Medicine, and a Fellow of the American Association for the Advancement of Science. In recent years she has become a distinguished visiting lecturer in great demand, the Merrimon lectureship being one of her significant 1979 efforts.

## The Evolution of Medical Uncertainty

Uncertainty has been central to my work in the sociology of medicine since its inception. The importance of uncertainty in modern medical practice as a theoretical concept, an empirical phenomenon, and a human experience was first impressed on me by my teacher, Talcott Parsons (Parsons, 1951). He also conveyed to me the paradox and poignancy—for both physician and patient—of the fact that our great twentieth-century progress in medical science and technology has helped to reveal how ignorant, bewildered and mistaken we still are in many ways about health and illness, life and death.

When I subsequently moved from his classroom into the field to study patients and physicians on a research ward, I became a participant observer in a tragi-comic hospital world of men facing the unknown, where uncertainty and death were the only certainties. From Ward F-Second, one could catch a glimpse of a white, Greek temple-style medical school building, into whose stone facade had been chiseled the famous aphorism of Hippocrates:

Life is short  
And the art long,  
The occasion instant,  
Experiment perilous,  
Decision difficult.

*Experiment Perilous* became the title of the book I wrote about that ward (Fox, 1959, 1974a) and the aphorism a kind of motto for me, personally and professionally. Ever since then, whether I have been exploring the process of clinical investigation, the making of a physician, or the development of a new form of therapy, in the United States, Europe, or Africa, the theme of uncertainty has appeared and reappeared as a motif in my research, teaching, and writing.

I shall not try to explain why this is so. A complete answer could not be given in purely intellectual terms; and it would carry me more deeply into my biography, and how I see and feel the world, than would be appropriate to this occasion. But it can be said that various factors in my person and life have made me unusually aware of the uncertainty dimension in medicine, and preoccupied with it, so that for thirty years, as a sociologist, I have been a watcher, chronicler and analyst of uncertainty in numerous medical settings. It now seems to me that over these past three decades, and particularly during the last ten years, while I have been absorbed in studying problems of uncertainty in various medical contexts, a more pervasive interest in these problems and a greater concern about them have grown up around me. Something has been progressively happening in American medicine and in the larger society that has led Lewis Thomas to write:

The only solid piece of scientific truth about which I feel totally confident is that we are profoundly ignorant about nature. I regard this as the major discovery of

the past hundred years of biology. . . . It is this sudden confrontation with the depth and scope of ignorance that represents the most significant contribution of twentieth-century science to the human intellect. . . . Because of this, these are hard times for the human intellect. (Thomas, 1979:73-74)<sup>1</sup>

All sorts of things seem to be turning out wrong, and the century seems to be slipping through our fingers here at the end, with almost all our promises unfulfilled. I cannot begin to guess at all the causes of our cultural sadness, . . . but I can think of one thing that is wrong with us and eats away at us: we do not know enough about ourselves. We are ignorant about how we work, about where we fit in, and most of all about the enormous, imponderable system of life in which we are embedded as working parts. . . . This is, in a certain sense, a health problem after all. For as long as we are bewildered by the mystery of ourselves, and confused by the strangeness of our uncomfortable connection to all the rest of life, and dumbfounded by the inscrutability of our own minds, we cannot be said to be healthy animals in today's world. (Thomas, 1979:174-175)

As a people, we have become obsessed with Health. . . . We do not seem to be seeking more exuberance in living as much as staving off failure, putting off dying. We have lost all confidence in the human body. The new consensus is that we are badly designed, intrinsically fallible, vulnerable to a host of hostile influences inside and around us, and only precariously alive. . . . The new danger to our well-being . . . is in becoming a nation of healthy hypochondriacs, living gingerly, worrying ourselves half to death. . . . Indeed, we should be worrying that our preoccupation with personal health may be a symptom of coping out, an excuse for running upstairs to recline on a couch, sniffing the air for contaminants, spraying the room with deodorants, while just outside, the whole of society is coming undone. (Thomas, 1979:47-50)

Health, illness, and medicine appear to be epicenters of the increased malaise about uncertainty, and the anxiety about danger and risk that have surfaced in our society. This uneasiness has risen to the point where cautionary articles on the possible harmful side-effects of measures taken to forestall harm are being published:

#### Informed Consent May Be Hazardous to Health

. . . A considerable body of psychological evidence indicates that humans are highly susceptible. . . . This alone would lead one to suspect that adverse reactions might result from the information given during an informed consent discussion.

An examination of the medical evidence demonstrates that there is . . . a dark side to the placebo effect. Not only can positive therapeutic effects be achieved by suggestion, but negative side effects and complications can similarly result. . . .

If protection of the subject is the reason for obtaining informed consent, the possibility of iatrogenic harm to the subject as a result of the consent ritual must

<sup>1</sup>From *The Medusa and the Snail*, by Lewis Thomas. ©1979 by Lewis Thomas. Originally appeared in *The New England Journal of Medicine*. Reprinted by permission of Viking Penguin Inc.

be considered. This clear cost must be weighed against the potential benefit of giving some people an increased sense of freedom of choice about the use of their bodies. (Loftus and Freis, 1979)

Other authors, disturbed by the potentially damaging consequences of such “uncertainty-of-uncertainty,” “risk-of-risk,” and “danger-of-danger” admonitions are responding to them with such counterbalancing notions as “necessary risks” (Jarvik, 1979) and “risk acceptance” (Comar, 1979).

This escalation of concern (and counterconcern) is as perplexing as it is striking. Like Lewis Thomas, I cannot begin to guess what all the causes of it may be, or where it is taking us. But it also seems to me that it has something to do with urgent problems that we are facing in the whole society and what he calls our “cultural sadness,” as well as with advances in science and technology, and the so-called biomedical revolution that they have brought forth.

I would like to devote my Merrimon Lecture to an examination of the evolution of medical uncertainty taking place in our society: what it is, and what it means. I will begin with an overview account of some of the insights that have emerged from my own microcosmic inquiries into medical uncertainty. From there, I will move on to consider the more macroscopic ways in which the problem of medical uncertainty (and its concomitants—risk, hazard, error, and limitation—) is manifesting itself at the present time. Finally, by linking up the two planes of observation and levels of analysis, I hope to offer a tentative interpretation of what appears to be the more-than-medical uncertainty crisis through which we are now passing.

### *My Research on Medical Uncertainty*

It was through my involvement in studying the education and socialization of medical students in the 1950s that I first had a chance to observe the “training for uncertainty” sequence that they undergo as part of the process of becoming a doctor (Fox, 1957). These observations were made in the context of the Columbia University Medical School Project: a research team, under the aegis of Columbia’s Sociology Department and Bureau of Applied Social Research, that studied the socialization of medical students as it occurred in the 1950s, in the medical schools of Cornell University, the University of Pennsylvania, the University of Colorado, and Western Reserve University (Merton, 1975b). As the chief fieldworker at Cornell University Medical College, where I spent the years 1953 to 1958 in the role of participant observer, I identified, shared, and subsequently analyzed the training-for-uncertainty sequence experienced by medical students (Fox, 1957). The research physicians of Ward F-Second, I retrospectively realized, had all known such training in their medical school days. It had not only introduced them to the uncertainty that they later faced as clinicians and investigators, but had also taught them ways of thinking about, and coping with it. The four-year-long process of training for uncertainty in medical school centered around three basic types of uncertainty:

The first results from incomplete or imperfect mastery of available knowledge. No one can have at his command all skills and all knowledge of the lore of

medicine. The second depends upon limitations in current medical knowledge. There are innumerable questions to which no physician, however well trained, can as yet provide answers. A third source of uncertainty derives from the first two. This consists of difficulty in distinguishing between personal ignorance or ineptitude and the limitations of present medical knowledge (Fox, 1957:208-209).

This exposure to the worlds of “experiment perilous” and of “the student-physician” also furthered my appreciation of the emotional, moral and existential implications of these types of medical uncertainty for physicians and their patients. To be puzzled, ignorant, unable to understand; to lack needed knowledge or relevant skill; to err, falter, or fail, without always being sure whether it is “your fault” or “the fault of the field” (as one medical student put it), is especially painful and serious when the work that you do is medical. For, however familiar and routine it may be, or seemingly unthreatening and non-tragic, no medical action or interaction that involves a patient is trivial or completely ordinary. Below their medical scientific surface, medical acts and events intersect with the human condition of patients, their relatives, and of medical professionals themselves—their most profound aspirations, hopes, and fulfillments, their deepest worries, anxieties, and fears.

Talcott Parsons and Ward F-Second had made me keenly aware that health, illness, and medical care in our society, as in all others, are integrally connected with some of the most elemental and basic, and some of the most transcendent and ultimate aspects of the human condition. The conception of human beings, their birth, survival, and growth, their physical, emotional, and intellectual capacities and development, their sexuality, aging, mortality, and death, I recognized, are core foci of health, illness, and medicine, as are the quality of their lives, and some of the significant forms of pain, suffering, accident, and *angst* that human beings experience. In this sense, our “coming in,” our “staying in,” and our “going out” are continuously linked with our health, and with the medical care that we seek and receive. The experience of illness and the practice of medicine also summon up critical problems of meaning—fundamental questions about the “whys” of pain, suffering, the limits of human life, and death, and about their relation to evil, sin, and injustice. My participant observation in the medical school acquainted me with the forms in which physicians-in-training first encounter these aspects of their future work and their initial reaction to them.

This kind of experience, I felt, was epitomized in the anatomy laboratory and in the autopsy (of which I made special studies) (Fox and Lief, 1963; Fox, 1979). Here, I saw medical students learning about the structure and pathology of the human body by cutting into and dissecting it, and meeting the mystery of life and the enigma of death in the form of a naked, fellow human being laid out on a stainless steel table. Dissecting a cadaver and participating in an autopsy initiated students into the life-death-nudity-probing-cutting nature of medical work. I knew that, later, they would have little to do with cutting and dissecting the human body, unless they decided on anatomy, pathology, or

surgery as their special field. But virtually all physicians take medical histories, do physical examinations, and carry out diagnostic, therapeutic, and prognostic procedures. These more everyday facets of their work oblige and allow them to see, peer into, touch, manipulate, explore, and penetrate the bodies of their patients, handle and analyze their urine, feces, mucus, blood and other bodily substances and secretions, and inquire into their personal lives and intimate feelings in analogous ways. Observing rigorous norms of asepsis and noncontamination, dressed in professional starched white or astringent green, they enter orifices and inner chambers of the human body physiologically and symbolically associated with its highest and lowest functions, to extract and deal with substances like human blood, considered culturally to be both sacred and profane, dirty and pure. In clinical pathology, physical diagnosis, and on their various clinical clerkships, I watched medical students learning not only to master the techniques that these examinations involve, but also to manage their emotional reactions. What students found particularly “disquieting” (to use their own word), were those medical situations in which problems of uncertainty and problems of meaning were joined—when they attended an autopsy, for example, from which no definitive explanation of the cause of the patient’s death emerged; or, when they had contact with a patient who was incurably and painfully ill with cancer, suffering from the severe side-effects of physicians’ therapy.

Some of the collective ways of coming to terms with uncertainty that medical students progressively developed were junior versions of the coping mechanisms that the physicians of Ward F-Second employed. These mechanisms included achieving as much cognitive command of the situation as possible, through the acquisition of greater medical knowledge and technical skill, and the increasing mastery of the probability-reasoning logic with which modern medicine approaches the uncertainties of differential diagnosis, treatment decisions, and prognosis-setting (“... learning to conjure possibilities and probabilities,” as one student put it). Students gradually evolved what they referred to as a more “affirmative attitude” toward medical uncertainty. They became more able to accept uncertainty as inherent in medicine, to sort out their own limitations from those of the field, meet uncertainty with candor, and to take a “positive, philosophy-of-doubting” approach. In clinical situations, they were more prone to feel and display sufficient “certitude” to make decisions and reassure patients. At the same time, the fact that students made numerous jokes about uncertainty, like Ward F-Second’s physicians, indicated that this continued to be a source of stress. Counterphobic, ironic, medical humor, laced through with impiety and self-mockery, helped students to deal with uncertainty, although they never went so far as to engage in the “game-of-chance” behavior of their F-Second seniors. Confronted with extraordinary and often tragic uncertainty, the research physicians of Ward F-Second took laughter-accompanied bets on such serious matters as the diagnosis of a patient’s illness, the impact of their therapy, its prognosis, the outcome of a particularly important or risky experiment that



they conducted on a patient-subject and, most audacious of all, whether one of their patients would live or die.

One of the interesting consequences of the publication of my "Training For Uncertainty" essay (Fox, 1957) was the unexpected amount of appreciative response that it evoked from faculty and students in nursing, social work, law, divinity, and business schools, as well as from medical faculty and students. I received many invitations to be a guest lecturer in those settings, as well as requests for permission to reproduce the essay so that it could be distributed to large numbers of students and teachers. The response suggested that the problem of uncertainty and training for uncertainty were applicable to more than medicine, and were considered to be especially relevant in preparing for and undertaking particular kinds of professional work. I will return to these reactions when I consider the changed atmosphere in which problems of uncertainty and training for it are currently taking place.

Through the writings of physiologist Walter B. Cannon (1945: 68-78), and of sociologists Talcott Parsons (1951) and Robert K. Merton (1957a:103-108), and my first-hand observation of how the research physicians of Ward F-Second thought and worked, I had become interested in the "serendipity pattern" in medical science: the role that happy (and not-so-happy) "chance" or "luck" played in the process of discovery. A chance happening that occurred in the course of my own research activities at Cornell Medical School gave me the opportunity to study "an instance of serendipity gained and serendipity lost." Lewis Thomas, then professor and chairman of medicine at the College of Medicine of New York University, and Aaron Kellner, associate professor of pathology at Cornell University Medical College, had each intravenously injected rabbits with the proteolytic enzyme papain, as part of their laboratory investigations. Both had observed unexpected "floppiness" in the rabbits' ears after the papain had been administered. But whereas Thomas had eventually gone on from there to make a discovery based on this "accidental" collapse of the rabbits' ears, Kellner had not.

A sociologist colleague, Bernard Barber, and I decided to make a comparative case study of the factors that had led one investigator down the path to discovering that the injection of papain had significantly altered the rabbits' cartilaginous tissues, and the other to follow a trail away from that discovery. The results of our inquiry into "the case of the floppy-eared rabbits" have been published and need not be discussed here (Barber and Fox, 1958). However, there is one set of observations about Kellner's and Thomas's shared outlook on medical uncertainty that I now feel we did not sufficiently emphasize. It is worth underscoring because their attitudes towards uncertainty in the mid-1950s when this case happened stand in sharp contrast to some of those that have become salient in the altered perspective on uncertainty of the 1970s. Kellner and Thomas viewed errors and mistakes, as well as uncertainty and chance, as perennial parts of the biological, medical, and human condition. Both investigators were as familiar with negative as with positive serendipity, preferring the latter, but were also convinced that

mistakes were not inevitably unfortunate or dangerous. Quite to the contrary; in nature, in the laboratory, and in man's scientific and nonscientific activities, they believed mistakes could lead to unexpectedly felicitous—even wonderful—knowledge, capacities, developments, or change.

Until the end of the 1950s, my sociological studies of medical research, medical education and socialization, and chronic and terminal illness were all located in American laboratory, hospital, and medical school settings. In 1959, I began an investigation of how social, cultural, and historical factors affect medical research and research careers in a contemporaneous European society. Belgium became the primary site of this study, and since then has been one of the major loci of my sociological research (Fox, 1978). Belgium, in turn, led me to Zaïre (the ex-Belgian Congo) where, from 1962 to 1967, I was affiliated with the Centre de Recherches Sociologiques in Kinshasa, and became involved in more wide-ranging research, which included studies concerned with the sociology of health, illness, and medicine phenomena (De Craemer and Fox, 1968). It took these foreign field experiences to make me realize gradually that my studies of uncertainty and ways of coming to terms with it on Ward F-Second, at Cornell Medical School, and in Thomas's and Kellner's laboratories had been inadvertently ethnocentric and culture-bound. My analyses had failed to recognize that the problems of uncertainty I had identified were distinctively modern, Western, and, perhaps, uniquely American in a number of ways. I had not even considered the possibility, for example, that the *concepts* of uncertainty, probability, and chance might not exist in some cultural traditions, or that our type of scientific reasoning about them might be incompatible with the the cognitive assumptions and modes of thought of other societies and cultures. It was, above all, certain nonmodern, non-Western, Central African, aspects of Zaïre's system of thought that brought me to this realization:

Most happenings—illness figuring prominently among them—are interpreted either as adverse or felicitous, relatively few experiences are regarded as neutral or without meaning, and virtually none are considered to be fortuitous. They are viewed as being determinatively caused, primarily by supernatural, psychic, and interpersonal forces, within a closed system of thought and belief, whose inner logic is cogent, self-confirming and self-fulfilling. Explanations for events like illness are preestablished, limited in range, and fixed. When evidence contrary to traditional interpretations presents itself, there is a tendency to develop what Evans-Pritchard has termed "secondary elaborations," that "excuse" or explain away the untoward occurrences and thereby protect established premises. There is no room for the concept of probability in this way of thought, nor for the formal acknowledgement of an ultimate, irreducible degree of uncertainty as an inherent property of man's attempts systematically to understand, explain, and predict physical, biological, social, cultural, and psychological phenomena. (Fox, 1976b:780)

In our studies of characteristic features of the many religious movements that have developed in Zaïre throughout its known history, colleagues and I found this same deterministic, fortune-misfortune-oriented way of thought to



dominate and focus on the most highly valued goals of the society, including health. Among the other paramount goals with which these movements were centrally concerned was the attainment of a risk- and chance-free state of invulnerability. (De Craemer, Vansina, and Fox, 1976)

I mention the new perspective on uncertainty I gained from Zaïre because it throws into bas-relief the latent bias I originally brought to the study of uncertainty: a bias that is not purely personal, but built into the society and culture of which I am native. This bears on a hypothesis I will venture later in this lecture: namely, that the degree and kinds of ferment over error, risk, hazard, and the like that are now occurring in our society may be indicators that we are in the midst of questioning and altering some of our fundamental, cultural ways of thinking about, and dealing with, uncertainty. For the capacity even to speculate on such a possibility, I am especially indebted to the first-hand opportunity that Zaïre gave me to explore a world view radically different from my own.

The next major piece of research I undertook involved a return both to an American context and to an old subject. In 1968, in collaboration with Judith P. Swazey, a biologist and historian of science, I began a study of organ transplantation and hemodialysis in a representative cross-section of the main American medical centers where these modes of treating patients with end-stage renal, cardiac, and liver diseases were being carried out and further developed. (Our study later came to include bone marrow transplantation as well, but in 1968 this form of organ transplantation was not yet being clinically tried on a sufficient number of patients to incorporate it into our research.) In the years 1951 to 1954, as a participant observer on Ward F-Second, I had been introduced to dialysis and transplantation at the stage when they were totally experimental therapies. During that period, the physicians of Ward F-Second (the metabolic research ward of the Peter Bent Brigham Hospital in Boston) had conducted pioneering work on the artificial kidney machine and performed the world's first kidney transplants. Some fifteen years later, coming back to these therapeutic innovations gave me a chance to study the phase movements through which they had passed, and to look at them in a broader social as well as time perspective.

Judith Swazey and I thought of transplantation and dialysis as constituting a paradigmatic case exemplifying the attributes and process of therapeutic innovation, and emblematic of the "collective conscience" issues with which the "new biology," medicine, bioethics, and American society more generally had begun to be preoccupied in the 1960s. Problems of uncertainty comprised one of the major themes around which our research and later our book on organ transplants and dialysis, *The Courage to Fail* (Fox and Swazey, 1974), were structured. We focused our attention on the research physicians working with these therapeutic innovations, in their socially shaped professional roles as "specialists in uncertainty." We described and analyzed the diverse range of phenomena that the uncertainties associated with transplantation and dialysis

posed for them: "the biological mysteries of the rejection reaction, the ambiguities of the relationship between clinical experimentation and therapy, the problematic aspects of the clinical moratorium, and the dilemmas involved in allocating various kinds of scarce resources." (Fox and Swazey, 1978:xiii-xiv).

The year 1968, when we began our study, was heralded by the mass media as "Year of the Transplant." Over a hundred human heart transplants were performed world-wide, accompanied by much ballyhoo concerning the astronaut-like daring adventure it represented. However, at the year's end, the number of heart implants per month took a sudden, deep plunge, reached a plateau during 1969 and 1970, and decelerated so greatly that a moratorium on the procedure was said to have been called.

This sequence of events led us to identify what we termed "the clinical moratorium," to define it as the temporary cessation or marked slowdown in the use of a still-experimental form of therapy on patients, which could last for weeks, months, or years. We recognized that such moratoriums have taken place repeatedly in the development of therapeutic innovations, and set out to make a detailed study of the origins and consequences of particular moratoriums in recent medical history (Fox and Swazey, 1978:108-134; Swazey and Fox, 1970; Swazey, Sorenson and Wong, 1978). From our inquiries, we learned that the moratorium is a recurrent, quasi-institutionalized event, most likely to take place during the early, "black-years" period of the use of a new drug, device, or procedure with patient-subjects, when problems of uncertainty are especially salient and acute for physician-investigators, and when the risks and mortality rate are so high they are judged to outweigh the possible benefits. The shared conviction that to continue the clinical trials is neither bearable nor justifiable, and the collective pressure to desist, we observed, could come from the reactions of the physician-investigators themselves to the situation, from their colleagues, the institution in which they work, or from patients and their families. These sentiments and sanctions could be expressed and enforced in informal or formal ways. Quite unexpectedly, our interest in and exploration of the phenomenon of the moratorium acquired more general significance. For, as the 1970s unfolded, and the concerned cultural mood about uncertainty, risk, and biohazards associated with health, medical practice, and medical research escalated, this kind of professional and societal response to medical uncertainty increased in prominence, frequency, and scope.

Finally, there are two additional areas of inquiry in which I have been involved since the mid-1960s; like the study of clinical moratoriums, they have given me a strategic vantage point from which to watch the evolution of medical uncertainty during the past decade. Both grow out of my earlier work.

The first is my role as participant and observer in the field of bioethics that has developed in the last fifteen years. This interdisciplinary sphere of research and action has brought biologists, physicians, philosophers, theologians, jurists, legislators, and social scientists together in various contexts and organizations

to consider a cluster of issues connected with certain biomedical advances and practices—especially those involving research with human subjects. Such issues are considered empirically and symbolically to be part of the “biological revolution” of the twentieth century. Ward F-Second and *Experiment Perilous*, organ transplantation, dialysis and *The Courage to Fail*, and my analyses of medical and “human-condition” uncertainty in hospital, laboratory, and medical school settings cast me in the role of a pioneer member of bioethics. Uncertainty and the principle of risk-benefit analysis figure centrally in bioethical discussions and deliberations. They are analyzed and weighed in relation to other cultural issues and precepts that are brought to bear upon the main concern of bioethics: what ought we, and what ought we not, be doing biomedically in our society at the present time?

My involvement has enabled me to study the cultural linkages that are currently being made between uncertainty and other value and belief themes that have preoccupied us medically and societally since the 1960s: individualism and individuality, social reciprocity and solidarity, universalism and particularism, allocation and scarcity, the quality of life and of death, and the necessity and hubris of our vigorous interventions in the physical, biological, and social universe (Fox, 1974b; 1976a). I have been allowed to study, from within, what amounts to a social movement that has grown up, significantly influencing the ways that Americans are currently thinking and deciding about these questions.

The one other observation-post from which I have been viewing the uncertainty problem has been from inside medical schools of the 1970s, as much through my role as a teacher and adviser of medical students, as in the capacity of a researcher. Whether or not the content and process of medical education and socialization, and the background and attitudes of the men and women who undergo medical training, are very different from those I studied in the 1950s is a controversy that swirls around the American medical school at the present time. This debate, stimulated by the widespread criticism to which the medical profession and delivery of care are now subject, focuses on changes that supposedly have and have not occurred in the medical school, and their implications for improving the health care system. Sufficient reliable and valid data to evaluate how “new” the medical school and the medical students of the 1970s really are, do not yet exist. There is, however, tentative evidence to suggest that students of the seventies do not experience and react to some of the core aspects of the physician’s role—the uncertainty dimension among them—in the same ways as their predecessors.

With regard to current training for uncertainty, I have been struck by the way today’s medical students tend to be “late deciders.” Compared with the students of the fifties, they take a long time to make up their minds about medicine as a career, and they come to it via a complicated, often circuitous route. They “Hamletize” about medicine and their commitment, audibly and continuously: about the rightness of their decision to become a physician, about

all that doctorhood asks, and whether or not they will have the motivation and stamina to resist being molded by the medical school, the hospital, and the profession into replicating sentiments and behaviors of their predecessors of which they disapprove. Insofar as they are "new," medical students appear to be more involved in thinking about the sorts of questions with which bioethics deals, convinced that physicians ought to be doing the same, and more inclined to consider the problem of medical uncertainty in this framework, than were their counterparts of twenty years ago. In this regard, they are highly concerned that virtually all medical and surgical interventions, no matter how beneficial, have harmful side-effects, about the relation between these iatrogenic properties, the dramatic increase in malpractice suits, and their own vulnerability as practicing physicians. Doubting, self-doubting, and philosophizing notwithstanding, many of today's medical students tend to account for problems of medical uncertainty, and other problems, by invoking explanations that are more economically and politically deterministic, accusatory of outside forces and persons, and, therefore, more self-exonerating than was generally characteristic of pre-1960 medical students (Fox, 1974c).

In any case, regardless of how different these future physicians do, or do not, turn out, the "uncertainty scene" in medicine they are facing has changed considerably. It is to that situation that I now want to turn.

#### *Recent Increase in Awareness of Medical Uncertainty*

The amount of concerned attention that has been fixed on uncertainty and medicine in the past decade, by a variety of scientific, professional and business organizations and journals, health associations, legislative and judicial bodies, regulatory agencies, consumer and self-help groups, publishing houses, and the mass media, is striking. A newspaper editorial dealing with the national absorption in the problems of medical uncertainty today might aptly begin: "The American public is being swept by a medical epidemic characterized by doubt of certitude, recognition of error (Cournand, 1977:700), and discovery of hazard.

This preoccupation with medical uncertainty is multiform. Awareness of the "long list of formidable human diseases whose underlying mechanisms are not at all clear, and [that] are presently unapproachable by such precisely targeted techniques as the use of penicillin against streptococci" (Thomas, 1977) has grown. Cancer leads this list. Consciousness of "the frail basis" (Mike and Good, 1977:678) on which many medical decisions still have to be made appears to have increased both inside and outside the medical profession. The fact that problems that are not only unprecedented but also "entirely unpredicted" continue to arise in medicine is frequently discussed with a mixture of amazement and alarm (Talk of the Town, 1979a). What is regarded as the high technical and human fallibility and error that persist in medical research and practice, in the laboratory and in the clinic, evokes an exceptional amount of troubled commentary. The phrase "biological revolution" or "biomedical

revolution” is continually applied to the scientific and technological advances in understanding disease, and to the advances in diagnosis, treatment, and prevention that have been made in the last sixty years. However, the potential hazards and serious side effects of these discoveries and developments—the capacity of the drugs, devices, and procedures they have made possible, and of the human agents who wield them to do harm—are emphasized far more than the problems they have solved or the benefits they have brought. The many allusions that are constantly made to the “power” of medicine usually refer to its scientific and moral dangers—dangers that are described as potentially “catastrophic,” rather than just “serious,” when such phenomena as “human carcinogens” or “DNA damage” are discussed. The ability to cure disease is seldom mentioned. In those rare instances when it is, the term “cure” is either used ironically, or (as in recent, more hopeful reports on the outcome of therapy for childhood leukemia), with tentativeness and caution. Given the current state of medical knowledge, “an objective definition of cure has not been possible . . . the state of complete remission based on our current ability to detect residual disease, is not distinguishable from a true disease-free state . . .” (George et al., 1979:272). Controversies about the basic methodology of medicine and its underlying way of thought are repeatedly aired: the pros and cons of randomized clinical trials, for example, of clinical decision analysis and, above all, of various approaches to risk assessment and containment. The need for reducing uncertainty and regulating risk is affirmed and reaffirmed, accompanied by a cacophony of opinions about who should do it, and how. The problems of uncertainty that lie on the borderline between medicine, public policy, and ethics, which are felt to touch on the “ultimate conditions . . . [and] reality” of man’s existence (Bellah, 1974:359) —for example, the uncertainties of “genetic engineering”—have elicited the greatest attention, the “most severe chills,” (Callahan, 1979:9) and the deepest “Orwellian shadow[s].”<sup>2</sup>

Both collective awareness of problems of medical uncertainty and uneasiness about them seem to have grown significantly since the 1950s when I wrote the “Training For Uncertainty” essay. At that time, it was primarily through the professional education and socialization process they underwent that medical students came to recognize these problems, formulate them as such, and attach to them considerable importance. They generally did not arrive in medical school with the insight that uncertainty was generic to medicine and the role of physician, or with a social kind of concern about the subject. Whatever common anxiety they experienced in this regard was focused primarily on the individualistic question of how competent and composed each of them could learn to be in the face of this uncertainty. It is true that the publication of “Training For Uncertainty” evoked a response from more readers than I had expected, but this came from a limited range of professional and educational

<sup>2</sup>Phrase used in the opinion rendered by the Court of Appeals of New York State on the consolidated cases of *Becker v. Schwartz* No. 599, and *Park v. Chessin* No. 560, December 27, 1978. Both these cases concerned issues relevant to genetic counseling and amniocentesis.

milieux: from those who were training persons to be nurses, social workers, lawyers, clergymen, and business executives, as well as physicians, who felt there was a special relation among these roles, the knowledge, skill, responsibility, and human relations concerns they entailed, and the uncertainty dimension. They expressed more pride than worry in the uncertainty component and the challenge of these roles; and they were appreciative of an article that acknowledged and analyzed them. Nothing like the outpouring of popular and professional discussion and writings on uncertainty that characterizes the 1970s existed at that time. In fact, if anything distinguished the appearance of "Training For Uncertainty" in the 1950s, it was its singularity.

The amplification of professional and public interest in medical uncertainty, and the accompanying apprehension since then, result, in part, from the organized way in which uncertainty, error and risk and their implications for health have been continually highlighted by the mass media, environmentalist and bioethics groups, the courts, the legislatures, and various federal government bodies, such as the Food and Drug Administration, the Department of Health, Education, and Welfare, the Occupational Safety and Health Administration, the Environmental Protection Agency, and the Nuclear Regulatory Commission. Whatever contributing role these and other agencies may have played, why have they become intensively involved in dealing with the phenomenon of medical uncertainty in the last decade, and emphasized its perilous aspects? Why is there a reservoir of general interest and disquietude in this area?

The heightened preoccupation with uncertainty, as mentioned earlier, is associated partly with the scientific and technological transformation medicine has undergone in this century. Some of the most fundamental and impressive advances in biomedical knowledge and successes in diagnosing, treating, and preventing disease have occurred quite recently, since the 1940s. One of the consequences is that the stakes have become very much higher in medicine than in the past. The modes of investigating and treating diseases are now much more powerful. They are also potentially a great deal more dangerous. As knowledge of disease and therapy have grown (as the case of therapy for childhood leukemia cited earlier), the difficulties of sorting out what physicians call "natural" remissions and reversals of disease and transient placebo effects of treatment, from the enduring biological impact of a regimen of therapy, have become greater. The research procedures and designs that have been devised to try to cut through this type of uncertainty so that clinical results can be more accurately evaluated have become more complex, both methodologically and ethically, and, in many cases, more risky. Uncertainty and risk, and awareness of them, have been increased by medical progress in both these regards. Medical advance also seems to have created a rise in expectations about health and well-being, longevity, and elimination of disease, which has had a boomerang effect on attitudes toward uncertainty. Public tolerance of medical uncertainty appears to have diminished, and indignation about its persistence has grown.

The development of scientific medicine, then, has both uncovered and created uncertainties and risks that were not previously known or experienced. Some of these problems are so new, and raise such intricate and important questions of fact, technique, judgment, authority, and values, that they cannot be quickly or neatly resolved. The indeterminateness of these perplexing issues has contributed to the sense of uncertainty about uncertainty, and augmented the sense of risk about risk. For example, in mid-1978, the World Health Organization declared that smallpox, an epidemic viral disease that has killed millions of persons over the course of human existence, is now on the verge of being eliminated from the earth:

These events cast in sharp relief a difficult problem that science and mankind never has [sic] had to face before: If an ancient, deadly and historically feared disease is at last eradicated through the marvels of modern medicine, should the laboratory stocks of the virus that caused it be kept for important related research? Nine laboratories, three in the United States, are known to have retained smallpox virus. What steps are being taken so that none will escape again in the distant future, as it did in Birmingham, conceivably causing a major epidemic in a population that by then may have lost its immunity, a population treated by doctors who may have all but forgotten the disease? And how reliable are these precautions? (Stockton, 1979: 36)

The Birmingham (England) case, referred to above, involved two tragic deaths: that of Janet Parker, a 40-year-old medical photographer at the Medical School of Birmingham University, who contracted a fatal case of smallpox in late August 1978 from a laboratory situated on the floor below her darkroom in the medical school; and the death by suicide (on September 1, 1978, five days before Janet Parker's) of 49-year-old Dr. Henry Bedson, the virologist who ran the laboratory. The laboratory specialized in smallpox research and, it was later revealed, failed to meet the standards of precaution and safety recommended for the handling of dangerous pathogens. Although these two interconnected deaths did not lead to a general outbreak of smallpox, they become *causes célèbres*, because they were felt to epitomize some of the potential uncertainties, dangers, and damage that medical progress has brought and the many unsolved problems of how to deter, contain, and control them (Hawkes, 1979).

To a much greater and more sustained extent than the intrinsic and laboratory-borne hazards of work with smallpox virus, research with recombinant DNA (the compound deoxyribonucleic acid) has become a center of deep worry and impassioned controversy over the uncertainties of new and contemplated biomedical developments. The questions concern the potential benefits of these developments and the postulated risks; whether, how, and by whom these hypothesized benefits and risks can be proved and/or disproved; and the issue of whether, why, how, and by whom such research can or should be controlled.

DNA is the molecule in which encoded genetic information is stored, and the material vehicle of the instructions by which hereditary traits are passed from

one generation of organisms to the next. So-called recombinant DNA is the new technology that enables scientists to take DNA from one organism and splice it onto DNA from another, using a recently discovered class of ordinary enzymes (the restriction enzymes). This process allows the genetic information in DNA molecules to be specifically rearranged, so that new living molecules and genes—in effect, new forms of biological life—are created. Usually, the recipient organism is a bacterium that will replicate the “foreign” DNA along with its own genes, distributing both to “daughter” cells during cell division. Since bacteria divide rapidly, large amounts of the DNA segment can be synthesized by this means. This is considered a major breakthrough in genetic research, with great potential benefits. On a basic research level, because recombinant DNA technology makes it possible to obtain many copies of genes from higher organisms, it provides a valuable medium and resource for working out the detailed structure of the chromosomes and the dynamics of gene action in these organisms. Scientists believe that such advances in knowledge could, in turn, further our understanding of the fundamental mechanisms involved in immunological responses, resistance to antibiotics, the growth and spread of cancer cells, and other crucial medical phenomena. Scientists also hope that the recombinant DNA techniques may enable them to select segments of DNA that are templates for valuable therapeutic products, such as human insulin and the antiviral agent interferon, which might be multiplied and produced in copious amounts by inserting these segments into cultures of *Escherichia coli* (*E. coli*), or some other bacteria. Still another benefit envisioned is the prospect of extending the climatic range of food crops by equipping plants to secure their nitrogen supply from the air.

With the development of this new technology, however, and as these promising lines of research have opened up, concern about the possible biohazards of recombinant DNA has grown and become more audible, along with assertions about its advantages. The voiced concern started within the scientific community itself, coming at first from those scientists most directly connected with the research, and it has progressively come to include representatives of the government, lawyers, social scientists, private citizens, public-interest groups, and the media. The stormy debates triggered by these expressed apprehensions, debates that still continue, have been focused not only on specific and proximate technical risks of recombinant DNA research, but also on their broader, more long-term evolutionary and ecological dangers:

Simultaneously . . . with the arrival of this new technology, some of us [began] to wonder whether it might also have unexpectedly bad consequences, such as through the creation of new types of organisms never yet subjected to the pressures of evolution and which might have disease-causing potentials that we do not now have to face. In particular, we worried about the creation of bacteria selectively tailored to be resistant to all known antibiotics or the insertion of the genes of tumor viruses into bacteria known to multiply in humans. (Watson, 1978: 3)

And if such alterations inadvertently did occur, what would happen if they



escaped from the laboratory into the environment? It has been urgently asked whether their effects would be malignant or toxic, and their spread irreversible.

This is not the place to chronicle the long history and vast implications of the recombinant DNA research controversy. (Swazey, Sorenson, and Wong, 1978). (An archive of documents, interviews, and audio and video tapes on the history of recombinant DNA and the issues associated with it has been created as part of the Oral History Project of the Massachusetts Institute of Technology.) But I do want to identify some of the ways in which this important case of actual and incipient biomedical developments both involves and illuminates the new societal and cultural uneasiness about medical uncertainty that I am exploring.

To begin with, however vehement the statements and counterstatements about the potential benefits and biohazards of recombinant DNA techniques, the fact remains that both are largely a matter of conjecture. Most forms of recombinant DNA research are so new that there is little in the way of a laboratory past to guide scientists. Although probability reasoning and risk-benefit logic can be and have been applied to the problem of assessing, comparing, and evaluating the likelihood and magnitude of various risks and benefits recombinant DNA research may entail, the unknowns are too great for essentially qualitative judgments to be more quantitatively, precisely, reliably, or conclusively expressed. To scientifically prove or disprove the risk-benefit appraisals that have been made would require much more laboratory, genetic, metabolic, and ecological information than is currently available.

Partly for this reason, the perspectives of scientists as well as non-scientists on the uncertainties of recombinant DNA, and the positions that have been taken by various individuals and groups on its possible benefits and hazards, have been based as much on personal and social sentiments, values, and beliefs, as on scientific concepts, facts and methods. A powerful sentiment that has been repeatedly expressed in the discussions about DNA is awe: a mixture of wonder, reverence, and fear over how fundamental this molecule is to all forms of life. This sense of awe underlies some of the almost messianic hopes about the benefits to humanity that recombinant DNA may bring, along with "facts that may be necessary to the [very] survival of our . . . advanced societies." (Watson, 1976:15). This same conviction about the relation between DNA and the essence and continuation of life has also contributed to the even more conspicuous sense of foreboding and potential catastrophe that the capacity to manipulate genes has helped to arouse. This research has been referred to as a "manipulation of life" that constitutes an "ultimate experiment" in "man-made evolution" (Wade, 1977), an intervention that might "counteract, irreversibly, the evolutionary wisdom of millions of years" (Chargaff, 1976) by crossing a supposed "natural barrier" between species.

As Thomas observes:

The recombinant line of research is . . . upsetting not because of the dangers now

being argued about but because it is disturbing in a fundamental way to face the fact that genetic machinery in control of the planet's life can be fooled around with so easily. We do not like the idea that anything so fixed and stable as a species line can be changed. The notion that genes can be taken out of one genome and inserted in another is unnerving. Classical mythology is peopled with mixed beings—part man, part animal or plant—and most of them associated with tragic stories. Recombinant DNA is a reminder of bad dreams. (Thomas, 1979: 71)

And indeed, the huge body of scientific and popular literature that has been published on recombinant DNA is full of such mythic and “bad dreams” imagery, including Frankensteinian allusions to the production of new, uncontrollable, destructive creatures (Gaylin, 1977).

The interweaving of “deliverance” and “disaster” metaphors in the discussions of recombinant DNA, and the ambivalence expressed about whether “disturbing the universe” in this way (Dyson, 1979), or desisting from doing so, is the more dangerous, are related to another set of attitudes and beliefs around which these debates have turned: differing conceptions and philosophies about errors and mistakes, and the role they play in the physical universe, the biosphere, and human affairs. One of the premises on which some of the more sanguine and serene opinions about the potentialities of recombinant DNA is based is the notion that to err is neither exclusively human nor primarily regrettable. Rather, it is a basic life process: “Errors are made by nature . . . replication is not perfect . . . [and] evolution is built up by the perpetuation of errors” (Thomas, 1979: 28-30). In this view, DNA itself shows this “capacity to blunder”—this “driving force in evolution” (Cohen, cited in Powledge, 1977: 19). The making of mistakes, and the exploration of them, are also considered to be central to imaginative, creative human thought and discovery, in science as in art.

Along with the celebration of error, a skeptical, anxious, and vigilant outlook on “natural” and “human” mistakes has been forcefully expressed throughout the debates on recombinant DNA. “The evolutionary wisdom of nature has given us bubonic plague and cancer,”<sup>3</sup> is the wry comment that a professor of medicine, involved in the recombinant DNA controversy, made on the supposedly benign and beneficent properties of errors in and by nature. What many observers and commentators assume are the less predictable and controllable consequences of human error have elicited still greater apprehension. These consequences, above all, have brought forth feelings of cosmic dread and primal sin, as in the following poem, “Original Synthesis”, on “the Man-Made Gene,” by a microbiologist:

<sup>3</sup>Statement by Stanley Cohen, professor of medicine at Stanford University School of Medicine, and a signatory to the 1974 letter calling for a moratorium on certain types of recombinant DNA research that was drafted by researchers working on it, and published both in *Science* and in *Nature* in July 1974. Cohen's remark is quoted in Powledge (1977:19).

One can't help but admire the craftsmanship.  
Half a dozen years for assembly, forty synthetic  
frag-  
ments joined end to overlapping end.  
Larger than life it sits there,  
the 126 ribs all in place.<sup>1</sup> You can almost hear it rattling its terminator.

If only it didn't look so much  
like a goddamned serpent! Archetypes  
crowd in, insistent as base-pairs.  
Even now, in some bounteously  
equipped laboratory,  
a tyrosine suppressor transfer-DNA template  
sidles up to an unwary investigator,  
slyly whispering in vitro, "*Eritis sicut Deus,*  
*scientes bonum et malum.*  
Take the apple  
and improve on it.  
Be fruitful and replicate."  
Or Hermes—unerring messenger—  
tires of the scene, suppresses  
a yawn,  
unwinds his doubly-snake staff and transfers  
to future generations  
the gene for winged feet.

Deoxyribonucleic acid sounded once  
strange as Quetzalcoatl and as remote.  
High on the stepped pyramid  
we encounter  
now  
the unmasked visage of the twofold god:  
We look upon the bringer of maize.  
We look upon the Feathered Serpent. (Isaacs, 1977)

This shuddering sense of metaphysical danger is premised not only on the belief that human error is unnatural, ungovernable, and peculiarly difficult to rectify or reverse; but also on the belief that it is made more lethal by the moral and spiritual weaknesses and imperfections of human beings and human societies—above all, by the evils that result from their self-centeredness, and their temptation to play God. This latent conception of human fallibility seems to have been brought to the surface and made more acute by biological and medical developments, such as recombinant DNA, and by the risks involved in the use of nuclear power—such as the accident at Three Mile Island—widely regarded as potentially generative of unique events that could menace life as we know it on a worldwide basis:

One characteristic of the new class of disaster is simple magnitude; for some reason, we seem to tolerate losses more easily when, as in highway accidents, they occur separately, and to recoil when a large number occur at once. Another, perhaps more significant characteristic, is peril to some large and irreparable or irreplaceable piece of nature—such as a species, or the ozone in the upper

atmosphere, or the birds in the spring—or to some large piece of human civilization, such as New York City, or to a particular tribe or people.

In attempts to prevent one-time catastrophes, the usual tools of prediction are useless. (Talk of the Town, 1979b)

In addition to these scientific and suprascientific questions about the uncertainties and hazards of recombinant DNA research, another cluster of concerns has been prominent in the controversy. The “limits” of scientific inquiry and its “regulation” are the key words that have been used most frequently to refer to these issues, along with the reiterative question: “Who decides who decides?” The development of recombinant DNA has not only precipitated impassioned discussion about whether, when, to what extent, in what ways, and by whom decisions and actions should be taken to constrain risk-fraught scientific work. This research has also constituted a dynamic, widely publicized, *in vivo* experiment in the application and appraisal of a wide gamut of controls intended to govern it responsibly.

Over the course of the past six years of its complex and turbulent history, recombinant DNA has been the object of several moratoriums in certain types of potentially troublesome experiments, invoked nationally and internationally by molecular biologists themselves; by the formulation and issuance of guidelines by National Institutes of Health specifying physical and biological containment levels and procedures, and proscribing particular experiments; a whole series of local controversies and actions involving universities and research institutes, citizens’ groups, and city and state governments in at least a dozen different American localities; congressional hearings; the introduction of regulatory bills in the United States Senate and House of Representatives; lobbying and counterlobbying on the part of numerous scientific, community and special interest groups; and by the consequent, perhaps temporary, forestalling of national legislation to control work with recombinant DNA.

The attitudes toward uncertainty and risk that have been expressed in the context of these DNA deliberations have been far from olympian. They have included a detailed and sometimes impassioned consideration of the “possible scenarios of misfortune” and fortune that might result from work with recombinant DNA (Sinsheimer, 1978: 27-28). They have also been punctuated by attempts to assign responsibility, exact accountability, and affix blame to particular individuals, groups, and forces in the society for the handling or mishandling of uncertainty, the biohazards, medical risks, and adverse health effects that could result. A line of distinction between fault-accompanied and fault-free uncertainty has not been maintained. Nor has the concept of no-fault been considered acceptable, in this context, any more than it has in other areas of medical uncertainty and risk.

Throughout these debates, the issue of whether to regulate or not to regulate, and how, have brought a wide variety of concerns to the surface. These have ranged from freedom of inquiry anxieties and affirmations, to holocaust- and civil-rights-movement-associated protests against “genetic engineering” and

trying to “perfect the human race” (“We shall not be cloned . . .”),<sup>4</sup> to philosophical uneasiness about the extent to which our scientific and technological endeavors continue to rest on “our faith in the resilience, even the benevolence of nature . . . . Ought we to step more cautiously as we explore the deeper levels of matter and life?” (Sinsheimer, 1978:24). The “risk-regulation” question has not only increased these uncertainties and made them more manifest, but has also generated new forms of methodological and moral uncertainty specifically associated with the regulation process:

Risk regulation itself carries risks. . . . [T]here are two different kinds of uncertainty that plague risk regulation. Some uncertainty is inherent in regulating activities on the frontiers of scientific progress [where we] simply do not know enough. . . . In the face of such uncertainty society must decide whether or not to take a chance—to wait for more information before going ahead . . . , or to go forward and gamble that solutions will be found.

The other kind of uncertainty that infects risk regulation comes from a refusal to face the hard questions created by lack of knowledge. It is uncertainty produced by scientists and regulators who assure the public that there are no risks, but know that the answers are not at hand. Perhaps more important, it is a false sense of security because the hard questions have never been asked in the first place. (Bazon, 1979: 279)

In the case of recombinant DNA, the hard questions *have* been asked, repeatedly, often dramatically, and on a wide local, national, and international scale. In fact, recombinant DNA constitutes a particularly important and conspicuous set of scientific and technological developments around which many of the cultural themes and social issues associated with the growing significance of medical uncertainty and its broader implications have clustered. This is only one such instance. Even more than the supposed dangers of recombinant DNA, for example, the accident that occurred last March at the Three Mile Island nuclear plant in Pennsylvania has brought forth anguished alarm and indignation over the potentially disastrous cosmic significance of experimenting and tampering with nature in basic ways; of error, particularly in its human form; and of too much scientific audacity and technological pride. These fears are clearly reflected in comments that appeared in *The New Yorker*:

A recent headline in the *Washington Post* concerning the afflicted nuclear power plant on Three Mile Island, in Pennsylvania, read, “Aides Wonder if Contamination May Close Plant Forever.” . . . The appearance in news stories of words like “forever” is one more clear signal, if we still need it, that with the discovery of nuclear energy events of a new order of magnitude, belonging to a new dimension of time, have broken into the stream of history. In unleashing nuclear

<sup>4</sup>Such allusions to the “superior race” eugenics of Adolph Hitler and to “We Shall Overcome,” the hymn of protest and affirmation of the civil rights movement, were made in the course of public meetings about recombinant DNA research and its potential dangers that took place in Cambridge, Massachusetts, in the last half of 1977. See Swazey, Sorenson, and Wong (1978:1071).

chain reactions, we have brought a cosmic force, virtually never found in terrestrial nature, onto the earth—a force that, both in its visible, violent form of nuclear explosions and in its invisible, impalpable form of radiation, is alien and dangerous to earthly life, and can, through damage to life's genetic foundation, break the very frame on which the generations of mankind are molded. . . .

Another headline that caught our attention was one in the *News* which read, "Human Error Probed in Leak." The concept of "human error" has cropped up often during the Pennsylvania crisis. . . . The main thing that the planners concerned with nuclear power left out of their scenarios was not the correct workings of some valve or control panel. It was the thing that no scenario can ever take into account: simple human fallibility per se—an ineradicable ingredient in the actions not only of power-plant operators but also of power-plant designers, of government officials, and of the general public as well. . . . At the deepest level, then, the human error in our nuclear program may be the old Socratic flaw of thinking that we know what we don't know and can't know. The Faustian proposal that the experts make to us is to let them lay their fallible human hands on eternity, and it is unacceptable. (Talk of the Town, 1979a)

Experimentation, in which the consequences of certain kinds of catastrophes can sometimes be gauged, is also sharply limited. Just as one cannot remove the ozone layer in order to find out how important it is to the earth's environment, one cannot release large amounts of radiation into the atmosphere in order to discover its effects on human society. Lacking these experiments, the earth itself becomes the laboratory: it is on the earth that the effects of a particular one-time catastrophe must originally become known. First, by accident, we release the radiation; then, twenty years later, we find out how many cancer deaths have been caused. In the last analysis, therefore, the limit that restrains our nuclear pioneering is the singularity of the earth. Because there is only one earth, and one mankind living on it, all our experiments with nuclear devices and other lethal substances and machines are at the same time actions taken in real life. Of course, science is capable of many wonders, including, for example, the cloning of a frog. Maybe one day, in some other solar system, our scientists will succeed in cloning the earth itself. . . . Until then, though, they would do well to leave our present earth—the parent of us all and our only home—alone. (Talk of the Town, 1979b)

Whereas such apprehensions about the advertent and inadvertent consequences of nuclear energy and recombinant DNA are indicative of the apocalyptic modes of response that are occurring to some of the ways in which we have "probed . . . dissected [and] rearranged [the] components of nature . . . bend[ing] its forms and divert[ing] its forces to human purposes," (Sinsheimer, 1978:24), the increased concern about potential hazards of natural and man-made chemicals is more closely associated with a cluster of cognitive, procedural, and value problems to which the mounting preoccupation with risk, its assessment and its regulation has contributed.

A particularly telling indicator of the magnitude of this concern about chemicals can be found in the area of drug development. The Center for the Study of Drug Development in the Department of Pharmacology and Toxicology of the University of Rochester School of Medicine and Dentistry conducted searches for me in their vast computer files of literature on drugs.

Eileen Thomas, the research assistant who made the searches, found that a major part of the drug development literature was concerned with the topics of risk assessment and risk benefit. She identified 2,212 articles on these topics in the Center's files that have been published during the past five years in medical and in lay literature.

There is a sense in which the concern about the noxious effects of chemicals on the environment and human health, like the disquietude about recombinant DNA and nuclear energy, involves anxiety about possible (individual and collective, short- and long-term) disaster. For it is especially focused on the dangerous possibility that many chemicals may be human carcinogens and/or mutagens: major causes of cancer and of genetic birth defects in the population. To an even greater extent, the concern highlights the difficulties and dilemmas of finding scientifically adequate, culturally appropriate, and socially effective ways of appraising and governing risk, now that it has become defined as such a central and far-reaching problem.

To begin with, the sheer number of chemicals that could be carcinogenic or mutagenic is overwhelming. And the resources available for assessing them are inherently limited:

The American Chemical Society estimates that there are 4 million chemicals in existence, with some 6,000 new ones emerging every week. Some 44,000 of these chemicals are believed to be in common use in the United States. . . . (Staff Paper, 1979:1)

. . . A key method for detecting carcinogens is the animal bioassay. . . . The utility of animal cancer tests for cancer prevention, however, is limited by several important factors. Animal cancer tests are too expensive (currently about \$350,000 per chemical for a thorough test) and take too long (about 3 years) to be used for the testing of the many thousands of chemicals to which humans are exposed. . . . There are not enough pathologists to read the slides even if it was decided to test only the thousand or so new chemicals introduced into commerce each year, not to mention the 50,000 untested commercial chemicals already in use and the even greater number of chemicals in the natural world. . . . An environmental carcinogen causing cancer in 1 percent of 100 million people would result in a million cases of cancer. Detection of a chemical causing cancer in only 1 percent of the test animals would require the use of 10,000 rats or mice and would be extraordinarily expensive. A test group of only 50 mice or rats of each sex at each of two doses is the usual size of the most thorough cancer experiments. This limitation is somewhat overcome, though not entirely satisfactorily, by exposing the animals to as high a dose as possible (the "maximum tolerated dose") which, by increasing the tumor incidence, partially off-sets the statistical problems inherent in the small sample size. (Ames, 1979:587-589)

As the foregoing suggests, the procedures that are utilized to identify, evaluate and control the human risks associated with chemicals that could cause mutations or cancer pose various methodological uncertainties of their own. Primary among these are two issues. What role should human epidemiological studies, on the one hand, and animal bioassays and short-term *in vitro* laboratory

tests, on the other, play in assessing the riskiness of chemicals? There is the problem of deciding in what ways and to what extent findings extrapolated from animal studies can and ought to be applied to the human level, especially when high dose testing is used on laboratory animals as a means of dealing with some of the sampling, cost and scarcity difficulties inherent in such inquiries. What does the finding of cancer in animals at such high doses, for example, imply for the carcinogenic potency and hazard of these same substances for human beings?

Despite these major uncertainties, quantitative-risk assessment is widely employed. However, its adoption has been accompanied by a great deal of heated public, as well as professional, discussion over the quality and meaning of the numbers it produces:

The qualitative phase of risk assessment is followed by the quantitative phase, and here the science is highly speculative and replete with uncertainty. From the carcinogenic response data obtained at the high dose levels administered in the laboratory it is, of course, necessary to extrapolate downward to arrive at an estimate of the tumor incidence in very low doses expected in the environment. Then, another leap of faith is necessary if this extrapolation of the carcinogenic response from high dose to low dose is to be accepted as even a crude approximation of human risk. The susceptibility of the highly heterogeneous human population that would be exposed to the carcinogen could differ greatly from the susceptibility found in the small number of relatively homogeneous laboratory animals tested. Also, because humans are exposed to countless pollutants, additive or synergistic effects are always possible. . . . [W]hatever the advantages of risk quantification, to reach firm conclusions as to the comparative response of laboratory animals and humans to a given carcinogen is still impossible. (Carter, 1979:813)

When the potential uncertainties and errors of the methods and techniques of risk assessment and of the reasoning underlying them are so great that, according to Arthur C. Upton, director of the National Cancer Institute, "an estimated risk of 4.2 cancers . . . per 220 million people, as calculated by extrapolation from mouse or rat data, might turn out in reality to be as low as no human cancer, or as high as 420,000 cancers" what is the worth of a quantitative analysis? How should it be interpreted and utilized?

The debate about these kinds of methodological and procedural matters has been intensified by their relationship to the progressively expanding role of government in evaluating and regulating risks to public health and safety, and to still another category of uncertainty that this role has engendered:

Federal decision-making in the control of carcinogens is a hot subject that seems to invite more controversy all the time. Disagreement exists within the government itself over "cancer policy" and especially over whether the science of quantifying cancer risks is far enough advanced to be safely used by regulatory agencies in setting standards for human exposure to carcinogens.

The director of the National Cancer Institute, Arthur C. Upton, has recently circulated a memorandum warning that the misuse of risk quantification could



lead to public health catastrophes. Although citing no specific instances of misuse, Upton has told *Science* that he is worried lest regulatory officials make the mistake of minimizing cancer risks on the basis of estimates that fail to reflect the underlying uncertainties in the mathematical modeling.

On the other side of the risk assessment issue are the government officials and scientists, including some at the White House Office of Science and Technology Policy, who are afraid that risk quantification will either be neglected by some agencies or misused to overestimate risks in support of exposure standards that are too strict and costly. (Carter, 1979:811)

Within this framework, how does one determine whether particular chemical substances pose low, moderate, or high human risks; whether these risks have been accurately characterized, underestimated or overestimated; and, in the light of these assessments, whether they are being appropriately regulated, underregulated, or overregulated? Here the uncertainties of scientific knowledge and political governance intersect with the uncertainties of value and belief. For, as Judge David L. Bazelon has stated, virtually all risk regulation decisions entail an intricate mix of “fact and value questions:”

In determining questions of fact, such as the magnitude of risk from an activity, we as a society must rely on those with the appropriate expertise. Judges and politicians have no special insights into this area. Where questions of risk regulation involve value choices such as how much risk is acceptable, we must turn to the political process.

But even this formulation leaves many problems unanswered. There is no bright line between questions of value and of fact. Even when a problem is appropriately characterized as one of scientific fact, consensus and certainty may very often be impossible even in the scientific community. Many problems of scientific inference lie in the realm of “trans-science” and cannot be resolved by scientific method and experimentation. . . .

The growing use of analytic tools such as cost-benefit analysis magnifies the chance that unrecognized value judgments will creep into apparently objective assessments. Even the most conscientious efforts by experts not to exceed their sphere of competence may be inadequate to safeguard the validity of the decision-making process. (Bazelon, 1979:278-279)

#### *From Medical to Metamedical Uncertainty*

Dealing with medical uncertainty and risk in ways that do not go beyond the boundaries of competence has become increasingly difficult, partly because many of the questions that uncertainty and risk now pose do not easily fit into established disciplinary, professional, or institutional frameworks of analysis or decision making. Four relevant cases that have occurred in the course of the past year, and received a considerable amount of public attention, are illustrative of the kinds of metaquestions currently arising out of the matrix of medical uncertainty. (These are questions that would have been far less likely to present themselves in the 1950s when I first began my medical uncertainty-watching, or to be brought before a court of law, as they were in 1978 and 1979.)

The first case is associated with the potentialities, uncertainties, and risks of organ transplantation, and with what Judith Swazey and I have called its "gift-exchange" aspects (Fox and Swazey, 1978:5-39, 381-384). Robert McFall, an unmarried asbestos worker suffering from a terminal case of aplastic anemia, filed suit in a Pittsburgh court seeking an injunction to compel the unwilling David Shimp, his cousin, to become the donor in a bone marrow transplant that might save his life. The issues with which the judge in this case had to wrestle included the question of whether we are obliged to be "our cousin's keeper"; whether we have a duty to try to "rescue" another person and, if so, when; whether there is such a thing as a "compulsory donation"—a mandatory and coercible gift of self or life (Meisel and Roth, 1978).

The second case is one that "presents a perplexing problem spawned by modern nuclear warfare" and by "the dangers of radiation from nuclear detonation," the case of "Stanley Jaffee and Sharon Blinn Jaffee, individually and Stanley Jaffee, on behalf of others similarly situated *v.* United States of America."<sup>5</sup> This case turned around Jaffee's avowal that, in 1953, when he was serving in the United States Army, he and other soldiers were ordered to stand in an open field near the test explosion of a nuclear device at Camp Desert Rock, Nevada, without any protection from radiation and, without their knowledge and consent, despite the fact that the government knew of the "grave risks of injury from such exposure." Jaffee further alleged that he developed inoperable cancer because of his exposure to this radiation. In reviewing the way the district court ruled on this case, the United States Court of Appeals for the Third Circuit found itself face to face with the question of whether "under the extraordinary facts of this case, in which it is alleged that many soldiers have been exposed to nuclear radiation," the "sovereign immunity" of the United States from suit could and should be waived by the judiciary or by Congress; and, whether the United States should be directed to provide "warning relief" to Jaffee "and all members of the class about the medical risks facing them," and/or relief in the form of subsidized medical care.

The third case, a composite one, concerns genetic counseling, amniocentesis, and new concepts of genetic predictability. Two cases, those of Dolores Becker and of Hetty and Steven Park, were consolidated by the State of New York Court of Appeals. Dolores Becker, at the age of thirty-seven, became pregnant and gave birth to a child with Down's Syndrome. Mrs. Becker alleged that she was never advised of the increased risk of Down's Syndrome in children born to women over age thirty-five, or of the availability of amniocentesis to detect the condition in utero, during the period she was under the care of her obstetrician. She would have had an abortion, she contended, if the test had indicated her fetus was affected.

<sup>5</sup>Jaffee *v.* United States of America No. 78-2041, United States Court of Appeals for the Third Circuit, argued November 17, 1978. (Opinion filed February 9, 1979.)

Mr. and Mrs. Park claimed that they consulted the obstetricians who had cared for Mrs. Park during her first pregnancy about the likelihood of their having a second child with polycystic disease. They were informed that the chances of another child's being born with this condition were "practically nil" since the disease was not hereditary. Based on this information, the couple decided to have a second child, a child they would not have chosen to conceive, they contended, if they had been "correctly informed of the true risk of reoccurrence of this disease." The Parks, whose first child, afflicted with polycystic disease, died five hours after birth, had a second child, born with the same disease, who lived for two-and-a-half years.

Both the Beckers and the Parks sued for physical injuries, for psychiatric and emotional distress to themselves, for medical costs, and for institutional expenses in caring for the children born with genetic defects. They also sought damages on behalf of these children for "wrongful life." In rendering its decision on the companion cases, the court affirmed that "seeking compensation for the wrongful causation of life itself cast an almost Orwellian shadow . . . of genetic predictability," and this question would have to be resolved in a way that "transcends the mechanical application of legal principles":

Whether it is better never to have been born at all than to have been born with even gross deficiencies is a mystery more properly to be left to the philosophers and the theologians. Surely the law can assert no competence to resolve the issue, particularly in view of the very nearly uniform high value which the law and mankind has placed on human life, rather than its absence. Not only is there to be found no predicate at common law or in statutory enactment for judicial recognition of the birth of a defective child as an injury to the child; the implications of any such proposition are staggering. Would claims be honored, assuming the breach of an identifiable duty, for less than a perfect birth? And by what standard or by whom would perfection be defined? . . .

Simply put, a cause of action brought on behalf of an infant seeking recovery for wrongful life demands a calculation of damages dependent upon a comparison between the Hobson's choice of life in an impaired state and nonexistence. This comparison the law is not equipped to make. . . .

Who then can say, as it was essential to the parents' causes of action that they say for themselves, that had it been possible to make the risk known to the children-to-be—in their cellular or fetal state or, let us say, in the mind's eye of their future parents—that the children too would have preferred that they not be born at all? To ordinary mortals, the answer to the question, obviously, is "no one." Certainly, the answer does not lie in the exercise by the children, if their mental conditions permit, of subjective judgments long after their births. Therefore, whatever be the metaphysical or philosophical answer—speculative, perhaps debatable, but hardly resolvable—and, however desirable it may be for society to otherwise treat with these problems with sensitivity, I am compelled to conclude that the matter is just not justiciable.<sup>6</sup>

<sup>6</sup>*Becker v. Schwartz* No. 558, and *Park v. Chessin* No. 560, State of New York Court of Appeals, December 27, 1978.

The fourth case is one that has received the most coverage from the media. Chad Green,<sup>7</sup> a two-year-old boy with acute lymphocytic leukemia, received the antileukemic chemotherapy regimen at present considered to be the treatment of choice. In the second phase of this program, bone marrow tests indicated the boy's leukemia was in complete remission. However, his parents, Gerald and Diana Green, were reluctant to have their son continue chemotherapy, because of their deep concern about what they felt were the emotional and behavioral, as well as physical, side-effects Chad had suffered as a result of the treatment. They were skeptical about the cause and effect relation that is assumed to exist between chemotherapy and remission. In their opinion, none of the data or evidence they had seen "prove[d] that chemotherapy cures leukemia" (The New York Times, 1978). As one of the parents said, "Chemotherapy does not give anybody any hope as far as I am concerned. They cannot prove to me that chemotherapy works. . . . Half of the children are still dying when they are on these drugs. . . . In my opinion, chemotherapy isn't so good that it should be forced down anybody's throat" (Steinmann, 1978: 172). Without telling their physicians, the Greens withdrew their son from the maintenance chemotherapy schedule he was expected to follow at home for two or three years. Instead, they treated him with the diet of distilled water, vegetarian foods, and high doses of vitamins they had initiated while he was receiving chemotherapy, one they believed to be more beneficent than chemotherapy. They prayed, and began to give Chad laetrile, the controversial substance derived from apricot pits that many cancer patients in this country have been taking illicitly because it has not been recognized or approved by the medical profession, the National Cancer Institute, or the Food and Drug Administration.<sup>8</sup>

In February 1978, Chad Green's physician first went to court to seek the appointment of a temporary guardian for the child so that his chemotherapy could be resumed. The judge so ruled, and the Greens appealed the decision. Subsequently, the Greens, the physician, and the hospital where Chad was treated moved through a series of Massachusetts courts in legal confrontation over such questions as whether parents have the right to refuse and terminate certain forms of medically prescribed treatment for a child with a life-threatening illness, to opt for alternative forms of treatment that are not regarded as "consistent with good medical practice," to choose what they define

<sup>7</sup>See the Direct Appellate Review of this case ("Custody of A Minor"), ordered by the Supreme Judicial Court of Massachusetts, Plymouth, Mass. Adv. Sh. (1978) 2002, July 10, 1978.

<sup>8</sup>On September 27, 1978, in an attempt to clear up the twenty-year-old laetrile controversy, Arthur C. Upton, director of the National Cancer Institute (NCI), called for an NCI clinical trial of laetrile. In order to carry out such a trial, the NCI must apply for an Investigational New Drug permit from the Food and Drug Administration (FDA). Once this application is made, the FDA evaluates it, and decides whether or not to approve the clinical trial. At this writing, that decision is still pending.

as a “full life” rather than a long life for the child. However, there is an even more basic sense in which the case of Chad Green involved an examination of the medical profession’s probabilistic way of thinking about uncertainty, benefit, and risk. In this regard, the case could aptly be considered one in which probability reasoning itself went on trial, with the Greens alleging that the quality of the (physician’s) numbers was strained. What the court called the Greens’ “pessimism” concerning the child’s chance of cure by chemotherapy not only constituted a rejection of chemotherapy per se, but of the probability-based logic on which medical diagnosis, evaluation of therapy, and prognosis-setting are premised. In weighing the Greens’ perspective on their son’s prognosis, the court considered and, in the end, supported the medical opinion that “there is a substantial chance for cure and a normal life for the child if he undergoes chemotherapy treatment.” The court did so in a way that set forth the analytic framework within which medical experts had reasoned, as well as the facts and opinions they had stated:

According to the experience of medical experts in this case, the effect of this type of treatment on the long-term survival of leukemic children has been gratifying. After one year of treatment, 90% of the children are found to be disease free. In the second year of treatment, 70% are in a state of remission. At the end of the third year, 65% are still in remission. In the fourth year the survival rate curve flattens to show a steady survival pattern of approximately 50%.

Two other factors are relevant. First, it has been shown that survival rates vary according to the type of leukemic cells found in the child. Because in this case the child is afflicted with a “null-cell” type of leukemia, his chances of survival with chemotherapy are slightly higher than 50%. Second, because the child falls within an age group which has a higher probability of potential cure and long-term survival, the chances for successful treatment in his case are stronger.<sup>9</sup>

Thus, in affirming that “acute lymphocytic leukemia in children is fatal if untreated, chemotherapy is the only available medical treatment offering a hope for cure, the risks of the treatment are minimal” and the chances for cure are “substantial,” the court upheld probability reasoning as well.

In January 1979, Diane and Gerald Green petitioned the court to reopen the case. They sought to show that laetrile treatments should replace chemotherapy treatments. When the judge ruled that chemotherapy should be continued, and that laetrile should be stopped, on the grounds that it was slowly causing cyanide poisoning in the boy, the Greens moved to Mexico with their son. There, under the supervision of a clinic in Tijuana, the boy allegedly received a combined regimen of chemotherapy and laetrile. On October 12, 1979, three-year-old Chad Green died in the rented apartment near the clinic where he and his parents resided.

Central to the problems posed by all these cases are the uncertainties connected with relatively recent scientific and technical advances (human

<sup>9</sup>Verbatim quote from the Supreme Judicial Court of Massachusetts’ review of the case, Mass. Adv. Sh. (1978) 2002, July 10, 1978.

organ transplantation, the use of nuclear energy and power, genetic screening and counseling, chemotherapy for leukemia and other types of cancer), their potential risks in comparison with their possible benefits, and, especially, the hazardous consequences they may have for health, survival, and the quality of life. The fact that they were deliberated in court is indicative of the great proliferation of law and lawsuits that has taken place in American society during the past decade, the accelerating degree to which judicial and legislative bodies are being asked to make decisions about such complex scientific and technical matters:

Multiplying even more quickly than lawyers are laws and lawsuits. In 1977, the legislative bodies at the federal, state and local levels enacted approximately 150,000 new laws and each of these new laws, on the average, required the issuance of ten new regulations. Between 1969 and 1972, the case load of the federal courts (corrected for the increase in population) rose by half. If the federal appellate case load, which accounts for only 10 percent of all federal cases, continues to grow as it has in the past decade, over one million federal appellate cases a year will flood the courts by the year 2010. And four times as many suits are filed each year in the state courts of California alone as in the entire federal system. (Tribe, 1979:25)

Courts are often thrust into the role of authoritative decision-makers. But in recent years there has been growing concern about the ability of the judiciary to cope with the complex scientific and technical issues that come before our court. Critics note, quite correctly, that judges have little or no training to understand and resolve problems on the frontiers of nuclear physics, toxicology, hydrology, and a myriad of other specialties. And the problem is growing. Hardly a sitting in our court [United States Court of Appeals for the District of Columbia Circuit, Washington, D.C.] goes by without a case from the Environmental Protection Agency, the Occupational Safety and Health Administration, or the Nuclear Regulatory Commission. These cases often present questions that experts have grappled with for years, without coming to any consensus.

But the problem . . . is not confined to the judicial branch. Legislators are daily faced with the same perplexing questions. They, too, lack the expertise to penetrate the deepest scientific mysteries at the core of important issues of public concern. (Bazelon, 1979:278)

The McFall, Jaffee, Becker-Park, and Green cases described are characteristic of the uncertainty- and risk-associated scientific and technological cases that are increasingly coming before the courts and legislatures, although many of the questions they raise surpass a judge's, lawyer's, or legislator's domain of professional competence. What is more, the perplexing questions each of these cases entails extend far beyond scientific and technical issues, or even "the deepest scientific mysteries." In every instance, they open onto questions fundamental to the polity, the societal community, and the human condition itself. The issues with which all the participants in these cases have been asked to cope, and that the judges have been asked to judge, include problems of nonexistence, birth, life, survival, and death; identity, individuality, integrity, and autonomy; humanness, fulfillment, and meaning; equality and sovereignty; solidarity and reciprocity; responsibility, accountability, and immunity; impairment and

imperfection; injury and suffering; solace and relief; rescue and deliverance; compassion; and causality and chance. As the judge in the Becker-Park case recognized, many of these questions are essentially moral and philosophical; some of them are metaphysical. They cannot easily be resolved or even properly addressed through the law or under it. ("They are just not justiciable.") Certain of the questions—such as "the wrongful causation of life itself"—are what philosopher Simone Weil (1970:335) called "insoluble problems in all their insolubility." Others are "telic" questions, ones no "ordinary mortal," in the words of the judge, can answer: What is the fetus? How are we to regard its being?

As can be seen in these cases, when questions of this order and magnitude emerge from a consideration of problems of biomedical uncertainty, risk and predictability, there is a marked tendency to draw back from them. This drawing back is occurring repeatedly in American society at the present time. Awed recognition of what is ethically and existentially involved and at stake frequently causes even the most experienced and poised experts to shrink from the essential nature of the inquiry. One of the characteristic ways in which physicians, scientists, lawyers, legislators, and judges deal with these mysteries is by declaring them to lie outside of their own trained and legitimate sphere of competence, affirming that they are more properly to be left to the philosophers and theologians. But when confronted with such ultimate perplexities, philosophers and theologians draw a similar line and make analogous disclaimers. In the end, what generally happens is that the questions are recast in more narrowly disciplinary and practically manageable ways. The issues are operationalized and reduced so they can be analyzed and decided upon within the framework of existing scientific, technological, legal, and ethical theory, knowledge, and procedures.

An instructive example of the way in which such difficult ethical and religious questions are acknowledged but set aside can be seen in the conclusion of the Ethics Advisory Board, appointed by the secretary of the Department of Health, Education, and Welfare, that "it is acceptable from an ethical standpoint to undertake research involving human *in vitro* fertilization and embryo transfer," provided that certain conditions are met (Final Report, Ethics Advisory Board, 1979). As Margaret O'Brien Steinfels (1979) points out, in the end, the board paid relatively little attention to the issue that it cited as one of the major questions it had to face: namely, what is the moral status of the fertilized human egg, and the embryo and fetus that develop from it? Nor did they give much attention to the kinds of "soft ethical issues" brought before them by Leon R. Kass, in his testimony to the board at its Boston meeting on October 13-14, 1978, questions such as "the meaning and worth of one's body"; "the meaning of the bond among sexuality, love and procreation"; "lineage, identity and self-identity, respect and self-respect"; "the *idea* of the *humanness* of our human life and the meaning of our embodiment, our sexual being, and our relations to ancestors and descendants" (Kass, 1979). Rather, the board focused more narrowly on ethical issues of special concern to researchers, particularly

the problem of risk, and on a range of questions of immediate, practical importance to the Department of Health, Education, and Welfare. "Although never phrased in these words, the board's dominant question became: how can determined couples be protected from unknown risks in undertaking in vitro fertilization without recommending public funds for research and clinical trials? Proceeding in the manner of a body that hopes to reach a consensus, the board both acknowledged and finessed the issues on which it could not agree by careful attention to the wording of its conclusions" (Steinfels, 1979:5).

At the same time, however, new institutional arrangements for handling such questions are being developed and tried: bioethics institutes, for example, science courts, institutional review boards, ethics advisory boards, mixed scientist and public-interest groups, national and presidential commissions for the protection of human subjects and the study of ethical problems in medicine, biomedical and behavioral research, and an unprecedented array of moratoriums both on basic and clinical types of medical inquiry. The creation of these groups and mechanisms indicates there is, at least, a latent collective awareness that our established political, legal, and professional institutions cannot totally encompass or adequately resolve the deepest meaning of the moral and metaphysical questions about health- and medicine-relevant uncertainty.

What is the deeper and larger significance of the way that medical uncertainty has evolved in American society? The phenomena we have explored in examining the development of medical uncertainty suggest a macrointerpretation I would like to offer as a speculative conclusion.

The increased professional and public preoccupation with medical uncertainty notable throughout the 1960s and 1970s has been centered on problems of error and risk, hazard and harm, as well as probability and predictability. Although they encompass a wide spectrum of health-, illness- and medicine-associated matters, these uncertainty concerns have been especially focused on matters pertaining to molecular biology, genetics, and human reproduction; the transplantation and implantation of tissues, organs, and organisms; the use of chemicals and nuclear energy; and both innate and environmental factors that might play a role in the development of birth defects, genetic mutations, and cancer.

Central to these concerns, then, are particular advances and particular limitations in biomedical knowledge, therapy, and technology considered to have extraordinarily powerful and fundamental implications for human life, normalcy, health, mortality, and death. In this connection, for example, recombinant DNA technology is viewed not only as a recent development in biology, but also as a prototype and portent of genetic engineering, the emerging capacity of mankind to lay its hands on the evolution of all forms of life on this planet, including, and especially, on its own. Cancer is regarded not only as a set of malignant diseases with which biology and medicine are still unable to deal knowledgeably and effectively, but also, in the minds of many, as the most



pernicious, invasive, and lethal type of suffering to which human beings are subject.

The increased interest in medical uncertainty and its consequences is accompanied by a highly ambivalent outlook on various modes of intervening in the universe and the human condition, in order to discover new knowledge, achieve new certainty, and make progress by enhancing the quality and prolonging the length of human life. There is a curious inconsistency, if not paradox, in the fact that indignation over the continuing incapacity of medical science and technology in dealing with unsolved problems of health and well-being coexists with anxiety about medical "hubris" and the "nemesis"-borne side-effects of medical attempts to master these problems (Illich, 1976). Conviction about the need for more energetic steps to deter or limit scientific and technological interventions that are hazardous to health and, beyond that, to the world of life, go hand-in-hand with concern about the adverse consequences of exercising and imposing such restraint.

There is an "uncertainty-about-uncertainty," "ambivalence-about-ambivalence" quality to this process of worrying, prescribing, and worrying about the prescription we noted earlier. Its boundless irresolution suggests that something more culturally disorienting is happening besides the re-examination of such social values as vigorous meliorism and unbridled inquiry. The very axes of our way of thinking about uncertainty seem to be involved. Debates and deliberations, which raise systematic doubts about the intellectual appropriateness and moral adequacy of our scientific and legal logic for dealing with the kinds of problems of uncertainty that are now before us, are continually occurring. Probability reasoning, qualitative and quantitative modes of risk assessment, and the application of legal principles have all been thrown into question.

"These are hard times for the . . . intellect," Lewis Thomas (1979: 74) has observed. Within the framework of an advanced, secularized, modern society, we are being asked not only to consider collectively whether our Chad Greens have a "substantial chance for cure," but also whether we are "our cousin's keepers," and if there is such a thing as the "wrongful causation of life." Furthermore, we are called upon to do so at a stage in our societal evolution when certain aspects of our world-view seem to be shifting. Our sense of the beneficence and "resilience of both natural and man-made phenomena" (Sinsheimer, 1978: 25) has somehow been shaken in ways that heighten our sense of ignorance, mystery, fallibility, frailty, vulnerability "to a host of hostile influences inside and around us" (Thomas, 1979: 47), danger, capacity to harm, and potential catastrophe. We are not sure how to think lucidly and responsibly about a kind of unease and bewilderment that cannot be resolved in our laboratories, field stations, and clinics, or dispelled by the principle-based reasoning of the moral philosophers whom we are consulting increasingly. In our nontheocratic society, there is no official church that can deal with such matters on behalf of us all.

This is where the broadest significance of the evolution of medical uncertainty in American society lies. Leon Kass comes close to articulating it:

How should we think about the ethical issues, here and in general? There are many possible ways, and it is not altogether clear which way is best. For some people ethical issues are immediately matters of right and wrong, of purity and sin, of good and evil. For others, the critical terms are benefits and harms, risks and promises, gains and costs. . . . (Kass, 1979:34)

Our current preoccupation with medical uncertainty, error, risk, and harm is a symbolic language through which we are communicating some of our deepest questions about the cognitive, moral, and also the metaphysical foundations of our cultural tradition and outlook. It is also a primary medium through which fundamental aspects of our social, cultural, and cosmic way of thinking, feeling, and believing about ourselves, our society, this planet, and the universe are gradually being altered.

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## REFERENCES

- Ames, B.N. 1979. Identifying Environmental Chemicals Causing Mutations and Cancer. *Science* 204: 587-592. ©1979 by the American Association for the Advancement of Science. Reprinted by permission.
- Barber, B., and Fox, R.C. 1958. The Case of the Floppy-Eared Rabbits: An Instance of Serendipity Gained and Serendipity Lost. *American Journal of Sociology* 64: 128-136.
- Bazelon, D.L. 1979. Risk and Responsibility. *Science* 205: 277-280. ©1979 by the American Association for the Advancement of Science. Reprinted by permission.
- Bellah, R.N. 1974. Religious Evolution. *American Sociological Review* 29: 358-374.
- Callahan, D. 1979. The Moral Career of Genetic Engineering. *Hastings Center Report* 9 (April): 9.
- Cannon, W.B. 1945. *The Way of an Investigator*. New York: Norton.
- Carter, L.J. 1979. How to Assess Cancer Risks. *Science* 204: 811-816. ©1979 by the American Association for the Advancement of Science. Reprinted by permission.
- Chargaff, E. 1976. Letter to the Editor. *Science* 192: 938-940. ©1976 by the American Association for the Advancement of Science. Reprinted by permission.
- Comar, C.L. 1979. Risk: A Pragmatic De Minimis Approach. *Science* 203: 319. ©1979 by the American Association for the Advancement of Science. Reprinted by permission.
- Cournand, A. 1977. The Code of the Scientist and Its Relationship to Ethics. *Science* 198: 699-705. ©1977 by the American Association for the Advancement of Science. Reprinted by permission.
- De Craemer, E., and Fox, R.C. 1968. *The Emerging Physician: A Sociological Approach to the Development of the Congolese Medical Profession*. Stanford, Calif.: Hoover Institution Press.
- \_\_\_\_\_, Vansina, J., and Fox, R.C. 1976. Religious Movements in Central Africa. *Comparative Studies in Society and History* 18: 458-475.
- Dyson, F. 1979. *Disturbing the Universe*. New York: Harper and Row. Reprinted by permission of the publisher.
- Final Report, Ethics Advisory Board. 1979. *Federal Register*, June 17.
- Fox, R.C. 1957. Training for Uncertainty. In Merton, R.K., Reader, G., and Kendall, P.L., eds., *The Student-Physician*, 207-241. Cambridge, Mass.: Harvard University Press.
- \_\_\_\_\_. 1959. *Experiment Perilous: Physicians and Patients Facing the Unknown*. Glencoe, Ill.: Free Press.
- \_\_\_\_\_. 1974a. \_\_\_\_\_. Paperback edition. Philadelphia: University of Pennsylvania Press.
- \_\_\_\_\_. 1974b. Ethical Existential Developments in Contemporaneous American Medicine: Their Implications for Culture and Society. *Milbank Memorial Fund Quarterly/Health and Society* 52 (Fall): 445-483.
- \_\_\_\_\_. 1974c. The Process of Professional Socialization: Is There a "New" Medical Student? A Comparative View of Medical Socialization in the 1950s and the 1970s. In Tancredi, L.R., ed., *Ethics of Medical Care*, 197-227. Washington, D.C.: National Academy of Sciences.

- \_\_\_\_\_. 1976a. Advanced Medical Technology: Social and Ethical Implications. *Annual Review of Sociology* 2: 231-268.
- \_\_\_\_\_. 1976b. Medical Evolution. In Loubser, J.J., Baum, R.C., Effrat, A., and Lidz, V.M., eds., *Explorations in General Theory in Social Science* 2: 773-787. New York: Free Press. Reprinted with permission of the publisher.
- \_\_\_\_\_. 1978. Why Belgium? *Archives Européennes de Sociologie* 19: 205-228.
- \_\_\_\_\_. 1979. The Autopsy: Its Place in the Attitude-learning of Second-year Medical Students. In *Essays in Medical Sociology: Journeys into the Field*, 51-57. New York: Wiley.
- \_\_\_\_\_, and Lief, H.I. 1963. Training for "Detached Concern" in Medical Students. In Lief, H.I., Lief, V.F., and Lief, N., eds., *The Psychological Basis of Medical Practice*, 12-35. New York: Harper and Row.
- \_\_\_\_\_, and Swazey, J.P. 1974. *The Courage to Fail: A Social View of Organ Transplants and Dialysis*. Chicago: University of Chicago Press.
- \_\_\_\_\_. 1978. \_\_\_\_\_. 2nd edition, revised. Chicago: University of Chicago Press. ©1974, 1978 by the University of Chicago. Reprinted by permission.
- Gaylin, W. 1977. The Frankenstein Factor. *New England Journal of Medicine* 297: 665-667.
- George, S.L., Aur, R.J.A., Mauer, A.M., and Simone, J.V. 1979. A Reappraisal of the Results of Stopping Therapy in Childhood Leukemia. *New England Journal of Medicine* 300: 269-273. Reprinted with the permission of the *New England Journal of Medicine*.
- Hawkes, N. 1979. Science in Europe: Smallpox Death in Britain Challenges Presumption of Laboratory Safety. *Science* 203: 855-856.
- Illich, I. 1976. *Medical Nemesis: The Expropriation of Health*. New York: Pantheon.
- Isaacs, L. 1977. Original Synthesis. *Hastings Center Report* 7 (April): 24. Reprinted with permission of Leonard Isaacs and the *Hastings Center Report*. ©Institute of Society, Ethics and the Life Sciences.
- Jarvik, M.E. 1979. Necessary Risks. *New England Journal of Medicine* 300: 1130.
- Kass, L.R. 1979. "Making Babies" Revisited. *The Public Interest* (Winter): 32-60. Reprinted by permission.
- Loftus, E.F., and Freis, J.F. 1979. Informed Consent May Be Hazardous to Your Health. *Science* 204: 11. ©1979 by the American Association for the Advancement of Science.
- Meisel, A., and Roth, L.H. 1978. Must a Man Be His Cousin's Keeper? *Hastings Center Report* 8 (October): 5-6.
- Merton, R.K. 1957a. *Social Theory and Social Structure*. Glencoe, Ill.: Free Press.
- \_\_\_\_\_. 1957b. Some Preliminaries to a Sociology of Medical Education. In Merton, R.K., Reader, G., and Kendall, P.L., eds., *The Student-Physician*, 3-79. Cambridge, Mass.: Harvard University Press.
- Mike', V., and Good, R.A. 1977. Old Problems, New Challenges. *Science* 198: 677-678. ©1977 by the American Association for the Advancement of Science.
- New York Times*, 1978. Boy with Leukemia Focus of Court Fight. April 6. ©1978/79 by the New York Times Company. Reprinted by permission.
- Parsons, T. 1951. Social Structure and Dynamic Process: The Case of Modern Medical Practice. *The Social System*, chapter 10, 428-479. Glencoe, Ill.: Free Press.

- Powledge, T.M. 1977. Recombinant DNA; The Argument Shifts. *Hastings Center Report* 7 (April): 18-19. ©Institute of Society, Ethics and the Life Sciences.
- Sinsheimer, R.L. 1978. The Presumptions of Science. *Daedalus* 107 (Spring): 23-25. Reprinted by permission of *Daedalus*, Journal of the American Academy of Arts and Sciences, Boston, Massachusetts. Spring 1978, *Limits of Scientific Inquiry*.
- Staff Paper, 1979. Office of Science and Technology Policy, Executive Office of the President. February 1.
- Steinfels, M.O. 1979. In Vitro Fertilization: "Ethically Acceptable" Research. *Hastings Center Report* 9 (June): 5-8. ©Institute of Society, Ethics and the Life Sciences.
- Steinman, M. 1978. A Child's Fight for Life: Parents vs. Doctors. *New York Times Magazine*, December 10. ©1978/79 by the New York Times Company. Reprinted by permission.
- Times Company. Reprinted by permission.
- Stockton, W. 1979. Smallpox Is Not Dead. *New York Times Magazine*, February 4. ©1978/79 by the New York Times Company. Reprinted by permission.
- Swazey, J.P., and Fox, R.C. 1970. The Clinical Moratorium: A Case Study of Mitral Valve Surgery. In Freund, P.A., ed., *Experimentation with Human Subjects*, 315-357. New York: George Braziller.
- \_\_\_\_\_, Sorenson, J.R., and Wong, C.B. 1978. Risks and Benefits, Rights and Responsibilities: A History of the Recombinant DNA Research Controversy. *Southern California Law Review* 51: 1019-1078.
- Talk of the Town, Notes and Comment. 1979a. *The New Yorker*, April 16: 27-28. Reprinted by permission.
- \_\_\_\_\_. 1979b. *The New Yorker*, June 25: 21-22. Reprinted by permission.
- Thomas, L. 1977. Biostatistics in Medicine. *Science* 198: 675. ©1977 by the American Association for the Advancement of Science.
- \_\_\_\_\_. 1979. *The Medusa and the Snail*. New York: Viking.
- Tribe, L.H. 1979. Too Much Law, Too Little Justice. *Atlantic Monthly* (July): 25-30. Copyright ©1979, by the Atlantic Monthly Company, Boston, Mass. Reprinted with permission.
- Wade, N. 1977. *The Ultimate Experiment: Man-Made Evolution*. New York: Walker.
- Watson, J.D. 1976. In Defense of DNA. *Annual Report*, 1976, Cold Spring Harbor Symposium. Reprinted with Dr. Watson's permission.
- Weil, S. 1970. *First and Last Notebooks*. London: Oxford University Press.