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MAKING ETHICS: THE STRUGGLE FOR INFORMED CONSENT IN AMERICA, 1945-1995

by

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THESIS

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This thesis is dedicated to Jack Pressman

and to everyone who learned from him.

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CONTENTS

"Matters of practical conduct have nothing invariable about them, any more than matters of health. This is true of ethics in general, and it is true even more of moral issues arising in particular cases. These are not a scientific or technical matter: rather as in medicine or navigation, *they require human beings to consider what is appropriate to specific circumstances and to specific occasions..*"
Aristotle, Nicomachean Ethics. (X) II.2.1104a. (1)

I. INTRODUCTION

On July 29, 1975, Chauncey D. Leake donated a copy of the second edition of Percival's *Medical Ethics*, of which he was editor, to the Main Library of the University of California in San Francisco. (2) Leake penned a note to the library staff on the flyleaf, with the comment that "this [is] the second edition of a book issued 48 years ago, when it fell flat as a mudpie". In the Preface to the new edition, Leake explains that he was encouraged in this second attempt by "the amazing and sometimes amusing excitement these days over various aspects of ethical problems arising in the current practice of the health profession." (3). Leake had in mind the intense exchanges of the 1970's about "abortion and contraception in their various ramifications; euthanasia in its diverse forms; human experimentation; the "right" [sic] of a patient to know the truth; the right of a patient to die; genetic manipulation; the use of addictive or mood changing drugs, and even the use of food additives."

It is notable that 23 years later, each item on Leake's list is still actively contested, yet his expectations of renewed interest in Percival's work were not fulfilled. He might have been unsettled to discover that the "amazing excitement" flowed not from Percival's world of gentlemanly healers - the AMA Code of Medical Ethics was copied from Percival's monograph in 1847 - but from sources imposed on the medical profession from outside. A closer reading of Leake's inventory of contested ethical issues hints at a thoroughgoing epistemological transformation in the years since he wrote the Preface to the second edition. Today, an ethicist or moral philosopher of Leake's stature would consider the informed consent principle as anything but controversial. Nor would he or she position it anywhere but at the top of a list of contemporary bioethical concerns; no one even remotely familiar with the development of the informed consent doctrine from a contextual framework of self-determination in the late 70's and early 80's would place quotation marks around the word 'right', as Leake did in 'the patient's '"right" to know the truth'. (4) While the controversies remain, the cultural framework has shifted, turning yesterday's hermeneutic insights into today's historical dilemmas - and vice versa. Leake was planning his second edition just as the AMA's Judicial Council prepared to eliminate the last tenuous ties of its Code of Medical Ethics with Percival's language and format.

The anecdote about Leake was meant to introduce and to contextualize the underlying premise of this paper that medical ethics 'principles' are historically contingent, rather than being immutably anchored in ancient deontological

injunctions. Insofar as such codes organize and rationalize the interactions of physicians with patients, and of researchers with study subjects, these texts become useful objects for historical analysis and explanation. (5) To discover how these moral guidelines have reflected the ambivalence, tension and conflict which existed between practitioners and researchers, the two leading journals of clinical practice in America, the *Journal of the American Medical Association*, and the *New England Journal of Medicine*, and the two foremost American journals of clinical and basic science, the *Journal of Clinical Investigation*, and *Science*, were scanned for items relating to professional ethics, focusing specifically on issues of patient autonomy, disclosure and consent, and their contextual origins in the social setting of medicine from the time of the Great Depression to the near-present. These four journals were selected because they contain information and representative opinions spanning the entire professional horizon. Most importantly, these journals represent the views, concerns and activities of the organized profession, as the official organs of the most influential and politically active professional organizations.

Much has been written about the stormy relationship between basic (i.e. non-clinical) science and clinical practice in the late 19th and early 20th centuries. (6) This literature stresses the divergent aspirations and epistemological issues between the worlds of the basic scientist and the clinician, and the "persistent skepticism" of practicing doctors toward basic scientists' claims of relevance at the bedside. (7) Nevertheless, a hermeneutics of medicine beginning in the latter half of the 19th century reveals a gradual intersection of two divergent epistemologies: the traditional

holistic healing 'art', focused empirically on the individual patient and her suffering, crossed in more recent times by a hard-edged ethos of expert knowledge derived from experiments in groups of people (human subjects); in brief, medicine based on scientific knowledge, or, in a phrase coined by the president of the AMA in 1930, 'mechanistic medicine'. (8) Together, these two barely compatible epistemologies produced a professional paradigm relentlessly promoted by organized medicine (namely, the AMA) as 'scientific medicine'.

In parallel with tensions between the clinician and the basic scientist, a less conspicuous but not less significant family feud within the professional brotherhood has received little notice. Profound ideological and definitional polarities separate two *clinical* professional prototypes, the clinical practitioner and the clinical researcher. Indeed, Percival's rules of etiquette have provided a kind of cover over this cleft at the heart of 'scientific medicine', with direct and important implications for public health. Each side found common ground in their shared status of physician, with unchallenged authority for all negotiations with patients, research subjects and society prescribed by Percival. My intent is to show how the conflation of the clinician and the researcher served to promote the status of both, but also led to moral confusion within the profession. In this paper, I shall attempt to track the evolution of a new ethics, alternative to Percival's deontological edicts, which began to emerge in the late 1960's. (9)

Counterpressures to the absolute autonomy of American medicine had already surfaced between World War I and the Great Depression as movements to provide 'free' health care to the indigent, the veterans and native tribes. (10) The tendency toward centralized social control gained momentum through increased involvement of government agencies from the '30's on. The twinned specters of 'socialized medicine' and 'government control' became the main targets of the AMA's House of Delegates, who represented in this singular instance the autonomy interests of both sides of the professional divide. During and after World War II, the monopolistic grip of the medical profession gradually weakened and drove the polar extremes of the medical spectrum further apart. Percivalean etiquette could no longer hold the ends together, and was eventually abandoned altogether. Clinician and researcher drifted further apart, no longer held by the perception of shared interests. Each followed separate career paths, authorized since the late 1960's or early '70's by new codes. For the clinician, the struggle for professional autonomy ended with a profoundly altered relationship with patients, underpinned by juridical decisions; for the researcher, state and institutional regulations stabilized and reinforced the new arrangements.

The growth of biomedical research stimulated by World War II produced increasing concern about the protection of experimental human subjects. Emphasis shifted away from the traditional physician-centered beneficent ethics model to a new regulatory structure grounded in patients' civil rights. For the first time, medical ethics was forced to concern itself with moral contingencies encountered on the formally designated research ward. (11) The momentous challenges to normative medical

conduct represented by simultaneous pressures to grant patients greater autonomy, while at the same time increasing the possibilities of using them as means to reach other ends, found a deontological anchor in the set of moral guidelines promulgated by judges at the so-called Doctors' Trial in Nuremberg, which produced a tale of crimes committed by physicians who used people precisely as means to ends. (12) The Code of Nuremberg began to replace the Code of Percival. The immediate task of this paper is to illuminate the way this transition took place, and how a new ethical framework was 'made'.

The historicity of medical ethics offers an opportunity to ask questions rooted in specific moments, hence vulnerable to change; to ask, in the Fleckian manner, about the genesis and development of an ethical "fact". (13) Ludwik Fleck developed his thesis on *The Genesis and Development of a Scientific Fact* (14) around the cultural representations of an ancient disease (syphilis), using case studies (for example, the Wasserman reaction) to probe and expose forces operating in the social construction of scientific discovery. I intend to combine Fleck's methodology with Aristotle's dictum in three ways: first, by following the AMA's Code of Ethics through its several revisions in response to changes in the larger culture; second, by tracing the contemporaneous trajectory of the Nuremberg Code from its creation through a period of eclipse, and its recruitment as the source and inspiration of a new set of moral guidelines required by the altered sensibilities of the time; third, to illuminate the 'real world' in which these epistemological changes played themselves out. For this purpose, the events surrounding the "genesis and development" of a 'release'

document at the Laboratory of Cancer Research in San Francisco between 1947 and 1953 will be presented as a heuristic tool with which the vagaries of the Nuremberg Code in the postwar era may be better understood. (15) With this strategy, I hope to bring into sharper relief the central cleavage between the scientific and practice cultures at the poles of modern medicine, and to illustrate how the main actors in the 'two cultures' reflected the social forces at work on them and their professional concerns and commitments.

II. THE PERCIVALEAN PARADIGM.

1. *Practical ethics*. In the first half of the nineteenth century, 'regular' or allopathic medicine was practiced by unaffiliated individuals whose credentials and skills were acquired in a wide assortment of unregulated proprietary 'medical schools'. 'Regulars' practiced in an environment of intense competition with sectarian healers, mainly homeopaths and eclectics. This situation changed dramatically with the beginnings of 'organized' medicine in the United States, which can be conveniently dated from the founding of the American Medical Association in 1846. (16) The AMA had two chief goals at its beginning: to establish uniform requirements for a scientific medical education, thereby gaining institutional control over standards of practice; and to exclude non-allopathic practitioners. (17) Medical licensure requirements had been repealed by several states in the period between1826 and 1844, leaving the profession open to untrained "impostors", poorly educated graduates of proprietary medical schools, and sectarian practitioners - mainly homeopathic healers and eclectics - whom the 'regulars' regarded as *unscientific* "charlatans and quacks." (18) In lieu of

licensing, the AMA inaugurated its own professional code of ethics in 1847, grounded in proper conduct among physicians, excluded sectarian and untrained practitioners, and provided general guidelines for dealing with patients. (19)

The AMA's Code was based on Percival's Medical Ethics published in 1803. Why was Percival's manual chosen from among several texts on medical ethics available at the time? In his 1927 edition of Percival's text, Leake observed that the work had more to do with physician-to-physician etiquette than with moral principles governing patient-to-physician relationships. (20) Others have interpreted Percival's objectives as intended to preserve the monopolistic position of physicians, to forestall or resolve professional boundary disputes, and to enhance doctors' influence over apothecaries, sectarian healers, and patients. (21) Percival had been a prominent physician on the staff of the Manchester Infirmary at a time of persistent and occasionally violent disputes among physicians, surgeons and apothecaries. The institution engaged Percival in drawing up a "scheme of professional conduct" which would serve as a practice guide and a manual for arbitrating disputes. Completed in 1794, the practical manual set forth principles of conduct in dealing with day-to-day intraprofessional issues (fees, consultations, seniority regulations, interactions with apothecaries, lawyers, etc.) and proper approaches to patients. In the latter context, Percival advocated minimal disclosure of information and opinions between doctors and patients. Above all, he cautioned against "gloomy prognostications". His counsel was "not to enter discussions concerning the nature of the case...before the patients... because misapprehension

may magnify real evils or create imaginary ones." However, physicians could "on proper occasions" warn the patient's friends of danger "when it really occurs and even to the patient himself, if absolutely necessary". Percival's steadfastly utilitarian tone and simple instructions for control over competitors and clients met the requirements of the fledgling AMA exactly.

In a lengthy introduction to the new Code, John Bell, the member of the drafting committee who presented the document to the AMA convention on June 15, 1847, inveighed against "quackery in all its forms..." and bemoaned the fact that "the laws...are silent, and of course inoperative, in the cases of both fraud and poisoning so extensively carried on by the host of quacks who infest the land."(22) Bell singled out the apothecaries for exceeding all others in the sale and distribution of "quack medicines and nostrums". On the issue of a proper professional education, Bell proposed an approach based on scientific expertise:

> "The greater the inherent difficulties of medicine, *as a science*, and the more numerous the complications that embarrass in its practice, the more necessary is it that there should be minds of a high order and thorough cultivation, to unravel its mysteries and to deduce scientific order from apparently empirical confusion."

Thus, from its founding, the organization promoted itself as the sole representative of 'scientific doctors', and its Code of Medical Ethics the bulwark and guarantor of professional integrity. As we shall see, the AMA succeeded brilliantly in achieving both primary goals. It is of interest, therefore, that the Code, having been introduced at a time of scientific awakening, and using science as the defining principle of the

profession, mentions neither the moral dilemmas of clinical research, nor ethical contingencies which may actually distinguish scientific from empirical practice.

2. *The Creation of a Scientific Elite.* The organized medical profession's success in eliminating its competition was rooted in the fact that regular medicine was associated with demonstrable scientific advances, while the sectarians remained committed an immutable therapeutic orthodoxy. As Jay Katz has written "The magical promise of science to wipe out disease contributed to the public's willingness to turn away from other healers and allow allopaths, the 'regular' doctors, whose *handful of scientific brethren* had been associated with these discoveries, to take charge of the nation's health needs." (23) Beginning at the turn of the century, the demand for sectarian practice dwindled; the number of homeopathic schools declined from 22 in 1900, to 12 in 1910, to 6 in 1918, to none within the next several years. Eclectics followed a similar course. (24)

The main strategy used by organized medicine to eliminate the competitive threat of sectarian schools and practices, and to standardize the practice of 'regular' medicine, centered on the German model of laboratory science as the mainstay of medical education and the clinic. Johns Hopkins Medical School became the flagship of the reform movement in 1893. At the center of educational reform stood experimental medicine. As William Welch, the eminent Johns Hopkins pathologist and later dean of Johns Hopkins School of Medicine, put it: "The medical school should be a place where medicine is not only taught but studied."

(25) . The new formula joined science and research firmly to clinical inpatient practice. At Johns Hopkins, the innovative 4-year program required a college degree for entry, students and the research-oriented faculty were recruited nationally, and students spent the first two years with basic laboratory sciences. (26).

Essential to the operation of the German educational model was the hospital environment where therapy and research could be combined at the bedside. "Both physicians and their hospitals were to cloak themselves in the mantle of an ever-improving, increasingly effective, and necessarily unselfish medical science..." writes Charles Rosenberg. (27) The rise of the hospital system, driven by advances in diagnostic and therapeutic technology and a growing demand for expertise in surgery, gynecology, radiology, and pathology reflected the essential role of science in structuring the hospital as a technological environment for healing.

Yet, voices were raised questioning the relevance of the new laboratory tests to everyday practice. Physicians learned the new technical and laboratory skills associated with "hospital-based" specialties, but few fulltime staff positions were available. As William Osler observed "...the young man may start with an ardent desire to devote his life to science, [but] he is soon dragged into the mill of practice, and at forty years of age, the 'guinea stamp' is on all his work." (28) The hospital often became a stage for wider conflicts about the role of research in practice and the use of hospitalized patients for "the science of the prevention of disease". (29) The rise of the hospital reconfigured the practice of medicine, particularly after the turn

of the 20th century, first, with hospital residency programs which introduced a new generation of young physicians to clinical research; second, by making possible the development of medical specialties, hospital-based practices in particular, with access to scientific diagnostic laboratories and expensive imaging equipment. In academic centers, hospitals also offered opportunities for clinical research by medical staff members.

The AMA established a Council on Medical Education in 1904, charged with standardizing medical education. Only 82 of 160 inspected schools received Council approval in 1906; 46 others were graded "imperfect" and 32 were rated beyond salvage. (30) These findings were wrapped in secrecy, for the Code of Medical Ethics disapproved washing one's dirty linen in public. At the Council's request, the Carnegie Foundation conducted a similar investigation, with Abraham Flexner, a young non-physician educator appointed to lead the project. Flexner personally visited every medical school in the US. His famous report, *Bulletin Number Four,* pointed squarely at the proprietary training programs, whom Flexner blamed for the large gap between medical education and the progress of medical science. (31) By 1915, the number of medical schools declined from 131 to 95, while the number of schools requiring a minimum of one year's college increased from 35 to 83. Eventually, approximately 70 medical schools survived. (32) Promoted and implemented by the AMA, the Flexner report created an essential framework for the reinvention of all US medical schools as science-based, university-affiliated institutions, according to the prototype at Johns Hopkins University. At roughly the

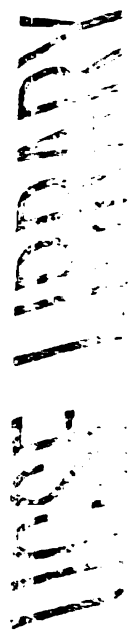
same time, the Federation of State Medical Boards (established in 1912), recognized the AMA's three-level ABC medical school rating scheme as official and authoritative. (33) The AMA's decisions on education now carried the force of law.

The identification of the Flexner report with the Carnegie Foundation had another profound effect on the linkage between medical education and medical science: the leading foundations provided major funding for the creation of endowed research units at the top medical schools, imposing a model of education centered on research rather than on practice. The total contribution of foundations to medical education and research has been estimated at 154 million dollars by 1936, with 91 million dollars donated by the General Education Board of the Rockefeller Foundation to a select group of leading schools. (34) A new cohort of medical leaders emerged from these elite institutions - scientifically trained, technically competent, *and distanced from private practice.* These men occupied full-time academic positions in clinical medicine, recently created to provide intensive clinical research and laboratory experience for students. In contrast, clinical instruction remained in the hands of part-timers who maintained private practices. (35) Traditional practitioners were often alienated from these academics, with whom they had little in common. As we shall see, academic science-trained physicians and traditional private practitioners diverged in the 20th century in their interests, priorities, and epistemological values.

3. *Making Ethics: Evolution of the AMA's Ethics Code.* The steadily rising tide of scientific knowledge and procedural expertise in the last half of the 19th century and the first quarter of the 20th permeated the culture of clinical practice as it did the general culture. The status of physicians in society was secured: 'scientific medicine' helped reduce sectarian competition and rationalized a professional monopoly. Linkage with science made possible the emergence of medical specialties, determined the content and organization of medical education and, in turn, profoundly influenced the image and substance of the modern physician. According to promoters of these changes, the 'new' superbly trained practitioner entered the practice of medicine comfortable with the centrality of science in clinical work. But did the advances and novel applications of scientific medicine lead to new standards of professional conduct, perhaps even to a different understanding of the relationship between patients and doctors? Did the AMA's relentless promotion of medicine as science translate into explicit ethics rules in the Code (Principles after 1903) of Medical Ethics governing the proper conduct of experimentation on patients?

The next hundred years experienced a progressive erosion of Percivalean principles in the Code, without introducing new guidelines for the conduct of science-based specialty practice, or for regulating clinical research. The AMA's 1847 Code of Medical Ethics underwent its first revision in 1903; the second revision was precipitated a mere 9 years later by a revolt for the right to accept referrals from sectarian practitioners, launched by the New York delegates. (36) After an interval of another 47

years, the AMA's House of Delegates approved the third revision in 1949. The fourth revision finally abandoned Percival's format, if not his principles, in 1957. The text of the Code was reduced from its original 5600 words to 4000 by 1903, 3000 by 1912, dwindling by 1957 to 500 words. The final revision of 1980 condensed the Code to 10 Principles sparingly expressed in 250 words. (37) This steady decline in Percivalean rules ordering the conduct of clinical practice to its nadir in the late 1950's coincided and contrasted strikingly with the emerging trend toward legal and governmental regulation of clinical research. By the time Leake noted the "excitement" around ethical issues in the mid-1970's, the AMA had effectively abandoned Percival and his practical manual. As we shall see, the AMA soon had an opportunity to play a direct role in the framing of a new code. The successor to Percivals' physician-centered etiquette was the Code of Nuremberg, with its main focus firmly on the patient.



The unflinching emphasis of Percival's Principles on intraprofessional issues is evident from the format of the revised code of 1912: 31 sections deal with "The Duties of Physicians to Each Other and to the Profession at Large", 5 sections are devoted to "The Duties of Physicians to their Patients" and the remaining 4 concern "The Duties of the Profession to the Public. " (38) All revisions up to 1980 contain no references to experiments or to science of any kind, nor do the Articles mention the obligations of researcher to subject. More impressive still is the silence of the Principles on ethical dilemmas which may arise in the everyday practice of 'scientific medicine'. For example, does a 'scientific' physician have an obligation to seek scientific evidence for or against a proposed treatment regimen? Is there an ethical requirement to evaluate

benefits versus risks based on probabilistic statistical evidence rather than on subjective and necessarily limited clinical experience? The only reference which offered even an indirect hint of science as a factor in practice surfaced in the 1912 revision, where AMA members were rhetorically urged to join their county and state medical societies in order "[to promote] the advancement of medical science." The AMA's failure to deal with moral issues inherent in the proactive, aggressive, often invasive setting of a scientific clinical center is all the more remarkable in the years 1903 and 1912, a period of active debates about professional ethics conducted in medical publications and professional societies. (39)

In contrast with the virtual absence of concern with science-based practices in all six versions of the Code, other modifications of the 1903 Code and the 1912 Principles were clearly drafted in response to the contemporary political setting of organized American medicine. Pressure to provide health care to a growing population of indigent and poor patients produced a radical break in the sliding scale policy which was the most distinctive feature of the original 1847 Code; at the same time, the prohibition against providing free services to institutional clients represented an attack on "contract practice" by salaried physicians. The provision of unlimited prepaid services to members of a paying organization was regarded by the AMA as a dangerous departure from the autonomy principle that only the physician may set the value of his services. Thus, the 1903 Code carried an injunction that "Poverty, mutual professional obligations, and certain...public duties...should always be recognized as presenting valid claims for gratuitous services; but neither institutions endowed by

the public or the rich, or by societies for mutual benefit, for life insurance, or for analogous purposes, nor any profession or occupation, can be admitted to possess such privilege." (40)

The AMA's main efforts between the years 1912 and 1949 were devoted to damage control against perceived outside threats to the professional autonomy of the physician. The AMA opposed all schemes which could shift the economic base of medical practice from fee-for-service to cooperative payment schemes by organizations, corporations and hospitals, and, above all, any government encroachment in medical care. (41) An episode described by Susan E. Lederer in her book *Subjected to Science* sheds a significant light on the medical culture of the day, revealing epistemological tensions associated with the conflation of research and practice by the medical leadership of the day. (42)

The eminent Harvard physiologist Walter Cannon chaired the AMA's Council on the Defense of Medical Research, which dealt with attacks by anti-vivisectionist groups against *involuntary* research in people and animals. Cannon used advertisements in medical journals to "...let the fact be stated that the patient or his family were fully aware of and consented to the [research] plan." Much to Cannon's chagrin, the Rockefeller Institute's *Journal of Experimental Medicine* published a study in which rabbits were inoculated with syphilitic treponemes extracted from brain tissue obtained with biopsies in patients at a Michigan mental institution without consent. When the mass media carried this story, several physicians

countered that being hospitalized implied permission for any experiment performed by the physician. In 1916, Cannon proposed an amendment to the AMA Principles of Medical Ethics codifying the necessity to obtain the potential experimental patient's consent and cooperation, and to place the relationship between clinical investigator and patient on a formal, prescriptive basis.

Cannon's proposal met with an unenthusiastic reception from clinical authorities. Simon Flexner, editor of the *Journal of Experimental Medicine* and brother of Abraham Flexner, and Rufus Cole, director of the Rockefeller Hospital, were concerned that "laboratory men" would not understand the position of the clinicians. More to the point, Cole feared that a discussion before the AMA House of Delegates would "open the way for a discussion of the importance of obtaining the consent of the patient before any investigations are carried on which are not primarily for the welfare of the patient." The respected clinician Francis Peabody of Harvard asserted that "in medical wards, the patients do virtually give their consent to what is done to them, and if they raise any objection the procedure is not carried out." Peabody felt that the only occasion when a "formal consent" should be obtained from a patient is for procedures which could produce injury, such as surgery or anesthesia. In his opinion, guidelines for experimentation and the formal consent of a patient were not critical safeguards, only the good character of the clinical researcher afforded meaningful protection; those who chose a career in scientific medicine were "among the more high-minded of the profession". The AMA's delegates refused to discuss Cannon's amendment, but he was able to go on

record against using patients in scientific experiments without their consent. He also stated his views in an editorial on the ethics of human experimentation: "There is no more primitive and fundamental right which any individual possesses than that of controlling the uses to which his own body is put. Mankind has struggled for centuries for recognition of this right. Civilized society is based on the recognition of it. The lay public is perfectly clear about it." (43) In his focus on the patient's right to consent, Cannon was 50 years ahead of his time.

The resistance of individual clinicians and the AMA's House of Delegates to ethical guidelines applicable to human medical research, compared with their willingness to tinker with other regulations in the Code, in part reflected the reality that in 1916 *experimental* science was of little practical significance as an operational or heuristic tool in general or specialized practice. Cannon's attempt to bring patients' rights issues into mainstream medicine exposed some confusion in the minds of practitioners and researchers about what constituted an experiment. The comments of the pure clinicians, Cole and Peabody, quoted above, reflected their belief that a patient's willingness to undergo treatment implied authorization for non-harmful experimentation which did not require a patient's consent, being a natural extension of therapy from reliable and conservative to innovative or 'heroic' measures. The training and professional mind-set of these eminent physicians provided no context in which contact with the patient could involve anything but a therapeutic calculus. The patient's welfare was all that really mattered. Therefore, Cole and Peabody were opposed to codifying explicit permission even for non-

harmful research, which they equated with therapy and hence regarded such regulation as unnecessary and potentially disruptive. The idea of patient consent seemed culturally foreign and potentially troublesome to the leading minds of the profession.

4. *Two Cultures in a Single Frame.* The professionally advantageous political alliance between science and clinical medicine remained shaky and ambiguous before the First World War. Heralded by the Cannon episode of 1916, the coming cleavage between these two inimical conceptions of medicine was still barely visible. But soon, situated on a cultural fault line, the traditional Hippocratic general practitioner ineluctably lost ground to the science-based specialist in the years after World War I. Scientific medicine provided "a new plausibility for physicians and their institutions... legitimated an impressive new style of medical identity: that of master of laboratory science and 'instruments of precision' as contrasted with the more traditional ideal of wise and intuitive manager of elusive and idiosyncratic clinical situations." (44) Physicians clearly benefited from the rising influence of science. Yet, it seems safe to generalize that science in the clinical context was often regarded as reductionist and technological, while clinical medicine was usually perceived as holistic and humane. The impassioned tone of speeches by leading professors and practitioners bear testimony to the intensity of cultural attachment to this binarized divisive conception. The new class of hospital-based specialists was the most directly dependent on scientific or technical expertise - pathologists, anesthesiologists, radiologists, surgeons - and their practices were the most intrusive

and, indeed, experimental. (45). The specialist acquired a practice style during years of residency training focused on a single organ or set of diseases, coupled with research experience on "clinical material" abundant in teaching hospitals and university clinics. Such investigations helped develop the defining competencies of specialty careers, but were less concerned with taking care of the sick.

The changing relationship between the science and art of medicine in the '20's and '30's has been well documented. One example of that complex historic argument may suffice here. Francis Peabody, whose opinions on voluntary consent were noted above, wrote in a famous essay published in 1927: "The practice of medicine is an art, based to an increasing extent on the medical sciences, but comprising much that still remains outside the realm of any science. The art of science and the science of medicine are not antagonistic but supplementary to each other." (46) Writing 40 years later from the clinical researcher's point of view, William McDermott is less sanguine: "Somehow, somewhere, in this question of human experimentation, as in so many other aspects of our society, we will have to learn how to institutionalize "playing God" while still maintaining the key elements of a free society."(47) The chill wind of Nuremberg blows through McDermott's words. As we shall see, the transition in American professional values from Percival's Manchester at the beginning of the nineteenth century, to their ultimate destination in mid-twentieth century Nuremberg, occupied the entire 40-year span separating Peabody and McDermott.

These unresolved tensions between the "two cultures" of medicine have not received the analytical attention they deserve. If Charles Rosenberg is correct that science served merely as a cloak to provide plausibility for clinical practice, (48) what hid beneath? The following series of contemporary pronouncements on medical ethics, patient disclosure and consent suggest at least two underlying preoccupations of the general practitioner conflicting with 'scientific practice': first, dread of 'socialized medicine' in all its forms, to be countered with appeals to the individualistic 'art' of medicine; second, rejection of 'mechanistic medicine' as generally practiced by specialists, and particularly by academic clinical researchers, also by invoking the practice of a personal, subjective 'art'. The presidential speeches at the annual convention of the AMA traditionally address the 'state of the union' of American medicine. In 1930, in the worst period of the Great Depression, 'union' was not on the minds of thousands of embattled general practitioners who formed the largest and by far the most active contingent of the membership. The first and perhaps the only substantive issue for these physicians was the Depression-driven threat of 'government control'. President William Gerry Morgan's blunt and desperate words transmit the flavor and the intensity with which these battles, largely unremarked by the public, were fought. (49) In calling for resistance to "state medicine, so-called" Morgan enumerated:

> "...the long and steadily growing list of agencies, medical and quasimedical and plainly nonmedical, which have for their object some form of oversight, 'guidance', 'education', 'social service', 'case work' and whatnot, all directed toward the physical, mental, moral or emotional life of parents or their children, and all under the guise of physical or mental 'betterment'.

All these potential occupants of the house of medicine, Morgan insisted, were reinforced by

> "the idea of specialization, leading the public to view with some sort of suspicion the average practitioner. Yet,...he gives as good service diagnostically and therapeutically within the limits of the equipment at his disposal as do the glorified institutions of *mechanistic medicine.*" (emphasis added)

In a lengthy statement at the climax of his speech, Morgan laid the first evil, that of state medicine, at the door of the second, the specialists and their mentors, the medical scientists:

> "But there is a school of medicine today, reared in the laboratory atmosphere and blessed with an arrogance unsurpassed in the entire history of medicine, which seems to consider the patient as its pet guinea pig. Far too little attention is paid to his [the patient's] individual psychological reactions. Far too little attention is paid to the remote history of the case with the numerous factors that may have contributed to the present pathology. To no extent is the patient taken into the physician's confidence, he is passed perhaps from one department to another or from one specialist to another. If he rebels he is, so to speak, thrown out on his ear as "non-cooperative". The plain truth of the matter is that eventually the public will be non-cooperative with such methods. And since the public is entitled to demand in our present age of civilization adequate medical and health service, it will turn to its official servants, the government agencies, to obtain such service, i.e., the dreaded state medicine."

Having presented the view from the private doctor's office, Morgan ended his address on a warning note which identified the core concern of the AMA's political activities for the next forty years: "Indubitably, the medical profession is confronted with the danger of losing its independence of action." Issues of patient self-determination were about to be completely subsumed in the struggle for physician autonomy.

Five months after Morgan's address, a speech by David Riesman, Professor of Clinical Medicine at the University of Pennsylvania, reflected the uneasy epistemological balance implicit in an abstract and inherently unstable chimera of art and science. (50) Riesman addressed the students at Harvard University Medical School on the *Art of Medicine:*

> "When I contrast the two branches of medicine - the art and the science - it must not be inferred that they are separable in the doctor's daily work... art uses one eye and science the other but wisdom uses both. It is for that wisdom arising through a union of science and art for which we must strive as students and as practitioners of medicine."

Nevertheless, Riesman warned that one can have too much science but not too much art:

> "In certain places there is indeed a definite tendency to minimize the importance of the art of medicine and to imbue the student with profound faith in the laboratory as the Alpha and Omega of medicine. I doubt whether Hippocratic...could get a chair today in some of these super-scientific medical schools."

Speaking at the end of 1930, Riesman observed that in Germany, *Heilwissenschaft* (the science of healing) had displaced *Heilkunst* (the art of healing), and cautioned that "in their zeal for scientific methods, [medical men] are coming to realize that they have forgotten the true essence of their calling - the healing of the sick."

Remarkably for his time, Riesman devoted an entire journal page to a detailed discussion of disclosure of information to patients. Disagreeing with those who would tell "the whole truth" to the patient, he advised that a physician must

"temper his statements so as not to crush the spirits of the patient or his dear ones". Riesman concluded with an upbeat restatement of his personal credo: "The American...a practical idealist, can combine the art of medicine with the ideals of the laboratory...more scientific in the sense of understanding better the physiologic basis of life and health, and a nobler art in its profound insight into the human soul which can not be weighed in the balance or seen through the microscope."

The George W. Gay Lecture is an annual event intended to "bring issues of proper conduct and other moral issues of fundamental concern to the medical profession", to the attention of medical students at Harvard and Tufts Universities, and widely disseminated by publication in the *New England Journal of Medicine.* Passages from these prestigious and influential didactic addresses delivered before, during and immediately after World War II provide a window through which may be glimpsed leaders of medicine as they transmitted to future physicians the explanatory and ethical codes by which the medical profession defined itself.

James Herrick, the Gay lecturer for 1936, was a retired professor of medicine and former physician-in-chief of Harvard's Peter Bent Brigham Hospital. Herrick left the students a mixed message: "Research investigators are rare, i.e. those who can originate and independently carry on research. These men frequently make poor practitioners." Incongruously, Herrick insisted that it would be a mistake to set up "a real or fancied barrier" between research and practice. The successful doctor "must possess the dual personality, he must be scientist and human or humane."

As for disclosure of clinical information to patients, Herrick advised a relativistic approach: "do as little harm as possible, not only in treatment with drugs or with the knife, but also in treatment with words." (51)

Next year's Gay lecturer, Lawrence K. Lunt, M.D., addressed the explicit connection Morgan had introduced in linking socialized medicine with scientific thinking. (52) Lunt raised "...ominous rumblings about 'state medicine'... Compulsory health insurance can result only in wholesale abuse and the inevitable lowering of medical standards, with a consequent wholesale loosening of wholesome ethical restraints." Moral decay may also come from the direction of science. Lunt warned the students against adopting the opinions of another influential physician, M. I. Leff, whom Lunt quoted in disapproval: "Our ethical concepts and spiritual values have been subjected to a thorough-going revision and sweeping reevaluation by the same *scientific method* by which more material problems are solved...we still do *lip service to a code of ethics* which came down to us from the good old days when medicine men really were different...Let us be done with sham and place our Code in the Museum where it belongs". (emphasis added) The blueprint for a future transformation in "ethical concepts and spiritual values" was clearly on the horizon in 1937, a time when the Nazi plan to exploit medical science for state purposes was taking shape in Germany. (53)

Lunt admitted that "it is true that, in some instances the patient is getting better scientific treatment, and more lives are being saved, but the doctor-patient

relationship suffers deeply." The problem was that "yesterday's complaints against specialization in medicine" have been largely silenced by "natural growth", and a great increase in industry which "has given rise to the double specter of "the industrial doctor and to contract practice." (54)

On consent issues, Lunt resurrected a rule which had been deleted from the AMA's Principles in 1912 as "controversial": "He [the patient] should never permit his own crude opinions to influence his obedient attention to the physician's prescription." Lunt even cautioned medical men that when one of them is ill, "he is like anyone else in his incapacity to use sound judgment concerning himself and generally needs, even more than does the layman, definite and rigid direction." On the issue of communication between patient and physician, Lunt provided a differentiated opinion, which still came down on the side of non-disclosure: "How much should one tell a patient about his condition? It is generally agreed that one should use great care in what is divulged...some individuals want to know...even the worst about themselves...some are going to be made sicker thereby...many, perhaps wisely, do not want to know". Lunt's advice to the medical students: "It hardly seems possible that anyone could maintain that the whole truth, when asked for, should always be given; and yet there are those who feel it inconsistent with their honor to do otherwise." Unfortunately, he did not divulge their identity, but change was in the air. (55)

The US was still a relative spectator in World War II when the 1941 Gay lecturer spoke on February 13 at Harvard. David Cheever, M.D., a retired associate professor of surgery and consulting surgeon at Peter Bent Brigham Hospital, explained his position on codes of professional behavior: "Inevitably, the manners and social attitudes of the physician are related to the ethical customs, which in turn are interwoven with important problems inherent in the art as distinguished from the science of medicine." Cheever dealt with the disclosure question by limiting truth-telling issues to "cases of cancer". According to Cheever, three types of people should be distinguished in making disclosure decisions: mature adults who ask for the truth with convincing "sincerity... [they] are exercising their right to information and should be told; those who ask half-heartedly and do not press the question; and those who do not ask." Cheever suggested that in the latter cases, the practitioner should explain the exact situation "to the nearest relative or friend". However, in the majority "Tact and evasion will usually suffice." Cheever's final message to the medical students: "At our school here you have gained factual knowledge, clinical experience and an appreciation of the scientific method, but it would be a sorry thing indeed if you had not found and admired in your teachers those qualities of the heart and spirit that are *more potent than science itself* to make our profession a noble one". (56)

There were no further Gay lectures during World War II. When the series resumed in 1945, Gay lecturer Ben Ames Williams continued where his predecessors had left off - in pursuit of dilemmas generated by the cultural divide between scientific specialist

and artful generalist. Speaking of common pitfalls in the practice of medicine, Williams identified a fundamental failure of discourse between the specialist and the general practitioner: in the former, the greatest handicap was that "he does not know his patient," hence "cannot accurately appraise what the patient tells him"; in the latter, the problem was the inability of the patient's own doctor, the general practitioner, "to pass on his knowledge to the specialist. He may know, yet not know how he knows. There are so many intangibles in medicine." Williams concluded his lecture with remarks about disclosure. Truth-telling, said Williams, was "the doctor's most persistent psychiatric problem", because "to decide who should be told the hopeless truth is a problem impossible of positive solution; but he who oftenest solves correctly is the best doctor." (57)

On the research side, leaders of 'scientific medicine' were not interested in practitioners' definitions of science, nor in a romantic theory of medicine defined by 'art'. Authoritative speakers ignored the problems which agitated practicing clinicians and 'organized medicine', particularly issues of physician autonomy and truth-telling. Students and prospective clinical researchers usually received cryptic instructions on survival as serious full-time and fully-trained scientists within the culture of traditional medicine, and were warned against the monetary seductions of practice. The concern with defections to the 'other side' had been voiced as early as 1931 by Hans Zinsser, professor of bacteriology and immunology at Harvard University, who remarked on the occasion of dedicating a new hospital: "The complaint that we cannot expect to recruit the best brains in the country into

academic life owing to the meager economic future offered in these occupations is to some extent justified in fact. Not so long ago science in America was a calling at which one could not make a living until after death." (58). S.J. Meltzer, the first president of the American Society for the Advancement of Clinical Investigation, precursor of the elite American Society of Clinical Investigation (ASCI), had set the tone in his inaugural address of 1909 for the conflict between practice and research from his point of view: "In the first place", Meltzer began his speech, "I wish to discuss the problem of clinical medicine as a science"; and concluded with "The constitution does not keep you down exclusively to science, but let me tell you: beware of practice. It is a bewitching graveyard in which many a brain has been buried alive with no other compensation than a gilded tombstone." (59)

This flashback to 1909 gains in historical and epistemological significance with evidence that the confrontational stance toward the clinical medical culture survived intact for at least the next forty years: Meltzer's final lines were quoted approvingly by Wesley W. Spink in his presidential address at the annual meeting of the ASCI in 1949. Spink's speech focused on familiar themes which clearly differentiated researchers from clinicians, particularly in the post-war period: the trend to team research versus solo practice; the comparatively penurious full-time academic salaries, which forced able individuals to enter more lucrative fields, "especially private practice"; and the unbridgeable divide between the two cultures for which Spink used a quotation from Sir Thomas Lewis: "No investigator can be

successful who allows , or is forced by circumstances to allow, solicitude for his patients to preoccupy his mind". (60)

The speeches and articles of medical practitioners and medical scientists summarized above reveal an absence of ethical concerns about the conduct of experiments in patients by either side of the professional divide. This alone would bring attention to the only treatment of the subject published before 1953. However, the presidential address by William Bennett Bean at the 24th meeting of the Central (i.e. Midwestern) Society for Clinical Research on November 2, 1951, was a remarkable harbinger of so much that was to follow; the address deserves to be quoted in substance. (61) Bean himself was astounded that "morality" had never been the theme of a presidential talk before the Central Society,*or any other society concerned with research.* Taking Claude Bernard's famous definition of permissible research in patients as his point of departure - "The principle of medical and surgical morality, therefore, consists in never performing on man an experiment which might be harmful to him in any extent, even though the result might be highly advantageous to science, i.e. to the health of others" - Bean focused on the "wide cleavage which separates clinician from investigator in his split personality." (62) As physicians, the prime concern is "intimate, personal responsibility in caring for sick people." As investigators, they are "goaded by divine discontent and impelled by curiosity as well as ambition for renown. Such stimulus sometimes suppresses the physician altogether." Bean had observed "fire as well as acrid smoke" generated by the friction between an "excited" investigator and a resident with his mind set on care for the patient. In this

situation, "potentially dangerous experiments may be done without the subjects' knowledge or express permission...such practice is a measure of the moral obliquity which exists in some places of research today." Bean felt that although such neglect of moral values may have been rare in his time,

> "the recent degradation of physicians in Nazi Germany exemplifies the decline and fall of a group whose moral obligations went by default in a single generation. *The house would not have fallen had not many timbers been rotten.* Descent into the gas chamber by doctors of infamy had its beginning in disregard for the patient. Never forget that the difference between an experiment on human beings without clear understanding and freely granted permission, and the determination of the mean lethal dose in man is one of degree, not of kind. The patient...has sacred rights..." (63)

Bean concluded with a ringing declaration: "Morality is the keystone in the arch of medicine, supported by and joining the pillar of art and the pillar of science." This was the first American echo of Nuremberg; it fell on deaf ears.

At the threshold of the '60's, Maurice B. Strauss, chief of the medical service at the Veterans Administration hospital affiliated with the schools of medicine of Boston University and Tufts University, took the separation of medical research from medical practice for granted. In his John Punnett Peters Lecture delivered at Yale University School of Medicine on November 17, 1959, Strauss discerned two trends which had considerable impact on the "cultivation of clinical research" on the contemporary horizon: "The divorce of the medical scientist from the bedside, and a preoccupation with mathematical, biochemical and biophysical techniques." In sharp contrast with previous speakers who were concerned with the lure of practice, Strauss wondered whether this separation might drive the most promising young

researchers into the arms of the *basic* sciences. "One can hardly blame the young man of today," said Strauss, "if in wishing to get ahead, he retreats from the rigors of the hospital ward and the study of the patient in favor of the calm of the enzyme in the Warburg." (64)

5. *The "Cultivation of Clinical Research"*. The strident tone of the competition for commitments and career paths of young physicians, evident in speeches to medical students and young graduates by leaders of both sides in the dispute between empirical clinical practice and scientific medicine, indicated that divergent perceptions of proper and ideal professional identity had not abated since the original energetic debates had erupted about a new relationship between science and practice in the latter half of the 19th century. (65) Hence, at least up to this point in the discussion, my sequential presentation should not be understood as reflecting a gradual resolution or narrowing of differences. Rather, these discourses were not 'evolutionary' steps toward a single 'consensus' view, but instead manifestations of independently fluctuating ethical constructs operating in historically contingent frameworks, and changing social, cultural and political situations.

Still at stake at the beginning of the post-World War II era, as in the analogous disputes of the 1860's to 1890's, were two divergent interpretations of medical propriety and clinical morality. In speaking of "art", traditional practitioners in the 1860's and 1960's saw the quality of their personal interactions with patients as the ethical foundation of medical effectiveness and the mainspring of their authority.

This moral subtext was evident from the twin themes of beneficent non-disclosure and physician autonomy which so many leading spokesmen evoked in the quoted speeches and writings. The sense of moral outrage they felt when "subjected to science" - in Susan Lederer's apt phrase from another context - was palpable in pronouncements dismissive of reductionist science, such as the quote from H.J. Müller cited by Strauss in his presidential address: "To say that a man is made up of certain chemical elements is a satisfactory description only for those who intend to use him as a fertilizer." (66) Yet, the other side in this dispute also implied that science is a moral as well as an intellectual activity, but never confronted the ethical dimension explicitly - with the singular exception of Bean. From the fate of Bean's admonitions, it was clear that the ethical dimensions of their work were not yet conceptualized by the disciples of science.

The influence and prestige of scientific knowledge in the general culture had advanced immeasurably in the century since the AMA had codified the rules of professional conduct, yet the practice of medicine had proven resistant to perceived challenges from science to the practitioner's authority. As things turned out, Spink's anxiety about losing the able young men to clinical practice, and Straus's concerns about losing them to the basic science laboratory both proved unfounded. The story of successful coordinated medical research efforts during World War II, and their continuation in the post-war era, represented a turning point in the social and political role of medicine which has become a historiographic commonplace. (67) In the coming decades, growing numbers of young, clinically and

scientifically trained researchers flocked from fellowships in basic science departments and MD/PhD programs to research wards in university hospitals, drawn by unprecedented opportunities. Large infusions of government money and the new prestige of medical science, symbolized and propelled by the therapeutic success of a laboratory fungal extract called penicillin, guaranteed stable careers in pursuit of 'truth'. At that moment of "logarithmic growth in medical progress," as the president of the ASCI put it in 1956, (68) the AMA's original Code of Ethics, the moral standard for the "young physician going forth into a life full of moral conflicts" in words spoken by the AMA president exactly one hundred years before, (69) had dwindled to two short, outdated and unenforceable paragraphs. New ethics were needed for clinical research, but no one had as yet dared interfere with progress. further distanced

The new academic culture and its competitive system of incentives facilitated an epistemic shift which placed the full-time clinical researcher within a conceptual framework from which patients were perceived as socially sanctioned instruments for discovery of scientific knowledge, and further distanced the academic physician from the solo practitioner's concentration on the care of the individual patient. The legitimizing epistemologies of general practitioners and medical school faculties had never been further apart. Products of traditional medical culture, clinicians were increasingly unable to function as caregivers within the impersonal limitations dictated by random selection, untreated control subjects, and rigid study designs. The clash of cultures was dramatically amplified in academic settings where influential doctors, still operating within their cultural framework, strongly resisted

any experimentation with human beings other than uncontrolled therapeutic trials in patients suffering from intractable chronic, or imminently terminal diseases. (70) This Bernardian position was perpetuated by a transitional generation of senior medical school faculty who also served as 'principal investigators' on many clinical research grants as early authorities in the practice of medical specialties. The conflation of medical practice with clinical research was thus rationalized by a cultural extension of Hippocratic ethics to 'human experimentation' ("every time a doctor treats a patient, he conducts an experiment"). Since practitioners and academicians needed and legitimized each other in the larger society, 'scientific medicine' continued to be presented as normative medicine to the public, the mass media and the state.

The latter half of the 20th century witnessed a striking transformation in the epistemology of clinical practice, from the artful application of scientific knowledge to individual patients to the very different project of turning the 'art' of decision-making into a 'science' of probabilities across aggregates of patients. Development of thousands of drugs, diagnostic devices and surgical interventions depended on new quantitative approaches for evaluation of clinical treatment regimens. The randomized, controlled trial (RCT) was the most important of these innovations (71) The introduction of the RCT is an excellent subject for historical analysis: investigators who pioneered the first controlled clinical studies faced a series of revealing conceptual, social, organizational, and professional obstacles. Demanded by the Food and Drug Administration from the pharmaceutical industry for drug trials,

RCT and other decision-support techniques eventually supplanted all other trials used to assess benefits and risks of any new therapy or procedure; their implementation cemented the divide between the autonomous solo physician and the team of medical experimentalists. (72)

Designed to guarantee an impersonal standard of scientific integrity, these procedural innovations enshrined distrust of the clinician's judgment of individual patients in the structure of clinical investigation, and effectively removed many aspects of therapeutic decision-making from the hands of the individual physician. Incorporating randomized assignments of patients and "blinded" assessments of outcome, RCT's made the bedside clinician irrelevant to the modern research enterprise. The strategy of conflating organized medical research with standard medical practice could no longer sustain the pretense that care and experimentation could be practiced side by side, at least in the majority of cases. The simmering disputes about the identity and moral order of medicine ended where they began. Science had won a place at the bedside.

The following brief account of postwar developments in shaping medical practice to the fit of clinical research, borrows elements from Marc Berg's conceptualization. (73) While organized medicine welcomed the achievements of medical research, the cognitive and moral divide between practice and clinical research had never been wider. Articles in the *Journal of the American Medical Association* and the *New England Journal of Medicine* extolled the benefits of scientific discovery,

continuing to conflate the roles of caregiver and researcher. (74) "Science is nothing more than a method of reasoning equally applicable to the laboratory or the clinic," declared David Rutstein, but by 'clinic' he meant clinical research. As for clinical practice, it consisted in the application of science in 'artful ways' centered in the physician's informed subjective assessment of the patient's needs. (75) The epistemological confusion in these postures was often reflected in contradictory perceptions, when, medical care was seen as degraded by the same scientific applications which elsewhere attracted praise for their life-saving contributions to the management of disease. Thus Harvard anesthesiologist Henry Beecher complained in 1953 that 'scientific paraphernalia' in his specialty threatened to turn physicians into robotic technicians;Walter C. Alvarez raised the specter of "decerebrate medicine" from an overabundance of pushbutton laboratory tests and "so-called miracle drugs". (76)

Organized medicine during the years of rapid expansion of medical research attempted to contain these paradoxes and ambiguities by upholding the primacy of art over science: the importance of science was as a means for successful execution of the art. The AMA and its component regional societies appropriated 'scientific medical practice' as part of an all-encompassing strategy to intertwine the power of the scientific image with professional medical politics aimed at preserving the central position of the physician, and to secure control of health care by the profession of medicine. In pursuit of these goals, the AMA needed to maintain the appearance of active involvement in research activities. A Committee on Scientific

Research and a Therapeutic Trials Committee were established, and another Committee, on Scientific Exhibits, was charged with preparation and presentation of important scientific advances to general practitioners attending annual meetings of the AMA. Representative reports of the Committees in the immediate post-war period show expenditures totaling $3,715 for 5 new grants, ranging from $250 to 1,200 per grant in 1945; and a total of $14,524 for 16 new grants, ranging from $250 to $2,600 per grant in 1946 (77) Somewhat smaller amounts were expended annually by the Therapeutic Trials Committee, established in 1944 (78). The modest scope of these efforts is indeed striking for an organization whose annual budget had climbed into the millions of dollars.

Various appeals for revisions of the Principles of Ethics were made by regional medical societies to the Judicial Council of the AMA on the basis of new contingencies arising in practice and research which were not covered by the "outmoded" existing Principles. The Council resisted all demands to change "Medicine's constitution". The first revision since 1912 was finally implemented in 1947, to meet "changing conditions". (79) The Judicial Committee routinely reminded its members that "The AMA has no laws to compel its membership to care for the sick or the public at large. That would be foreign to our conception of the Principles of Medical Ethics, which reflect our pride in 'a rule of right action, consciously adopted. It is the full knowledge of the conditions surrounding the patient -not the doctor- that determines whether a practice is ethical or unethical." (80) Thus, modifications in the Principles applied to patients in a care relationship.

Specification of treatment parameters for research subjects, as distinct from ordinary patients, was contrary to the professional and political interest of the AMA, and the Council saw no need to focus attention on the problematic and divisive subject of experimentation versus practice. The AMA's lobbying and publicity effort, spent in resisting the perceived increase in government incursions and regulation intensified in the 1930's and continued unabated through the 1940's. These activities occasionally crossed paths with attempts of the research community to move toward greater involvement with federal agencies which supported their research. In one of the many such speeches by presidents and other officials, the president of the AMA for 1946, Roger I. Lee, expressed before the House of Delegates the sense of crisis which permeated their deliberations:

> "I think we must all agree that it is likely that from now on the constituted governmental authority will inject itself to an increasing degree in medical affairs....the United States government is manifesting a great interest in science and there is likelihood of a very large expenditure of governmental funds for science. Your Association has teamed up with other scientific organizations in favoring the development of a National Science Foundation. But while the intent of such legislation is wholly benevolent, the administration and execution of such legislation may be of a different order. Science is a coy and jealous mistress, and her enduring charms are often not purchasable for a fixed price and do not always go to the highest bidder. Then too the practice of medicine is an applied science. While the art of medicine is very old, medical science is new. Like it or not, there is an aristocracy of science, which on occasion may be a bit intolerant...I believe that dangers to the profession lurk there just the same as in the more obvious attempts of government intervention, as in the case of the Wagner-Murray-Dingell bill [for compulsory national health insurance]". (81)

The case against clinical research had just been bolstered by a new, and powerful, political argument.

Lee's immediate successor, H.H. Shoulders, speaking on the 100th anniversary of the AMA, began on a positive note: "Beyond question it is true that more progress was made in the science and art of medicine in this period and in the adaptation of this science and art to human needs in the United States than in any other nation in the world. " Nevertheless, in a section of his speech entitled *Campaign to Undermine Faith in American Medicine,* Shoulders continued the theme of a profession under siege:

> "A campaign has been going on for some years now aimed at four objectives: 1. the destruction of the faith of the people in the medical profession. 2. Destruction of the faith of the people in our American system of medical care. 3. Destruction of the freedom of doctors and patients. 4. The establishment of a totalitarian system of medical care...This campaign culminated in the introduction in both Houses of Congress of a series of Wagner-Murray-Dingell bills...to make medical and hospital care matters of federal patronage to a large extent...Doctors, hospitals and nurses would become beholden to a federal administrator for a contract to serve the beneficiaries or else not serve them...The beneficiaries would receive no insurance contract but would accept whatever benefits were arranged for them by the administrator...This bill constitutes the boldest bid for power over more people and for greater patronage than any other measure that has ever been introduced into the Congress." (82)

In the eyes of the medical profession, loss of autonomy was the key moral issue and the greatest evil imaginable. It would lead to "the assembly line type of practice so greatly deplored elsewhere". (83) Countless editorials, committee reports, House of Delegates resolutions in the two decades centered in World War II, were devoted to combating all forms of state control, including the double-edged sword of support for research. An editorial in Hygeia, the AMA's journal written for the general public, stated the position succinctly: "Vastly impressed by the success of the government-

supported, intensified and coordinated research that led to the development of the atomic bomb, many people are ready to conclude that a similar technique would yield the cause and cure of cancer... Medical scientists...are more skeptical..." (84)

The other prong of the fight for professional autonomy was a publicity campaign building up a larger-than-life image of the masterly physician and his proper social role of protector and friend. In line with a strategy based on cementing the old social contract between patients and physicians, Hygeia published a series of cartoons along with editorials, which blended images of the benevolent and omnipotent 'doctor' with graphic depictions of impending disaster for "the little man" should the government take over the role of health care provider. (Appendix A) The first cartoon/editorial in the series was reproduced in the Journal of the American Medical Association with the legend 'There can be but one master in the house of medicine, and that is the physician' (85). The giant figure of the doctor looms over a landscape threatened by the darkening storm of politics, as ranks of aggressive new health professions march toward 'the nation's homes', these dangers and 'the nation's hospitals' - all held in check by 'The Doctor's' protective powers (Appendix B). There was absolutely no room for patient autonomy in this picture. The other drawings for the lay readers of Hygeia, covered the threatened moral coordinates of the practitioner's world: loss of freedom for physicians, aka socialized medicine (Appendix C); (86) loss of freedom for patients, aka compulsory sickness insurance plans (Appendix D); (87) loss of freedom for all, aka government manipulation of doctors, patients, hospital administrators, and relief agents (Appendix E); (88) and

arrayed against these treacherous blandishments, the doctor's enduring and dedicated beneficence depicted as 'the doctor's 24-hour day in the service of his patients (Appendix F). (89) Here there was no time for informed consent.

III. THE NUREMBERG COMMANDMENTS

1. *The Code in Historical Perspective.* The Nuremberg Code (Appendix G) was simply absent from the professional and popular consciousness of the immediate postwar period. This was a time when Reader's Digest, The Saturday Evening Post, and The New York Times ran upbeat human interest stories about eccentric yet noble volunteers for radioactive tracer studies, new vaccine tests, high altitude experiments and 'guinea pigs' for malaria trials. (90) To take a measure of the epistemological distance traveled, a glance at the situation 50 years later seems warranted. The popular media frequently carried sensational stories of unethical research and malpractice suits side by side with reports of scientific 'breakthroughs', while prestigious medical journals in the 1980's and 1990's frequently referenced the Code's central importance in protection of study subjects' human rights and, in its emphasis on consent, the universally recognized foundation of clinical morality. "The Nuremberg Code is the most important document in the history of the ethics of medical research" began a recent Special Article in the New England Journal of Medicine. (91) Another opened with "The most famous document resulting from the Nuremberg Medical Trial is the Nuremberg Code, and the most celebrated element of this Code is the opening consent clause," which states that "the voluntary consent of the human subject is absolutely essential." (92) "Nuremberg has a special

resonance in the annals of law and biomedical ethics. Though it was not the first jurisprudential appearance for the principle of patient autonomy, the Nuremberg judgment gave central importance to this principle that should govern physician-patient relations", proclaims a third. (93) One book has been entirely devoted to the Code and its universal impact (94). In its 50th anniversary year, the Code has been the focus of several international conferences, dozens of chapters in books on medical ethics, and countless scholarly articles. The Code is clearly on a trajectory from cultural oblivion in its own time to iconization in the global culture of the present. All this activity leads to two interrelated questions: where did this unmistakable reshaping of cultural cognition originate, and what was the historical context which nurtured it? The answers lead back to the AMA.

2. *Making the Code.* Sometime in the spring of 1946 the American prosecution team preparing for the Doctors' Trial in Nuremberg asked Secretary of War Robert P. Patterson for an expert in medical research. Patterson contacted Army Surgeon General Norman T. Kirk, who turned to the Board of Trustees of the AMA. In May, 1946, the AMA appointed Andrew C. Ivy as its official consultant to the prosecutors in Nuremberg. Ivy was a leading medical scientist whose personal research experience included areas of investigation pursued by the accused at Nuremberg, including experiments in seawater desalinization and high altitude research (with himself as a subject). Ivy had been active as the founding secretary-treasurer of the National Society for Medical Research, an organization established to ward off the challenges of antivivisectionists. Considering the tenuous relationship of the AMA with the world of medical science, and its concern with potential political damage to

the image of physicians everywhere emanating from Nuremberg, the House of Delegates decided that Ivy could be trusted to represent the interests of organized medicine at the trial. Ivy's contributions to the prosecution, and his central role in framing the Code have been repeatedly described in recent years. (95) The brief account below highlights those aspects of the story which echo and reverberate against the broader debate waged at that time by the clinical and scientific sectors of the medical profession.

After Ivy met with the Nuremberg prosecutors in the summer of 1946, he returned to the U.S. convinced that the ethical aspects of human experimentation would become a central issue in the prosecution's case. (96) In August, Ivy met with the AMA's Board of Trustees and agreed to produce a report "as to the manner in which these experiments [were] infringements of medical ethics." According to Ivy, the twenty two-page report contained "the rules" of human experimentation, which had been "well established by custom, social usage and the ethics of medical conduct." Ivy submitted the report to the AMA in September, with a copy to the Nuremberg prosecutors. Ivy's 'rules' were arranged in 3 sections which dealt with consent of the "human subject" (language adapted from the anti-vivisectionists?), appropriate design of the study, and awareness of risks. (97) A comparison of Ivy's text with the language of the Nuremberg Code shows that important elements of clause 1, and clauses 2, 3, 4, 5 and 8 essentially in their entirety, were incorporated by the judges who framed the final version of the Code. The judges also accepted Ivy's assertion

that these rules were already widely understood and followed by medical researchers. Accordingly, the preamble to the Code begins "All agree..."

Ivy took the stand at the trial in the middle of June 1947 (the trial ended on July 19,1947), as the expert witness the prosecution brought to Nuremberg expressly to rebut the claims of the defense that no standards for proper conduct of human experimentation existed prior to the trial. The counsel for the prosecution read the three AMA principles into the record, then asked whether these rules "purport to be the principles upon which all physicians and scientists guide themselves before they resort to medical experimentation on human beings in the United States". Ivy responded: Yes, they represent the basic principles approved by the American Medical Association for the use of human beings as subjects in medical experiments." In answer to a question from presiding Judge Harold E. Sebring, Ivy asserted that the principles of the AMA were "identical, according to my information" with principles of medical ethics "over the civilized world generally." The defense eventually forced Ivy to admit that the AMA guidelines were written expressly for the purpose of the trial, and no written instructions existed before December, 1946. Still, Ivy insisted that the rules "were understood only [sic] as a matter of common practice." (98)

We have seen that the AMA's Code of Ethics contained no language dealing with scientific experimentation. Accordingly, the AMA's Judicial Council, custodians of Percival's ethics, presented a severely truncated version of Ivy's rules before the

House of Delegates on December 10, 1946, the day *after* the opening of the Doctors' Trial in Nuremberg. The chair of the Judicial Council, E.R.Cunniffe, characterized the experiments described in Ivy's report as "gross violations of standards already inherent in the existing Principles of Medical Ethics of the AMA." The Council conceded that such guidelines were not *explicitly* stated in the Principles and presented a distillation of Ivy's text to the House of Delegates for approval, which was granted on the morning of the next day. The full text of the now official AMA policy on human experimentation was as follows:

> In order to conform to the ethics of the AMA, three requirements must be satisfied: (1) the voluntary consent of the person on whom the experiment is to be performed [must be obtained]. (2) the danger of each experiment must be previously investigated by animal experimentation (3) the experiment must be performed under proper medical protection and management. (99)

Records of deliberations by the delegates for all of the 1940's have been lost, (100) but the brevity of their final policy statement, the fact that informed consent was not endorsed, and the single admonition they added -"This House of Delegates condemns any other manner of experimentation on human beings than that mentioned herein"- suggest that the delegates were not anxious to deal with the idea of experimentation for social benefit, and with protocols which placed healthy individuals in harm's way. The *Journal of the American Medical Association* printed these rules in fine type in the middle of several lengthy miscellaneous items concealed in the voluminous minutes of the meeting.

The record summarized above suggests that a single individual, operating in a regulatory vacuum single-handedly crafted the format and the main sections of the Nuremberg Code, as well as the official policy of the AMA on research in humans. However, another American physician, Leo Alexander, an American Army psychiatrist working with an Allied intelligence organization, had an equal, some believe even greater, claim to the title of "Father of the Code." Alexander had been assigned shortly after the war to gather evidence for the Nuremberg trials, and to examine some of the witnesses who had been victims. Alexander prepared a memorandum entitled *Ethical and Non-Ethical Experimentation on Human Beings* in which he identified three ethical, legal and scientific requirements for the conduct of human experimentation: the first established the right of the *competent* experimental subject to consent or refuse to participate ("the subject should be willing to participate of his own free will..."). The second restated the Hippocratic duty not to harm in terms of experimentation ("The medical Hippocratic attitude prohibits an experiment if the ...probability...exists that death or disabling injury of the experimental subject will occur"). The third characterized good research practices. The chief prosecutor, Colonel Telford Taylor transmitted Alexander's statement to the judges. (101)

Careful examination of Alexander's text reveals that it contains almost all of the principles that appear in the final 10-point Nuremberg Code. (102) It is also known that Alexander attempted to assemble his and Ivy's testimony for the judges in making their final statement. This the judges accomplished with a strong

reinforcement of the informed consent requirement in the first clause ("absolutely essential"); and added the 9th clause which affirmed the research subject's right to withdraw from the experiment. (see Appendix for the complete text of the Code) The remaining 8 points appear to have been constructed with language provided by both Alexander and Ivy.

As the primary architects of the Nuremberg Code, Ivy and Alexander offered support for their opinions based on a variety of historical sources. Both specifically cited Hippocrates as the major foundation for their views on medical ethics. (103) Ivy responded with an affirmation of the Oath to a question about the sources of his belief in the morality of human experimentation. "According to my knowledge, it [Hippocratic Oath] represents the Golden Rule of the medical profession... And in that way [it states] how a doctor should treat his patient or experimental subject." Alexander noted: "Every professional relationship between the physician and another human being, irrespective of whether the physician treats the patient, examines him, or performs an experiment upon him with his permission , is bound by the principles laid down in the Hippocrates [sic] oath. "

These statements of principle immediately evoked two related conflicts: first, Hippocratic morals deal with benefit to the patient, while experiments may cause potential harm; second, the trial concerned experiments on prisoners not therapeutic treatment of patients. Hippocrates evinced no interest in "research" which was non-therapeutic. These points were made by the defense to demonstrate that the

Hippocratic ethos could not provide a solid foundation for the purposes of the trial. More directly pertinent to the subject of this paper is the fact that Hippocrates had everything to say about the benevolent, paternalistic physician and nothing about the consenting, autonomous patient. Percival's medical ethics, and hence the AMA's Code, reinforced the Hippocratic ideal of the all-knowing physician. Percival does refer to "new remedies and new methods of surgical treatment" which should be devised "...scrupulously and conscientiously, governed by sound reason, just analogy, or well-authenticated facts. And no such trials should be instituted without a previous consultation of the physicians or surgeons according to the nature of the case." It is important to note that Percival's conclusions on this point provided the rationale and moral authorization for the conflation of therapy and experiment promoted by the medical profession in the past one hundred years. (104)

Ivy and Alexander shared in that conflation inherited from Hippocrates and reinforced by Percival which characterized the traditional part-time clinical 'investigator' in the first two decades after World War II. As mentioned, professionals replaced hyphenated doctors when the randomized, doubly-blinded and controlled clinical trial swept aside all other approaches to the research ward. Furthermore, its central preoccupation with informed consent made the Nuremberg Code incomprehensible, unenforceable or threatening to practitioners and *part-time* clinician-investigators alike, groups who shared a common epistemology and comprised the Fleckian thought-commune of medicine during the first half of the 20th century. Informed and authorized by a shared culture, these practitioners saw

the world through Hippocratic eyes. There was no place for "absolute" requirements in it except, perhaps, to do no harm.

3. *A new mosaic from old beliefs.* On June 13, 1947, Ivy was asked during cross-examination by defense counsel to reconcile his opinion,that dangerous experiments are ethically acceptable, with the Hippocratic injunction not to "administer a poison to anyone, even when asked for it." Ivy admitted under oath that "this Hippocratic commandment refers to the function of the physician as a therapist, not as an experimentalist, and what refers to the Hippocratic oath is that he [the physician] must have respect for life and the human rights of his or her experimental patient." (105) With the evident weaknesses in Ivy's testimony exposed by the defense, the judges at Nuremberg realized that the Hippocratic physician's commitment to preserve patients' lives and protect their welfare was not sufficient to safeguard their human rights in medical research. Accordingly, in drafting the indictment, the judges accepted the physician-centered suggested provisions of their two medical experts, but reinforced them with two additional principles which transfered control into the hands of the patient: the first clause, with its strong consent statement, and the ninth, guaranteeing the right to withdraw from the experiment at any time.

The logic and unequivocal severity of the judiciary argument suggested that all Hippocratic clinician/researchers, including Alexander and Ivy, may in their own research encounter difficulties in complying with the stringent consent requirements of the Nuremberg Code. Indeed, as Evelyne Shuster has pointed out, Alexander was

unable to distinguish research from treatment in his psychiatric practice. (106) Limited by a Massachusetts decree to a specified number of electroconvulsive treatments per patient, Alexander complained that "something has come between us and our patients...thus creating a conflict between temporal and temporary laws, and the eternal basic and unwavering law of medical ethics, compelling us to do always what we consider best for our patients." (107)

By 1973, Alexander had reinterpreted the Code which he himself had helped create, as a bulwark *not for individual rights but against the power of the state.* And since the convicted physicians at Nuremberg were servants of the Nazi state, it was that state which was ultimately responsible for the crimes. (This, of course, had been the standard defense at the trial). The lesson to be drawn was that the state should never have the power to dictate to physicians - precisely, as we have seen, the core position of the AMA in its never-ending struggles against "government control."

Writing in 1973 toward the end of his career, Alexander summarized his position on the Nuremberg Code as follows:

> "This is a conflict between the laws of the state on the one hand, and the ethical conscience and the professional responsibility of the physician on the other...Should we submit to the capriciousness of temporary-temporal political laws, or stick to our immutable laws of medical ethics? It is my firm belief that the latter outranks the former, as Divine law outranks government law, a fact unanimously established by the Nürnberg [sic] War Crimes Court... All this is being carried out in the name of independence and civil rights. But long before independence there was interdependence: the patient and his doctor trusting each other, forming with solidarity an alliance against the illness." (108)

Alexander had reason for concern. Parcivalean deontological etiquette ("Divine law") was rapidly becoming outmoded around the time Leake published his second edition of Percival's rules and Alexander wrote the lines quoted above. Just as Leake was unable to discern that Percival's era was ending, Alexander could not grasp that his beloved Code had been lifted out of its '40's context, and reframed to fit the new paradigm of the civil rights/human rights revolution: "All this is being carried out in the name of independence and civil rights." This was an invasion of the physician's authority by the regulatory authority whom Alexander, still laboring under his "Hippocratic obligation", was neither equipped to recognize, nor prepared to endure. Leake and Alexander saw their world through the lens of an increasingly obsolete cultural framework.

Ivy experienced a similar "conversion" to an anti-state interpretation of the Code. As did Alexander, Ivy confused research with therapy, devoting most of his postwar career to therapeutic trials of the ineffective biological compound he had named Krebiozen in terminal cancer patients. (109) Even more intensely than Alexander, Ivy interpreted his Nuremberg experience as a lesson against government interference in medical affairs. The subtitles of Ivy's paper on Nazi war crimes in the *Journal of the American Medical Association* signal the arguments for this point of view: "Totalitarian Philosophy; What Happened to Organized Medicine? The Contribution of Hippocrates; Materialistic Scientific and Technological Philosophy has no Survival

Value; State Medicine and Compulsory Sickness Insurance Introduce Deteriorating Evils." (110) The AMA could not have been more explicit.

Otto Guttentag, a moral philosopher and noted scholar of medical ethics, recognized Ivy's inconsistency on the central meaning of the Code. In a review of an eyewitness report of the proceedings in the Doctors' Trial observed from the German side, with an introduction by Ivy (111), Guttentag cited "discrepancies between his [Ivy's] statements in *Doctors of Infamy* [title of the report] and in his article entitled "Nazi War Crimes of a Medical Nature." In *Doctors of Infamy*, Ivy had written "From all evidence available, it is necessary to conclude that, far from opposing the Nazi state militantly, part of the German medical profession cooperated consciously and even willingly, while the remainder acquiesced in silence...Therefore, our regretful but inevitable judgment must be that responsibility...rests in large measure also upon the bulk of the German medical profession, because the profession without vigorous protest permitted itself to be ruled by such men." In his article in the *Journal of the American Medical Association*, Ivy stated "It should be emphasized that the larger portion of German medicine remained ethical. " Guttentag characterized Ivy's flip-flops as "unfortunate". (112)

The ultimate irony for Alexander's and Ivy's generation of clinician/researchers lay in the fact that the Code had become the treasure rescued from the dustbin of the 1950's for one reason only: its "majestic", "complete and authoritative", "unique" informed consent clause - the one part of the Code in which neither man had a hand

- had become the signature of the new bioethics which they abhorred. (113) The historic movement from Percivalean practitioner to modern clinical investigator and patients with "rights"used the Code's interweaving of legalistic and Hippocratic elements as a rhetorical device to create a moral framework for a new kind of medicine functioning in a radically transformed explanatory system.

4. *Near-Total Eclipse.* The response of organized medicine to the opening of the Doctors' Trial in Nuremberg was, to put it mildly, muted. In the year the trial began, the official organ of the AMA carried two editorials on German medical research during the war. The first, on March 2, 1946, recounted Alexander's report to the Secretary of War with the details of Sigmund Rascher's freeze-thaw experiments in the concentration camp Dachau. (114) The anonymous writer(s) castigated Rascher for "allowing frozen people to die in bed with naked women in order to demonstrate the relative ineffectiveness of that method of rewarming, while standing ready to measure the rectal temperature of those who recovered sufficiently to carry out sexual intercourse under those circumstances." They implied that the great failure, "not only of men of Rascher's caliber but a number of men once important in the German scientific world," was that "out of this revolting mess...came a single practical suggestion, namely that rapid rewarming is more effective in the treatment of shock due to chilling than slow rewarming." And, after all that, the editorial concluded "even that suggestion was not original, for it was advocated as far back as 1880 by a Russian physician." (115)

The topic of research in aviation medicine for the German Air Force was taken up again in a second lead editorial on March 23, 1946. (116) This time, the material was gathered by "our investigators who visited the experimental laboratories and interviewed the research workers." The unusually technical review included several human experiments concerning tolerance of acceleration, effects of altitude on visual acuity, ability to "work" at high altitudes, and a study of cooling and rewarming in parabiotic rats. The data were presented without noting that the animals reacted identically with the humans in the Dachau experiments described in the Journal just three weeks earlier. The apparent "take home" lesson and rationale for this highly uncharacteristic focus on scientific procedural detail in the Journal, let alone in its editorials, was stated in the final sentence: "The information is interesting chiefly because it offers a basis for comparison...on the whole, the German aviation science does not reveal any successful solving of problems that our own investigators have not tackled and solved." JAMA's editorial writer was thus demonstrably focused on comparative technical achievements and research outcomes, and ignored moral contextual questions.

A follow-up report on studies by German scientists for the Luftwaffe sent in by JAMA's "special correspondent" in Washington, DC, appeared on September 14, 1946. The report is reproduced here in its entirety, in order to transmit a sense of the prevailing utilitarian world-view three months before the opening of the Doctors' Trial:

> "Army Air Forces Headquarters has disclosed after study of captured enemy medical reports that 'human guinea pigs' were 'successfully' used in German pressure chamber tests up to 30,400 feet without oxygen. The research was carried out in German Laboratories in the

> Dachau internment camp by Nazi scientists and doctors during April 1942. Tests were made on human subjects at the direction of Heinrich Himmler, Gestapo chief. Records in the Office of the Air Surgeon reveal that tests placed human beings at a higher artificial attitude without oxygen than ever before reached. The U.S. Navy in operation 'Mount Everest' raised volunteer personnel to 29,025 feet." (117)

The final editorial on wartime German medical experiments appeared in JAMA on November 23, 1946. (118) The editorial contained a synopsis of Ivy's travels as the AMA's representative to the trial, a summary of his report, a condemnation of the 'experiments' described in the report, and pointed a finger squarely at the AMA's German counterparts: "Perhaps most serious of all is the failure of the German medical organizations and societies to express in any manner their disapproval of these widely known experiments." The editor appeared to be oblivious of the fact that JAMA's Foreign Letters section had carried since 1933, without commentary, reports of atrocities the new government in Germany had committed against Jewish and socialist physicians. The suggestion was: "It was the fault of the Nazi government. We stand up to ours, why couldn't you stand up to yours?"

The editorial attracted a single letter to the editor, published on December 28, 1946. (119) The writer, Cortez F. Enloe, Jr., had interrogated "hundreds" of German physicians after the war and had "failed to reveal any evidence that they were aware of what was going on in the name of medical science in the concentration camps or that, being aware, they had any power to exercise even such a faint gesture as the voicing of disapproval. So it was wrong to condemn the German profession as a body." The conclusion the writer drew from his experience was that "no medical

group can withstand the threat of violence that is the major characteristic of the police state." Enloe's letter in turn brought a single response from another reader, Frederic Wortham, who recalled that rumors of "very serious...brutalities in American psychiatric hospitals" ought to be investigated because here, as in Germany, "not to know is not an excuse, it is an indictment." (120) These exchanges constituted the reaction, in its entirety, of organized medicine in the US to the news from Nuremberg.

The outcome of the trial was reported in the Foreign Letters section of the Journal without editorial comment four months after it ended. The Letter included lists of the 14 "experiments", and the ten "basic principles", subsequently dubbed the Code of Nuremberg, which "must be observed in order to satisfy moral, ethical and legal concepts." (121) An adjoining item from Bad Neuheim in West Germany, announced that the anonymous Foreign Letters reporter attended a meeting of German Medical Societies from the three Occupied Zones, at which details from the trial in Nuremberg "shocked" the representatives into passing a resolution which mandated a newly drafted oath required for a license. The full text of the lengthy oath was reproduced in the Letter. (122) The contrast with the American reaction reinforced the impression that the trial and the issues raised in the proceedings were strictly a German affair.

Several authors have commented on the relative silence with which the medical profession and the general press reacted to the news from Nuremberg. (123) The

favored rationale to account for this lack of interest is a putative failure to identify with the crimes and criminals processed in Nuremberg. David Rothman has given an account of the scanty news coverage of the trial by major newspapers, and has asserted that the general feeling among physicians at the time and after the trial was "nothing these Nazi criminals did has any relevance to the United States." Jay Katz visualized a similar scenario: "It was a good code for barbarians, but not for fine upstanding people." (124)

Interviews conducted in 1995 by historians for the Ethics Oral History Project of the Advisory Committee on Human Radiation Experiments (ACHRE) with medical scientists active in the U.S. in the 1950's and 1960's yielded a mixed picture which was interpreted by ACHRE as consistent with Rothman's and Katz's postulations. (125) However, while many interviewees reported that they had not followed the events in Nuremberg for lack of interest, Herbert Abrams, a resident in radiology at the time, remembered "We were all aware of it...at least in the environment I was in." The environment which made Abrams conscious of medical crimes committed by Nazi doctors was Montefiore Hospital in New York City, a place where a number of Jewish refugee physicians who had fled Germany were employed. Several other interviewees appear to have had second and third thoughts at follow-up interviews, which featured anachronistic reactions in conformity with current cultural expectations. "And as you ask me now, I'm astonished that we were not hanging on the TV at the time, watching for each twist and turn of the argument to develop." and "As I see it now, I'm saddened that we didn't see the connection, but that's what was

done...It's hard to tell you now ...how we rationalized, but the fact is we did." (126) Such remarks diminish the heuristic value of these oral representations.

Another approach to the question concerning the initial eclipse of the Code is to recall that "the Code" is itself a later construct. These clauses were framed for indictment purposes and were perceived as an integral part of the trial. To analyze the initial lack of interest in the Code is to begin with the observation that the public was introduced to the Code in conjunction with the trial. As noted previously, the Code had to be separated from the specific trial setting and placed in a context which removed it from the scandalous and 'foreign' aspects of the trial. Only then, after the trial itself had become history, could the Code reemerge as holy writ for the legitimization of a new bio-scientific morality. The perception of the Code as a stand-alone legal product may date from the mid-1950's. In 1953, the new Clinical Center of the National Institutes of Health (NIH) adopted guidelines for acceptance of subjects for research. The rules for handling of normal volunteers were introduced as follows: "The rigid safeguards observed at the NIH are based on the so-called 'ten commandments' of human medical research, which were adopted at the Nuremberg War Crimes trials after the atrocities performed by Nazi doctors had been exposed." A secular Decalogue had been unveiled. (127)

A third way to gain historical perspective on the eclipse of the Nuremberg Code is to ferret out of the historical record the exceptional insight invisible to contemporaries, therefore ignored in its time. Paul Dufault's speech to a group of physicians in

Western Massachusetts belongs in that rare category. Speaking from the vantage point of a state sanitarium superintendent, Paul Dufault addressed the Medical Society of Worcester District on October 12, 1949. Dufault's speech is remarkable for its presentation of the Nuremberg trial in an entirely novel hermeneutic perspective for its time. Dufault was the first to focus on the *universal* meaning of the Nuremberg trial in the American medical literature after Alexander's and Ivy's reports. He sensed a close connection with the German doctors on trial, and recognized the implications of their behavior for all physicians working in the progressivist Western scientific tradition. (128)

Dufault adopted the rhetorical device of pretending to be a physician looking out toward the more distant future from the immediate future ("Medicinae Doctor 1950"):

> "In this year 1950, Medicinae Doctor stands alone, a puzzled, self-conscious person. Disturbed by events abroad affecting the status of his *brethren*, uneasy about some tendencies at home, and at the same time fascinated by the rapid advances in his own field of endeavor, he turns a searching eye on his profession and a critical one on himself."

The editors who published Dufault's insights less than three years after the end of the Nuremberg trial might have been oblivious to his meaning. Who could imagine these physician murderers as "brethren"? Further on:

> "The world, accustomed for generations to this teaching [a crime to perform castration for non-medical reasons], witnessed with unmixed horror...the appalling practices condoned by a philosophy according to which political and utilitarian factors were allowed to prevail over spiritual considerations. The conscience of civilized men was also shocked by reports of experiments, potentially detrimental to life, carried out on defenseless political prisoners without their consent."

In the same essay, Dufault also defined two epistemologically diverse ways of looking at a patient: "Specialists and men in the higher echelons, seeing the patient only in their offices and in the hospital, have come to look at him too much as a *sick man* and not enough as a *man*... The practitioner of old who visited the sick in their homes was less exposed to this pitfall of the modern streamlined hospital system." These few words contained the germ and gist of David Rothman's influential *Strangers at the Bedside* published 42 years later.

Dufault then proceeded to challenge the central dogma of the medical profession, the proscription against external control :

> "The very idea of extended medical care...is accepted as undeniable proof that health is now regarded as the inalienable right of man as much as individual liberty, and of equal value. *Medicine has sold itself to the world, and the world wants to make it public property.* The means to attain this end are being debated heatedly between the proponents and the opponents of socialization. "

Dufault's essay ends with a return to Nuremberg:

> "The events of the last decade have shaken the faith of many who hoped *that virtue would keep faith with science.* ..And if some depraved sadists were recently let loose, they perpetrated their crimes in the secrecy of concentration camps..."

5. *A Solar Flare At The Margin Of The Eclipse.* As was true of his contemporaries, Dufault could not conceptualize the Code outside the trial, but what he saw or foresaw was extraordinarily different from everybody else's vision. Exactly two years later, virtue did attempt to catch up with science, using the Nuremberg Code itself for the first time as its instrument. The first attempt to contextualize the Nuremberg

Code explicitly for American medical researchers took place at a symposium held at the University of California in San Francisco on October 10, 1951. The meeting brought together four distinctive and representative voices: the research worker, the physician, the legal expert and the military advocate, each given equal billing in the resultant four-in-one publication. (129)

The antecedents, motivation and organization of this unlikely event have puzzled previous commentators. (130) The Final Report of ACHRE (131) comments enigmatically "Dr. Michael B. Shimkin organized the symposium in response to some confidential criticism that he had received for research carried out under his direction with patients at the University of California's Laboratory of Experimental Oncology." The criticism convinced Shimkin that a more open discussion of clinical research might be of benefit to his colleagues. According to his recollection, "there was an almost visible thawing of attitude by the airing of the problem at the symposium." (132) These tantalizing allusions to criticisms by unnamed parties of sufficient strength to force the Laboratory's director into "open discussions of clinical research" and even greater exposure at a public symposium, raised the possibility of conflict between clinicians and researchers over control of cancer patients in clinical studies. When the published proceedings turned on a discussion of the Nuremberg Code from the researcher's point of view, and the discussant who represented the "physician's point of view" was Otto Guttentag, professor of medicine at the University of California in San Francisco and noted philosopher of medical morality, a closer look appeared warranted.

While Guttentag was well known as a pioneer and authority on moral aspects of the patient-physician relationship, Michael Shimkin, a much younger man, was still relatively unknown outside the walls of the NCI in 1951. He was a career Public Health Service medical scientist who had spent twenty five years at the National Cancer Institute (NCI), joining as one of NCI's original group of research fellows in 1938. During World War II, Shimkin had been involved in cancer research for an extension of the Manhattan Project at the NCI. There he encountered Robert S. Stone, a senior medical director in the Manhattan Project and chairman of Radiology at Shimkin's alma mater, the University of California Medical School in San Francisco (UCSF). In discussions with Stone, Surgeon General Thomas Parran, and director of the NCI, Roscoe R. Spencer, Shimkin conceived the idea for an extramural clinical-laboratory unit for cancer research in an academic environment. "I wanted to demonstrate that biomedical research programs of the National Institutes of Health (NIH) could develop as colonies of full partnership with universities..." (133)

The Laboratory of Experimental Oncology (LEO) was established in 1947 as a clinical research facility operated jointly by the NCI and UCSF under Shimkin's direction. The LEO was "disbanded" in 1954, victim of a policy shift which favored intramural control at the NIH, and was replaced by a central facility built in 1953 to implement that policy, the NIH Clinical Center in Bethesda, MD. Shimkin retired from the Public Health Service in 1963, and subsequently held professorships at Temple

University and at the University of California at San Diego, served as editor of *The Journal of the National Cancer Institute* for six years, and was elected president of the American Association for Cancer Research in 1974. Shimkin died of a stroke in 1989. The symposium Shimkin organized on *The Problem of Experimentation on Human Beings* came in response to complaints he had received from UCSF's clinical faculty about the treatment of patient/subjects at the LEO. (134)

Keeping in mind that the symposium was presented "for the benefit" of his colleagues (researchers or clinicians?) at the University of California at San Francisco, and perhaps to preempt shadowy but powerful critics, Shimkin began his address at the symposium with the admission that "the use of human beings for experimental purposes often encounters vigorous opposition."(135) Shimkin went on to acknowledge potential abuse of subjects, but "abuse does not preclude use." Then Shimkin set the agenda with a question rhetorically addressed to his clinical critics and beyond: What are the "proper rules of conduct" (Percival's language) that can be utilized in judging whether human beings should be involved in experimentation? His proposed answer: "Perhaps the closest formulation of such rules was made at the Nuremberg medical trial." Shimkin next recited the Code (not yet a code in 1951 but a "set of rules") in its entirety, marking the first appearance of the complete text in a major American scientific journal. To adapt the Nuremberg guidelines for contemporary clinical researchers, Shimkin condensed the ten clauses to "two primary principles": First, the investigator must be thoroughly trained in the scientific disciplines of the problem, and must

and must understand and appreciate the ethics involved; second, the human experimental subject must understand and voluntarily consent to the procedure, and must not be selected upon any basis such as race, religion, level of education or economic status. In other words, *"the investigators and the subjects are human beings with entirely equal, inalienable rights."* Shimkin also felt that research on humans is "too hazardous," with "too many responsibilities to be undertaken by lone investigators," but it should be "a group effort supported by a proper consultative body." This was the first suggestion on record for a regulatory mechanism for clinical research based on an institutionally organized review committee. As we shall see, the revolutionary idea of consultations with clinicians about research protocols originated in an attempt to pacify his critics by bringing them into the process.

Guttentag's part the story of the Laboratory of Experimental Oncology (LEO) will be discussed later. At the symposium, Guttentag's presentation dealt with at least two issues directly related to the controversy involving Shimkin: the use of "hopelessly incurable" patients, and "increased technicalities all around." As a refugee from Vienna from the early '30's and a recent reviewer of the report by Mitscherlich and Mielke, the two German physicians assigned as official observers at the Nuremberg trial for the West German equivalent of the AMA, Guttentag was familiar with the most important contemporary sources of information about the trial. (136) Yet, he expressed an optimism about the durability of the patient-physician relationship in American culture, believing that "...the overwhelming majority of physician-

experimenters...are so deeply rooted in the democratic spirit that they agree...that the use of force is not justifiable on a single person, even if millions of other lives could be saved by such an act." The rationalization Guttentag offered for his faith in the American clinical researcher was his perception that saving millions of lives at the expense of one person's rights was an immoral act which "from the standpoint of democratic brotherhood might create millions of amoral sequels, and that the moral history of mankind is more important than the scientific."

The "problem of the 'hopelessly incurable'" was for Guttentag the one area which "challenged tremendously the basic concepts of the original patient-physician relationship." Guttentag feared "encroachments" upon the patient's rights from society, but more urgently, from the medical profession itself. "The literature suggests that the classification of persons as 'hopelessly sick'...by its characterization as 'hopeless' is intended to justify an experimenter's self-permit for greater boldness...when in performing experiments that endanger the lives of the experimented-on sick, the experimenter restricts himself to those 'marked by death.' Guttentag noted that the Principles of Medical Ethics of the AMA "nowhere forbid experimentation,"and provided an explanation for the general tendency of physicians, and his own, to conflate therapy and research:

> "Experimentation for the patient's immediate good forms an integral part of the physician's care of his patients; and experiments to confirm or disprove a biological generalization with regard to man certainly cannot be better performed than by the profession that is trained more completely than any other in comprehending the somatic and psychological aspects of human life..." (137)

Guttentag concluded that only physicians could fill both roles of caregiver and experimenter, and was cognizant that "present types of experimentation on the sick clearly challenge tremendously the basic concepts of the original patient-physician relationship." Guttentag therefore introduced the notion, borrowed from the legal adversarial system, of separating the two functions with the appointment of a 'physician friend' to represent the patient's interests before the 'physician-experimenter.' "The responsibility for the patient as patient would rest, during the experimental period, with the physician-friend, unless the patient decided differently." (138)

Finally, Guttentag addressed the issue which would later become iconized as 'informed consent'. Under the rubric of "technicalities" to characterize "the forms that patients must sign when about to volunteer for experimentation, or even to undergo an operation," Guttentag recognized that "...following explanations of the seriousness of an operation and the nature of the patient's disease, it was 'agreed' between patient and physician to operate can be true only in the vaguest sense of the term 'agree'." Finally, Guttentag came to grips with the crucial difference between therapy and experiment: "How much greater is this difficulty in an experimental procedure, where selfishness plays a role?" As far as oversight can afford protection for the experimental subject, Guttentag placed his faith in a paternalistic "physician friend"; as far as formal acknowledgment of the patient's right to self-determination was concerned, none existed. True to his time, Guttentag suggested that the "forms...might be so phrased as to state not only the patient's consent, but also the

physician's affirmation of his utmost effort to protect the patient from harm..." In the 50's, the normative paternalistic Hippocratic physician still could be the patient's friend and best protector.

In its commentary on Guttentag's scheme to separate the functions of personal physician from medical researcher, ACHRE suggested in its Final Report that "among physicians Guttentag was nearly unique in medicine in those days in raising such problems in print." Further, the Committee seized Guttentag's contribution to the symposium to make the general historic point that "difficult and inconvenient as it might have been for researchers in the boom years of American medical science following World War II to confront the fundamental differences between therapeutic and non-therapeutic relationships with other human beings, it was not impossible. ..." (139) 'Nearly unique' yet 'not impossible', the Committee clearly experienced difficulty in fitting Guttentag's presentation into its primary framework, which was to reconstruct the ontogeny of ethical thinking about human experimentation in post-World War II America. Shimkin's pioneering recognition of "rules made at the Nuremberg medical trial" as "the clearest formulation of rules...of conduct that should be utilized in judging whether human beings should be involved in experimentation," presented an even greater challenge to the historiographical commonplace that American medical researchers regarded the Nuremberg 'rules' with disdain in the 1950's and 1960's. (140) It was telling, also, that this construction of the Code as an important document for American medical research scientists came from the director of a major federally promoted and NCI- supported prototype clinical research facility.

Shimkin's idiosyncratic contribution at the symposium was invisible to the members of ACHRE and went unmentioned in the Committee's Final report.

A circumstance which brought together a research professional in charge of a facility dedicated to experimentation in terminal cancer patients, and an eminent theorist of the moral foundations underpinning the patient-doctor relationship, would be unusual at any time and place; in 1951, it was probably unprecedented. ACHRE indirectly acknowledged the epistemological potential of the mysterious situation at the LEO in remarks about "confidential criticism," but had to admit that "the exact nature of this criticism is unclear from the records that remain from the episode." In any case, the Committee realized that the charges against him prompted Shimkin to take "remedial steps" in addition to organizing the symposium. These measures included "written protocols for all new departures in clinical research, which we asked the cancer board of the medical school to review." (141)

It seems worthwhile to recall at this point, that the main task of this paper is to document the emergence of modern bioethics from social and cultural reforms which altered the self-definition of American medicine after World War II. Perhaps it may be evident by now that the notion of complete silence on the ethics front in the first two postwar decades requires qualification: perhaps the regulatory vacuum of the time reflected a cultural framework not yet cognitively ready to accept the new post-Percivalean paradigm even when it surfaced fully grown and equipped with its signature, the Nuremberg Code. One major milestone had been erected in San

Francisco in 1951, but there was as yet no clear road leading to "the field of human experimentation, performed not for the good of the individual patient, but made to confirm or disprove a...biological generalization." (142) The contingencies which created a context making possible this curious epistemological non-event - for it had no impact in its time - may shed light not so much on the eventual direction taken but on the situation of clinical research ethics in the U.S. in the first few years after the Nuremberg trial - the period described by Rothman as the Gilded Era of Research. (143) In particular, the story of the LEO may help explain the environment in which the first skirmishes over informed consent took place.

6. *Shimkin's Lost Colony.*

> "In the fight between you and the world, back the world."
>
> Franz Kafka, The Great Wall of China.(144)

The historical archives at UCSF contain records of the Laboratory of Experimental Oncology (LEO) for the years of its existence, 1947-54. (145) In addition, Shimkin has written a memoir published in limited typeset edition in 1978 (146); an abridged version of the essay on the LEO in the memoir was published in the *Journal of the National Cancer Institute* (147) Shimkin also included remarks about the LEO in his presidential address to the American Association for Cancer Research in 1974. (148)

At the time when Shimkin initially broached the idea for a regional, university-affiliated cancer research center located in San Francisco to Stone, in 1946 a member of the powerful National Advisory Cancer Council, Stone's reaction was not

enthusiastic. Direct intervention by the Surgeon General of the Public Health Service, Thomas Perran, with the President of the University of California, soon helped establish the Laboratory of Experimental Oncology as a combined operation of the National Cancer Institute (NCI) and the School of Medicine at the University of California in San Francisco (UCSF). As previously noted, Shimkin was appointed director. (149) The rationale for new medical research centers like the LEO originated in the empirical and psychological contingencies of war. (150) After the war, these trends crystallized around defined major national health problems. The most visible and accessible target was cancer. The money began to flow from the NIH, the Atomic Energy Commission, the Department of Defense and the Veterans' Affairs Administration into the universities. Underwritten with contracts transferred to the public sector after the end of the war, and with extramural grants from the NIH, the medical schools were propelled into a hurried transition from their traditional role as bastions of empirical science and practical teaching, to a vastly expanded new partnership with the state, modeled after the Manhattan Project. (151)

Space for the LEO was arranged on two floors of Laguna Honda Home, the city's facility for the aged poor operated by the Department of Health: the upper floor housed the clinical facilities (15 beds); the lower floor was for basic laboratories, physiological equipment, and animals. The basic allocation from NCI was under Shimkin's control, whereas the experimental ward was financed by a NCI grant to the medical school, which meant that Shimkin's clinical research budget was under

university rules; and a small budget was set up by the medical school to cover certain teaching requirements. The entire medical staff held clinical appointments at the medical school in Experimental Oncology, administered by the Department of Medicine, but the supply of patients, effectively the core of the relationship between the LEO and UCSF, was funneled through the interdepartmental Cancer Board, chaired and controlled by Stone. During the war Stone was a leading figure in the human plutonium project, and the main advocate after the war of total body radiation experiments on healthy volunteers. Stone was the *éminence grise* of cancer at UCSF, according to Shimkin. (152)

In its relatively brief existence, the LEO followed a trajectory evoked by Shimkin with the subtitles in Lost Colony: The Launching; In Flight; At Apogee; Descent; The Crash. (153) Picking up the story at its "apogee" in mid-1951, the LEO's research staff then included 9 professional investigators, 12 administrative and technical assistants, 8 nurses, and others for a total of 49 people. Research projects in progress were wide-ranging: studies of leukocyte dynamics, cross-transfusion experiments between patients with leukemia and patients with disseminated neoplasms, development of arteriographic methods to reach visceral tumors, induced virus infection in leukemia patients, and experimental chemotherapeutic trials of about a dozen compounds. LEO publications numbered 61 by 1951, with 10 more in press.

Despite the appearance of productive success, Shimkin's administrative and political position was inherently unstable from the beginning. "It was my purpose to

demonstrate two arrangements," Shimkin recalled telling Stone at their original meeting:

> "(a) that biomedical research programs of the NIH should develop as colonies of full partnership with institutions of higher learning throughout the United States; and (b) that biomedical research in the clinic and in the laboratory should be pursued by full-time research teams working in this partnership." (154)

Shimkin's first objective, to wed the programs of the NIH to institutions of higher learning, was as yet an untested idea based on opportunities generated by the government's new policies to fund extramural research. In 1944, Congress empowered the Surgeon General to make grants to universities, laboratories and individuals, to encourage development of NIH extramural programs. (155) Hence, in effect, Shimkin was Perran's emissary in the San Francisco "colony". The LEO reported to the medical school and to the NCI. Dependent on the medical school for patient-subjects, financial arrangements and regulatory legitimization, Shimkin was particularly vulnerable to the machinations of insiders like Stone. Serving two masters, the LEO was subject to pressures from both sides. The medical school had a major interest in maintaining good relations with the NCI, not only because of the money provided to the school for LEO's clinical operations, but to safeguard a one million dollar building grant for construction of a cancer research facility in the main university hospital. At the time, regional expansion was NCI policy. Should one or the other side of the arrangement falter, the entire structure could collapse around the LEO. This is what eventually happened.

According to Shimkin's memoir, Stone had an interest in controlling the LEO as a preliminary step to gaining the directorship of the planned Cancer Research Institute at UCSF, which was to be constructed with NCI funds and intended to house the LEO in the University of California Medical Center. (156) Stone's strategy was to "volunteer his participation in budgetary and administrative matters in the laboratory...I finally realized that the planned institute was being set up for Stone as its director, and that I was seen as a competitor for the position..."(157) In the meantime, the LEO's -and Shimkin's - most important promoter, Surgeon General Parran, "resigned precipitously or was fired" in 1948, and the NIH decided to build its own Clinical Center in Bethesda. Leonard A. Scheele, the new NCI director had "little background or sympathy for the [LEO's] arrangements or goals." (158)

Instability in the geographical and political position of the LEO as a rare West Coast outpost of the NCI camouflaged a deep-seated clash of medical cultures inherent in the second goal of Shimkin's campaign. Inevitably, (if the argument presented in this paper is valid), Shimkin's second objective led to frictions with the clinical staff at UCSF. Shimkin's very language sent "all the wrong messages" from the clinicians' perspective: the new, impersonal 'biomedical research', the lumping of 'clinic and laboratory', the exclusionary notion of 'full-time research', the invidious 'teams' with connotations of impersonal practice provided by salaried M.D.'s whose interests and incentives lay in objectifying the patient (the fundamental conflation). From a perspective of twenty five years later, and with insight derived from a new

epistemology, Shimkin would recognize the LEO as "a *premature* regional cancer center." (159)

The first "rumblings" of criticism came in 1951. "The professor of medicine had a long friendly chat with me, informing me that we were being accused of performing drastic, deleterious procedures on patients and that the release form we had devised for admission to the research ward was 'psychologically harmful'." The source of the criticisms was not revealed to him, but Shimkin realized there would be trouble ahead because "we were in the middle of the sticky area of experimentation on human beings." Soon after the "friendly chat", the new director of the NIH accused Shimkin of "experimenting on man". Confronted with a deteriorating situation on both fronts, Shimkin took "remedial steps" which included: 1. Revision of the "release form." 2. Written protocols for all new research, to be reviewed by the Cancer Board at UCSF. 3. A symposium on the subject of human experimentation. (160).

The symposium was Shimkin's idea; the matter of the release form, and the demands for written protocols and tighter control by the Cancer Board, were imposed on Shimkin by the clinicians. The release form was the passport for admission to the LEO. Shimkin described the entry procedure:

> "The patients were screened carefully before admission. They had to *understand* the experimental nature of our work, and every procedure was again *explained* to them; the initial *release form* even included agreement to an autopsy. The understanding did not absolve us of negligence nor deprive patients of recourse to legal actions, but it did set the tone and nature of our relationships. In all our 5 years of

> operations, not a single threat or implied threat of action against us was voiced. Two patients did instruct us to terminate our attempts at therapy. We certainly had less trouble with our patients than with our doctors and nurses..." (161)

What went wrong with this 'entry' process? Archival records indicate that the first release form for the LEO was developed on Shimkin's initiative in 1947, in consultation with attorneys for the University and for the City of San Francisco as owner of Laguna Honda. Shimkin introduced the matter in a letter to Dean Smyth on January 27, 1947, in which preparation of a form was requested which stated the patient's written permission to be "used for experimental therapy of his condition," and permission for an autopsy to be signed by patient and the nearest relative. The form was to be used with trials of chemotherapeutic agents, and carried a statement "that if these conditions are not carried out, the patient or the heirs become liable for the full cost of hospitalization and medical treatment." (Appendix H) All seemed to go smoothly, as far as Shimkin was aware, until 1951.

T. L. Althausen, professor of medicine and soon to be chair of medicine, had "a long, friendly chat" with Shimkin on March 6, 1951 , informing him of accusations from unidentified sources of carrying out drastic, deleterious procedures on patients in the LEO, and of having devised a "psychologically harmful" 'release form'. Shimkin responded to the criticisms in a letter one week later: (1) All LEO paperwork was open for inspection. (2) LEO manuscripts submitted for publication first had to be approved by the Department of Medicine. (3) All clinical work at the LEO was governed by the rules of the Cancer Research Institute at UCSF - major projects were

reviewed by the Cancer Board of the School of Medicine, from whom he [Shimkin] had never received a single complaint or comment; weekly ward rounds were held with staff and consultants from other departments; these staff members had veto power over research projects. (4) Terminal patients welcomed "certain experimental procedures which they themselves often demand." (5) "Hopeless patients" required different rules and considerations. (6) Procedures (a bone of contention) were performed by specialists and carried calculated risks. (7) He had resisted "fragmentation of effort" by refusing studies of interest to"certain" UCSF investigators. Also, he had refused to admit patients on grounds of financial need, only scientific ones. (162)

Regarding the release form, Shimkin agreed that it was "harsh", as it had been drafted by University lawyers and reviewed by the Attorney General in 1947 at the specific request of the University and the City of San Francisco. However, the form had been reviewed by the Cancer Board also, and approved. The form was always explained to the patient (Shimkin did not specify by whom), and discussed with relatives and the referring physician before admission. "We have found the release form useful during our 4 years of operation in that it clearly states the situation to the patient, and that with its help we have maintained an autopsy rate of exactly 100%."

Shimkin proposed two specific measures in response to the criticisms:

1. The Dean should appoint a committee to review all clinical research at the LEO.
2. A review of the release form should be made by legal advisors of the university.

On April 11, Dean Smyth appointed a committee chaired by Otto Guttentag, to review the form together with legal advisors, and "by one or more physicians not connected with the LEO, and by someone connected with it." The dean named three other members and Shimkin to the committee; he apparently ignored Shimkin's other suggestions for keeping the peace at the LEO. Guttentag and Shimkin seemed on friendly terms, as is suggested by a "Dear Mike" letter from Guttentag on May 8. By July 11, the revised document had been approved by university and city counsels and was ready for submission to the Dean. At this point, Shimkin requested that the form be approved also by Althausen or the chairman of the Department of Medicine, William J. Kerr (copied to Althausen and Smyth). Guttentag responded to Shimkin's request with a carefully worded note, also copied to Smyth and Alhausen, which indicated that the request "fell outside the realm of our Committee," but "I am glad that you sent copies...to Dean Smyth and Dr. Althausen." Guttentag assured Shimkin that the Dean would "initiate the actions necessary to...bring our mission to a successful conclusion." On August 8, Dean Smyth instructed Shimkin to have the new version of the release form printed; on the same day the Dean thanked Guttentag: "I think the revised form is excellent. It meets with my entire approval." The new release form was printed in September, less than one month before the symposium arranged by Shimkin with Guttentag's assistance was held. The records of the LEO contain no documents about the symposium or the proposed review of research.

A comparison of the original release form of 1947 with the revised version of 1951 (Appendices H and I) reveals surprisingly few and minor changes: a reference to negligence was deleted; a new clause was added to the effect that the patient agreed to pay the costs of transportation to and from the hospital; the substitutions and deletions made the new form seem kinder at the expense of unvarnished truth. Perhaps the most remarkable aspect of the revised form was that the 1951 version, outside of the strictly legal references, was prepared by Guttentag, a leading physician-ethicist of his day. The contents had not a whiff of patient autonomy. However, limited as it may appear by later standards, Shimkin's policy of having a special 'release form' for research was at the time itself exceptional. An NIH-sponsored survey of 86 departments of medicine conducted in 1962 regarding research procedures received 52 responses; only 16 departments used special "consent" forms for research. Louis Welt had previously published similar results: of 66 responding departments, "eight have a procedural document..."(163)

Shimkin's experience at the LEO provides a narrower and sharper insight into factors responsible for the tight grip practice held over clinical research. He had great difficulty in maintaining the flow of patients from referring physicians because of his insistence that there would be no financial arrangements between the patients and the investigators. Later, Shimkin wrote "The world of the real, even in 1947, was out of focus with my beliefs." (164) The medical school faculty derived much of their income from private practice - "open, hidden, or rationalized." Shimkin soon discovered that even seeing patients in consultation and not charging, "embarrassed

the physician and the patient." Since there were no fiscal arrangements with the patients, the LEO had to be guarded against becoming a convenient destination for incurable and indigent patients. "By insisting on complete control over admissions, we avoided the problem quite successfully at the cost of being considered uncooperative by some of our confreres." Clearly, Shimkin was not exactly popular with the Department of Medicine. The subject of payment by patients was reopened when the new director took over the Cancer Research Institute at UCSF. Shimkin managed to deflect this scheme also, but the days of the LEO were numbered.

The experience Shimkin and Guttentag had shared seems to have impressed and affected both. Guttentag's discussions with Shimkin in revising the release forms probably stimulated Shimkin's awareness of the Nuremberg "rules", reminiscent of the "Nuremberg standards" terminology Guttentag used in his review of *Doctors of Infamy* (the idea of a Code was not yet in evidence). (165) The concept that the clinical researcher and the physician may differ in their "point of view" was an original insight, challenging Percivalean ethics and a medical profession whose perceived interest lay in blurring those boundaries. At stake at the LEO for the clinicians was exclusion from all access to the experimental bedside, and displacement of regular physicians by salaried government employees;for Shimkin, the successful operation of the LEO was paramount. He had landed squarely on the fault line between these incompatible positions, and any 'remedial steps' short of closing down would be unlikely to make a difference.

Guttentag may have sensed that the solution to both the ill research subject's suffering and the clinician's problem was to place a personal physician at the bedside. Further, exposure to the existential plight of the 'hopeless patient' at the LEO alerted Guttentag to the need to separate caregiving from experiment. He turned these insights into the concept of the 'physician-friend', a figure who neatly separates the roles of investigator and caregiver but does not eliminate the fundamental conflict between them. Thus, Guttentag's experience as chair of the Release Form Committee seems to have reinforced his awareness of "...technicalities, the forms that patients must sign when about to volunteer for experimentation, or even to undergo an operation...not only the patient's consent, but also the physician's affirmation..." (166) The word consent does appear, but its meaning here stems from a cultural context which equated a research procedure and a therapeutic surgical operation, reflecting the prevailing instinctive view of clinical practice and research on patients as a continuum. In this framework, the patient could not be 'informed' because, with the exception of another physician as patient, a layman's understanding of medical issues was assumed to be necessarily limited and therefore dangerous.

Shimkin invited the participation of a "consultative body" to help shoulder the many hazards and responsibilities of research on patients, as he had in his response to Althausen. Whereas the LEO release form spoke of patients' "permission", Shimkin's condensation of the Nuremberg principles contained the phrase "the human experimental subject must understand and voluntarily consent". I doubt

whether Shimkin could have been aware of any substantive difference between "permission" and "voluntary consent", but what seems clear from the connotational changes in the meaning of these phrases, is how far the conceptual framework had shifted, and how profoundly the language of the judges at Nuremberg had influenced or assisted in that transformation. Writing his memoirs in 1978, Shimkin was, of course, aware that "complete informed consent by the subject...is now accepted dogma and a stringent requirement." (167) However, he recalled "there was also ample evidence in our experience how little reality was contained in the demand... A much more realistic safeguard is the independent doctor-counselor suggested by Guttentag" (168) . Shimkin clearly distinguished disclosure from consent. "Patients had to know they had cancer before admission, and almost all of them did. A woman with disseminated breast cancer, however, would ask us not to tell her husband; her husband just before had asked us not to tell her. Cancer was seldom mentioned after that..." (169)

In April, 1953, Shimkin received official notification that the clinical activities of the LEO would not be funded after June 30. The LEO closed after 7 years, 500 patients, 2.6 million 1950-vintage dollars and over 130 publications. "The director of the Cancer Research institute offered sympathy; the dean became unavailable; the local press was indignant; but the decision was final...The research floor that had been added to the new medical school building for our use, quickly acquired other occupants..."

To complete the historical legacy of the LEO, it should be mentioned that the NIH "stopped" the publication of the four papers presented at the symposium. (170) The proceedings were eventually published in *Science* 16 months after the event. Shimkin mused in his reminiscences that "in some way, an enunciation from California was considered contrary to possible policy. They [NIH] too, were grappling at that time with this 'sticky' problem and formulating their guidelines for the Clinical Center that was going up in Bethesda." Shimkin recalled that letters and telegrams were exchanged, with the dean emerging as "a champion of academic freedom". Approval for publication finally arrived, "with instructions that I not be identified with the NIH". (171) As discussed further in connection with the foundation of the NIH Clinical Center, this curious episode reflected uncertainties regarding the ethics of clinical experimentation conducted by a government agency, and disputes about patient consent and non-therapeutic research.

IV. THE STRUGGLE FOR INFORMED CONSENT

1. *The Shifting Paradigm: From Beneficence to Self-determination.* The postwar expansion in government-sponsored research has been thoroughly described. (172) The flagship of organized, state-supported American medical research was the NIH, from which unprecedented amounts of funding radiated to universities and research institutes across the country. The growth of NIH budgets provides an estimate of how big a business the business of medical research had become: from $700,000 in 1945, the budget climbed to $36 million in 1955, $436 million in 1965, and

over $1 billion by the late 1960's. As mentioned in connection with the LEO, the NIH opened its Clinical Center in 1953.

With establishment of the world's largest clinical facility devoted to scientific studies, the ethical problems associated with clinical research came sharply into focus. Every patient admitted to the Center was there as a research subject, although the brochures for patients assured them that "they would...[be provided]the best possible medical and nursing care." The director of the NIH declared that "use of experimental procedures for patients was part of the doctor-patient relationship; a positive decision was made that it would be intrusive for an administrative body to interfere with that relationship." (173) The blurring of the lines between therapeutic and potentially harmful experimental procedures was now institutionalized. The need for normal controls required healthy volunteers who were not under a physician's care and, therefore, needed special protection. The director of the NIH recalled that "a fairly extensive effort was made to devise a set of guidelines and procedures governing the use of normal controls in clinical investigations within NIH..." (174) A major question which occupied NIH officials was "the kind of information ...we felt should be made available to these [volunteers] people ." (175)

Shimkin had guessed correctly that Clinical Center administrators were wrestling with the "sticky" problem of guidelines for research in human subjects at the time he had come out with his Nuremberg solution. Indeed, the director of clinical investigations at the NCI noted that researchers could not agree among themselves

on what to disclose to study subjects, much less how. (176) The NIH and the extramural programs in the universities were not interested in codes, but in keeping science unfettered by regulations and "red tape". A policy which conveniently equated the researcher-subject relationship with the doctor-patient relationship meant that the researchers were on their own as far as essential decision-making was concerned. It was generally taken for granted that lay people lacked the scientific background for meaningful informed consent. "The usual patient wants to avoid the necessity of grappling with painful facts related to his own welfare", explained a research director at the NIH. Leave it to the investigator, he's your doctor, patients at the Clinical Center were told in 1953. The research community would have agreed with Henry Beecher that "the problems of human experimentation do not lend themselves in most cases to a series of rigid rules." (177)

As presented by Rothman, the fate of the Kefauver-Javitts legislation of 1962 illustrates how the care/research conflation correlated with resistance to change in ethical approaches to informed consent. After extensive hearings concerning regulation of the drug industry, Senator Estes Kefauver proposed a bill which gave the Food and Drug Administration a mandate to test new drugs for efficacy, in addition to its usual testing for safety. (178) The bill was aided significantly in its passage by the scandal involving the drug thalidomide which had caused severe malformations of the upper limbs in children whose mothers had taken the drug during their pregnancy. During hearings on the bill, many of the women testified

that they were not informed of being part of a drug trial, nor had they given their consent. An amendment to the Kefauver bill was attached by Senator Javits, directing the Department of Health, Education and Welfare to disallow the experimentation with any untested drug unless the study subject has been informed of its unproved safety record.

The senators' opposition to the bill was based on a confusion of experimentation with therapy, and of the researcher with the physician; they feared that the physician treating a patient with a new drug might be compelled to reveal a life-threatening diagnosis to the patient or be prevented from using the drug in an emergency. As one senator put the argument against the bill, it might be experimental, but it might give him a chance to live. Thus lawmakers were no more able than NIH officials to distinguish the research subject from the patient, "so that efforts to regulate experimentation were translated into attempts to regulate therapy." David Rothman has pointed out that many senators also reflected the general optimism about the promise of research in the society of the early 1960's, and ignored the lessons of thalidomide. The outcome was ineffectual legislation which favored consent for experimental drug research, "except where [the investigators]deem it not feasible or ...contrary to the best interests of such human beings."

Sensational revelations of unethical research conduct reported between July 1963 and July 1972 appeared to break the calm trust in 'the Master in the House of Medicine'. The turning point came when the public and the government became

aware that the beneficence of the physician was insufficient guarantee of protection from harm in a research setting. The research physician finally began to be perceived by the public as distinct from a 'regular' doctor, and both less benevolent and less trustworthy. Calls for protection of patients and experimental subjects enrolled in scientific studies began to come from every sector, including the media, the government and academe. The "excitement" Leake had observed at its height in 1975, had begun to build. The rallying cry of all was for "informed consent". Even the AMA's Judicial Council decided that the time had finally arrived to unbundle the images of the clinician and the researcher, distancing the one from the other for the first time since 1847.

The first of the highly publicized research scandals involved a study conducted at the Brooklyn's Jewish Chronic Disease Hospital in July, 1963, when twenty two elderly patients were injected with cancer cells without their consent (some were not competent to give consent). The two physicians involved were found guilty of fraud, deceit and unprofessional conduct by the Board of Regents of the State University of New York, and suspended. (179) This 'early' case had few public repercussions. However, the research was partly funded by the NIH; the case made officials aware of the inadequacy of their procedures, and forced them to recognize that "in the setting in which the patient is involved in an experimental effort, the judgment of the investigator is not sufficient as a basis for reaching a conclusion concerning the ethical and moral set of questions in that relationship." Eventually, the case influenced the development of federal guidelines in 1966. (180)

The second case involving consent illustrates the epistemic shift in public awareness of autonomy issues in the next six or seven years. Beginning in 1956, a series of inoculations with live hepatitis virus was used to infect severely mentally retarded children at Willowbrook State School on Staten Island in an attempt to develop an effective vaccine. (181) The children were admitted to a special research unit with written parental permission. Ten years and several publications later, Beecher included this study in his exposé article listing twenty two "ethically dubious" studies. (182) The work continued, the highly respected researchers published their results in prestigious journals, including the *New England Journal of Medicine,* and little public attention was paid to Beecher's accusations. Another work of Beecher's, the book-length treatise on *Research and the Individual,* published in 1970, reiterated his accusations against the Willowbrook group; this time, the theologian ethicist John Ramsay joined in the criticism, and a critical article appeared in *The Lancet.* (183) Strongly supported by the editors, who apologized for not dealing with this issue sooner, the article accused the Willowbrook investigators of abusing the children and manipulating the parents to agree to unethical experiments with their children. The principal investigator of the Willowbrook study, Saul Krugman, defended the study on the grounds that the study had been reviewed and approved by various local, state and federal agencies, including the Armed Forces Epidemiological Board, the U.S. Army Medical Research and Development Command, the Health Research Council of the City of New York, and several committees at New York University School of Medicine,

especially its Committee on Human Experimentation. The editors of the *Journal of the American Medical Association*, the *New England Journal of Medicine*, and the *Journal of Infectious Diseases* defended the research. (184)

During the 10-year period from the beginning of the study at least up to the year Beecher's article appeared, the Willowbrook researchers were viewed as clinicians doing important research. Indeed, Krugman was the world's foremost expert on hepatitis in children and the consultant on liver diseases for Willowbrook. By 1970, the roles of the researcher and clinician had been separated. Suddenly, even written consent from parents of affected children was suspect, and the motives of the researchers inflected with deep suspicion. Stephen Goldby, the British writer who had attacked the study in the Lancet, did so from the perspective of a British legal system which prohibits experiments on children, and the Medical Research Council of Britain which considers parental consent invalid. The Lancet had previously published one of Krugman's scientific reports (185), for which act of imprudence the editors apologized profusely a mere three years later. Yet, authoritative and dedicated panels of experts had given their explicit informed consent to a study which all sorts of people now perceived as evil. Attitudes toward medical research had changed dramatically, even abruptly, not only in the United States but in Britain as well. The editors and other experts who continued to defend the study were operating in a frame in which the researcher was still the physician taking care of children. They did not yet realize that Dr. Jekyll and Mr. Hyde had finally been separated, and Jekyll the experimenter was receiving all the opprobrium.

By far the greatest negative impact on the reputation of medical researchers came with the exposure of the so-called Tuskegee syphilis study. (186) This study was faulted for non-treatment rather than for harmful manipulation. A report appeared in July, 1972, that the Public Health Service had for forty years neglected to treat 400 black men known to be infected with syphilis. The aim of the protocol had been to determine the natural course of the untreated disease in comparison with a group of uninfected control subjects. The study began in 1932 in Alabama: at least 28 of the participants died of untreated syphilis and approximately 100 may have suffered crippling effects such as blindness and insanity. As in the case of Willowbrook, reviews conducted between 1932 and 1970 by PHS officials and medical societies saw nothing wrong, and after 13 articles in prestigious journals, the study continued uninterrupted and unchallenged until the summer of 1972. When the story appeared, the repercussions were immediate. The U.S. Department of Health, Education and Welfare appointed an ad hoc advisory panel to review the study and the department's policies and procedures for protection of human subjects. The panel found that neither DHEW nor any other governmental agency had an adequate policy for reviewing experimental procedures or securing subjects' consents. This time no one objected to change. The time had come to make a new ethics. The struggle for informed consent was almost over.

Many explanations have been put forward for this unusually abrupt turn in social trends. Concerns in the wider culture about individual liberties and social equality

collided with the increasingly technical, impersonal world of the health care system. The new rights orientation may have contributed its challenge to authority. It is clear that in common with other professions, the world of medicine was swept along on a tide of civil rights, women's rights, the consumer movement, and the rights of prisoners and the mentally ill. Informed consent was central to the aspirations of all these groups for self-determination. (187) In the new rights-oriented climate, human rights abuses against vulnerable subject populations - elderly, mostly female and frequently incompetent patients at the Brooklyn Jewish Chronic Disease Hospital, severely retarded children at Willowbrook State School, and impoverished black subjects in the Tuskegee study - became a rallying cry the Congress could no longer ignore.

It is pertinent to the thesis presented in this paper that the categories of potentially incompetent or otherwise vulnerable research subjects would have been specifically excluded had the Nuremberg Code been adopted, following Shimkin's lead in 1951, that the Nuremberg 'rules' constituted "the clearest formulation... of the proper rules of conduct that can be utilized in judging whether human beings should be involved in experimentation". In response to the outcry to Tuskegee in 1972, the Department of Health, Education and Welfare (DHEW) appointed the Tuskegee Syphilis Study Ad Hoc Panel to review the study and the Department's policies and procedures for protection of human subjects. The panel urged suspension of the Tuskegee "experiment" and recommended that Congress establish "a permanent body with the authority to regulate at least all federally supported research

involving human subjects." (188) Several bills were introduced in Congress dealing with experimentation on children, poor women, and prisoners; and the need for a national Commission to consider the ethics of research as recommended by the Tuskegee Ad Hoc Panel. DHEW developed regulations for the use of human subjects requiring grantee institutions to establish Institutional Review Boards responsible for controlling the conduct of federally funded research, along lines also originally proposed by Shimkin; Congress passed the National Research Act which endorsed the new disclosure- and consent-based DHEW regulations and established the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. (189)

The AMA recognized informed consent as a "basic social policy" in 1981. (190) In the AMA document, consent clauses for standard care and research are placed in different sections. Paragraph 8.07 deals with clinical aspects only, and states that patients should make their own choices, *even if their physician disagrees;* the guidelines for disclosures necessary to obtain consent for clinical investigations are in paragraph 2.05. (emphasis added) In situations where novel treatments blur the line between innovation and therapy, the Council remained firmly on the side of the therapeutic advantage. Thus, in dealing with organ transplantation, paragraph 2.09 (4) advised physicians to "be objective in discussing the procedure, in disclosing known risks and possible hazards, and in advising of the alternative procedures available... The physician's interest in advancing knowledge must always be secondary to his primary concern for the patient." (191)

The 1981 Judicial Council statements signaled an impressive divergence of interests between the patient and the experimental subject on the one hand, the caregiver physician and the clinical researcher on the other. For the first time, 'organized medicine' formalized the separation of the two polarities in language derived from the Percivalean and Nurembergian lineages I have traced in this paper. The lines quoted in the preceding paragraph about objectivity, risk disclosure, and alternative procedures, reiterate the three conditions for research in human subjects the AMA rushed into print in 1946, just missing the opening of the Doctors' Trial in Nuremberg. In sharp contrast, the AMA's new consent rules for therapeutic patient-doctor relationships are copied *verbatim* from the legal brief in the landmark 1972 case *Canterbury v. Spence.* (192)

Both the Judiciary Council's paragraph 8.07 and the core judiciary opinion in *Canterbury v. Spence* read as follows:

> "...the patient's right of self -decision can be effectively exercised only it the patient possesses enough information to enable an intelligent choice . The patient should make his own determination on treatment. Informed consent is a basic social policy for which exceptions are permitted (1) where the patient is unconscious or otherwise incapable of consenting and harm from failure to treat is imminent; or (2) when risk-disclosure poses such a serious psychological threat of detriment to the patient as to be medically contraindicated. Social policy does not accept the paternalistic view that the physician may remain silent because divulgence might prompt the patient to forego needed therapy. Rational, informed patients should not be expected to act uniformly, even under similar circumstance, in agreeing to or refusing treatment."

Having abandoned the last vestiges of Percival's professional etiquette, the AMA voluntarily relinquished control over proper conduct of clinical practice to the law.

2. *Informed Consent for Research: The State Steps In.* In contrast with the situation regarding informed consent in practice vis à vis the law, virtually no case law exists on the basis of which legal standards for consent to research, as distinguished from practice, might be defined. (193) The law has never recognized experimentation outside the therapeutic context. Accordingly, there have been no court decisions involving non-therapeutic experimentation, whether in healthy volunteers or in patients, and as a consequence, a "common law" for human experimentation has not developed. No experiments resulted in lawsuits in the 1940's, 1950's and 1960's. We have seen how the scandals which erupted around clinical research projects, and changing social conditions which provided the framework for the impact of these events, prompted the AMA to appropriate the umbrella of case law, as the single source of meaningful control over issues of primary importance to the practice of medicine, namely malpractice, negligence or incompetence in the provision of health care.

Disclosure and informed consent policies of the AMA regarding research were essentially limited to Percival's 1803 warning against "gloomy prognostications." This was the standard on disclosure for the AMA until 1957, when that year's revision deleted Percival's wording and substituted the admonition that "physicians should make available to their patients...the benefits of their professional

attainments." In 1969, the Judicial Council interpreted these "principles" as an obligation by the "experimenter", when using new drugs or procedures, to obtain "the voluntary consent of the person." (194) The AMA endorsed the Declaration of Helsinki as the international standard for the ethical conduct of research. The Declaration was the first set of new medical ethical Principles based on the Nuremberg Code, adopted by the World Medical Association (WMA) in June 1964. (195) The WMA was founded in 1947 by physicians in reaction to the revelations of medical atrocities at the Nuremberg Doctors' Trial which ended that year. At its second assembly in September 1948, the WMA adopted a set of principles for the moral practice of medicine, known as the Geneva Declaration. However, the process of drafting a similar document for the conduct of human experimentation took the WMA's Committee on Medical Ethics from 1953 to 1964 when the 18th World Medical Assembly meeting in Helsinki adopted the first set of guidelines based on the Nuremberg Code. However, the hallmark voluntary consent principle of the Code was relegated to a secondary position, and qualified with distinctions between "Clinical Research Combined with Clinical Care" and "Non-Therapeutic Clinical Research." The international gathering of leading physicians was not yet prepared in 1964 to grant complete autonomy to patients nor to disentangle practice from research. Not surprisingly, the Helsinki Declaration underwent three additional revisions in 1975, 1983 and 1989. Even in the latest version, all decisions remained in the hands of the beneficent physician. (196) The AMA House of Delegates, in its endorsement of the Helsinki Declaration, asked investigators engaged "in clinical [research] primarily for treatment" to make relevant disclosures

and obtain the voluntary consent of patients. The AMA had nothing to say about other kinds of research.

Unlike physician's associations and their voluntary ethics codes, the State held the twin cards of the peer review mechanism and funding in the area of biomedical research. As we have seen, prompted by the revelations of unethical research, the U.S. Congress appointed the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research in 1974. The Commission developed a scheme of basic ethical principles - Respect for Persons, Beneficence, Justice - which placed informed consent first, in imitation of the Nuremberg Code. (197) Further evidence of the centrality of informed consent in the thinking of government officials and bioethics consultants came in January, 1980, when the U.S. President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research was convened with informed consent as the main item on its agenda. By 1982, the Commission had produced an exhaustive three-volume report devoted to informed consent issues. (198) The Commission described the principle of self-determination as the "bedrock" of medical ethics. Informed consent had finally arrived at the university.

V. CONCLUSION

The final separation of clinical practice from clinical research has enabled society to perceive a clear need for different rules of conduct for each. The law has assumed the main responsibility for safeguarding the rights of individuals in the therapeutic

encounter; the researcher is regulated by institutional, state and federal regulations which are centered on concepts of patient self-determination and informed consent. Since the mid-1960's, the Nuremberg Code has become the international instrument and a source of most new ethics codes governing the proper conduct of research in human beings. The Code had been originally formulated for the express purpose of creating standards for non-therapeutic research in normal subjects, and contained as its centerpiece, a legalistic formulation of informed consent. The first clause of the Code , designed by the judges at Nuremberg, supports and demands a standard of patient autonomy foreign to the traditional precepts of medical practice.

The tension between Hippocratic medical ethics and human rights receded as practicing physicians withdrew behind the protections of the law, leaving the Code as the ultimate "ten commandments" intended to protect the human rights of research subjects. With a human rights perspective that acknowledged the centrality of informed consent and the right of the subject to withdraw, the Nuremberg Code changed the way people, physicians amongst them, view the proper conduct of medical research on human subjects. In line with the rest of the contemporary world, the UCSF Committee on Human Research now proudly displays the Nuremberg Code in its web site. Shimkin, thou shouldst be living at this hour.

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119. Cortez F. Enloe Jr, Brutalities of Nazi Physicians, JAMA 132 (1946), 1104.

120. Frederic Wortham, JAMA 133 (1947), 645.

121. The Nuremberg Trial Against German Physicians, JAMA 135 (1947), 867.

122. The Bad Neuheim Physicians' Convention, Foreign Letters, JAMA 135 (1947), 868.

123. Rothman, Strangers at the Bedside. 62-3 (see note 11) ; Ruth R. Faden and Tom L. Beauchamp, A History and Theory of Informed Consent. 153-58 (see note 11); Advisory Committee on Human Radiation Experiments. 74-96 (see note 95); for an opposing view, see Marks. The Progress of Experiment. 157 (see note 72).

124. Jay Katz, The Consent Principle of the Nuremberg Code, in Annas and Grodin. The Nazi Doctors and the Nuremberg Code. 227-39 (see note 12)

125. ACHRE member and historian Susan Lederer organized the Ethics Oral History Project with assistance from staff, including two historians specialized in the techniques of oral history. The Committee conducted twenty two interviews, focusing on

researchers who had "exhibited some particular interest in research ethics during their careers." Advisory Committee on Human Radiation Experiments. 86 (see note 95);

126. American Medical Researchers' Reactions to News of the Nuremberg Medical Trial, Advisory Committee on Human Radiation Experiments. 85-88 (see note 91).

127. U.S. Department of Health, Education, and Welfare, *Healthy Volunteers Help Scientists Conquer Disease,* PHS Pub. No. 714 (Washington, D.C.:Public Health Service, NIH, 1959), 14.

128. Paul Dufault, Medicinae Doctor, 1950, N. Eng. J. Med. 242 (1950), 429-36; emphases added in text.

129. Shimkin et al. *The Problem of Experimentation in Human Beings,* op. cit., (see note 15).

130. A recent reiteration of comments previously made in her book Ruth R. Faden and Tom L. Beauchamp, A History and Theory of Informed Consent. (see note 11), appears in Ruth R. Faden, et al., US Medical Researchers, the Nuremberg Doctors Trial, and the Nuremberg Code, A Review of Findings of the Advisory Committee on Human Radiation Experiments, JAMA 276 (1996), 1667-71.

131. Advisory Committee on Human Radiation Experiments. 87-88 (see note 91).

132. ibid., 87-88.

133. Michael B. Shimkin, Lost Colony, in *As Memory Serves: Six Essays on a Personal Involvement with the National Cancer Institute, 1938-1978* (Prepared under PHS Contract NIH 263-76-C-0419 from the National Cancer Institute, 1978), 3.

134. Ibid., 19.

135. Shimkin et al. *The Problem of Experimentation in Human Beings*, op. cit., 205 (see note 15); emphasis in the original.

136. Mitscherlich and Mielke, *Doctors of Infamy*. (see note 111).

137. Guttentag, *The Problem of Experimentation in Human Beings*, op. cit., 208 (see note 15)

138. Ibid., 210.

139. Advisory Committee on Human Radiation Experiments. 80-81.
(see note 95).

140. For references and discussion, see Rothman. Strangers at the Bedside. 63 (see note 110; Advisory Committee on Human Radiation Experiments. 86 (see note 95).

141. Michael B. Shimkin, Lost Colony,19 (see note 133); cited in Advisory Committee on Human Radiation Experiments. 88 (see note 95).

142. Guttentag, *The Problem of Experimentation in Human Beings*, op. cit., 210 (see note 15)

143. Rothman. Strangers at the Bedside. 51-70 (see note 11).

144. Epigram, Lost Colony, in Michael B. Shimkin,As Memory Serves,1 (see note 133).

145. All records are kept in the UCSF Archive in the Special Collections Library, in boxes marked Laboratory of Experimental, Oncology, 1947-54.

146. Shimkin. Lost Colony, *in* As Memory Serves. (see note 133).

147. Michael B. Shimkin, Lost Colony: Laboratory of Experimental Oncology, San Francisco, 1947-54: Historical Note. J Natl Cancer Inst, 60 (1978), 479-88.

148. Michael B. Shimkin, Upon Man and Beast - Adventures in Cancer Epidemiology: Presidential Address, Cancer Research 34(1974), 1525-35.) Nicholas Petrakis, M.D.,

Professor Emeritus of Epidemiology at UCSF, who served under Shimkin in the original LEO staff, and Mary Shimkin of La Jolla, California have been valuable sources of firsthand information.

149. Michael Shimkin, Lost Colony, 479 (see note 147). During the war, Stone had served as chief of the Manhattan Project's Metallurgical (euphemism for plutonium and other heavy metallic elements) Laboratory Health Division involved in the human plutonium project, had pioneered in total body radiation experiments, and was known for his advocacy of using healthy volunteers for total body radiation experiments after the war. Advisory Committee on Human Radiation Experiments. 231-236 (see note 95).

150. Virginia Sharpe and Alan I. Faden, *Medical Harm,* Cambridge:Cambridge University Press, 1998), 36-60.

151. Daniel J. Kevles, The National Science Foundation and the Debate over Postwar Research Policy, 1942-45. A Political Interpretation of Science-The Endless Frontier, , Isis 68 (1977), 5-26.

152. Shimkin, Lost Colony. 481 (see note 147).

153. Ibid., 479-488 .

154. Shimkin, Upon Man and Beast. 1525 (see note 148).

155. Donald C. Swain, The Rise of a Research Empire: NIH, 1930 to 1950, Science 138 (1962), 1235; Advisory Committee on Human Radiation Experiments. 10-11 (see note 95).

156. Shimkin, Lost Colony, 481 (see note 147).

157. Ibid., 481.

158. Michael B. Shimkin, An Informal History of the National Cancer Institute, 1937-57, in *As Memory Serves,* 92 (see note 133).

159. Shimkin. Upon Man and Beast. 1525. (see note 148); emphasis added in text.

160. Shimkin, *As Memory Serves.* 19 (see note 133).

161. Ibid., 22.

162. Letter from Shimkin to Althausen, March 13, 1951., LEO Records, UCSF Historical Archives.

163. Law-Medicine Research Institute of Boston University, Final Report to USPHS, Mark S. Frankel, Guidelines Governing Research, (1963) 18; Louis.G.Welt, Reflections on the Problems of Human Experimentation, Connecticut Medicine 25 (1961), 75-78.

164. Shimkin, Lost Colony. 480 (see note 147).

165. Guttentag, Review. (see note 111).

166. Guttentag. The Problem of Experimentation. 210 (see note 15).

167. Shimkin. *As Memory Serves*. 23 (see note 133).

168. Guttentag. *The Problem of Experimentation*. 210 (see note 15).

169. Shimkin. *As Memory Serves*. 24 (see note 133).

170. Shimkin. Lost Colony, 484 (see note 147).

171. Ibid, 485.

172. Swain, The Rise of a Research Empire: NIH, 1930 to 1950, 1233-37 (see note 155); Rothman. Strangers at the Bedside, 51-69 (see note 11); Starr, The Transformation of

American Medicine, (New York:Basic Books, 1982) 340-47 (see note 10); George Rosen, Patterns of Health Research in the United States, 1900-1960, Bull. Hist. Med. 39 (1965), 220; for postwar planning of research policy, see Kevles, The National Science Foundation. 5-26 (see note 151).

173. Interview by Mark S Frankel with James A, Shannon, former Director of the NIH, May 13, 1971, in The Development of Policy Guidelines Governing Human Experimentation in the United States: A Case Study of Public Policy-Making for Science and Technology, in Ethics in Science and Medicine, Vol. 2 (Oxford:Pergamon Press, 1975), 43-59.

174. Interview with Joseph S. Murtagh, former Director of the Office of Program Planning, NIH, March 26, 1971, ibid., 47.

175. Interview with Irving Ladimer, former Assistant Director of Research Planning, NIH, May 14, 1971, ibid, 47.

176. Rothman. *Strangers at the Bedside.* 57 (see note 11)

177. Henry K. Beecher, *Experimentation in Man,* (Chicago:Charles C. Thomas,1959),4.

178. Drug Industry Act of 1962, Congressional Record, (1962), 17391, cited from Rothman, Strangers at the Bedside, 65-7; (see note 11).

179. Hyman v. Jewish Chronic Disease Hospital, 251 NY, 2d 818 (1964).

180. Interview with Joseph S. Murtagh, former Director of the Office of Program Planning, NIH, March 26, 1971, in The Development of Policy Guidelines. 50 (see note 159).

181. Saul Krugman, Joan P. Giles, and Jack Hammond, Infectious Hepatitis, JAMA 200 (1967), 365-73.

182. Henry K Beecher, Ethics and Clinical Research, New Engl J Med, 74 (1966), 1354-60.

183. Stephen Goldby, Experiments at the Willowbrook State School, Lancet I (1971), 749; Paul Ramsey, *The Patient as Person* (New Haven:Yale University Press, 1970), 47-56.

184. Proceedings of the Symposium on Ethical Issues in Human Experimentation:*The Case of Willowbrook State Hospital Research*, Urban Health Affairs Program, New York University Medical Center, (1972).

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188. U.S. Department of Health, Education and Welfare, Final Report of The Tuskegee Syphilis Study Ad Hoc Panel (Washington, DC: GPO, 1973), 23

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191. Cited from Katz, *The Silent World*. 23-4 (see note 23).

192. *Canterbury vs. Spence* (1972) 464 F,2d 772 (D.C. Circuit) cert. denied 409 U.S. 1064. The correspondence between the two statements was noted in Tom L. Beauchamp and Ruth R. Faden. Informed Consent. 1236 (see note 4). The paragraph below is quoted from their article.

193. For detailed accounts of medical research issues in the courts, see George J. Annas, Leonard H Glantz, and Barbara F Katz, *Informed Consent to Human Experimentation: The Subject's Dilemma.* (Cambridge, MA:Ballinger, 1977); Charles Fried, *Medical Experimentation: Personal Integrity and Social Policy,* (Amsterdam:North-Holland, 1974).

194. The informed consent provisions do not appear in the 1980 revision of the Principles of Medical Ethics, but in the Judicial Council's Current Opinions promulgated in 1981 to accompany the 1980 principles. (American Medical Association, Judicial Council, Current Opinions of the Judicial Council of the AMA, (Chicago: American Medical Association, 1981.

195. Annas and Grodin. The Nazi Doctors and the Nuremberg Code. 157-60 (see note 12).

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Overview, in Annas and Grodin. The Nazi Doctors and the Nuremberg Code. 149-73, 331-42 (see note 12).

197. U.S. National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Biomedical and Behavioral Research, DHEW Publication (OS) 78-0012 (Washington, D.C.:Department of Health, Education and Welfare, 1978.

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MASTER IN THE HOUSE OF MEDICINE

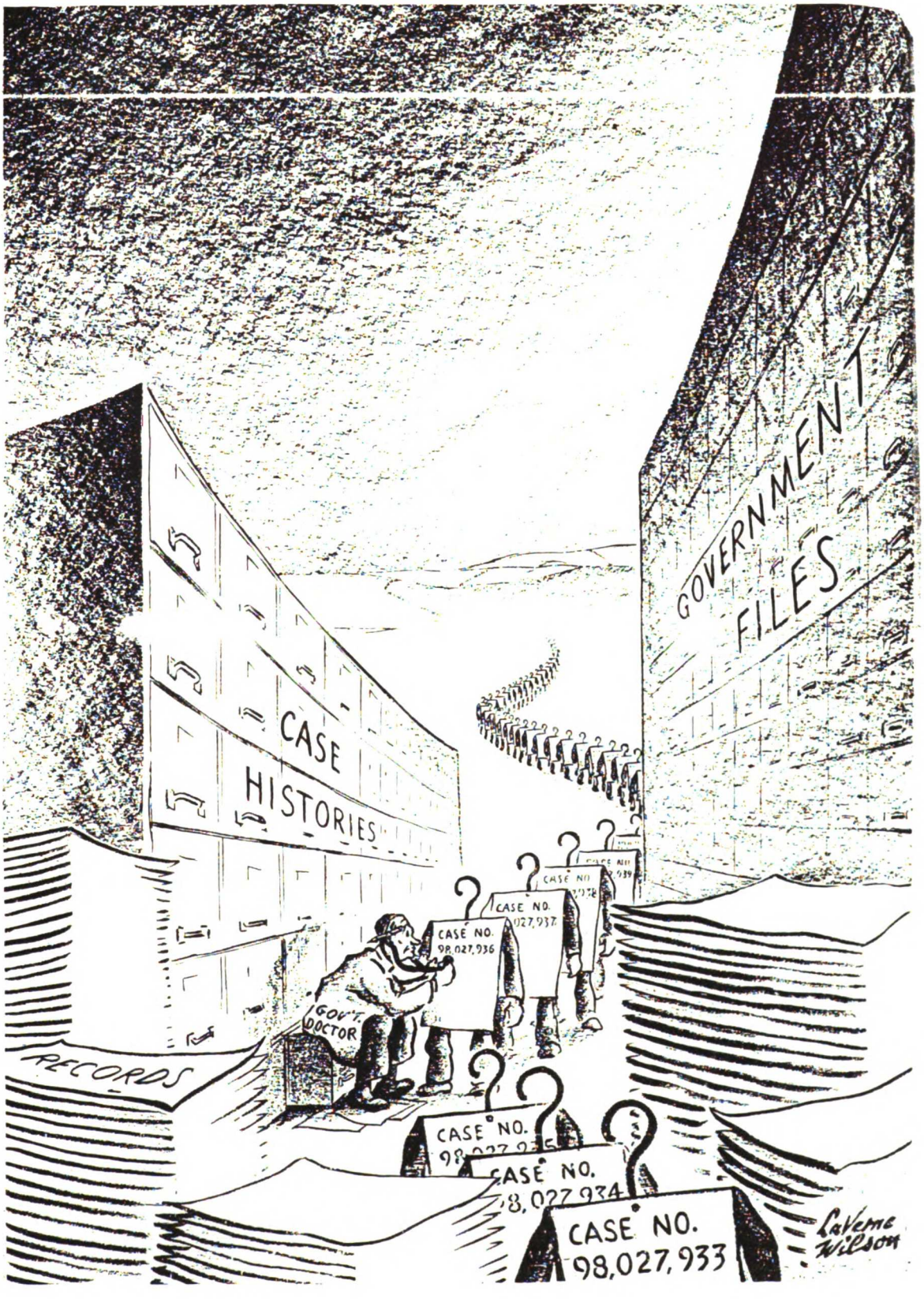
The cartoon on this page is taken from the current issue of *Hygeia*, the Health Magazine, published by the American Medical Association. It epitomizes the gathering lines of cleavage in current debates regarding the future of the practice of medicine in this country. Medicine, once practiced almost exclusively by the physician, is now an activity in which hundreds of thousands participate, giving their full time to the prevention of disease and the diagnosis and treatment of the sick. Only the physician in this group is entitled by training, by experience and by law to assume responsibility for the sick patient, yet the great numbers of persons concerned and the vested interests involved would in some instances wish to intervene in the situation. The question as to whether or not the hospital shall dictate the terms of medical practice is being pointed as an issue by the difficulty of establishing satisfactory circumstances under which the roentgenologist, the pathologist and the anesthetist may function without losing professional status. There are those who insist that the dominance of the hospital in this field is paramount and that doctors who are associated with hospitals will realize that it is to their interest to support the hospital's point of view. Another group now looming large in its numbers and in its influence in this country is the social worker group. While they are concerned with the circumstances surrounding the delivery of medical service, including environmental and financial competence, they would in many instances make professional service subservient to environmental factors. As these lines of cleavage in opinion develop, there seems to be but one answer to this question—that is the answer which *Hygeia* makes in its cartoon and in the leading editorial about that cartoon in the August issue. There can be but one master in the house of medicine, and that is the physician.

There can be but one master in the house of medicine, and that is the physician.

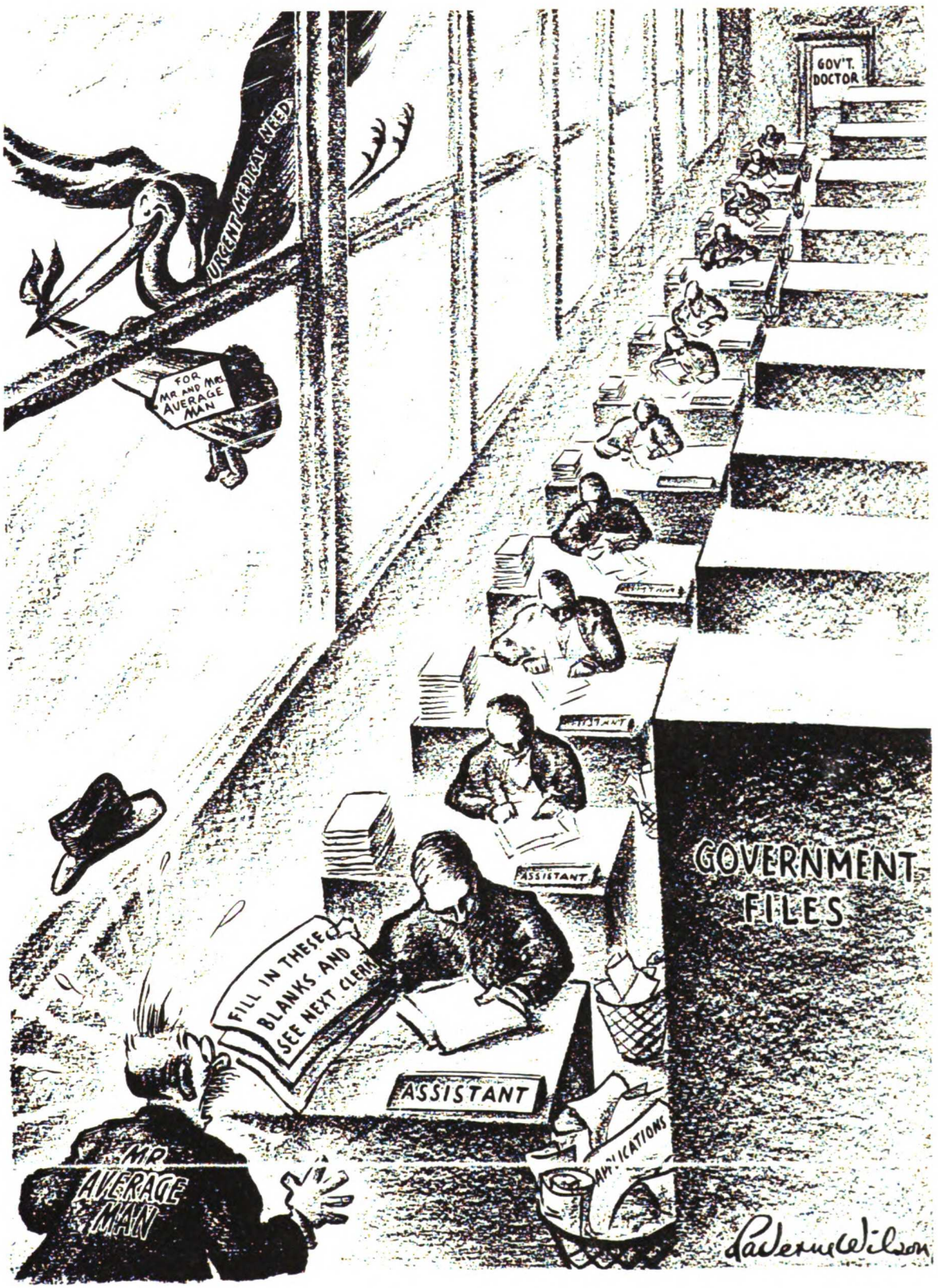
THE STUDENT SECTION

In this issue of THE JOURNAL appears for the first time a section devoted wholly to the interests of the medical student; it will, however, be concerned not only with the educational interests, training and welfare of medical students but also with problems affecting interns and residents in hospitals. This section of THE JOURNAL has been established after careful consideration by the Board of Trustees of the relationship of the student and the intern to the medical profession. The students, interns and residents of today are the practicing physicians of tomorrow. Unless they are familiar with the problems which concern the practicing physician and with the policies and principles established by the organized medical profession of the United States, they can hardly be expected to participate actively in medical affairs immediately after entering into the organized medical profession. The student section as now planned will appear once each month in the fourth issue of the month. While much of the material for the student section is developed by educators and those interested in the problems of medical education, opportunity will be given to students, interns and residents to be heard as to their views on problems which intimately concern them. Material submitted for this department of THE JOURNAL needs merely to be addressed to the headquarters of the Association, with a letter indicating that it is submitted particularly for the student section.

There can be but one master in the house of medicine, and that is the physician.



Mechanized Medicine



Little man, what now?


POLITICS
DOCTOR
HOSPITAL SUPT.
RELIEF AGENT
PATIENT
NOW SHOWING
"MEDICINE A LA MODE"
LaVerne Nelson

OTHER MEN WORK FROM SUN TO SUN,—BUT THE DOCTOR'S WORK IS NEVER DONE!

The "Nonstop" Champ Spends a Day with a Doctor

G

THE NUREMBERG CODE

1. The voluntary consent of the human subject is absolutely essential.

This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, overreaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision. This latter element requires that before the acceptance of an affirmative decision by the experimental subject there should be made known to him the nature, duration, and purpose of the experiment; the method and means by which it is to be conducted; all inconveniences and hazards reasonably to be expected; and the effects upon his health or person which may possibly come from his participation in the experiment.

The duty and responsibility for ascertaining the quality of the consent rests upon each individual who initiates, directs or engages in the experiment. It is a personal duty and responsibility which may not be delegated to another with impunity.

2. The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature.

3. The experiment should be so designed and based on the results of animal experimentation and a knowledge of the natural history of the disease or other problem under study that the anticipated results will justify the performance of the experiment.

4. The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.

5. No experiment should be conducted where there is an *a priori* reason to believe that death or disabling injury will occur; except, perhaps, in those experiments where the experimental physicians also serve as subjects.

6. The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment.

7. Proper preparations should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability, or death.

8. The experiment should be conducted only by scientifically qualified persons. The highest degree of skill and care should be required through all stages of the experiment of those who conduct or engage in the experiment.

9. During the course of the experiment the human subject should be at liberty to bring the experiment to an end if he has reached the physical or mental state where continuation of the experiment seems to him to be impossible.

10. During the course of the experiment the scientist in charge must be prepared to terminate the experiment at any stage, if he has probable cause to believe, in the exercise of the good faith, superior skill, and careful judgment required of him, that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject.

UNIVERSITY OF CALIFORNIA MEDICAL SCHOOL
Laboratory of Experimental Oncology

See 4(b)

I, ..., of _____, have been advised that I am suffering from a disease diagnosed as ....., and I do hereby apply to the United States Public Health Service, the Department of Public Health of the City and County of San Francisco, State of California, and the Medical School of the University of California to be used as a subject for experimental purposes in the study of my case and to be given such experimental diagnostic procedures and treatment (hereinafter referred to as "treatments") as may be determined or prescribed by the physicians representing the said United States Public Health Service, the Department of Public Health of the City and County of San Francisco and the Medical School of the University of California, or any of them, in charge of said treatments.

I have been informed that the hereinabove mentioned treatments are purely experimental and that the results thereof are unpredictable.

In consideration of my being used as a subject of said treatments and receiving the same, I assume all risk of injury (including death) to myself, and release the United States Public Health Service, the City and County of San Francisco, State of California, and The Regents of the University of California and any employee or employees, representative or representatives, agent or agents of them and each of them participating in the conduct of said treatments from all liability therefor, and hereby for myself, for my heirs, executor, administrator and assigns agree that in no event will I present to or prosecute against the said United States Public Health Service, the City and County of San Francisco, State of California or The Regents of the University of California, or any employee or employees, representative or representatives, or agent or agents of them or any of them participating in the conduct of said treatments, any claim or action for damages or compensation for any injury (including death) suffered by me arising out of or incidental to the said treatments, whether the said injury be occasioned by the negligence of the said the United States Public Health Service, the City and County of San Francisco, State of California, or The Regents of the University of California, or by the negligence of any employee or employees, representative or representatives, agent or agents of them or any of them, or otherwise.

I understand and agree that transportation to and from the place or places where said treatments are to be given shall be at my expense; also, that in the event of my death, all costs of burial, including transportation of my body, shall be charged against and paid from my estate.

I hereby consent that records and other information relative or pertaining to my case may be made available to the person or persons conducting said treatments by the person or persons in whose care or custody said records or information may be.

I agree that the need for and length of my hospitalization shall be determined by the physicians in charge and that I will abide by their decisions; that at regular, but reasonable, intervals following the termination of the hereinabove mentioned treatments I will report in person, or by letter, at such intervals as may be determined by the physicians conducting said treatments, regarding my physical status and progress; also, I agree to request my heirs or legal representatives to inform said physicians of my death and to permit an autopsy to be performed upon my body.

DATED:.....

.....

WITNESSES TO SIGNATURE:

.....

.....

H

Form No. O 1-1m-9'47 (A5508)

University of California Medical School

Laboratory of Experimental Oncology

I, ..., of . . . . have been advised that I am suffering from a disease diagnosed as . . . . I do hereby AGREE to VOLUNTEER as a subject for INVESTIGATIVE purposes in the study of my CONDITION IN THE FACILITIES of the United States Public Health Service, the Department of Public Health of the City and County of San Francisco, State of California and to UNDERGO such INVESTIGATIVE procedures CONCERNING FURTHER CLARIFICATION OF MY CONDITION AND CONCERNING RESTORATION OF MY HEALTH (hereinafter referred to as "treatments") as my be determined or prescribed by the physicians representing the said United States Public Health Service, the Department of Public Health of the City and County of San Francisco and the Medical School of the University of California, or any of them in charge of said treatments.

I have been informed that the hereinabove mentioned treatments are FOR THE MOST PART IN A purely experimental STAGE and that the results thereof CANNOT BE PREDICTED AT PRESENT, ALTHOUGH EVERY ENDEAVOR HAS BEEN MADE TO PROTECT ME FROM HARM.

In consideration of my VOLUNTEERING TO BE a subject TO said treatments and receiving the same, I assume all risk of UNTOWARD EFFECTS (including death) to myself, and release the United States Public Health Service, the City and County of San Francisco, State of California, and The Regents of the University of California and ANY PHYSICIAN OR PHYSICIANS or other employee or employees, representative or representatives, agent or agents of them and each of them participating in the conduct of said treatments from all liability therefor, and hereby for myself, for my heirs, executor, administrator and assigns agree that in no event will I present to or prosecute against the said United States Public Health Service, the City and County of San Francisco, State of California or The Regents of the University of California, PHYSICIAN OR PHYSICIANS or any other employee or employees, representative or representatives, or agent or agents of them or any of them participating in the conduct of said treatments, any claim or action for damages or compensation for any injury (including death) suffered by me arising out of or incidental to the said treatments.

I hereby consent that MEDICAL records and other information relative or pertaining to my case may be made available to the PHYSICIAN OR PHYSICIANS conducting said treatments by the person or persons in whose care or custody said records or information may be.

I agree that DURING THE PERIOD OF RECEIVING THE HEREINABOVE MENTIONED TREATMENTS the need for and length of ANY hospitalization shall be determined by the physicians in charge; that following the termination of the hereinabove mentioned treatments I will report in person, or by letter, at such intervals as may be determined by the physicians conducting said treatments, regarding THE status OF MY HEALTH; also, I agree to request my heirs or legal representatives to inform said physicians of THE EVENT OF my death WHENEVER IT OCCURS and to permit an autopsy to be performed upon my body.

I understand and agree that ALL COSTS OF transportation to and from the place or places where said treatments are to be given shall be at my expense; also, that in the event of my death WHEREVER IT OCCURS, all costs of burial, including transportation of my body, shall be charged against and paid from my estate.

DATED: . . . .

WITNESSES TO SIGNATURE:

. . . .

. . . .