Innovation and Public Accountability in Clinical Research

EVAN M. MELHADO

University of Illinois at Urbana–Champaign

WHAT IS CLINICAL RESEARCH AND WHAT SHOULD become of it? This vexatious and long-standing question was analyzed in a recent study by the Institute of Medicine (IOM 1994). The study reflected dramatic changes in the field: the displacement among practitioners of a clinical orientation by a molecular one, the attrition of physician–scientists from its ranks and the declining recruitment of new ones, the intrusion of PhDs into its domain, and the tightening of funding that is likely to intensify with the advance of managed care. The very survival of clinical research as an enterprise dominated by physicians seemed to be at stake. The study sought to articulate policy measures that would sustain the field by reversing losses, stabilizing careers, and fostering among its leaders the—rarely achieved—consensus that effective policy making requires.

The IOM study portrayed clinical research with a curious mixture of old and new. It characterized the endeavor as a bridge between basic (or laboratory) research and clinical practice and public health. The researcher could either produce (or at least stimulate) novelties in basic science or generate from them new applications. The former mode recalled older conceptions of clinical science as the pursuit, undertaken without immediate concern for practical applications, of basic knowl-

The Milbank Quarterly, Vol. 77, No. 1, 1999

edge of human disease. The latter mode, however, which the report described as "translation," reflected a new and increasingly common belief that the clinical researcher had become a principal agent for improving medical practice. Also novel were the claims of the study that translation could rest in part on the evaluative sciences and the inclusion within clinical research of clinical decision making, outcomes research—in general, health services research—all social-scientific practices that traditionally have been foreign to the field. However, the principal policy recommendations of the study—adjustments in funding mechanisms, institutional arrangements, and training programs—were devised more to restore and preserve the older conception of clinical research as a disinterested pursuit of basic knowledge. Moreover, these measures scarcely differed from ideas discussed for over two decades in the upper reaches of academic medicine and in the higher echelons of the federal agencies and private foundations that support clinical research. Indeed, some policies that were instituted to realize a number of these ideas had failed to diminish concern about the decline of the field. Clearly, its leaders have hesitated to articulate "translation" or pursue its implications.

Despite its novelties, therefore, the IOM study is but one outcome of ongoing discussions which, although elicited by major scientific and political changes, produced only incremental and ineffective remedies inspired by a conservative vision. Rehashing long-standing themes will not enable researchers to bring closure to their discussions and reach consensus on policy. Instead, this essay argues, the novel, but as yet scarcely exploited, ideas about the pertinence of health services research are most likely to offer a viable foundation for publicly accountable policy governing clinical research, and therefore a major reorientation of its practitioners and leaders is needed.

These conclusions rest on historical analysis. This essay portrays the discussions as the latest episode in nearly a century of effort by academic clinicians to establish and maintain clinical research as a field for the autonomous practice of science by physicians. Initially, it was physicians in the laboratory sciences (e.g., biochemistry, microbiology, and physiology), located in the "preclinical" or "basic science" departments of medical schools, who carried the ethos of research into American academic medicine. Seeing clinical practice as the application of laboratory novelties, they authorized the still common usage that opposes "basic" and "clinical" research as the medical version of the broader distinction between "basic" and "applied" science. However, some research-oriented

academic clinicians joined these basic scientists to create a clinical science that was not applied; that is, it would create knowledge of human disease without immediate concern for practical utility, an aspiration articulated several generations earlier by Rudolf Virchow (1847). Its advocates struggled for legitimacy in a setting, the medical school, in which laboratory sciences possessed greater prestige, their practitioners often disdained clinical science as derivative, the demands of clinical teaching and patient care distracted clinicians from research, and the conditions permitting a scholarly approach to disease were unstable. As MDs ceded the preclinical sciences to PhDs, clinical departments became the principal sites where physicians could pursue their scientific aspirations, and there these long-standing problems persisted.

The recent alarm about clinical research marks a new stage in this struggle. Advances in both science and medicine raised the costs of entry into a research career but lowered its likelihood of success. Many physicians shifted to either laboratory or applied science or left research for teaching and patient care. As recruitment of MDs into clinical research suffered, PhDs, who typically possessed more rigorous scientific training but had little immediate interest in medical practice or public health, entered territory traditionally claimed by physicians. Physician–scientists responded by trying to restore traditional forms of research while securing public legitimacy through the portrayal of their enterprise as a source of practical innovations. Theirs was a conservative vision.

That vision emerged under the aegis of two standard elements of postwar American science policy: a manpower model that invoked a labor market in which, in this instance, federal funds created the demand for researchers and medical institutions both supplied and employed them; and a model of applied science that considered medical practice a relatively straightforward application of innovations in basic science. However, labor-market models assume the persistence of institutional arrangements that arose under earlier conditions but that otherwise might become targets of novel policies. The standard view of applied science inhibited researchers from delineating desired kinds of applications, the skills needed by researchers to produce them, and the policies that would supply and effectively exploit such scientists. As a basis for public policy, both "translation" and the means for its cultivation are unclear. Although some figures have linked translation to health services research, this theme, heretical in the light of traditional views, has scarcely been explored or exploited.

This essay analyzes the policy discussions among researchers in the light of these historical precedents. It traces the history of medical research in the laboratory sciences, which generated the model of applied science in medicine, provided a context for the rise of clinical research, and incorporated standards against which clinical research would be judged. The discussion then turns to clinical research itself, exhibiting its difficulties in meeting prevailing standards and in preserving its scholarly character. Against this background, the essay explores the political and scientific changes that elicited the recent discussions, the resultant policy proposals, and researchers' failure to achieve closure. It traces that failure to their conservative vision, to their predilection for labor-market thinking, and to their disquiet in the face of the new emphasis on applications. Finally, the essay notes that some researchers have at least suggested the utility of health services research in crafting a new approach to policy for clinical research, and it argues that such an approach, although likely to be difficult, is probably the best foundation for achieving the long elusive policy consensus.

The Laboratory Sciences and the Public Interest

The growth of medical research in twentieth-century America has been sustained by public faith in its social utility. In the Progressive Era (roughly, the first two decades of this century), scientific rationality seemed the best foundation for organizing society, and the emergent professions appeared to be the best instruments for applying science (Wiebe 1967; Hollinger 1984; Nelson 1987, esp. 52–4). Physicians successfully claimed that their new laboratory-based medical science was the proper foundation for the interpretation of disease, and they could illustrate its powers by pointing to innovations in public health (such as the antidiphtheria campaigns) and progress in surgery and in obstetrics and gynecology (Starr 1982, esp. ch. 1 and 134–44; Vogel 1980, esp. ch. 3; Howell 1995, ch. 2; cf. Rosenkrantz 1979, 6–9). In a reinvigoration of the Baconian vision of science as the instrument of social improvement, Americans perceived physicians as exploiting the fruits of laboratory research to relieve suffering and enhance public health. Research in the laboratory-based medical sciences gained legitimacy as the ostensible source of these gains.

Medical research at first drew its financial support from private philanthropy (notably Rockefeller funds), and later, after World War II, from the federal government (Shryock 1947; Strickland 1972; Harden 1986; Rothstein 1987, ch. 12). During the 1890s, philanthropists began to create an infrastructure for research in the preclinical departments of medical schools. They appropriated the goals of a small cadre of academic, research-oriented physicians, many of whom had taken advanced training in the laboratory sciences at German medical faculties. These research reformers aimed to realize in American medical schools what they perceived to be the German system of medical education, which emphasized the research careers of the professoriate and the training of students in institutes of advanced research. They aspired, that is, to remake American academic medicine, at least in the preclinical departments, into a university-based, scholarly discipline, in which academic physicians would pursue laboratory science, as opposed to medical practice, as a career (Ludmerer 1985; Berliner 1985; Huddle 1987; Rothstein 1987; Wheatley 1988; Bonner 1990; Fye 1991). From the 1890s through the 1920s, the reformers gradually established research as the dominant ethos in several elite medical schools, while their backers supplied resources for new professorial posts and research facilities. Especially after the war, this model came to dominate American medical education.

The research reformers did not regard scholarly values as inconsistent with practical progress. Early in the century, medical research appeared broadly relevant to medical practice and public health (Fye 1991; Huddle 1993; Harvey 1981, 81–2) and remained in close proximity to phenomena observable at the bedside. Historians have also suggested that, at least through the 1930s, laboratory scientists in fields like biochemistry and bacteriology chose research problems in part with reference to their practical value (Kohler 1982; 1985; Amsterdamska 1987). Moreover, reformers' commitment to research colored their ideas about medical training and the abilities of suitably trained doctors. Regarding practice as isomorphic with research, they argued that in diagnosis and therapy the physician used the same methods as the researcher (Flexner 1910, 25; Huddle 1987, 74–5; Reiser 1978a, 162–3; 1978b; Blake 1980, 41; Warner 1980, 65–6, 68; Bonner 1990), and they regarded the techniques of practice as relatively straightforward applications of basic science (Huddle 1987, 78). Scientific medical training would enable physicians to appreciate innovations from the laboratory, which,

reformers anticipated, could be readily exploited in clinical settings. These convictions also shaped the new system of medical education, which wrapped all medical students in the mantle of research by requiring extensive training in the laboratory sciences prior to clinical education (something not attempted in Germany). The reformers thus believed that practical applications would flow readily because scientific questions were tied to practical needs and physicians would be trained to exploit the discoveries of the laboratory.

However, new factors—scientific, epidemiological, and social—reinforced the scholarly values of laboratory scientists and shifted their attention away from the bedside. From the late 1930s, researchers in biochemistry broadened their interests, taking in biological oxidation, intermediary metabolism, and macromolecules (Kohler 1982, ch. 12), a shift later accelerated by the emergence of intracellular and, still later, molecular biology. Also from the 1930s, some observers, recognizing the growing incidence of chronic disease, pursued its implications for policy and research (Swain 1962, 1233, 1234; Shannon 1976, 14, 36; Fox 1989a; 1989b; Stevens 1998, xxiii–xxiv). Among them were laboratory scientists who turned to the basic biological processes taken to underlie chronic illness. Their search for basic knowledge garnered support from philanthropists, and, especially after World War II, from the federal government, which, through the National Institutes of Health (NIH), devoted much of its medical research budget to this goal (Rosen 1965, 218–19; Shannon 1967a; 1967b; 1987; Rothstein 1987, 239–41).

Indeed, NIH funding antedated and overshadowed direct congressional support for medical education and therefore became the principal factor molding medical faculties (Association of American Medical Colleges [AAMC] 1962; Stevens 1998, ch. 16; Strickland 1972, ch. 4 and 249–56; Lewis and Sheps 1983, 127–8). Moreover, because broader discussions of federal policies for health manpower typically ignored research manpower (e.g., Shannon 1976, 41), the NIH was free to develop research manpower as it saw fit. The agency pressed the turn toward fundamentals both by its use of "study sections," comprising groups of experts, to define the research front in various subfields and to assess the grant proposals submitted by researchers (Fox 1987; IOM 1984; cf. Ahrens 1992, 157), and by its support of research training, which grew prominent from the late 1950s and would loom large in the later policy discussions (Wyngaarden 1973; Stephenson 1974, 17-18; Shannon 1967b, 121; 1976, esp. 27, 35–7, 40–1, 65–7; National Re-

search Council [NRC] 1989, vol. 1: 17–31; 1994, appendix A). Research training took two principal forms: fellowships for individuals (usually at the postdoctoral level) and institutional training grants. The latter were awarded to departments both to train researchers (chosen locally by the grant-holding institutions) and to enhance the environment for research by contributing to faculty salaries, paying for supplies and equipment, and supporting the trainees. The institutional grants supported both predoctoral students (pre-PhDs in basic science departments and, from 1964, MD/PhD students in the NIH Medical Scientist Training Programs [MSTP]) and postdoctoral students (primarily PhDs, but also some MDs). Administrators at NIH could thus act on their perceptions of scientific needs and manpower shortages without regard to congressional scruples about federal support for medical education. A supply of highly trained basic science faculty, oriented toward the biological fundamentals of primarily chronic disease, was therefore made available to seek direct research support from the NIH and to take faculty positions in new or expanded medical schools.

NIH support accelerated a formerly gradual trend, beginning in the 1910s in biochemistry, toward the replacement of MDs by PhDs at diverse rates in preclinical departments. PhDs trained in the basic sciences possessed little interest in medical practice, and their lack of medical qualifications kept them remote from the clinic (trends reinforced by the gradual shift of laboratory service roles out of preclinical and into clinical departments [Lippard 1974, esp. 46–8]). Their research topics increasingly lost short-term clinical relevance. In a word, scholarship overshadowed practice (Cowan 1980, 113; Kohler 1982, 219; Rothstein 1987, 155, 250, 296; Geison 1987; NIH 1968, 82–3, 90; Stevens 1989, n.11, 396–7, and its text, 203; Ahrens 1992, 20–1. Cf. Aiken and Freeman 1984, 540; Latour 1988, 61, 68, 259 n.3, 261 n.9, and cf. 87; Melhado 1991; Berzelius 1808).

Researchers did recognize that congressional support rested on anticipated practical improvements, but World War II delayed any clash in values. Researchers supported the war effort by returning to practical work (Fox 1989a, 19). Their successes enhanced their prestige (Ginzberg and Dutka 1989, 52; Reiser 1978b, 14–16) and seemed to bear out the belief that knowledge, once generated, could be treated as a costlessly available, off-the-shelf component, ready for application (Mowery and Rosenberg 1989, 5–7, 15). Researchers thus obtained generous funding from a Congress seeking victory over the ills of humankind

(Strickland 1972; Rothstein 1987, 155–9 and ch. 12; Shannon 1967a; 1976; 1987; Murtaugh 1973; IOM 1990, chs. 2, 4). Even when practical benefits proved less than prompt, Congress was willing to wait. Through the early 1960s and, with lesser enthusiasm, still later, it accepted researchers' arguments that the infrastructure for research and its intellectual foundations must be built first; the conquest of disease required a firm basis in pure science (American Foundation 1955; Shannon 1967a; 1967b, 5; 1976, 48; 1987; Strickland 1972, esp. ch. 9; Fredrickson 1977, 160, 166–7). Researchers could therefore pursue scholarship without deferring to congressional expectations. Thus, ironically, it was generous public funding for research training, institutional expansion, and disciplinary development, supplied after the war in anticipation of practical advances, that intensified the turn toward fundamentals (Stevens 1998, 357–62; Shannon 1976, ch. 5; Rothstein 1987, 250–1).

Researchers' success in selling laboratory research also benefited in the postwar years from resistance to public health–insurance programs and socialized health care delivery or financing. Politicians and legislators could help ward off such innovations by invoking the Baconian expectation that, under conditions of economic growth, research would improve medical practice and public health (American Foundation 1955; Strickland 1972, esp. 213–14; Murtaugh 1973; Rosenkrantz 1979; Stevens 1989, esp. ch. 8; Fox 1985, 353–5; 1986b). That expectation was incorporated in and fostered by the widely accepted policy principle that Fox calls "hierarchical regionalism" (Fox 1983; 1985; 1986a; 1986b; 1988). It reflected the assumption that both the causes of disease and effective therapies for them are discovered in medical schools and their teaching hospitals and that these innovations can best be disseminated through a regionally organized hierarchy of institutions. Scientific research, more than reform of health care delivery and health services financing, would bring the benefits of medical research to society.

Congressional patience was of course not inexhaustible, but researchers long adeptly parried efforts to reorient them toward practical outcomes (Culliton 1991). During the heyday of congressional support (ca. 1955–67), James A. Shannon, director of the NIH (1955–68), warded off most pressure from both outside interests and Congress (and often direct instructions from congressional committees) for categorical programs, while sheltering research into fundamentals (Strickland 1972, 193–203). In President Nixon's war on cancer, researchers successfully resisted both removal of cancer research from NIH control and reallo-

cation of funds toward targeted programs, arguing that a broad research program was more likely to conquer cancer (Strickland 1972, ch. 12; Rettig 1977; Ginzberg and Dutka 1989, 27; Patterson 1987, 248–52). In the face of budgetary uncertainty early in the Reagan years, the NIH protected individual and research-project grants at the expense of clinical trials, contracted developmental work, and categorical research centers (Fredrickson 1981; Ginzberg and Dutka 1989, 31; Ahrens 1992, 77–8, 93–5). During the 1970s and 1980s, even direct congressional pressure on researchers to pursue practical payoffs often had only modest effects (Rothstein 1987, 245, 254). In general, researchers responded to political pressure for practical applications in ways that maximized their freedom to pursue their own priorities.

The structure of postwar support of research reflected competition between congressional interest in practical achievements and researchers' focus on basic science. Under pressure from activists seeking the conquest of specific diseases, a practically minded Congress imposed a categorical structure on the NIH: research was to be organized by disease, not by criteria arising from pure research (Swain 1962; Strickland 1972, 32–54; 135–57; Murtaugh 1973, 163–4; Shannon 1976; 1987, esp. 868; Lewis and Sheps 1983, 19–24; Kilbourne 1986, 51–2; Fox 1989a, 20). The agency grew by addition of new categorical institutes. Researchers could scarcely have resisted that approach, but in 1958 they created a basic-science counterweight, the Division of General Medical Sciences, which in 1962 became the National Institute of General Medical Sciences (NIGMS). It housed programs that explicitly supported basic science in an otherwise categorical agency. In public statements, researchers sought to accommodate both Congress and basic science (Shannon 1959; 1976; Strickland 1972; Fredrickson 1977; Association of American Medical Colleges 1983; Wyngaarden 1984b; Ahrens 1992, 130) and occasionally pointed to practical advances; most often the autonomy of laboratory science prevailed over congressional aspirations.

In summary, laboratory research in American medicine was created by philanthropists and research reformers in the basic medical sciences, who hoped to make of medicine a scholarly discipline. Researchers emphasized basic knowledge but at first anticipated that scientifically trained physicians would readily turn scientific findings into practical improvements. This claim gained them both social legitimacy and, especially after the war, vast public resources. Research also benefited as an alternative to controversial governmental health programs. However, spe-

cialization and disciplinary development in science, the prominence of chronic diseases, the rapid pace of institutional expansion, and the primacy of scholarly values oriented researchers toward narrowly scientific concerns, a shift ironically fostered by increased public funding. Researchers successfully argued that practical progress required a sound scientific basis. When Congress grew impatient, they often succeeded in deflecting its pressure and in sustaining their quest for basic knowledge. For about two decades (the 1950s and 1960s), medical research enjoyed enormous prestige, access to immense resources, and sustained growth.

Academic Clinical Research

The history of clinical research resembles that of the laboratory sciences. During the 1910s and 1920s, reform-minded physicians in the laboratory sciences, in league with a few research-oriented clinicians, sought to turn clinical as well as laboratory medicine into a scholarly discipline. Invoking the terms of philanthropic grants, reformers ended the traditional practice of recruiting clinical professors from among local practitioners, who typically continued to earn a living from private practice. Instead, clinical faculty would be recruited nationally, appointed to full-time posts, and expected to concentrate on teaching and research. In a few elite institutions (Johns Hopkins, Washington University, Yale, the University of Chicago), Abraham Flexner used Rockefeller funds to impose a "strict" full time, in which clinical professors would see patients only in university hospitals and their fees would revert to the medical school. However, he eventually sponsored elsewhere the more lenient "geographic" full time, in which clinical faculty retained consulting fees; this system became standard after World War II (Rothstein 1987, ch. 13). Full time thus did not relieve clinical professors from seeing patients; rather, it confined their practice, the better to orient them toward teaching and research. Also promoting the scientific clinician was the prototype provided by the Hospital of the Rockefeller Institute from its opening in 1910 (Meltzer 1909; Cohn 1924; Corner 1964; Rockefeller Archive Center 1977; Harvey 1977; 1978, 1981, esp. ch. 5; Kohler 1982, 238–9; Kilbourne 1986, 44–7, 49–50; Wheatley 1988, 30–1, 34–6, 40–1). Research was sustained by the development in hospitals of specialized wards and laboratories (Means 1958; Harvey 1977; 1981; Maulitz 1979; Petersdorf 1980, 490; Cangi 1982; Finland

1982–83; Berliner 1985; Ludmerer 1985, 207–13; Huddle 1987, ch. 6; Rosenberg 1987, 184–9; Rothstein 1987, chs. 8, 13; Peitzman 1988, 213–22; Wheatley 1988; Fye 1991). Clinical science thus found its moorings in the clinical departments of medical schools and their associated hospitals.

The nascent field aimed to elucidate bedside phenomena by combining clinical observation, new techniques of measurement, and deductive logic (Blake 1931; Lewis 1934; Lee 1938; Warren 1983, 341; Kunitz 1988; Peitzman 1992; see also Gill 1984, 354–5). New instruments, like the electrocardiograph, the x-ray machine, and the blood-pressure cuff, as well as methods from clinical chemistry and medical bacteriology, permitted bedside measurements of pathophysiological and biochemical changes. Measurements did not eclipse the patient but gave a scientific foundation for interpreting signs and establishing the natural history of disease; in a word, they helped characterize the clinical picture, which was paramount. The goals were primarily natural–historical and nosological: to identify the characters of disease, establish their clinical course, rationalize their nomenclature, and investigate at least their proximate causes. Understanding disease, rather than improving practice, was the researchers' goal, but their immersion in clinical phenomena often enabled them to help selected categories of patients (Blake 1931; Harvey 1980; 1981; Axelrod 1970; Cope 1966). Short-term payoffs from research were thus an ever-present reality.

Tensions developed between clinical and laboratory science, but they little affected clinical research. Thomas Lewis, a British researcher who trained a number of Americans (Harvey 1981), claimed that although clinical researchers could legitimately make excursions into physiology or microbiology, they should return from the laboratory to the territory of clinical phenomena in patients (Lewis 1934, 3; cf. Kunitz 1988, 282–3; Albright 1944, 921), a view consistent with that of leading American researchers (e.g., Meltzer 1909; Cohn 1924). Warnings appeared against excessive movement toward both the laboratory (e.g., Maulitz 1979, 103; 1987, 228; Harvey 1981, 151–2; cf. Albright 1944) and the clinic (Harvey 1981, 267: on Cohn), but most clinical researchers stressed clinical (as opposed to cellular and subcellular) phenomena, interpreted in the light of bedside measurements (e.g., Sinding 1989; 1990). Kohler's suggestion (1982, 221–2) that biochemistry in the 1920s and 1930s was a "basic–applied science" seems applicable to the clinical as well as laboratory research that he chronicles: through mutual ac-

commodation, laboratory and clinical scientists collaborated in ways that relieved their fear of defections from the ranks of one to the other. A hybrid discipline of clinical science, which took its concerns from the practical imperatives of medicine but approached them with a disinterested will to explore the phenomena of disease, seems to have taken root. At least until the late 1930s, what changed was not the role of the laboratory but the scale of the enterprise, as a new generation of clinical scientists became prominent in a growing number of research-oriented institutions (Harvey 1981; Warren 1983; Beeson and Maulitz 1988).

However, the same factors affecting laboratory science—the weight of scholarly values, institutional growth and disciplinary development, and the new importance of chronic disease—also pulled clinical researchers away from bedside phenomena and reduced their interest in practical innovations. In the 1930s, both Rockefeller philanthropy and the federal government began to support clinical research into the fundamentals of disease (Swain 1962; Fox 1989a). As in the basic sciences, this shift was interrupted by World War II but resumed thereafter, when clinical researchers participated in the efforts of medical scientists to parry pressure from Congress. Congressional interest in practical outcomes led to the opening of the NIH Clinical Center in 1955 and the start of NIH funding in 1960 of General Clinical Research Centers at universities (Ahrens 1992, 66–7, 70–2, 131–41, 145–51; DeCesare 1981), but the centers were modeled on the Hospital of the Rockefeller Institute, where, in the postwar years, clinical research sought basic knowledge of human disease and no longer seriously anticipated clinical applications (Ahrens 1977; Benison 1977, esp. 43–4; cf. Ahrens 1992, 60–2, 130, 138, 146). Like the laboratory scientists, clinical researchers secured the freedom to pursue scientific leads.

In enlarging the enterprise and altering the orientation of clinical faculty, the research-training programs of the NIH were again centrally important (Wyngaarden 1973; U.S. Senate 1973, 1–11; Stephenson 1974; Braunwald 1975; Shannon 1976). Whereas research training in the basic sciences lay in the NIGMS, clinically oriented postdoctoral training primarily of MDs remained in the categorical institutes, which organized and managed them in diverse ways that were consistent with administrators' judgments about the appropriate scientific foundations for clinical disciplines, scientific opportunity, and manpower needs. In clinical research, a shift in faculty interests toward disinterested study did parallel that in the basic sciences but took place more slowly and in

the company of opposing tendencies. Initially, research training aimed both to improve the scientific competence of clinical faculty (and thus support training in specialty practice) and to create a scientifically capable research faculty. From the mid-1950s, however, it grew clear that, in most disciplines, training produced not only new faculty members but also specialists, who entered private practice and there earned high incomes. The NIH therefore began to focus on training researchers as opposed to practitioners. However, as the next section shows, the lines between subspecialty practice and clinical research long seemed vague (e.g., Braunwald 1975; NRC 1976, 26), and other forces arose tending to foster applied science. The result was that, even as some researchers took up applications, NIH research training gradually created a body of faculty for whom the gap between their scientific interests and the short-term improvement of medical care had widened appreciably (Stevens 1998, xxii–xxiii).

The developments described here culminated in a "golden age" of clinical research that lasted about two decades (the mid-1950s to the early 1970s) (Ebert 1986, 69; Ahrens 1992, 47; Wyngaarden 1979b, 1259). Academic clinicians described themselves with the football term "triple threat" (a formidable player who could run, kick, and pass), as they committed themselves to simultaneous pursuit of research, teaching, and patient care. Research, however, was primary: with generous congressional support, research-oriented clinical departments blossomed, specialization advanced, and academic medicine expanded enormously (Rothstein 1987, chs. 8, 12–13; Lippard 1974, chs. 6, 8; Shannon 1976, esp. ch. 4; Ebert 1977; 1986; Thier 1977, 219–21; Petersdorf 1980; 1981). Enjoying immense prestige and resources, clinical research became a large-scale enterprise on which Americans placed their hopes for the conquest of disease.

In summary, clinical research emerged from the efforts of research reformers in the basic sciences and some research-oriented clinicians to impose the university model on clinical departments. Academic clinical medicine was to be a scholarly enterprise, producing fundamental knowledge of human disease, and faculty were to be chosen according to scholarly criteria and placed on salary. As these aspirations were realized, the immersion of researchers in the clinic allowed them to improve treatments for some patients. With the growth of research support and research training, clinical departments expanded, and clinical research entered a golden age. However, as in the laboratory sciences, much

clinical research shifted toward fundamentals, as researchers parried congressional pressure for practical outcomes.

The Dissolution of the Golden Age

The golden age was brief. From the 1940s, and especially after World War II, new forces buffeted clinical research. They pushed it toward the opposing poles of laboratory science (largely divorced from problems of disease) and applied science (focused on improvements in clinical practice), induced many academic clinicians to abandon research, and facilitated the entry of PhDs into the field. Fewer physicians took up research, the number of projects diminished, and physicians' dominance of what remained was under threat. Clinical research entered into decline.

A major factor pushing clinical research toward either the laboratory bench or applications was the instability of its foundation as a "basic–applied science." As noted earlier, such a discipline depended on collaboration with laboratory scientists, and changes in their interests, as occurred in biochemistry from the 1930s, could undermine the field. Similarly, Löwy's studies (1987; 1989) suggest that what enabled clinical scientists to produce basic knowledge about disease was their mutually supportive, but rare and contingent, relationships with laboratory scientists. More commonly, medical work was rewarded as an achievement of either laboratory science or medical practice and public health. Echoing Ben-David (1960), Löwy argues that in Britain and America the laboratory researcher and the clinical practitioner have constituted the stable social roles; the intermediate one of the clinical scientist has been only transitory.

This pattern seems to mark the evolution in the tensions noted above between laboratory and clinical science. After the discovery in 1953 of the double helix, the laboratory sciences were rapidly transformed, as researchers focused on cellular, subcellular, and molecular events, but a decade passed before clinical research felt analogous effects (a difference accounting for the slower separation, in clinical disciplines, of research from practice). In the eyes of laboratory scientists, the bedside phenomena of interest to clinical researchers were reflections of fundamental events, and clinical research was derivative (Grahn 1980; Landau 1980; Feinstein 1983; 1994). Previously muted professional jealousies grew palpable: precisely because clinical research required patients (however

objectified as "clinical material"), it enjoyed lower status among researchers than research conducted in their absence, as occurred in laboratory science (Abbott 1988, esp. 118–21; cf. Petersdorf 1980, 495–6; Wheatley 1988, 40). In addition, full-time clinical professors took seriously their obligation to teach future clinicians; they thus compromised their scholarly claims in the eyes of basic scientists (Peabody 1928; Castle 1960; Kunkel 1962; Seldin 1966; Warren 1972; 1983). The very distinction of "basic" from "clinical" research implied that the latter, whatever its pretensions to creating basic knowledge, was tainted by practice and applications. Scientifically and professionally, clinical research was losing prestige.

Leading researchers voiced concern. Wood (1963, 3), at the Association of American Physicians (AAP), claimed the revolution in biology had split preclinical from clinical faculty. The laboratory scientist descended to the cellular and subcellular levels, but the "clinical teacher and investigator ... has no choice but to deal with the bewildering complexities of the intact host." He hoped this split would heal, but others were less sanguine. Kunkel (1962), at the American Society for Clinical Investigation (ASCI), when asked whether clinical researchers should be trained in the basic sciences, found "little doubt" that at least some should be, but he worried that "the physician undertaking prolonged basic training may be completely lost to clinical investigation," "forsake entirely his disease orientation," and "encounter the rather widespread disparaging attitude of basic scientists toward clinical investigation" (quotations, 1355). Anxiety about the corrosive effect of the laboratory on clinical research has persisted (Strauss 1960; 1964; Beeson 1967; 1977; Ahrens 1992, 36, 147; 1993, 202; cf. Landau 1980, S4–S5, S7; Grahn 1980, S58; Sherman 1988; Thier 1977, 222; 1980, 249, 250). As noted below, clinical researchers, in trying to uphold the legitimacy of their field, have continued to insist on its scholarly character.

As basic science undermined clinical research, increased demand for accountability in research (Strickland 1972; Steinfels 1976; Holton and Morison 1979; Dutton 1988; Rothman 1991) and shifting federal health priorities highlighted applied science. In the 1960s and 1970s, Congress entered the once restricted realm of health services financing and delivery, establishing Medicare and Medicaid, sponsoring planning, and engaging in regulation (Strickland 1972, ch. 10; Fox 1986b; Roemer 1975; Rettig 1977; Somers and Somers 1977; Brown 1992), developments early seen as putting a premium on applications (Carey 1967,

54–5; Murtaugh 1973, 164; Shannon 1976). Moreover, these innovations did not imply consensus about the proper role of government in health care; practical innovations may have been endorsed to derail further controversial initiatives. Budgetary strictures also played a role. As new health programs took funds from biomedical research, the postwar economic expansion ended, and the costs of the Vietnam war mounted, Congress sought payoffs from its investments. The hope grew that applied science could replace expensive "half-way technologies" (Thomas 1977; Bennett 1977) with definitive (and therefore supposedly cheaper) treatments. Since the late 1960s, a growing proportion of federal research dollars has been devoted to targeted research, clinical trials, and disease management, and many researchers followed the dollars (President's Science Advisory Committee 1972, 19; Morgan and Jones 1976, sect. 4, and 5-19–5-20; Levine 1979; Landau 1980; Rushmer 1980; Ahrens 1992, 53–64, 112, 209, 218; cf. Grahn 1980, S60; Bever 1980; Whedon 1980, S42; Oates 1982).

Developments in clinical science enabled researchers to respond to demands for practical results. Perhaps most significant was the advent of clinical trials, particularly in application to drug therapies (Temin 1980; Lilienfeld 1982; Feinstein 1985, 683–90; Meldrum 1994; Löwy 1996, ch. 2; Marks 1997). Stimulating their use were the rise of biostatistics (Gehan and Lemak 1994; Marks 1997), the "spectacular success" (Feinstein 1985, 688) of the British streptomycin trial in the 1940s (Medical Research Council 1948), the rise of cancer chemotherapy (Löwy 1996, esp. ch. 1), and the thalidomide disaster and the ensuing Kefauver amendments of 1962 (Meldrum 1994, 16–18; NRC 1993, esp. 84–7; Marks 1997, esp. ch. 3). The latter in particular inaugurated a regulatory regime that mandated trials as proof of the safety and efficacy of treatments. Especially since 1960, Congress and the pharmaceutical industry provided funds for clinical trials, and researchers, especially in departments of clinical pharmacology, increasingly devoted themselves to this work.

Accompanying and reinforcing these developments were the rise of health services research, outcomes research, clinical epidemiology, and clinical decision making, practices that analyze the potential applicability, utility, and efficiency of medical innovations in clinical settings and public health. The history, methods, and substance of these fields lie outside the scope of this paper, but it can be noted here that they have been spurred by political emphasis on the public accountability of med-

ical research and the efficient operation of health services[1] and that they have attracted some clinical researchers. The new fields thus offer an avenue of collaboration with those clinical researchers who are oriented toward applications and can sustain efforts to create and evaluate novel interventions in medicine and public health. As noted below, those concerned with policy governing clinical research have largely kept their distance from these practices, but their support in conjunction with clinical research may lead to socially viable innovations in policy regarding clinical research. This theme is pursued in the concluding section.

As applied science lured some clinical researchers, others, inspired by the growth of molecular biology and the higher status, lesser complexity, and potentially greater academic rewards of laboratory research, took up laboratory projects (Relman 1979; Grahn 1980; Landau 1980; Ahrens 1992, 175–6; IOM 1994, 55; Goldstein and Brown 1997, 2803). Some of them likely conformed to Lewis's model, in which researchers returned to the clinic after excursions to the laboratory (e.g., Beeson 1977; Weissmann 1987), but much clinical research came to resemble basic science (Beeson 1967; Lippard 1974, 78–9; Krause 1980, 257–8; Fletcher, Fletcher, and Greganti 1981; Warren 1983, 343–5; Gill 1984; Herman and Singer 1986, 154–5; NRC 1989, vol. 1, 18–19; Ludmerer 1990, 482-6). From the late 1960s, papers at the joint annual meetings of clinical researchers' three professional societies (the AAP, the ASCI, and the American Federation for Clinical Research [AFCR]) have displayed "a distinct new trend in direction: less toward 'clinical' and more toward 'basic' phenomena"; and revealed "a decline in the percentages of human, disease-oriented, and patient-centered research, with a rise in the nonhuman-nondisease percentages" (Feinstein, Koss, and Austin 1967, 398, 410; Feinstein and Koss 1970; Gill 1984; cf. Forrest 1980; Ahrens 1992, 55, 59, 111–12). More recently, Ahrens (1992, ch. 8) has likewise shown that the research of physicians supported by the NIH has shifted from the bedside toward the bench.

Other stresses led academic clinicians to alter or even abandon their research. Clinical research seemed ever more onerous, requiring higher levels of scientific knowledge and research skill and deeper immersion in subspecialty practice (Thier 1980, 249; Thier, Challoner, Cockerham, et al. 1980, 87; Wyngaarden 1981, 424, 426; 1985, 97; 1986b, 267; Goldstein 1986; Ahrens 1992, 188–91; Martin 1991). A career in clinical research was becoming a dual professional life, scientific and

medical, requiring practitioners to develop and maintain two areas of expertise and skill, keep up with two bodies of abstruse literature, and attend two sets of professional meetings. It was a prospect made more daunting as difficulties in securing research funding threatened the payoff from such heavy investments in professional expertise (e.g., Wintrobe 1970; Beeson 1977; Thier 1977; Levine 1979; Wyngaarden 1979b; 1984b, 159; 1985, 97; Krause 1980, 258; Fredrickson 1981, 516; Healy 1988, 1062; Smith 1989, 110–12; Movsesian 1990; Martin 1991; cf. Culotta 1993; Swartz and Gottheil 1993; Williams, Wara, and Carbone 1997; Nathan 1998). Having abandoned the production of basic knowledge, many academic clinicians took up applied science or left it for teaching and patient care (e.g., Seldin 1966; Sherman 1980, S80; Petersdorf 1983, 1055–6; Beaty, Babbott, Higgins, et al. 1986; Ebert 1986, 74; Kelley 1988, 368-70; Ahrens 1992, 6–7, 59; Cadman 1994).[2] The era of the triple threat was ending, and an autonomous realm of clinical science was in peril as its prestige dropped and its practitioners turned to applications, bench research, or clinical teaching and practice.

More than alterations in the practices of academic clinicians threatened clinical research. With the intrusion of the laboratory into the field came its principal denizens, PhDs. As earlier in preclinical departments, so in clinical departments, PhDs, formerly rare, became commonplace, took on tasks once performed by physicians mindful of clinical practice, and both benefited from and fostered the shift away from the clinic toward the laboratory (Herman and Singer 1986; Gillis 1979; Wyngaarden 1979b, 1258; 1981, 421–2, 425; IOM 1983, 26–34; Petersdorf 1983, 1055; Ahrens 1992, 21–5, 110–12, 185–8). Moreover, PhDs seemed to enjoy at least two advantages over MDs: they spent no time on medical practice and clinical teaching, and they received research training as an inherent part of their education, while physicians received it through diverse postdoctoral programs of uneven quality (Stephenson 1974; Dolan and Morgan nd [1978]; Price 1981; Wyngaarden 1985, 97; 1986b, 267; Healy 1988, 1060–1; Ahrens 1992, esp. ch. 11; Swartz and Gottheil 1993, ch. 4; Nathan 1998). The preparation of clinical researchers lacks a "defined training path," and "[t]here are ma[n]y points . . . at which a physician can make a decision for a research career" (Dolan and Morgan nd [1978], 1; IOM 1994, 194); and these decisions were not irreversible. Not only was the character of clinical research at stake, but also the dominance of physicians over its practice. Problems of recruitment therefore became paramount in the minds of researchers.

In summary, by the 1970s, the model of clinical research established in the interwar years was in disarray. Constituted as a basic–applied science, it was inherently unstable. Changes in the scientific interests of basic scientists, the rise of the new biology, the public demand for accountability, the shift in federal funding toward applied science, and competing practices (clinical decision making, clinical trials, and the new outcomes research) all conspired to reduce the numbers of traditional clinical researchers. Some left research entirely, those remaining moved toward either basic or applied science, and recruitment suffered. As the population of clinical researchers declined and their practices changed, the rising number of PhDs threatened physicians' control of their now diminished turf. Alarmed, advocates of clinical research inaugurated the still ongoing policy discussions.

The Course of the Policy Discussions: The Supply of Physician–Scientists and the Dominance of Labor-Market Thinking

An early spark for the discussions was the attempt by the Nixon administration, in its budget proposal for FY 1974, to eliminate funding for NIH research-training programs (U.S. House 1973b, 14–17; U.S. Senate 1973, 19–22; Zapp 1973; Stephenson 1974, 24–9; Braunwald 1975; Walsh 1975; Shannon 1976, 64–7). Research training, especially the institutional training grant, had been under scrutiny even in the Johnson years, and it had suffered cuts in funding (Stephenson 1974; Shannon 1967b, 41, 60–2, 121–2), but the Nixon administration targeted research training early, sending its partisans among researchers and the NIH itself scrambling to justify the programs (AAMC 1971; 1974; NIH 1972; NRC 1976) and arousing the opposition of Congress (U.S. House 1973a; U.S. Senate 1973). Congress restored support for research training under the National Research Service Award Authority (NRSA), which was Title I of the National Research Act of 1974 (PL 93-348). However, the legislative history of the act (see, in addition to other citations in this paragraph, U.S. House [1973a; 1974]) and other contemporary sources [e.g., President's Science Advisory Committee 1972; Stone 1974] reveal that Congress shared at least two concerns of the administration: that stipends not be used to support training of clinical specialists who would leave research to earn high incomes in

private practice and that the awards should be "tuned" to the extent of need for research manpower in diverse disciplines. Reflecting the first concern, the act contained a provision that required trainees who did not ultimately pursue a research career either to pay back their training costs or to provide health services for underserved groups, a possible disincentive to enter training. Reflecting the second concern, the act centralized the diverse NIH programs to allow flexibility in the use of resources in response to need, and it also mandated studies by the National Academy of Sciences (NAS) of the need for biomedical research manpower (Culliton 1974).

The NIH itself tried to uphold its traditional reliance on administrators' judgments in distributing resources for research training, while acknowledging the propriety (for establishing background) of more formal manpower studies, for which it hoped to obtain the authority (NIH 1972; U.S. Senate 1973, 19–20). However, Congress insisted that the distribution of resources for research training should rest on formal analyses of need and that the NAS, not the NIH, should undertake them. Following an initial feasibility study (NRC 1975a), a series of NAS committees has regularly reported estimates of need for several categories of biomedical research personnel (NRC 1975b–79/1981; IOM 1983/85; NRC 1989; 1994 [in which see esp. Appendix A]; cf. Sherman, Jolly, Morgan, et al.1981) and analyzed supply. In effect substantiating one claim of the Nixon administration, that data were lacking for an adequate analysis of research training, the early studies showed that few formal efforts had been made to analyze the need for biomedical research personnel and that few sources of pertinent data existed. The studies devoted much effort to creating and analyzing databases and to generating formal labor-market models, which were aimed at short-term predictions of the extent of need and analysis of the sources of supply. Whether market institutions adequately served the national interest in biomedical research, or, more particularly, in clinical research, was not asked in the context of the NRSA. The act and the studies it mandated thus focused policy attention on short-term fluctuations in the existing distribution of monetary and institutional resources that generated both the need and supply of researchers.

The concern for the supply of physician–scientists sparked by the conflicts over the Nixon policies was intensified by reports of an apparently precipitous decline during the early 1970s in the flow of physician labor into clinical research. Lowered recruitment seemed to reflect de-

cline, or at least stagnation, from the late 1960s, in the overall level of federal support for medical research and for expansion of medical schools (Douglass and James 1973, 214; Shannon 1976; Challoner 1976, 241; NRC 1977, 111, 114, 119–20; Thier 1977, 222; 1980, 248; cf. Ahrens 1992, 101–4), but eventually additional factors were identified. As early as 1973, a study showed a reduced proportion of MDs among the principal investigators (PIs) in investigator-initiated research projects supported by the NIH from 1966 to 1972, a trend confirmed by an update of 1975 (Douglass and James 1973; Challoner 1976; cf. Cadman 1990). The first substantive report of the NAS committee (NRC 1976) showed decreasing numbers of MDs supported by NIH funds for postdoctoral training (see also Culliton 1976; IOM 1983; Burns 1984). Similar evidence in the early NAS reports was readily exploited by participants in the discussions who were concerned about the declining population of physician–scientists (e.g., Thier 1977, 221; Wyngaarden 1979b, 1255; DiBona 1979, 253; Forrest 1980, 246; Thier, Challoner, Cockerham, et al. 1980, 86; DeCesare 1981, D17, D25; Bickel, Sherman, Ferguson, et al. 1981, 1265). These sources gave prominence to the supply side of the labor market: given national need, could the institutions that produce researchers meet it? If not, what adjustments could permit them to do so?

During the 1970s, that concern shifted to a sense of crisis and prompted much analysis and discussion. In response to the budgetary proposals of the administration, the AAMC, while attempting to formalize its policies on research, conducted a preliminary survey that indicated the importance of training stipends to maintaining the supply of researchers (AAMC 1971). In 1973, the Association organized a meeting at which representatives of the universities most heavily involved in research training made recommendations for its support (AAMC 1974). It also performed a study, under contract with the NAS, of the training of clinical investigators (Dolan and Morgan nd [1978]); it later appointed an ad hoc committee to explore the causes of decline and propose remedies (Thier, Challoner, Cockerham, et al. 1980), and thereafter undertook another study of clinical research manpower for the NAS committee (Sherman, Jolly, Morgan, et al. 1981). Presidents of the AFCR expressed concern (Challoner 1976; Thier 1977; DiBona 1979), the organization articulated and published a formal policy on research training (Braunwald 1975), and it held a symposium entitled "The Young Clinical Investigator in the 1980s," which generated both data and analysis

(Forrest 1980; Thier 1980; Krause 1980). The IOM also held a conference in 1980 that documented the decline (IOM 1981, in which see esp. DeCesare).

Through most of the 1970s, these discussions took place largely among clinical researchers themselves, but at the end of the decade they entered a broader arena. In 1979, James Wyngaarden, a distinguished physician–scientist who served on the NAS committees that produced the first six of the reports mandated by the National Research Act and who was to become director of the NIH in 1982, coined the catchphrase, "the clinical investigator as an endangered species" (Wyngaarden 1979a). Under that title, he documented in the pages of the *New England Journal of Medicine* (Wyngaarden 1979b) the decline of the physician–scientist. The New York Academy of Medicine (1981) sponsored a conference that invoked his theme (Wyngaarden 1981) and published the proceedings for a broad audience. The Center for Policy Study at the University of Chicago also sponsored a national conference on "the plight of clinical investigation in the United States," and the resultant papers appeared the next year (Grahn 1980, S1). By the start of the 1980s, researchers had disseminated documentation of the crisis posed by declining numbers of physicians entering clinical research, together with a collection of ideas about causes and cures.

Wyngaarden's account (1979b) was grim. The NAS committee had sought to reserve 2,800 of 4,200 postdoctoral positions for research training in clinical disciplines, but the total was never reached for lack of sufficient MD applicants. In 1977, for example, only 2,304 places were filled, only 1,843 were filled by holders of clinical degrees, and some 460 were thus left to PhDs. Similarly a "precipitous decline in postdoctoral traineeship awards to M.D.'s" had begun in 1975, from over 3,000 to under 2,000 in 1977, accompanied by a linear increase in awards to PhDs. Annual awards of NIH research-training fellowships to MDs or MD/PhDs declined from about 900 to 400 over the decade from 1968 to 1977, making "inescapable" the conclusion "that there are substantially fewer M.D.'s undertaking research training today than a decade ago and that this trend antedates the Nixon administration." Among young faculty receiving Research Career Development Awards, the proportion of MDs diminished from 43.5 to 24.1 percent, while PhDs made "substantial gains." Holders of Young Investigator Awards showed similar changes: by the late 1970s, PhDs received the majority of grants. The proportion of MDs among PIs on NIH-funded research

projects similarly dropped, from over 41 percent in 1966 to 18 percent in 1975, recovering modestly to 23.5 percent in 1977. The number of MDs in this group was stable, but that of PhDs doubled (cf. Whedon 1980, S39–S41; Wyngaarden 1981, 422–3). Finally, the period from 1968 to 1975 revealed a dramatic drop (from 15,441 to 7,944) in the numbers of physicians reporting research as their primary activity, even though the numbers of medical graduates, medical faculty, and faculty in departments of medicine had doubled. Meanwhile, Wyngaarden observed, "the Ph.D. pool in the biomedical sciences is continually expanding," "an increasing percentage of the clinical-traineeship slots are occupied by Ph.D.-trainees," and "young M.D.-investigators are progressively being replaced by Ph.D.-research associates in the laboratories of physician-scientists of departments of medicine."

The message seemed clear: the supply of physicians in clinical research had been in decline for over a decade, whereas the recruitment of PhD scientists had grown substantially. In the AFCR symposium the next year, Forrest (1980, 246) called the decline "alarming," concluding (247): "There is no longer a need for more data; the data are in. Federally supported physician-research trainees have decreased [in numbers] precipitously since 1975 to a level approximately one-half of that deemed necessary for the national interest by the National Academy of Science[s]."

In analyzing these changes, clinical researchers came to recognize broader problems than the slowing of federal support in the 1970s or the policies of the Nixon administration. They enlarged their conception of the crisis by analyzing the supply side of the market for physician manpower and confronting it with the extent of need, usually as portrayed by the NAS committee. Often using the metaphor of the pipeline, they mapped the threat to the supply of physician–scientists across the educational spectrum from grade school through postgraduate research training and faculty careers. They portrayed the pipeline as a sequence of stages at which reversible decisions are made, identified the disincentives to choosing or persisting in a research career, and proposed policy remedies for the disincentives. This approach marked the NAS committees, which attempted to devise formal labor-market models of both demand and supply (NRC 1989, ch. 1; 1994, appendix A; cf. also Sherman, Jolly, Morgan, et al. 1981). In less formal discussions of supply, the pipeline metaphor was presaged early (e.g., Cooper 1973, 71–2; Wyngaarden 1973, 137; NRC 1976, 41, 61), the approach it mandated came to prominence at the turn of the decade (Dolan and Morgan nd

[1978]; Thier and Morgan 1979; Wyngaarden 1979b; Thier, Challoner, Cockerham, et al. 1980; Sherman. Jolly, Morgan, et al. 1981, esp. ch. 4), and it is still in routine use among analysts of the endangered species (e.g., Healy 1988; Ahrens 1993; Baker, Levey, and McGinnis 1993; Evans, Hendee, and Loeb 1993; Cadman 1994; Gallin and Smits 1997; Thompson and Moskowitz 1997).

Analysts of the supply side formulated polices to improve recruitment and retention of physician–scientists. This effort extends from the ad hoc committee of the AAMC (Thier, Challoner, Cockerham, et al. 1980) to Ahrens's book-length analysis entitled *The Crisis in Clinical Research* (1992), and the IOM study (1994) from which this essay began (cf. Dolan and Morgan nd [1978]; Thier and Morgan 1979; Levey, Sherman, Gentile, et al. 1988; Association of Professors of Medicine and AAMC 1989; Swartz and Gottheil 1993, pt. 1), into the present (Crowley and Thier 1996; NIH 1997; Nathan 1998). Typical proposals included the following: enhancing the attractiveness of medicine itself (in the face of its declining prestige) and of research careers (as opposed to socially sanctioned careers in primary care or more prestigious and lucrative specialty careers) by exposing medical students and residents early and often to research; identifying and encouraging potential recruits through mentoring and institutional arrangements; adding research training to the requirements for specialty certification; preserving and enhancing research training; assuring stability in the NIH budget (Fredrickson 1981, 515; Wyngaarden 1984b, 156–7; Seggel 1985); identifying sources of frustration and instability in research careers and stabilizing them with new NIH grant programs and other supports for various career stages (Wyngaarden 1984a, 573–4; 1984b, 97–8; 1986a, 47–8; 1987, 871–2; Healy and Keyworth 1985, 1451; Vaitukaitis 1991, 153–4; Ahrens 1992, chs. 7, 11); revising the policies of medical schools to facilitate entry into research careers and enhance their stability; and reducing economic disincentives, like the burden of medical student debt, the payback provisions of the National Research Act, and the lower incomes of researchers compared with those of specialized practitioners.

These analyses often pursued the distinctions, noted earlier, that put MD researchers at a disadvantage in comparison with PhDs and could discourage decisions to enter or persist in a research career. Many proposals therefore aimed to provide physicians with sustained, high-quality research training (Thier, Challoner, Cockerham, et al. 1980;

Bickel, Sherman, Ferguson, et al. 1981, 1267–8; Ebert 1986, 67–8; Wyngaarden 1979b, 1060; 1984b, 159; 1985, 97–8; 1986b, 267–8; Goldstein 1986; Levey, Sherman, Gentile, et al. 1988, 417, 418; Kelley 1988, 369–70; NRC 1989, vol. 1, 76–7; Neinstein and MacKenzie 1989; Smith 1989, 113–17; Martin 1991; Ahrens 1992, 7–8 and ch. 11, esp. 155; Baker, Levey, and McGinnis 1993, esp. 123–5; IOM 1994, 162–4, 191–3; Crowley and Thier 1996, 1159–60; Nathan 1998) and protected time (Wyngaarden 1979b, 1259; Thier 1981, 482–3; IOM 1981, 13, 35; Glickman 1985; Kelley 1988, 368; Healy 1988, 1063; Levey, Sherman, Gentile, et al. 1988; Ahrens 1992, 158; Thompson and Moskowitz 1997). Others aimed to ensure funding over the course of a career for which the intensive preparation might seem a risky investment (e.g., Wyngaarden 1983a; 1983b). Finally, some called for abandoning the ideal of the triple threat; to remain productive as clinical researchers, MDs would have to give up patient care (e.g., Glickman 1985; Petersdorf 1981; 1986; Healy 1988; 1992; Kelley 1988, 368–70; cf. Wintrobe 1970). Academic physicians not engaged in research could help finance departmental operations by providing practice income (compare endnote 2).

Especially during the 1980s, these analyses motivated new policies. The NIH established programs to support research careers at various stages, and the federal government maintained modest growth in the NIH budget (Wyngaarden 1984b; 1986b; 1987; Iglehart 1984). Wyngaarden (1984a, 569) therefore thought it an "exaggeration" to characterize clinical research as in crisis; it was rather "in a period of adjustment"; others too expressed some relief (cf. Kelley 1988; Evans, Hendee, and Loeb 1993, 136–8; Ahrens 1992, 171). The discussions have nevertheless persisted. Congress remained concerned about the effectiveness of research training (NRC 1989; Baker, Levey, and McGinnis 1993); some researchers regarded the new policies as uncertain and inadequate (Healy 1988; Ahrens 1992; 1993; NIH 1997); and others saw a mismatch between the numbers of researchers trained and the research support available to them (Wyngaarden 1986a, 46–7; 1987, 80–1; Healy 1988, 1061–2; Movsesian 1990; Ahrens 1992, 126–7; Cadman 1994). Some found continuing problems in the system of research training (IOM 1994, ch. 4; NIH 1997; Nathan 1998), believed that institutional arrangements at NIH have slighted clinical (as opposed to laboratory) research (Marshall 1994; NIH 1997; *Science* 1997; Agnew 1998; Williams, Wara, and Carbone 1997), and insisted (as noted in the next

section) that support for basic studies was inadequate (Ahrens 1992; 1993, Marshall 1994; Goldstein and Brown 1997). Meanwhile, declining recruitment and poor retention of physician manpower seem to have continued (Gallin and Smits 1997; Thompson and Moskowitz 1997; NIH 1997). What is striking about the recent literature (IOM 1994; NRC 1994, esp. ch. 5; Crowley and Thier 1996; NIH 1997) is the persistence of the same issues, modes of analysis, and policy ideas first articulated in the late 1970s. Short-term policy changes, aimed at incremental adjustments in existing institutional and financial arrangements, did not solve the long-term problems of clinical research or produce a consensus about how best to assure its future. New departures are needed.

In summary, concern among clinical researchers about the supply of physician–scientists and the growing prominence of PhDs emerged in the 1970s and persisted thereafter. Initially, researchers ascribed these problems to the assault by the Nixon administration on NIH research training and to declining federal support of research. However, the idea of a labor market and the metaphor of the pipeline broadened their vision and oriented them toward adjusting the institutional and financial arrangements that produce researchers to meet the extent of need demonstrated by the NAS committees. Researchers identified disincentives to entering or pursuing careers in medicine and clinical research and devised remedies. They invoked various policy levers, involving training programs, medical schools, and specialty boards. They aimed not only to remove disincentives, but also to improve the competence of physicians as researchers and enhance their ability to compete for funding with PhDs. Many participants in the discussions recognized that the era of the triple threat was gone and that research could not be combined with the typical demands placed on clinical practitioners, even in academia. Changes in institutional arrangements and funding mechanisms brought modest relief but did not eliminate concern about the viability of clinical research. Researchers continue to discuss and polish the same sorts of incremental measures first proposed more than twenty years ago.

Conservative Vision

Clearly, such measures did not do their job—to stem and reverse losses. This persistent failure might have suggested to researchers the need to

rethink their field in the light of novel conditions and reconfigure their policy goals. However, such a move has been inhibited by several factors. Because most researchers adhered to traditional conceptions of the field (even while conceding the importance of applications), their goal has been to recover or at least approximate the status quo ante. Because they perceived the problem as recruitment and retention and analyzed it in terms of short-terms changes in a labor market, their policy ideas have taken the form of incremental adjustments in standard funding mechanisms and institutional arrangements. Moreover, to justify their policy prescriptions, researchers recapitulated vague, and now discredited, claims about the relations of basic and applied research. However, if analyzed, their new emphasis on applications might force them to offer more concrete justifications for policy, but at the cost of reconceiving their field. This section explores their conservative views; the next shows how the labor-market thinking and vagueness prevent researchers from reformulating research policy governing their field.

Their conservatism was not univocal. Analyzing their diverse conceptions can signal how they understood changes in their field and illuminate the limits on their policy horizons. One vision embraced the laboratory but tried to avoid assimilation of clinical to laboratory research by stressing another (previously largely tacit) element of clinical research: its focus on intact patients. A second defended the traditional focus on clinical phenomena (as opposed to the cellular and subcellular ones of the laboratory) to preserve a more traditional realm of clinical research as a basic–applied science. A third, partially overlapping with the second, conceived of clinical research as a bridge between laboratory science and practice, supplying novel observations and theories for elucidation in the laboratory and generating practical applications from laboratory innovations. This position became predominant in the discussions. A fourth implied the need to reconceptualize the field, for its advocates (a small minority) held that the rise of the laboratory deprived clinical scientists of the means to generate basic knowledge of disease; for them, only applications are left to physician–scientists. These four positions are considered here in turn.

In the first, some researchers embraced the laboratory but articulated new foundations for an autonomous clinical science. They accepted the centrality of subcellular phenomena, but claimed that clinical, unlike laboratory science, concerned itself with intact patients (compare the discussion of Wood [1963] in the section above, "The Dissolution of the

Golden Age"). Ahrens (1977; 1992), for example, advanced the concept of "patient-oriented research" (POR), which took an integrative approach to the whole patient, unlike in vitro studies (for him the main form of laboratory research), which were reductionistic. He also distinguished "basic" from "applied" POR, believing the former to have been neglected in favor of applied science (1992, esp. ch. 12). To illustrate basic POR, he cited mechanistic study of fatty diets, undertaken with reference not to clinical states, but to such factors as "the concentration of circulating lipids and lipoproteins" or "changes in clotting mechanism, membrane permeability, or the rheologic qualities of blood" (178). As a commendable example (178; cf. Krause 1980, 258), he cited Weatherall's "description of the Mediterranean anemias" (1982), but no clinical picture of anemias appears in that book, which treats the "new [molecular] genetics" and "human molecular pathology" (Weatherall 1980, 408, for the quotations; see also his 1991).

These examples suggest how laboratory science had dissolved clinical pictures of disease into bundles of measured values of cellular products or molecular processes, causing clinical researchers to descend from the level of clinical to that of laboratory phenomena (Theodore M. Brown: private communication, 1995; cf. Engel 1980; Weissmann 1987, 147–60). Unlike the once prevalent basic–applied science, this version of clinical research did allow laboratory measurement to eclipse the clinician's account of the patient's condition. What would prevent assimilation of clinical to basic science was its integrative perspective (cf. Lipsett 1981, F-5). By emphasizing the whole patient as the field in which biological mechanisms operate, Ahrens hoped to fashion a standard to rally those resisting the reduction of the science of disease to the laboratory sciences. His standard excluded in vitro studies from POR (although not from clinical research [Ahrens 1992, 43]); however, its foundation was no longer the clinical picture presented by the patient but, rather, the basic biological phenomena at work within. The laboratory, not the clinic, defined the phenomena to be investigated.

Others offered similar ideas. Glickman (1985) acknowledged that the revolution in biology had at first left clinical researchers behind but now dominated their field. The laboratory would permit the physician to remain central to the production of basic knowledge of disease. Goldstein, in his presidential address before the ASCI (1986), found among clinical researchers a new malady, "PAIDS (Paralyzed Academic Inves-

tigator's Disease Syndrome)." Ostensibly seeking fundamental knowledge, its victims were instead pursuing only "pure clinical research" (853), that is, "observations on patients" made by "clinical scholars." He contrasted them with physicians who "learn to think like basic scientists" (853–4) and who, after an intense sojourn in basic-science departments, should return to clinical departments and there "be allowed to approach patients from a scholarly, academic viewpoint" (849). Like Ahrens, Goldstein sought to distinguish clinical from laboratory science by preserving the patient as the source of the phenomena under study and the arena for their analysis. Advocates of this position (henceforth, "basic POR") thus updated a traditional argument: physicians could still produce basic knowledge about disease of a sort that was unlikely to emerge from the basic sciences, that largely lacked short-term practical relevance, but that could create the foundation on which future practical improvements would rest (Ahrens 1992, ch. 12; Goldstein and Brown 1997).

The second conception of clinical research was more traditional because it stressed the centrality of clinical as opposed to laboratory phenomena. From at least the early 1960s, some clinicians responded to the biological revolution by citing evidence that clinical research, as a basic–applied science anchored in clinical phenomena, could still produce scientific knowledge about human disease. At the AAP, Castle (1960, 3) remarked that because investigation of disease had moved from study of patients to that of "laboratory animals, tissues, cells, and biochemical systems *in vitro,* the clinical investigator goes less often to the bedside and spends more time at the laboratory bench." However, the researcher should not "pursue too far problems that have become possible of solution by preclinical as well as by other [that is, nonmedical] basic scientists . . . . [A]dmiration for . . . basic science should not lead us as physicians to depreciate the unique opportunity and responsibility of the clinical investigator" (4). The achievements of clinical investigators provided "many examples of matters now under intensive scrutiny by basic scientists that became apparent originally from the bedside study of disease." He concluded (5) that "the all-important task of the clinical investigator is to take the essential first step away from the bedside toward the laboratory" and thereafter turn to a new problem centered on the clinic.

Beeson (1967) also defended traditional clinical research before the AAP. Although granting the propriety of any techniques for studying

clinical problems, he worried about the entry of basic-scientific methods into the field. Clinicians who used them studied simpler systems than human beings, approached problems in ways little different from basic scientists, and found collegiality among them but remained less competent than PhDs to undertake basic scientific research. Clinical researchers could "take a giant step by perceiving some previously unrecognized association, such as that between maternal rubella and congenital defects," he held, and he cited a newly recognized molecular disease, leucine-induced hypoglycemia, as having emerged from clinical observation. He also emphasized nosology, remarking that many supposedly single diseases were probably collections of disorders that the clinical researcher could discriminate. Beeson pursued this theme in several papers (e.g., 1977; 1979; 1980; Beeson and Maulitz 1988, 23–4); Beecher (1960) issued an entire book on it; and Strauss (1960; 1964) and Kunkel (1962) made similar claims.

In the recent discussions, several figures pursued this theme. Hirsch (1981, C2) and Warren (1983, 338) insisted that clinical research required substantive involvement with patients and excluded strictly in vitro studies. Thier (1980, 249–50) noted that after World War II, scholarship "was defined as research, and all too frequently as laboratory research. Clinical observation, critical reassessment of existing data, clinical trials, were all awarded lesser status than biochemically and physiologically based investigation." He objected that "departments of internal medicine had become departments of applied physiology and applied biochemistry more than of clinical medicine." He urged medical schools to adjust standards of scholarship in order to recognize the "clinical scholar who reassesses clinical data and comes up with a new concept of the natural history or management of a disease." The laboratory thus had threatened researchers' traditional focus on nosology, the long-standing anchor for its autonomy (cf. Moore 1964; Weatherall 1982, 407). Defenders of this tradition denied that the intrusion of the laboratory either diminished the significance of the task or undermined the methods of the clinical researcher; in the policy discussions, they aimed to preserve it against the tide of laboratory research through mechanisms of institutional and professional support.

Some advocates of this second view of clinical research created a third one by linking it to applied science. Thier and others, in defending traditional clinical science, portrayed it as bridging laboratory science

and practice, contributing both basic knowledge (by generating basic knowledge on its own or especially by supplying the results of clinical studies to the laboratory) and applications (by "translating" the results of basic science into practical novelties). This theme came to predominate in the late 1970s and after, appearing in the 1977 report of the NAS committee (NRC 1977, 110) and in the 1980 report of the AAMC, which attributed to clinical researchers a "cross-over role" (Thier, Challoner, Cockerham, et al. 1980, 87; reflected in NRC 1981, 25). At the IOM conference noted earlier, its president, David A. Hamburg, gave voice (1981) to this view in a passage that Wyngaarden quoted frequently (see also Paul 1981), and Oates (1982) adopted much the same position before the AAP.

In this discourse, Ahrens's term, "patient-oriented research" (POR), was occasionally appropriated to describe research likely to yield new applications (although Ahrens himself emphasized "basic" POR). In his paper, "The Priority of Patient-oriented Research for NIH" (1985), Wyngaarden defined POR broadly, recalled Hamburg's comments, and claimed (95) that "because much of the knowledge and understanding gained from ... molecular biology are now beginning to move toward clinical application ... we will need a steady supply of well-trained physician scientists to help in the incorporation of this new knowledge into the working motifs of medicine." Kelley (1988), Smith (1989), the IOM (1988), and Vaitukaitis (1991) followed much the same path, offering a spectrum of activities in clinical research and stressing its value as a source of practical improvements. A similar view marks two of the most recent substantial studies of clinical research (IOM 1994, 27 for "bridging scientist," 28 for "technology-transfer agents"; NRC 1994, esp. ch. 5; cf. Crowley and Thier 1996). The IOM offered (35) a broad definition of clinical research, but focused on "patient-oriented," "hands-on," or, simply, "human research" as the kind of research that permitted the translation of scientific novelties into new practices. This view juxtaposed a traditional conception of clinical research with the possibility of frequently generating short-run practical achievements. Advocates of this position emphasized that only MDs, who (unlike PhDs) are endowed with knowledge of disease and skills for clinical observation, could pursue these conjoint roles. The PhD might have a role in clinical research, but the physician must dominate. Proponents of this view have been among the most prominent voices in the policy discussions.

A fourth view questioned or disregarded the ability of clinical research to produce basic knowledge. The revolution in biology at last has enabled laboratory science to provide foundations, exploitable in the short run, for innovation in medical practice, but it has also shifted the locus of basic research out of clinical departments, and even out of medical schools, into nonmedical basic science departments (Barondess 1983, 262; Gill 1984, 364–5; Littlefield 1986; Kelley 1988; Smith 1989, 108; Ebert 1992, 739; cf. Castle 1960). Gill (1984, 368) found it "ironic that a separation [of physicians from scientists] occurred when physicians became scientists [i.e., practiced medicine on a scientific basis], and when the work of basic scientists became clinically relevant." The golden age was over, the high road to basic knowledge was no longer available to physicians, but the new world of clinical science qua development at least offered the potential for improving the care of the sick. Others pressed "translation" without commenting on the ability of clinical science to produce basic knowledge, in effect conceding that the field was an applied science (e.g., Morgan and Jones 1976, 5–23; Thier and Morgan 1979; Bickel, Sherman, Ferguson, et al. 1981; Sherman, Jolly, Morgan, et al. 1981, 1; Littlefield 1984; IOM 1988, 4; Martin 1991; Cadman 1994, 408). As Oates (1982) noted, the belief, to his mind unjustified, that clinical research is an applied science is what spurred the rise in the 1970s of more applied and targeted modes of research. It is a perspective that frankly—if reluctantly—acknowledged that the transformation of clinical research into an applied science was irreversible.

These four positions can be discerned from a close analysis of the discussions, but readers of this literature likely took home a simpler message: apart from the minority holding that only applications are left to physician–scientists, most researchers shared in a conservative consensus that gave scope to applied science but still anticipated gains in basic knowledge. The most prominent view, which was adopted in the IOM study (1994), was that of Thier, Wyngaarden, and their supporters: the best clinical scientist was a bridging scientist, who could generate scientific novelty and translate basic innovations into practical results. All agreed that it was physicians, not PhDs, who could best do this work. This consensus kept researchers focused on recruitment policies that supposed the traditional sources of manpower and the traditional career aspirations needed only modest revision. That dramatic changes implied the need for a wholly new approach to policy was scarcely suggested.

Elusive Closure

This conservative stance has been sustained by labor-market analysis and the pipeline metaphor. Although at first broadening researchers' perspectives, these tools discouraged them from pursuing the implications of recent changes in science, medicine, and politics and oriented them instead toward short-term measures. The NAS committees and other analysts of need (e.g., Sherman, Jolly, Morgan, et al. 1981; Ahrens 1992, 171–3) scarcely affected the prevailing belief in the inadequacy of supply because they never produced scientifically well-founded estimates (Ahrens 1992, 154, 181) of need. The 1989 report gave priority to judgment over projections; the "Panel on Estimation Procedures" serving the latest NAS committee questioned whether any well-founded forecasts of demand could be made (NRC 1989, vol.1, esp. 3, 63–6; 1994, 21–2); and the IOM study (1994) doubted that even an accurate census of active researchers could be obtained. These costly analyses therefore never enabled the fine-tuning envisioned by Congress between the resources it supplied for research training and the extent of need for researchers. Moreover, NAS committees never brought their recommendations to the level of individual disciplines; despite efforts to achieve that degree of discrimination, they stuck throughout to the broad categories (basic biomedical sciences, behavioral sciences, clinical sciences, and health services research first used in 1975, with the later addition of nursing and oral health research) (NRC 1975b; 1994; cf. NRC 1975a). The recommendations of the latest NAS committee thus differed little in character from those of twenty years before: the extent of need and recommendations about supply were predicated on informed guesses about short-term changes in prevailing arrangements (cf. Crowley and Thier 1996). More important, the committees did not inquire whether those arrangements were appropriate to altered conditions. Similarly, the perceived problems of supply and the solutions proposed in the IOM study (1994) and in the final report of the NIH director's Clinical Research Panel (CRP) (NIH 1997; Nathan 1998), as well as recent initiatives of the NIH (Shulman 1996; Marshall 1998; Agnew 1998), are similar to those articulated by the AAMC in 1980 (Thier, Challoner, Cockerham, et al. 1980). While deploring the persistent decline of their field, researchers have tinkered with incremental measures, even though they themselves have shown that its difficulties derive not from short-

term trends, but from profound changes in science, medicine, and public expectations.

Another obstacle to closure lies in the vagueness of the ideas that researchers drew from an earlier era to justify their proposals. Advocates of basic POR defended the usual policy measures by claiming that, in the past, success in research depended on personal and intellectual qualities[3] that they alleged had become rare. Past research-training programs supposedly fostered them; updated ones would restore what amounts to a moral environment for their renewed cultivation (Ahrens 1992; chs. 11, 15–16; Goldstein and Brown 1997). Moreover, support of basic POR rests on the nebulous and shopworn supposition that disinterested pursuit of knowledge would eventually improve medicine. Such a view is unlikely to be treated with sympathy in an environment that demands accountability from researchers in the form of medical progress. In addition, ideological arguments for manpower policies have increasingly met with skepticism (Fox 1996). Managed care also seems to threaten the capacity of medical schools to support research (Blumenthal and Meyer 1996; Crowley and Thier 1996; Mechanic and Dobson 1996; NIH 1996; Gallin and Smits 1997; Matherlee 1995; Reuter and Gaskin 1997; Skirboll 1997; Agnew 1998; Meyer, Genel, Altman, et al. 1998; Nathan 1998), particularly if it is costly and lacks practical application. Partisans of basic POR thus sustain their conservative vision with vague ideas about the virtues and promise of disinterested research that are likely to ring hollow in the current policy world. It is therefore not surprising that, just as some advocates of translation invoked Ahrens's term, POR, some supporters of basic POR have taken to labeling as "translational" forms of research that Ahrens (1992) had classified as basic POR (NIH 1996, 12; Shulman 1996, 398; for an early intimation, see Carpenter 1988, cxxxi). Advocates of applied science have held politically more viable goals than proponents of basic POR, but stated them equally vaguely. "Translation" appeals to researchers as being consistent with the traditional assumption that practical results would flow readily from scientific advances, but it has not been thoroughly articulated or studied,[4] and the concrete measures likely to foster it remain unclear (apart, perhaps, from the case of training for the conduct of clinical trials). If "translation" is to motivate policy change, however, it needs instead to be specified and linked with proposals well-tailored to advance it. Some implications of doing so are considered briefly below.

Conservatism, labor-market thinking, and vagueness thus inhibited researchers from conceiving clear and politically viable policy goals and measures well suited to achieving them. A telling illustration of these circumstances lies in the preference, among advocates of both translation and basic POR, for supplying researchers with intensive, high-quality research training heavily weighted toward the basic sciences. Such training seemed an appropriate response to the scientific advances that have made clinical research a more demanding career. The form of intensive research training most favored by all parties (with the salient exception of Ahrens) was the MD/PhD program. Among advocates of basic POR, intensive research training, especially via the MD/PhD, was seen as likely to instill the allegedly rare qualities of the successful researcher (Goldstein 1986; Goldstein and Brown 1987); and, among advocates of translation, MD/PhD programs were viewed since the late 1970s as inherently suited to producing the bridging scientist (NRC 1976, 26; 1977, 126). Thereafter, proponents of intensive research training invoked studies suggesting that, among all forms of research training, MD/PhD programs were the most successful in launching scientists on productive research careers (e.g., Thier and Morgan 1979; Bickel and Morgan 1980; Thier, Challoner, Cockerham, et al. 1980; Bickel, Sherman, Ferguson, et al. 1981, 1268; Wyngaarden 1984a; 1985; 1987; Ebert 1986; Martin 1991; IOM 1994, 55, 58–9; Goldstein 1986; Goldstein and Brown 1997).

However, advocates of translation did not consider what was implied by the housing of the Medical Science Training Program (MSTP) under the National Institute for General Medical Sciences (which supported the basic sciences), or by the decision of the NAS committee (NRC 1978, 12) to reclassify—consistently with NIH practice—the MSTP under basic instead of clinical sciences. Indeed, neither did the NAS committee itself, which noted (IOM 1983, 25) its "enthusiasm" for the MSTP. Nor did partisans of MD/PhD programs assimilate evidence, available at least since 1981, that MD/PhDs performed as much laboratory as clinical research (Sherman, Jolly, Morgan, et al. 1981, ch. 4; NRC 1981, 32; cf. NRC 1977, 126). Similarly, advocates of both translation and basic POR failed to take in Ahrens's evidence (1992, 169) that most research done by MSTP graduates was not clinical research but reductionistic laboratory research and that other forms of intensive research training in basic science would likely have similar results (cf. IOM 1994, 154–5). More recently still, Sutton and Killian (1996) offered

evidence that MD/PhDs were unlikely to do the translational research anticipated by its advocates (cf. NIH 1998). A policy measure—and an expensive one at that—has been pressed on the assumption that it will serve the conservative policy goals of its advocates, despite available evidence to the contrary. Vague and unexamined assumptions fostered by a backward vision can scarcely justify public expenditures or advance goals of public policy. Some observers have recognized that new sorts of MD/PhD programs may be needed (e.g., Swisher 1980; Littlefield 1984; Ross 1985; Ahrens 1992, 209; Shine 1998, 1443), but they have done little to flesh out these ideas or to exploit them in a major new policy initiative.

Among advocates of the bridging scientist, emphasis on traditional research training in standard institutional settings may also reflect disquiet in contemplating the applied-science end of the bridge. Analyzing applied science is likely to lead clinical researchers into the domain of outcomes research, evaluative sciences, clinical epidemiology, and medical decision making (broadly, health services research), activities that investigate the character and effectiveness of innovations in medical practice and public health. However, the leaders of clinical research have long kept these fields at arm's length, both intellectually and professionally. As noted earlier, the NAS committees used a fourfold taxonomy that separated clinical sciences from health services research and thus kept out ideas and practices that might afford a substantive conception of "translation." Indeed, Thier's address (1992) at a conference on outcomes research clearly suggests its "otherness" in the eyes of clinical researchers (cf. Schrier 1997). Vagueness in pronouncements about translation thus seems sustained by hesitation before the novel implications of articulating it substantively.

However, there have been signs of change. Although largely as asides or as part of an effort to model the diverse forms of research, some participants in the discussions have linked "translation" with health services research (e.g., DeGroot and Siegler 1979, 1287; Littlefield 1984; Kelley 1988; Larson 1988; Wennberg 1988; Martin 1991, 127; Weatherall 1991; Goldman, Cook, Orav, et al. 1990; Cadman 1994; Crowley and Thier 1996; NIH 1996), a view reflected in the IOM study (1994), as noted at the outset of this essay. The study also approvingly cited (56–7) the sponsorship, by the professional societies of clinical researchers, of symposia "for the novice" on clinical epidemiology and health services research, as well as (99–101) the health services research supported by the Agency for Health Care Policy and Research (AHCPR).

Similarly, the Clinical Research Panel (NIH 1997, 1; cf. Nathan 1998) defined clinical research to include "[e]pidemiological and behavioral studies" and "[o]utcomes research and health services research." In part, this breadth issued from the hope that managed care organizations, insurers, and the pharmaceutical industry might possess both exploitable data and willingness to help fund their analysis by clinical researchers (NIH 1997, 5–6; Skirboll 1997; Meyer, Genel, Altman, et al. 1998). Moreover, independently of the NIH or other agencies, some medical schools have begun to accommodate health services research within clinical research (Shulman 1996; Schrier 1997). Thus, some have recognized that social–scientific practices outside the traditional boundaries of the clinical research could anchor "translation," but this development remains exiguous and tentative.

In summary, despite modest successes in supporting recruitment, training, and careers, researchers have remained dissatisfied with the state of their field. They have persisted in assessing its problems in terms of labor-market models with short time horizons and tight links to standard modes of training and practice. While the traditional enterprise continued to erode, they adopted conservative visions of their field and espoused vaguely articulated polices that are little suited to meet their goals and unlikely to garner public support. Only a minority of observers acknowledged that changes in clinical research have pushed it definitively toward applied science, and, although a few glimpse the growing pertinence of health services research, most advocates of translation have kept their distance from the social–scientific practices and disciplines. However, there are good reasons for the leaders of clinical research to take health services research more seriously. Changes in science, medicine, and public expectations mandate a close analysis of applied science, the meaning of "translation," the kinds of research practice and collaboration—with PhDs in the social as well as biomedical sciences—that are likely to foster it, the implications for the training of researchers, and the policies appropriate to these goals (cf. Eisenberg 1993).

Reorienting policy for clinical research toward health services research will not be easy. It will require researchers not only to explore and engage themselves in the unfamiliar realm of the medical social sciences, but also to identify with and support institutions and policy spheres other than those centered on the NIH. The principal source of federal funds for health services research is the AHCPR. Its budget (for

FY 1998, $146.4 million) is a tiny fraction (about one-thousandth) of that of the NIH (for FY 1998, $13.6 billion), and its political strength and prestige are commensurately modest. Its future rests on its ability to respond, without offending powerful interests, to congressional demands for efficiency in the organization and provision of health care (Wadman 1996; Kahn 1998; Mendelson et al. 1998). If clinical researchers join forces with the agency and its constituencies, they would enter a policy world that is small and vulnerable. Although daunting, such an alliance may be the most promising way to halt the persistent decline of clinical research and to construct socially accountable policies for its guidance.

Conclusion

Clinical researchers have been discussing the status and future of their field for over twenty years, with little sign of closure. The discussions mark the latest stages in a history that spans the present century. Working in American medical schools that had been reformed by advocates and practitioners of laboratory science and their philanthropic patrons, clinical researchers attempted to establish what Kohler calls a basic–applied science. Dominated by academic clinicians, clinical science would exploit new measuring devices and clinical biochemistry to identify, characterize, and analyze human disease. To produce this sort of basic knowledge was the principal goal of researchers, but they also anticipated that improvements would readily follow in medical practice and public health. Through the 1930s, this project seemed successful despite its inherent instability. In the postwar era, clinical science, like laboratory science, benefited from the immense prestige that medical research had gained from its role in the war. Federal funding supported the training of numerous practitioners and fostered specialization and institutional expansion. However, even before the zenith of this "golden age," the biological revolution and the impatience of Congress for practical payoffs from its investments in research pushed clinical research toward the opposing poles of laboratory research and applied science. The Nixon administration's assault on research training and the leveling of federal funding elicited from researchers their still ongoing introspection, analysis, and discussion.

The discussions, cast largely in labor-market terms, allowed researchers to identify factors that inhibited recruitment, created deficiencies in training, and destabilized careers, and to recommend changes in institutional arrangements and funding mechanisms. Some of these recommendations resulted in policy measures in the 1980s that provided some stability, but researchers did not perceive sufficient improvement to abandon their repetitive scrutiny of their science; indeed, most believe the field remains in decline. They justified their recommendations by emphasizing either the production of basic knowledge of human disease or the bridging role that would permit "translation" of scientific novelty into practical improvements. However, their conservative vision has inhibited policy innovation, as suggested by their support of MD/PhD programs, which they assumed were well suited to support traditional forms of clinical research, but have been shown to be of doubtful value for that purpose. Conservatism also inhibits researchers from analyzing the traditional belief that scientific results can be straightforwardly turned into applications; under present conditions, "translation" implies that clinical research may have to embrace outcomes research, clinical decision making, and clinical epidemiology, areas from which it long held itself aloof. What seems to be in order among researchers is a frank recognition, thus far confined to a minority, that scientific changes, medical specialization, and intensified demand for public accountability have put an end to traditional clinical science. By analyzing what "translation" may be taken to mean under new conditions, how practitioners should be trained to foster it, and how best to collaborate with PhDs, not only in the basic sciences but also in the social sciences, researchers might at last achieve consensus on policy in support of their field and unite around efforts to attain its realization. Doing so, however, will involve a major reorientation toward health services research and toward the new and thus far little nourished institutions for its support.

ENDNOTES

1. For the context of both clinical epidemiology and clinical decision making, see Berg (1997); for programmatic statements and commentary on outcomes research, see Ellwood (1988), Relman (1988), Epstein (1990), Geigle and Jones (1990), Tanenbaum (1994). References affording entry into the pertinent literatures include (1) for clinical decision making: Lusted (1968); Raiffa (1968); Kassirer (1976); Weinstein, Fineberg, Elstein, et al. (1980); Beck, Pyle, and Lusted (1984); Eddy (1986); and Kassirer, Moskowitz, Lau, et al. (1987); (2) for clinical epidemiology: Sackett (1969); Feinstein (1968a; 1968b; and 1968c; 1972; 1985); and White (1991); (3) for out-

comes research: Brook, Ware, Davies-Avery, et al. (1979); Bergner (1985; 1989); Devo and Patrick (1989); Lohr (1989); Greenfield and Nelson (1992); Tarlov, Ware, Greenfield, et al. (1989); *Health Services Research* (1990); Testa and Simonson (1996); and Slater (1997); and (4) for health services research generally: Flook and Sanazaro (1973); Aiken and Mechanic (1986); Anderson (1991); and Ginzberg (1991).

2. This path was made possible by the growth of practice fees as a source of income that financed expansion of clinical departments (Ebert 1977; 177–8, 181; 1986, 74; IOM 1983, 21–3; Petersdorf 1983, 1055–6; Jones, Mirsky, and Keyes 1985; Chin, Hopkins, Melmon, et al. 1985; Herman and Singer 1986; Lewis and Sheps 1983, 89ff, 175; Beaty, Babbott, Higgins, et al. 1986; Healy 1988, 1061–2; IOM 1985, 4, 5, 19, 27–8; Ahrens 1992, 27–8; Taskel, Jolly, and Beran 1989; Jolin, Jolly, Krakower et al. 1992). However, competition threatens to erode traditional sources of practice income (Mechanic and Dobson 1996; Reuter and Gaskin 1997; Skirboll 1997).

3. E.g., physicians showing "technical courage" (Goldstein 1986, 849) or who "are broadly versed, intensely curious, and infectious in their ability to stimulate others to think deeply about human disease" (Goldstein and Brown 1997, 2803). Ahrens wanted to train the researcher in "the *meaning* of research—its style and historical background—and build on his eagerness to tackle a problem with probes that successfully explore the hypothesis," and he wanted "to ensure that this trained person becomes capable of recognizing new research opportunities and knows how to capitalize on them . . . *In . . . other words, support people, not projects*" (Ahrens 1992, 157; emphases in the original).

4. The idea of "translation" and the notion of "boundary objects" that enable and support it has been a theme of the field of science and technology studies. See, e.g., Latour 1987; Star 1989; Fujimora 1992. Although this literature has not been invoked in the discussions of clinical research, one recent monograph, Löwy (1996), explores translation in ways that speak to clinical research. She uses both history and sociology to argue that translation requires sustained effort to articulate and maintain links, both intellectual and material, between medical practitioners and laboratory researchers. In other words, what the clinical researchers call "bridging" was not constituted by a special kind of researcher strategically placed between the laboratory and the clinic, but by the work of scientists on the one side and clinical practitioners on the other to create objects and practices that mediated their distinct concerns. Here is further evidence for the difficulty in creating and maintaining a basic–applied-science.

References

Abbott, A. 1988. *The System of Professions: An Essay on the Division of Expert Labor.* Chicago: University of Chicago Press.

Agnew, B. 1998. New NIH Procedures to Shield Clinicians from Grant Bias. *Scientist* 12(10):1,14.

Ahrens, E.H., Jr. 1977. Changing Patterns in Clinical Investigation. In *Trends in Biomedical Research, 1901–1976.* Proceedings of the Second Rockefeller Archive Center Conference, December 10, 1976, 57–61. New York: Rockefeller Archive Center.

———. 1992. *The Crisis in Clinical Research: Overcoming Institutional Obstacles.* New York: Oxford University Press.

———. 1993. Institutional Obstacles to Clinical Research. *Perspectives in Biology and Medicine* 36:194–209.

Aiken, L.H., and H. Freeman. 1984. Medical Sociology and Science and Technology in Medicine. In *A Guide to the Culture of Science, Technology, and Medicine*, ed. P.T. Durbin, 527–80 (paperback ed.). New York: Free Press.

Aiken, L.H., and D. Mechanic. Eds. 1986. *Applications of Social Science to Clinical Medicine and Health Policy.* New Brunswick, N.J.: Rutgers University Press.

Albright, F. 1944. Some of the 'Do's' and 'Do Not's' in Clinical Investigation. *Journal of Clinical Investigation* 23:921–6.

American Foundation. 1955. *Medical Research: A Midcentury Survey.* Prepared by E.E. Lape (2 vols.). New York: American Foundation and Little, Brown.

Amsterdamska, O. 1987. Medical and Biological Constraints: Early Research on Variation in Bacteriology. *Social Studies of Science* 17:657–87.

Anderson, O.W. 1991. *The Evolution of Health Services Research: Personal Reflections on Applied Social Science.* San Francisco: Jossey–Bass.

Association of American Medical Colleges. 1962. Research and Medical Education: Report of the Ninth Teaching Institute, Association of American Medical Colleges, Colorado Springs, Colorado, December 3–7, 1961, ed. J.H. Comroe. *Journal of Medical Education* 37(12, pt. 2).

———. 1971. A Policy for Biomedical Research. *Journal of Medical Education* 46:691–743.

———. 1974. *Biomedical Research Manpower: Report of a Conference Held October 1–3, 1973 . . . .* Washington, D.C.

———. 1983. *Preserving America's Preeminence in Medical Research: Principles for Support of Biomedical Research.* Washington, D.C.

Association of Professors of Medicine and Association of American Medical Colleges. 1989. *Post-doctoral Research Training of Full-time Faculty in Departments of Medicine*. Prepared by N.O. Gentile, G.S. Levey, P. Jolly, and T.H. Dial. Washington, D.C.: Association of American Medical Colleges.

Axelrod, L. 1970. Bones, Stones, and Hormones: The Contributions of Fuller Albright. *New England Journal of Medicine* 283:964–70.

Baker, J.G., G.S. Levey, and R. McGinnis. 1993. Biomedical Research Scientists: Issues of Labor Supply and Training Quality. In *The Education of Physician–Scholars: Preparing for Leadership in the Health Care System,* eds. H.M. Swartz and D.L. Gottheil, 119–28. Rockville, Md.: Betz.

Barondess, J.A. 1983. The Doctor, the Patient, and the System: Reflections on Education for Clinical Careers. *Perspectives in Biology and Medicine* 26:261–73.

Beaty, H.N., D. Babbott, E.J. Higgins, P. Jolly, and G.S. Levey. 1986. Research Activities of Faculty in Academic Departments of Medicine. *Annals of Internal Medicine* 104:90–7.

Beck, J.R., K.I. Pyle, and L.B. Lusted. 1984. A Citation Analysis of the Field of Medical Decision Making, 1959–1982: Computer-aided Diagnosis and Clinical Decision Analysis. *Medical Decision Making* 4:449–68.

Beecher, H.K. Ed. 1960. *Disease and the Advancement of Basic Science.* Cambridge, Mass.: Harvard University Press.

Beeson, P.B. 1967. The Academic Doctor. *Transactions of the Association of American Physicians* 80:1–7.

———. 1977. The Development of Clinical Knowledge: With a Few Words about Targeted vs. Basic Research. *Journal of the American Medical Association* 237:2209–12.

———. 1979. The Growth of Knowledge about a Disease: Hepatitis. *American Journal of Medicine* 67:366–70.

———. 1980. Changes in Medical Therapy during the Last Half Century. *Medicine* 59(2):79–99.

Beeson, P.B., and R.C. Maulitz. 1988. The Inner History of Internal Medicine. In *Grand Rounds: One Hundred Years of Internal Medicine,* eds. D.E. Long and R.C. Maulitz, 15–54. Philadelphia: University of Pennsylvania Press.

Ben-David, J. 1960. Roles and Innovations in Medicine. *American Journal of Sociology* 65:557–68.

Benison, S. 1977. The Development of Clinical Research at the Rockefeller Institute before 1939. In *Trends in Biomedical Research, 1901–1976,* 35–45. Proceedings of the Second Rockefeller Archive Center Conference, December 10, 1976. New York: Rockefeller Archive Center.

Bennett, I.L., Jr. 1977. [Medical] Technology as a Shaping Force. In *Doing Better and Feeling Worse: Health in the United States,* ed. J.H. Knowles, 125–33. New York: Norton.

Berg, M. 1997. *Rationalizing Medical Work: Decision Support Techniques and Medical Practices.* Cambridge, Mass.: MIT Press.

Bergner, M. 1985. Measurement of Health Status. *Medical Care* 23:696–704.

———. 1989. Quality of Life, Health Status, and Clinical Research. *Medical Care* 27(3, suppl.):S148–S156.

Berliner, H.S. 1985. *A System of Scientific Medicine: Philanthropic Foundations in the Flexner Era.* New York: Tavistock.

Berzelius, J.J. 1808. Om nödvändigheten för jordbrukare och economer att äga insigter i chemien. [On the need for agriculturalists and economists to have knowledge of chemistry.] *Economiska Annaler {of the Royal Swedish Academy of Sciences}* 5(January):47–56.

Bever, A.T., Jr. 1980. A Quantitative Assessment of Fundamental and Targeted Clinical Research at NIAMDD. In: "Clinical Research: Elements for a Prognosis," ed. A. Grahn. *Perspectives in Biology and Medicine* 23(2, pt. 2): S25–S33.

Bickel, J.W., and T.E. Morgan. 1980. Research Opportunities for Medical Students: An Approach to the Physician-investigator Shortage. *Journal of Medical Education* 55:567–73.

Bickel, J.W., C.R. Sherman, J. Ferguson, L. Baker, and T.E. Morgan. 1981. The Role of M.D.–Ph.D. Training in Increasing the Supply of Physician-Scientists. *New England Journal of Medicine* 304:1265–8.

Blake, F.G. 1931. Clinical Investigation. *Science* 74:27–9.

Blake, J.B. 1980. Anatomy. In *The Education of American Physicians: Historical Essays,* ed. R.L. Numbers, 29–47. Berkeley: University of California Press.

Blumenthal, D., and G.S. Meyer. 1996. Academic Health Centers in a Changing Environment. *Health Affairs* 15(2):200–15.

Bonner, T.N. 1990. Friedrich von Müller of Munich and the Growth of Clinical Science in America, 1902–1914. *Journal of the History of Medicine and Allied Sciences* 45:556–69.

Braunwald, E. 1975. The Training of Manpower Needed for Biomedical Research. *New England Journal of Medicine* 292:290–3.

Brook, R.H., J.E. Ware, A. Davies-Avery, et al. 1979. Overview of Adult Health Status Measures Fielded in Rand's Health Insurance Study. *Medical Care* 17(7, suppl.):entire issue.

Brown, L.D. 1992. Political Evolution of Federal Health Care Regulation. *Health Affairs* 11(4):17–37.

Burns, T.W. 1984. Physician Investigators for Academic Medicine. *Annals of Internal Medicine* 101:708–9.

Cadman, E.C. 1990. The New Physician-Scientist: A Guide for the 1990s. *Clinical Research* 38(2):191–8.

———. 1994. The Academic Physician-Investigator: A Crisis Not to Be Ignored. *Annals of Internal Medicine* 120:401–10.

Cangi, E.C. 1982. Abraham Flexner's Philanthropy: The Full-time System in the Department of Surgery at the University of Cincinnati College of Medicine, 1910-1930. *Bulletin of the History of Medicine* 56:160–74.

Carey, W.D. 1967. Funding and Managing an Accelerated Program of Applied Biomedical Research. In *Research in the Service of Man: Biomedical Knowledge, Development, and Use.* U.S. Senate Committee on

Government Operations, Subcommittee on Government Research, 90th Congress, First Session. Senate document 55: 53–7. Washington, D.C.

Carpenter, C.C.J. 1988. Today's Challenge: Rigorous Biomedical Science, Globally Applied. *Transactions of the Association of American Physicians* 101:cxx–cxxxiii.

Castle, W.B. 1960. Functional Stresses within Full-time Departments of Medicine. *Transactions of the Association of American Physicians* 73:1–6.

Challoner, D.R. 1976. The AFCR—Administrative Ischemia. *Clinical Research* 24(4):237–43.

Chin, D., D. Hopkins, K. Melmon, and H.R. Holman. 1985. The Relation of Faculty Academic Activity to Financing Sources in a Department of Medicine. *New England Journal of Medicine* 312:1029–34.

Cohn, A.E. 1924. Purposes in Medical Research: An Introduction to the *Journal of Clinical Investigation*. *Journal of Clinical Investigation* 1(1): 1–11.

Cooper, J.A.D. 1973. Statement of Dr. John A.D. Cooper, president of the Association of American Medical Colleges. In *National Health Research Fellowship and Traineeship Act of 1973. Hearings . . . on H.R. 5640 and H.R. 5948*. U.S. House. Committee on Interstate and Foreign Commerce, Subcommittee on Public Health and Environment, 65–87. 93rd Congress, First Session. Serial, no. 93-13. Washington, D.C.

Cope, O. 1966. The Story of Hyperparathyroidism at the Massachusetts General Hospital. *New England Journal of Medicine* 274:1174–82.

Corner, G.W. 1964. *A History of the Rockefeller Institute, 1903–1953.* New York: Rockefeller Institute Press.

Cowan, D.L. 1980. Materia Medica and Pharmacology. In *The Education of American Physicians: Historical Essays,* ed. R.L. Numbers, 95-121. Berkeley: University of California Press.

Crowley, W.F., and S.O. Thier. 1996. The Continuing Dilemma in Clinical Investigation and the Future of American Health Care: A System-wide Problem Requiring Collaborative Solutions. *Academic Medicine* 71:1154–63.

Culliton, B.J. 1974. National Research Act: Restores Training, Bans Fetal Research. *Science* 185:426–7.

———. 1976. Biomedical Training: Time for a Slowdown. *Science* 193:747–8.

———. 1991. Shaping Science Policy: What's Happening to Biomedical Research in America. *Academic Medicine* 66:188–91.

Culotta, E. 1993. Doctor–Doctor: Growing Demand for M.D.-Ph.D.s. *Science* 261:1784–5, 1787.

DeCesare, W.R. 1981. Clinical Research—Perspectives from the General Clinical Research Centers Program. In *Clinical Investigations in the 1980s: Needs and Opportunities. Report of a Conference. . . .* Appendix D:1–28. Washington, D.C.: National Academy Press.

DeGroot, L.J., and M. Siegler. 1979. The Morning-report Syndrome and Medical Research. *New England Journal of Medicine* 301:1285–8.

Devo, R.A., and D.L. Patrick. 1989. Barriers to the Use of Health Status Measures in Clinical Investigation, Patient Care, and Policy Research. *Medical Care* 23(3, suppl.):S254–S268.

DiBona, G.F. 1979. Whence Cometh Tomorrow's Clinical Investigators? *Clinical Research* 27(3):253–6.

Dolan, K.S., and T.E. Morgan. nd [1978]. *The Training of Clinical Researchers, 1972–1976.* Final Report for the National Academy of Sciences. Washington, D.C.: Association of American Medical Colleges.

Douglass, C.D., and J.C. James. 1973. Support of New Principal Investigators by NIH: 1966 to 1972. *Science* 181:241–4.

Dutton, D.R. 1988. *Worse Than the Disease: Pitfalls of Medical Progress.* New York: Cambridge University Press.

Ebert, R.H. 1977. Medical Education in the United States. In *Doing Better and Feeling Worse: Health in the United States,* ed. J.H. Knowles, 171–84. New York: Norton.

———. 1986. Medical Education at the Peak of the Era of Experimental Medicine. In: "American Doctors, Medical Science, Medical Care," ed. S.R. Graubard. *Daedalus* 115(2):55–81.

———. 1992. Flexner's Model and the Future of Medical Education. *Academic Medicine* 67:737–42.

Eddy, D.M. 1986. Successes and Challenges of Medical Decision Making. *Health Affairs* 5(2):108–15.

Eisenberg, J.M. 1993. A New Bridge for Clinical Research. *Hospital Practice* 28(8):8, 13.

Ellwood, P.M. 1988. Shattuck Lecture: Outcomes Management, A Technology of Patient Experience. *New England Journal of Medicine* 318:1549–56.

Engel, G.L. 1980. The Clinical Application of the Biopsychosocial Model. *American Journal of Psychiatry* 137:535–44.

Epstein, A.M. 1990. The Outcomes Movement: Will It Get Us Where We Want To Go? *New England Journal of Medicine* 323:266–70.

Evans, R.M., W.R. Hendee, and J.M. Loeb. 1993. Physician–Researchers: An Endangered Species? In *The Education of Physician-Scholars: Pre-*

paring for Leadership in the Health Care System, eds. H.M. Swartz and D.L. Gottheil, 129–40. Rockville, Md.: Betz.

Feinstein, A.R. 1968a. Clinical Epidemiology, I: The Populational Experiments of Nature and of Man in Human Illness. *Annals of Internal Medicine* 69:807–20.

———. 1968b. Clinical Epidemiology, II: The Identification Rates of Disease. *Annals of Internal Medicine* 69:1037–61.

———. 1968c. Clinical Epidemiology, III: The Clinical Design of Statistics in Therapy. *Annals of Internal Medicine* 69:1287–312.

———. 1972. Why Clinical Epidemiology? *Clinical Research* 20:821–5.

———. 1983. An Additional Basic Science for Clinical Medicine: I. The Constraining Fundamental Paradigms. *Annals of Internal Medicine* 99:393–7.

———. 1985. *Clinical Epidemiology: The Architecture of Clinical Research.* Philadelphia: Saunders.

———. 1994. *Clinical Judgment* Revisited: The Distraction of Quantitative Models. *Annals of Internal Medicine* 120:799–805.

Feinstein, A.R., and N. Koss. 1970. The Changing Emphasis in Clinical Research. III. Follow-up Report for the Years 1965-1969. *Archives of Internal Medicine* 125:885–91.

Feinstein, A.R., N. Koss, and J.H.M. Austin. 1967. The Changing Emphasis in Clinical Research. I. Topics under Investigation. An Analysis of the Submitted Abstracts and Selected Programs at the Annual "Atlantic City Meetings" during 1953 through 1965. *Annals of Internal Medicine* 66:396–419.

Finland, M. Ed. 1982–83. *The Harvard Medical Unit at Boston City Hospital.* 2 vols. in 3. Charlottesville, Va.: Commonwealth Fund.

Fletcher, S.W., R.H. Fletcher, and M.A. Greganti. 1981. Clinical Research Trends in General Medical Journals, 1946–1976. In *Biomedical Innovation,* eds. E.B. Roberts, R.I. Levy, S.N. Finkelstein, et al., 284–300. Cambridge, Mass.: MIT Press.

Flexner, A. 1910. *Medical Education in the United States and Canada: A Report to the Carnegie Foundation for the Advancement of Teaching.* Bulletin. no. 4. New York: Carnegie Foundation for the Advancement of Teaching.

Flook, E.E., and P.J. Sanazaro. Eds. 1973. *Health Services Research and R & D in Perspective.* Ann Arbor, Mich.: Health Administration Press.

Forrest, J.N., Jr. 1980. Introduction [to the Symposium]: The Decline in the Training of Clinical Investigators: Data and Proposals from the 1970s. In: "Public Policy Symposium: The Young Clinical Investigator in the 1980s." *Clinical Research* 28:246–7.

Fox, D.M. 1983. The Decline of Historicism: The Case of Compulsory Health Insurance in the United States. *Bulletin of the History of Medicine* 57:596–610.

———. 1985. History and Health Policy: An Autobiographical Note on the Decline of Historicism. *Journal of Social History* 18:349–64.

———. 1986a. The Consequences of Consensus: American Health Policy in the Twentieth Century. *Milbank Quarterly* 64:76–99.

———. 1986b. *Health Policies, Health Politics: The British and American Experience, 1911–1965.* Princeton: Princeton University Press.

———. 1987. The Politics of the NIH Extramural Program, 1937–1950. *Journal of the History of Medicine and Allied Sciences* 42:447–66.

———. 1988. The New Discontinuity in Health Policy. In *America in Theory,* eds. L. Berlowitz, D. Donoghue, and L. Menand, 163–77. New York: Oxford University Press.

———. 1989a. Health Policy and Changing Epidemiology in the United States: Chronic Disease in the Twentieth Century. In *Unnatural Causes: The Three Leading Killer Diseases in America*, ed. R.C. Maulitz, 11–31. New Brunswick, N.J.: Rutgers University Press.

———. 1989b. Policy and Epidemiology: Financing Health Services for the Chronically Ill and Disabled. *Milbank Quarterly* 67(suppl. 2, pt. 2):257–87.

———. 1996. From Piety to Platitudes to Pork: The Changing Politics of Health Workforce Policy. *Journal of Health Politics, Policy, and Law* 21:825–44.

Fredrickson, D.S. 1977. Health and the Search for New Knowledge. In *Doing Better and Feeling Worse: Health in the United States,* ed. J.H. Knowles, 159–70. New York: Norton.

———. 1981. Biomedical Research in the 1980s. *New England Journal of Medicine* 304:509–17.

Fujimora, J.H. 1992. Crafting Science: Standardized Packages, Boundary Objects, and "Translation." In *Science as Practice and Culture,* ed. A. Pickering, 168–211. Chicago: University of Chicago Press.

Fye, W.B. 1991. The Origins of the Full-time Faculty System: Implications for Clinical Research. *Journal of the American Medical Association* 265:1555–62.

Gallin, J.I., and H.L. Smits. 1997. Managing the Interface between Medical Schools, Hospitals, and Clinical Research. *Journal of the American Medical Association* 277:651–4.

Gallin, J.I., and H. Varmus. 1998. Revitalization of the Warren G. Magnuson Clinical Center at the National Institutes of Health. *Academic Medicine* 73:460–6.

Gehan, E.A., and N.A. Lemak. 1994. *Statistics in Medical Research: Developments in Clinical Trials.* New York: Plenum.

Geigle, R., and S.B. Jones. 1990. Outcomes Measurement: A Report from the Front. *Inquiry* 27(1):7–13.

Geison, G.L. 1987. International Relations and Domestic Elites in American Physiology, 1900–1940. In *Physiology in the American Context,* ed. G.L. Geison, 115–54. Bethesda, Md.: American Physiological Society.

Gill, G.N. 1984. The End of the Physician-Scientist? *American Scholar* 53(summer):353–68.

Gillis, C.N. 1979. The Role of the Basic Scientist in an Academic Clinical Setting. *Federation Proceedings* 38:2355–8.

Ginzberg, E. Ed. 1991. *Health Services Research: Key to Health Policy.* Cambridge, Mass.: Harvard University Press.

Ginzberg, E., and A.B. Dutka. 1989. *The Financing of Biomedical Research.* Baltimore: Johns Hopkins University Press.

Glickman, R.M. 1985. The Future of the Physician Scientist. *Journal of Clinical Investigation* 76:1293–6.

Goldman, L., E.F. Cook, J. Orav, et al. 1990. Research Training in Clinical Effectiveness: Replacing "In My Experience . . ." with Rigorous Clinical Investigation. *Clinical Research* 38(4):686–93.

Goldstein, J.L. 1986. On the Origin and Prevention of PAIDS (Paralyzed Academic Investigator's Syndrome). *Journal of Clinical Investigation* 78:848–54.

Goldstein, J.L., and M.S. Brown. 1997. The Clinical Investigator: Bewitched, Bothered, and Bewildered–but Still Loved. *Journal of Clinical Investigation* 99:2803–12.

Grahn, A. 1980. Research Careers and Research Funding: Notes from the Discussion. In: "Clinical Research: Elements for a Prognosis," ed. A. Grahn. *Perspectives in Biology and Medicine* 23(2, pt. 2): S57–S61.

Greenfield, S., and E.C. Nelson. 1992. Recent Developments and Future Issues in the Use of Health Status Assessment Measures in Clinical Settings. *Medical Care* 30(5, suppl.):MS23–MS41.

Hamburg, D.A. 1981. Welcoming Remarks. In: *Clinical Investigations in the 1980s: Needs and Opportunities. Report of a Conference. . .* , 2–4. Washington, D.C.: National Academy Press.

Harden, V.A. 1986. *Inventing the NIH: Federal Biomedical Research Policy, 1887–1937.* Baltimore: Johns Hopkins University Press.

Harvey, A.M. 1977. Rufus Cole and the Hospital of the Rockefeller Institute. In *Trends in Biomedical Research, 1901–1976,* 13–25. Proceedings of the Second Rockefeller Archive Center Conference, December 10, 1976. New York: Rockefeller Archive Center.

———. 1978. Samuel J. Meltzer: Pioneer Catalyst in the Evolution of Clinical Science in America. *Perspectives in Biology and Medicine* 21:431–40.

———. 1980. Classics in Clinical Science: The Electrolytes in Diabetic Acidosis and Addison's Disease. *American Journal of Medicine* 68: 322–24.

———. 1981. *Science at the Bedside: Clinical Research in American Medicine, 1905–1945.* Baltimore: Johns Hopkins University Press.

Health Services Research. 1990. Patient Outcomes Research Teams: A New Strategy for Health Services Research on Medical Care Quality and Effectiveness (special section of six articles with editorial preface) 25:691–738.

Healy, B.P. 1988. Innovators for the 21st Century: Will We Face a Crisis in Biomedical-research Brainpower? *New England Journal of Medicine* 319:1058–64.

———. 1992. Cultivating the Shy Fruit of Science. In *Medical Education in Transition,* eds. R.Q. Marston and R.M. Jones, 67–70. Princeton, N.J.: Robert Wood Johnson Foundation.

Healy, B.P., and G.A. Keyworth. 1985. The NIH and Numbers: A Vital Concern's Concern. *New England Journal of Medicine* 312:1450–2.

Herman, S.S., and A.M. Singer. 1986. Basic Scientists in Clinical Departments of Medical Schools. *Clinical Research* 34(2):149–58.

Hirsch, J. 1981. Clinical Investigation: An Effort at Definition and Classification. In *Clinical Investigations in the 1980s: Needs and Opportunities. Report of a Conference* . . . , Appendix C, 1–11. Washington, D.C.: National Academy Press.

Hollinger, D.A. 1984. Inquiry and Uplift: Late Nineteenth-century American Academics and the Moral Efficacy of Scientific Practice. In *The Authority of Experts: Studies of History and Theory,* ed. T.L. Haskell, 142–56. Bloomington: Indiana University Press.

Holton, G., and R.S. Morison. Eds. 1979. *Limits of Scientific Inquiry.* New York: Norton.

Howell, J.D. 1995. *Technology in the Hospital: Transforming Patient Care in the Early Twentieth Century.* Baltimore: Johns Hopkins University Press.

Huddle, T.S. 1987. Science, Practice, and the Reform of American Medical Education. Ph.D. diss., University of Illinois at Urbana–Champaign.

———. 1993. Basic Science and the Undergraduate Medical Curriculum. *Perspectives in Biology and Medicine* 36:550–64.

Iglehart, J.K. 1984. Health Policy Report: The NIH Appropriation. *New England Journal of Medicine* 311:1132–6.

Institute of Medicine. 1981. Divisions of Health Sciences Policy and Health Promotion and Disease Prevention. In *Clinical Investigation in the 1980s: Needs and Opportunities. Report of a Conference* . . . . Washington, D.C.: National Academy Press.

———. 1983/1985. Committee on National Needs for Biomedical and Behavioral Research Personnel. *Personnel Needs and Training for Biomedical and Behavioral Research*. Washington, D.C.: National Academy Press.

———. 1984. Committee for a Study of the Organizational Structure of the National Institutes of Health. *Responding to Health Needs and Scientific Opportunity: The Organizational Structure of the National Institutes of Health*. Washington, D.C.: National Academy Press.

———. 1988. Committee for the Study of Resources for Clinical Investigation. *Resources for Clinical Investigation*. Washington, D.C.: National Academy Press.

———. 1990. Committee on Policies for Allocating Health Sciences Research Funds. *Funding Health Sciences Research: A Strategy to Restore Balance,* eds. F.E. Bloom and M.A. Randolph. Washington, D.C.: National Academy Press.

———. 1994. Division of Health Sciences Policy, Committee on Addressing Career Paths for Clinical Research. *Careers in Clinical Research: Obstacles and Opportunities,* eds. W.A. Kelley and M.A. Randolph. Washington, D.C.: National Academy Press.

Jolin, L.D., P. Jolly, J.Y. Krakower, and R. Beran. 1992. U.S. Medical School Finances. *Journal of the American Medical Association* 268: 1149–55.

Jones, R.F., M.F. Mirsky, and J.A. Keyes, Jr. 1985. Clinical Practice of Medical School Faculties: An AAMC Survey of Problems and Issues. *Journal of Medical Education* 60:897–910.

Kahn, C.N. III. 1998. Perspective: The AHCPR after the Battles. *Health Affairs* 11(1):109–10.

Kassirer, J.P. 1976. The Principles of Clinical Decision Making: An Introduction to Decision Analysis. *Yale Journal of Biology and Medicine* 49:149–64.

Kassirer, J.P., A.J. Moskowitz, J. Lau, and S.G. Pauker. 1987. Decision Analysis: A Progress Report. *Annals of Internal Medicine* 106:275–91.

Kelley, W.N. 1988. Are We about to Enter the Golden Era of Clinical Investigation? *Journal of Laboratory and Clinical Medicine* 111:365–70.

Kilbourne, E.D. 1986. The Emergence of the Physician-Basic Scientist. In: "American Doctors, Medical Science, Medical Care," ed. S.R. Graubard. *Daedalus* 115(2):43–54.

Kohler, R.E. 1982. *From Medical Chemistry to Biochemistry: The Making of a Biomedical Discipline.* Cambridge, U.K.: Cambridge University Press.

———. 1985. Bacterial Physiology: The Medical Context. *Bulletin of the History of Medicine* 59:54–74.

Krause, R.M. 1980. Research and Training Support from the National Institutes of Health. In: "Public Policy Symposium: The Young Clinical Investigator in the 1980s." *Clinical Research* 28: 256–60.

Kunitz, S.J. 1988. Classifications in Medicine. In *Grand Rounds: One Hundred Years of Internal Medicine,* eds. D.E. Long and R.C. Maulitz, 279–96. Philadelphia: University of Pennsylvania Press.

Kunkel, H.G. 1962. The Training of the Clinical Investigator. *Journal of Clinical Investigation* 41:1334–6.

Landau, R.L. 1980. Clinical Research: Elements for a Prognosis. In: "Clinical Research: Elements for a Prognosis," ed. A. Grahn. *Perspectives in Biology and Medicine* 23(2, pt. 2):S3–S8.

Larson, E.L. 1988. Organization and Structure of Clinical Research. In *Resources for Clinical Investigation,* 75–7. Washington, D.C.: National Academy Press.

Latour, B. 1987. *Science in Action: How to Follow Scientists and Engineers through Society.* Cambridge, Mass.: Harvard University Press.

———. 1988. *The Pasteurization of France,* trans. A. Sheridan and J. Law. Cambridge, Mass.: Harvard University Press.

Lee, R.I. 1938. Some Desirable Supplements to the Present Trends in Medical Investigation. *Annals of Internal Medicine* 12:692–8.

Levey, G.S., C.R. Sherman, N.O. Gentile, L.J. Hough, T.H. Dial, and P. Jolly. 1988. Postdoctoral Research Training of Full-time Faculty in Academic Departments of Medicine. *Annals of Internal Medicine* 109:414–18.

Levine, R.J. 1979. The Future of Clinical Research. *New England Journal of Medicine* 301:1295–6.

Lewis, I.J., and C.G. Sheps. 1983. *The Sick Citadel: The American Academic Medical Center and the Public Interest.* Cambridge, Mass.: Oelgeschlager, Gunn, & Hain.

Lewis, T. 1934. *Clinical Science.* London: Shaw and Sons.

Lilienfeld, A.M. 1982. *Ceteribus Paribus:* The Evolution of the Clinical Trial. *Bulletin of the History of Medicine* 56:1–18.

Lippard, V.W. 1974. *A Half-century of American Medical Education: 1920–1970.* New York: Josiah Macy, Jr. Foundation.

Lipsett, M.B. 1981. The Optimal Use of PhDs in Clinical Research. In *Clinical Investigations in the 1980s: Needs and Opportunities. Report of a Conference* . . . Appendix F: 1–7. Washington, D.C.: National Academy Press.

Littlefield, J.W. 1984. On the Difficulty of Combining Basic Research and Patient Care. *American Journal of Human Genetics* 36:731–5.

———. 1986. The Need to Promote Careers That Combine Research and Clinical Care. *Journal of Medical Education* 61:785–9.

Lohr, K.N. 1989. Advances in Health Status Assessment: Overview of the Conference. *Medical Care* 27(3, suppl.):S1–S11.

Löwy, I. 1987. The Impact of Medical Practice on Biomedical Research: The Case of Human Leucocyte Antigens Studies. *Minerva* 25(1–2): 171–200.

———. 1989. Biomedical Research and the Constraints of Medical Practice: James Bumgardner Murphy and the Early Discovery of the Role of Lymphocytes in Immune Reactions. *Bulletin of the History of Medicine* 63:356–91.

———. 1996. *Between Bench and Bedside: Science, Healing, and Interleukin-2 in a Cancer Ward.* Cambridge, Mass.: Harvard University Press.

Ludmerer, K.M. 1985. *Learning to Heal: The Development of American Medical Education.* New York: Basic Books.

———. 1990. The Origins of Mount Sinai School of Medicine. *Journal of the History of Medicine and Allied Sciences* 45:469–89.

Lusted, L.B. 1968. *Introduction to Medical Decision Making.* Springfield, Ill.: Charles C. Thomas.

Marks, H.M. 1997. *The Progress of Experiment: Science and Therapeutic Reform in the United States, 1900-1990.* Cambridge, U.K.: Cambridge University Press.

Marshall, E. 1994. Does NIH Shortchange Clinicians? *Science* 265:20–1.

———. 1998. New NIH Grants for Clinical Research. *Science* 279:1300.

Martin, J.B. 1991. Training Physician-Scientists for the 1990s. *Academic Medicine* 66:123–9.

Matherlee, K.R. 1995. The Outlook for Clinical Research: Impacts of Federal Funding Restraint and Private Sector Reconfiguration. *Academic Medicine* 70:1065–72.

Maulitz, R.C. 1979. "Physician versus Bacteriologist": The Ideology of Science in Clinical Medicine. In: *The Therapeutic Revolution: Essays in the Social History of American Medicine,* eds. M.J. Vogel and C.E. Rosenberg, 91–107. Philadelphia: University of Pennsylvania Press.

———. 1987. Pathologists, Clinicians, and the Role of Pathophysiology. In *Physiology in the American Context,* ed. G.L. Geison, 209–35. Bethesda, Md.: American Physiological Society.

Means, J.H. 1958. *Ward 4: The Mallinckrodt Research Ward of the Massachusetts General Hospital.* Cambridge, Mass.: Harvard University Press.

Mechanic, R.E., and A. Dobson. 1996. The Impact of Managed Care on Clinical Research: A Preliminary Investigation. *Health Affairs* 15(3):72–89.

Medical Research Council. 1948. Streptomycin Treatment of Pulmonary Tuberculosis. *British Medical Journal* 2:769–82.

Meldrum, M.L. 1994. "Departures from the Design": The Randomized Clinical Trial in Historical Context, 1946–1970. Ph.D. diss. Stony Brook, N.Y.: State University of New York.

Melhado, E.M. 1991. Mineralogy and the Autonomy of Chemistry around 1800. *Lychnos* 1990:229–62.

Meltzer, S.J. 1909. The Science of Clinical Medicine: What It Ought To Be and the Men to Uphold It. *Journal of the American Medical Association* 53:508–12.

Mendelson, D.N., C.S. Goodman, R. Ahn, and R.J. Rubin. 1998. Outcomes and Effectiveness Research in the Private Sector. *Health Affairs* 17(5):75–90.

Meyer, M., M. Genel, R.D. Altman, M.A. Williams, and J.R. Allen. 1998. Clinical Research: Assessing the Future in a Changing Environment. Summary report of a conference sponsored by the American Medical Association Council on Scientific Affairs, Washington, D.C., March 1996. *American Journal of Medicine* 104:264–71.

Moore, C.V. 1964. Behold Now Behemoth. *Transactions of the Association of American Physicians* 77:1–7.

Morgan, T.E., and D.D. Jones. 1976. *Trends and Dimensions of Biomedical and Behavioral Research Funding in Academic Medical Centers, 1964–1974.* Submitted to the President's Biomedical Research Panel. Washington, D.C.: Association of American Medical Colleges.

Movsesian, M.A. 1990. Effect on Physician-scientists of the Low Funding Rate of NIH Grant Applications. *New England Journal of Medicine* 322:1602–4.

Mowery, D.C., and N. Rosenberg. 1989. *Technology and the Pursuit of Economic Growth.* Cambridge, U.K.: Cambridge University Press.

Murtaugh, J.S. 1973. Biomedical Sciences. In *Science and the Evolution of Public Policy,* ed. J.A. Shannon, 157–87. New York: Rockefeller University Press.

Nathan, D.G. 1998. Clinical Research: Perceptions, Reality, and Proposed Solutions: National Institutes of Health Director's Panel on Clinical Research. *Journal of the American Medical Association* 280: 1427–31.

National Institutes of Health. 1968. Office of Resources Analysis. *Biomedical Research Manpower—For the Eighties*. Written by H.H. Rosenberg. Resources for Medical Research, report no. 11. Washington, D.C.

———. 1972. *The Training Programs of the Institutes of the National Institutes of Health, Fiscal Year 1974* (2 vols.). Bethesda, Md.: Office of the Director.

———. 1996. Director's Panel on Clinical Research (CRP). Interim Report. Bethesda, Md. (unpublished).

———. 1997. Director's Panel on Clinical Research (CRP). [Final] Report to the Advisory Committee to the NIH Director. Bethesda, MD. (unpublished).

———. 1998. National Institute of General Medical Sciences. The Careers and Professional Activities of Graduates of the NIGMS Medical Scientist Training Programs. Bethesda, Md. (unpublished).

National Research Council. 1975a. Report of the Committee on a Feasibility Study of National Needs for Biomedical and Behavioral Research Personnel. Washington, D.C. (unpublished).

———. 1976. Committee on a Study of the Impact of the NIH Research Training Programs on the Career Patterns of Bioscientists. *Research Training and Career Patterns of Bioscientists: The Training Programs of the National Institutes of Health*. Washington, D.C.: National Academy of Sciences.

———. 1975b–79/1981. Committee on a Study of National Needs for Biomedical and Behavioral Research Personnel. *Personnel Needs and Training for Biomedical and Behavioral Research*. Washington, D.C.: National Academy Press.

———. 1989. Committee on National Needs for Biomedical and Behavioral Research Personnel. *Biomedical and Behavioral Research Scientists: Their Training and Supply* (3 vols). Washington, D.C.: National Academy Press.

———. 1993. Panel on Monitoring the Social Impact of the AIDS Epidemic. *The Social Impact of AIDS in the United States,* eds. A.R. Jonsen and J. Stryker. Washington, D.C.: National Academy Press.

———. 1994. Committee on National Needs for Biomedical and Behavioral Research Personnel. *Meeting the Nation's Needs for Biomedical and Behavioral Scientists*. Washington, D.C.: National Academy Press.

Neinstein, L.S., and R.G. MacKenzie. 1989. Prior Training and Recommendations for Future Training of Clinical Research Faculty Members. *Academic Medicine* 64:32–5.

Nelson, R.H. 1987. The Economics Profession and the Making of Public Policy. *Journal of Economic Literature* 25:49–91.

New York Academy of Medicine. 1981. Symposium on the Academic Physician: An Endangered Species. *Bulletin of the New York Academy of Medicine* 57(6).

Oates, J.A. 1982. Clinical Investigation: A Pathway to Discovery. *Transactions of the Association of American Physicians* 95:lxxvii–xc.

Patterson, J.T. 1987. *The Dread Disease: Cancer and Modern American Culture.* Cambridge, Mass.: Harvard University Press.

Paul, W.E. 1981. Clinical Investigation—On the Threshold of a Golden Era? *Journal of Clinical Investigation* 68:823–6.

Peabody, F.W. 1928. The Soul of the Clinic. *Journal of the American Medical Association* 90:1193–6.

Peitzman, S.J. 1988. Nephrology in America from Thomas Addis to the Artificial Kidney. In *Grand Rounds: One Hundred Years of Internal Medicine,* eds. R.C. Maulitz and D.E. Long, 211–41. Philadelphia: University of Pennsylvania Press.

———. 1992. From Bright's Disease to End-stage Renal Disease. In *Framing Disease: Studies in Cultural History,* eds. C.E. Rosenberg and J. Golden, 3–19. New Brunswick, N.J.: Rutgers University Press.

Petersdorf, R.G. 1980. The Evolution of Departments of Medicine. *New England Journal of Medicine* 303:489–96.

———. 1981. Academic Medicine: No Longer Threadbare or Genteel. *New England Journal of Medicine* 304:841–3.

———. 1983. Is the Establishment Defensible? *New England Journal of Medicine* 309:1053–7.

———. 1986. Medical Schools and Research: Is the Tail Wagging the Dog? In: "American Doctors, Medical Science, Medical Care," ed. Stephen R. Graubard. *Daedalus* 115(2):99–118.

President's Science Advisory Committee. 1972. *Scientific and Educational Basis for Improving Health. Report*. . . . Washington, D.C.: Office of Science and Technology.

Price, V. 1981. The National Institutes of Health Medical Scientist Program. In *Clinical Investigations in the 1980s: Needs and Opportunities. Report of a Conference* . . . . Appendix G:1–21. Washington, D.C.: National Academy Press.

Raiffa, H. 1968. *Decision Analysis: Introductory Lectures on Choices under Uncertainty.* Menlo Park, Calif.: Addison–Wesley.

Reiser, S.J. 1978a. *Medicine and the Reign of Technology.* Cambridge, U.K.: Cambridge University Press.

———. 1978b. Human Experimentation and the Convergence of Medical Research and Patient Care. *Annals of the American Academy of Political and Social Science* 437(May):8–18.

Relman, A.S. 1979. Publications and Promotions for the Clinical Investigator. *Clinical Pharmacology and Therapeutics* 25(5, pt. 2):673–6.

———. 1988. Assessment and Accountability: The Third Revolution in Medical Care. *New England Journal of Medicine* 319:1220–2.

Rettig, R.A. 1977. *Cancer Crusade.* Princeton: Princeton University Press.

Reuter, J., and D. Gaskin. 1997. Academic Health Centers in Competitive Markets. *Health Affairs* 16(4): 242–52.

Rockefeller Archive Center. 1977. *Trends in Biomedical Research, 1901–1976.* Proceedings of the Second Rockefeller Archive Center Conference, December 10, 1976. New York: Rockefeller Archive Center.

Roemer, M.I. 1975. The Expanding Scope of Governmental Regulation of Health Care Delivery. *University of Toledo Law Review* 6:591–616.

Rosen, G. 1965. Patterns of Health Research in the United States, 1900–1960. *Bulletin of the History of Medicine* 39:201–21.

Rosenberg, C.E. 1987. *The Care of Strangers: The Rise of America's Hospital System.* New York: Basic Books.

Rosenkrantz, B.G. 1979. Damaged Goods: Dilemmas of Responsibility for Risk. *Milbank Memorial Fund Quarterly/Health and Society* 57:1–37.

Ross, R.S. 1985. Boundaries of the General Clinical Research Center in an Academic Medical Center. *Clinical Research* 33(2):105–10.

Rothman, D.J. 1991. *Strangers at the Bedside: A History of How Law and Bioethics Transformed Medical Decision Making.* New York: Basic Books.

Rothstein, W.G. 1987. *American Medical Schools and the Practice of Medicine: A History.* New York: Oxford University Press.

Rushmer, R.F. 1980. *National Priorities for Health.* New York: Wiley.

Sackett, D.L. 1969. Clinical Epidemiology. *American Journal of Epidemiology* 89:125–8.

Schrier, R.W. 1997. Ensuring the Survival of the Clinician–Scientist. *Academic Medicine* 72(7):589–94.

Science. 1997. NIH Leery of Clinical Research Bill. In "ScienceScope," ed. Jocelyn Kaiser. *Science* 278:375.

Seggel, R.L. 1985. *Stabilizing the Funding of NIH and ADAMHA Research Project Grants: A Background Paper.* Washington, D.C.: National Academy Press.

Seldin, D.W. 1966. Some Reflections on the Role of Basic Research and Service in Clinical Departments. *Journal of Clinical Investigation* 45:976–9.

Shannon, J.A. 1959. Factors Influencing the Substance and Dimension of Medical Research in the United States. In *Ciba Foundation's Tenth Anniversary Symposium on Significant Trends in Medical Research,* eds. G.E.W. Wolstenholme, C.M. O'Connor, and M. O'Connor, 303–16. Boston: Little, Brown.

———. 1967a. The Advancement of Medical Research: A Twenty-Year View of the Role of the National Institutes of Health. *Journal of Medical Education* 42:97–108.

———. 1967b. Statement by the director, National Institutes of Health, Public Health Service. In *Departments of Labor, and Health, Educa-*

tion, and Welfare Appropriations for 1968: Hearings . . . , National Institutes of Health, National Institute of Mental Health vol. 5, 4–8. U.S. Senate–House Committee on Appropriations, Subcommittee on Departments of Labor and Health, Education, and Welfare and Related Agencies. 90th Congress, First Session. Washington, D.C.

———. 1976. *Federal Support of Biomedical Sciences: Development and Academic Impact.* Washington, D.C.: Association of American Medical Colleges.

———. 1987. The National Institutes of Health: Some Critical Years, 1955–1957. *Science* 237:865–8.

Sherman, B. 1988. The Future of Clinical Investigation. In *Resources for Clinical Investigation,* 61-2. Washington, D.C.: National Academy Press.

Sherman, C.R., H.P. Jolly, T.E. Morgan, et al. 1981. *On the Status of Medical School Faculty and Clinical Research Manpower, 1968-1990: A Report to the Clinical Sciences Panel of the Committee on a Study of National Needs for Biomedical and Behavioral Research Personnel, National Academy of Sciences, National Research Council.* NIH pub. no. 82-2458. Bethesda, Md.: NIH Office of Program Planning and Evaluation.

Sherman, J.F. 1980. Toward an Adequate Pool of Clinical Investigators. In: "Clinical Research: Elements for a Prognosis," ed. A. Grahn. *Perspectives in Biology and Medicine* 23(2, pt. 2):S79–S81.

Shine, K.I. 1998. Encouraging Clinical Research by Physician Scientists. *Journal of the American Medical Association* 280:1442–4.

Shryock, R.H. 1947. *American Medical Research: Past and Present.* New York: Commonwealth Fund.

Shulman, L.E. 1996. Clinical Research 1996: Stirrings from the Academic Health Centers. *Academic Medicine* 71:362–3, 398.

Sinding, C. 1989. The History of Resistant Rickets: A Model for Understanding the Growth of Biomedical Knowledge. *Journal of the History of Biology* 22:461–95.

———. 1990. Clinical Research and Basic Science: The Development of the Concept of End-organ Resistance to a Hormone. *Journal of the History of Medicine and Allied Sciences* 45:198–232.

Skirboll, L.R. 1997. The Impact of Managed Care on Research: The Changing Face of Medicine. *Academic Medicine* 72:778–9.

Slater, KC.H. 1997. What Is Outcomes Research and What Can It Tell Us? *Evaluation and the Health Professions* 20:243–64.

Smith, L.H., Jr. 1989. Training of Physician/Scientists. In *Biomedical and Behavioral Research Scientists: Their Training and Supply,* vol. 3, 107–20. National Research Council, Committee on National Needs

for Biomedical and Behavioral Research Personnel. Washington, D.C.: National Academy Press.

Somers, A.R., and H.M. Somers. 1977. *Health and Health Care: Policies in Perspective.* Germantown, Md.: Aspen Systems.

Star, S.L. 1989. The Structure of Ill-structured Solutions: Boundary Objects and Heterogeneous Distributed Problem Solving. In *Distributed Artificial Intelligence,* eds. L. Gasser and M.N. Huhns, vol. 2, 37–54. London: Pitman.

Starr, P. 1982. *The Social Transformation of American Medicine: The Rise of a Sovereign Profession and the Making of a Vast Industry.* New York: Basic Books.

Steinfels, P. 1976. Biomedical Research and the Public: A Report from the Airlie House Conference. *Hastings Center Report* 6(3):21–5.

Stephenson, R.B. 1974. The NIH Training Activities: A Historical Background. In *Biomedical Research Manpower: Report of a Conference Held October 1–3, 1973*. . . , 15–29. Washington, D.C.: Association of American Medical Colleges.

Stevens, R. 1989. *In Sickness and in Wealth: American Hospitals in the Twentieth Century.* New York: Basic Books.

———. 1998. *American Medicine and the Public Interest,* rev. ed. Berkeley: University of California Press.

Stone, R.S. 1974. Current Status of the NIH/NIMH Research Training Program. In *Biomedical Research Manpower: Report of a Conference Held October 1–3, 1973* . . . , 45–52. Washington, D.C.: Association of American Medical Colleges.

Strauss, M.B. 1960. The Climate for the Cultivation of Clinical Research. *New England Journal of Medicine* 262:805–10.

———. 1964. Of Medicine, Men, and Molecules: Wedlock or Divorce? *Medicine* 43:619–24.

Strickland, S.P. 1972. *Politics, Science, and Dread Disease: A Short History of United States Medical Research Policy.* Cambridge, Mass.: Harvard University Press.

Sutton, J., and C.D. Killian. 1996. The MD–PhD Researcher: What Species of Investigator? *Academic Medicine* 71:454–9.

Swain, D. 1962. The Rise of a Research Empire: NIH, 1930-1950. *Science* 138:1233–7.

Swartz, H.M., and D.L. Gottheil. Eds. 1993. *The Education of Physician–Scholars: Preparing for Leadership in the Health Care System.* Rockville, Md.: Betz.

Swisher, S.N. 1980. Manpower Training for Fundamental Clinical Research. In: "Clinical Research: Elements for a Prognosis," ed. A. Grahn. *Perspectives in Biology and Medicine* 23(2, pt. 2):S62–S78.

Tanenbaum, S.J. 1994. Knowing and Acting in Medical Practice: The Epistemological Politics of Outcomes Research. *Journal of Health Politics, Policy, and Law* 19:27–44.

Tarlov, A.R., J.E. Ware, Jr., S. Greenfield, E.C. Nelson, E. Perrin, and M. Zubkoff. 1989. The Medical Outcomes Study: An Application of Methods for Monitoring the Results of Medical Care. *Journal of the American Medical Association* 262:925–30.

Taskel, L., P. Jolly, and R. Beran. 1989. U.S. Medical School Finances. *Journal of the American Medical Association* 262:1020–8.

Temin, P. 1980. *Taking Your Medicine: Drug Regulation in the United States.* Cambridge, Mass.: Harvard University Press.

Testa, M.A., and D.C. Simonson. 1996. Assessment of Quality-of-life Outcomes. *New England Journal of Medicine* 334:835–40.

Thier, S.O. 1977. Where Do We Go from Here? An Appeal to Reason. *Clinical Research* 25(4):219–24.

———. 1980. Clinical Investigation in the 1980s: Perspective from the Medical Schools. In: Public Policy Symposium: The Young Clinical Investigator in the 1980s. *Clinical Research* 28:248–51.

———. 1981. Recommendations for Remedies [for the Diminishing Number of Clinical Investigators]. In "Symposium on the Academic Physician: An Endangered Species." *Bulletin of the New York Academy of Medicine* 57:480–7.

———. 1992. Forces Motivating the Use of Health Status Assessment Measures in Clinical Settings and Related Clinical Research. *Medical Care* 30(5, suppl.):MS15–MS22.

Thier, S.O., D.R. Challoner, J. Cockerham, et al. 1980. Proposals Addressing the Decline in the Training of Physician Investigators: Report of the *ad hoc* Committee of the AAMC. *Clinical Research* 28(2):85–93.

Thier, S.O., and T.E. Morgan. 1979. The Other Medical-Manpower Problem. *New England Journal of Medicine* 301:1283–5.

Thomas, L. 1977. On the Science and Technology of Medicine. In *Doing Better and Feeling Worse: Health in the United States,* ed. J.H. Knowles, 35–46. New York: Norton.

Thompson, J.N., and J. Moskowitz. 1997. Preventing the Extinction of the Clinical Research Ecosystem. *Journal of the American Medical Association* 278(3):241–4; minor correction in 278(5):388.

U.S. House. 1973a. *National Health Research Fellowship and Traineeship Act of 1973. Hearings . . . on H.R. 5640 and H.R. 5948. . . .* Committee on Interstate and Foreign Commerce, Subcommittee on Public Health and Environment, 93rd Congress, First Session. Serial no. 93-13. Washington, D.C.

———. 1973b. *National Biomedical Research Fellowship, Traineeship, and Training Act of 1973: Report* [to accompany H.R. 7724]. Submitted by Mr. Staggers, from the Committee on Interstate and Foreign Commerce, 93rd Congress, First Session. Report. no. 93-224. Washington, D.C.

———. 1974. *National Research Act: Conference Report* [to Accompany H.R. 7724]. Submitted by Mr. Staggers, from the Committee of Conference, 93rd Congress, Second Session. Report. no. 93-1148. Washington, D.C.

U.S. Senate. 1973. *National Research Service Award Act . . . Report* [to accompany H.R. 7724]. Submitted by Mr. Kennedy, from the Committee on Labor and Public Welfare, 93rd Congress, First Session. Report. no. 93-381. Washington, D.C.

Vaitukaitis, J.L. 1991. The Future of Clinical Research. *Clinical Research* 39(2):145–56.

Virchow, R. 1847; tr. 1958; rpt. 1971. Standpoints in Scientific Medicine. In *Disease, Life, and Man: Selected Essays by Rudolf Virchow,* trans. L.J. Rather, 26–39. Stanford, Calif.: Stanford University Press.

Vogel, M.J. 1980. *The Invention of the Modern Hospital: Boston, 1870–1930.* Chicago: University of Chicago Press.

Wadman, M. 1996. Health Agency Avoids Congress's Axe. *Nature* 381:457.

Walsh, J. 1975. NIH Training Grants: The Uncertainty Factor. *Science* 188:1092–4.

Warner, J.H. 1980. Physiology. In *The Education of American Physicians: Historical Essays,* ed. R.L. Numbers, 48–71. Berkeley: University of California Press.

Warren, J.V. 1972. The Legacy of Soma Weiss. *New England Journal of Medicine* 286:658–9.

———. 1983. The Evolution of the Clinical Investigator. *Journal of Laboratory and Clinical Medicine* 101:335–50.

Weatherall, D.J. 1980. Toward an Understanding of the Molecular Biology of Some Common Inherited Anemias: The Story of Thalassemia. In *Blood, Pure and Eloquent: A Story of Discovery, of People, and of Ideas*, ed. M.M. Wintrobe, 373–414. New York: McGraw–Hill.

———. 1982. *The New Genetics and Clinical Practice.* London: Nuffield Provincial Hospitals Trust.

———. 1991. The Physician Scientist: An Endangered but Far from Extinct Species. *British Medical Journal* 302:1002–5.

Weinstein, M.C., H.V. Fineberg, A.S. Elstein, et al. 1980. *Clinical Decision Analysis.* Philadelphia: Saunders.

Weissmann, G. 1987. *They All Laughed at Christopher Columbus: Tales of Medicine and the Art of Discovery.* New York: Times Books.

Wennberg, J.E. 1988. The Need for Clinical Investigation to Consider the Issues of Outcome Assessment. In *Resources for Clinical Investigation,* 82–6. Washington, D.C.: National Academy Press.

Wheatley, S.C. 1988. *The Politics of Philanthropy.* Madison: University of Wisconsin Press.

Whedon, G.D. 1980. Further Analysis of Research Support at NIH. In: "Clinical Research: Elements for a Prognosis," ed. A. Grahn. *Perspectives in Biology and Medicine* 23(2, pt. 2):S34–S43.

White, K.L. 1991. *Healing the Schism: Epidemiology, Medicine, and the Public's Health*. New York: Springer-Verlag.

Wiebe, R. 1967. *The Search for Order, 1877–1920.* New York: Hill and Wang.

Williams, G.H., D.W. Wara, and P. Carbone. 1997. Funding for Patient-oriented Research: Critical Strain on a Fundamental Linchpin. *Journal of the American Medical Association* 278:227–31.

Wintrobe, M.M. 1970. Clinical Science, Clinical Research, and Academic Advancement. *Annals of Internal Medicine* 72:741–6.

Wood, W.B., Jr. 1963. Calling Mephistopheles. *Transactions of the Association of American Physicians* 76:1–7.

Wyngaarden, J.B. 1973. Statement of Dr. James Wyngaarden, Professor and Chairman, Department of Medicine, Duke University Medical Center. In *National Health Research Fellowship and Traineeship Act of 1973. Hearings . . . on H.R. 5640 and H.R. 5948*. U.S. House. Committee on Interstate and Foreign Commerce, Subcommittee on Public Health and Environment, 128-39. 93rd Congress, First Session. Serial no. 93-13. Washington, D.C.

———. 1979a. The Clinical Investigator as an Endangered Species. *Transactions of the Association of American Physicians* 92:1–15.

———. 1979b. The Clinical Investigator as an Endangered Species. *New England Journal of Medicine* 301:1254–9.

———. 1981. The Clinical Investigator as an Endangered Species. In: "Symposium on the Academic Physician: An Endangered Species." *Bulletin of the New York Academy of Medicine* 57:415–26.

———. 1983a. Careers in Academic Medicine. In *Academic Medicine: Present and Future,* eds. J.Z. Bowers and E.E. King, 129–38. Rockefeller Archive Center Conference, Pocantico Hills, North Tarrytown, New York, May 25–27, 1982. North Tarrytown, N.Y.: Rockefeller Archive Center.

———. 1983b. Encouraging Young Physicians to Pursue a Career in Clinical Research. *Clinical Research* 31(2):115–18.

———. 1984a. Irvine H. Page Lecture, 1983: The Future of Clinical Investigation. *Cleveland Clinic Quarterly* 51:567–74.

———. 1984b. Nurturing the Scientific Enterprise. *Journal of Medical Education* 59:155–61.

———. 1985. The Priority of Patient-Oriented Research for NIH. *Clinical Research* 33(2):95–9.

———. 1986a. Nurturing the Biomedical Research Enterprise. *Puerto Rico Health Sciences Journal* 5(2):43–50.

———. 1986b. The Role of Government Support in Biomedical Research. *Clinical and Investigative Medicine* 9:265–8.

———. 1987. The National Institutes of Health in Its Centennial Year. *Science* 237:869–74.

Zapp, J.S. 1973. Statement of Dr. John S. Zapp, Deputy Assistant Secretary for Legislation (Health), Department of Health, Education, and Welfare. *National Health Research Fellowship and Traineeship Act of 1973. Hearings... on H.R. 5640 and H.R. 5948.* U.S. House Committee on Interstate and Foreign Commerce, Subcommittee on Public Health and Environment, 8–12. 93rd Congress, First Session. Serial no. 93-13. Washington, D.C.

Acknowledgments: This essay has benefited from comments on diverse drafts by many colleagues; the author is grateful to all of them. With the most recent version, the two anonymous reviewers were particularly helpful, as were Theodore M. Brown, Stacie Colwell, Thomas S. Huddle, Robert E. Kohler, and Paula A. Treichler. Any deficiencies in the article remain the responsibility of the author. For highly capable reference work, graciously undertaken, the author is indebted to Victoria Pifalo and her staff at the Library of the Health Sciences, University of Illinois at Urbana–Champaign. For supplying documents, the author is obligated to Diane L. Gottheil at the Medical Scholars Program, University of Illinois at Urbana–Champaign; Ann Barry Flood at the Center for Evaluative Clinical Sciences, Dartmouth University; Jim Igoe at the National Research Council Library; Janet Smith in the Office of Human Subjects Research, the National Institutes of Health; and Keiko Ellis at the Association of American Medical Colleges.

Address correspondence to: Evan M. Melhado, PhD, University of Illinois, College of Medicine, Medical Sciences Building, 506 South Mathews Avenue, Urbana, IL 61801 (email: melhado@uiuc.edu).