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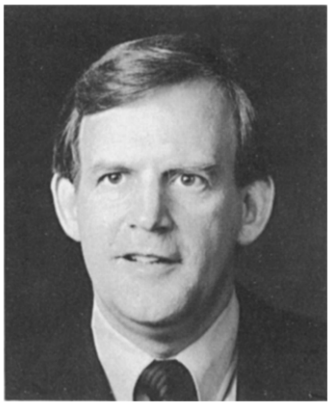

President's Page: Clinical Research in the United States— A Threatened Activity

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For some time, many people have been particularly concerned about the problems confronting clinical research in the United States. I was initially reluctant to discuss these problems because I am a clinical investigator and uncertain as to whether my perspective would be completely objective. However, several recent developments have highlighted the reality of these problems. One is the increasing proportion of clinical research performed outside the United States. For example, 39% of the abstracts submitted and 42% of those selected for presentation for this year's Annual Scientific Session originated abroad. In addition, surveys during our recent strategic planning process identified greater College support for clinical investigation as a high priority objective. I therefore believe that the perception that clinical research in the United States is facing serious difficulties that could threaten its worldwide leadership role is correct.

The fundamental requirements for all research are the availability of talented individuals and sound investigative protocols. In addition, the performance of clinical research requires time, equipment and patients. The current group of medical students, trainees and faculty clearly provides an abundant pool of capable and inquisitive individuals suitable for clinical investigation. However, significant problems are being encountered in obtaining the money and the patient populations necessary for such research.

Although no one debates the necessity of both time and equipment to perform excellent research, it is often assumed when discussing clinical investigation that these resources are readily available as part of the process of providing patient care. Despite the commonality shared by many forms of clinical research and patient care, access to equipment and technician time often cannot be borrowed from patient care resources, and protected investigator time is required for the planning, collection and analysis of research data. Accordingly, clinical research in the United States will be jeopardized until we reject the notion that the requisite resources for such research can be drawn from those provided for patient care and instead appropriate adequate money to fund these necessities.

Decreased support for clinical research from the NIH and other government and private agencies. Funding for clinical research in prior years was in large measure provided by the National Institutes of Health (NIH). However, the progressive reduction in the funding of clinical investigation by the NIH is evidenced by the increasing number of PhD investigators applying for and receiving NIH support and serving on NIH study sections, as well as by stated NIH emphasis on basic science and molecular biology. Discouraged by a failure rate of approximately 65%, MD investigators progressively decreased their applications so that between 1975 and 1987 the number of NIH grants awarded to MDs decreased from 27 to 22% of the total and MD investigators accounted for only 26% of awardees. Ancillary funding sources such as the American Heart Association (AHA) and the Veterans Administration have also increasingly directed support toward basic rather than clinical research. Thus, in 1988, MD researchers accounted for 25% of applicants for the AHA Established Investigator Award, but only 20% of awardees. With regard to AHA grants-in-aid, MD investigators accounted for 35% of applicants, but only 25% of those who were awarded money. A recent cardiology Merit Review Board of the Veterans Administration, which has no basic science divisions, comprised two PhDs, two MD-PhDs and two additional members with appointments in basic science departments of other institutions. From 1983 to 1986 the average rate of approval and funding for all Veterans Administration research proposals was 55%, but the rate for cardiology proposals was only 41%. Even in the College, programs such as the ACC/Merck Adult Cardiology Fellowship Training Awards, which were initially targeted toward

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the support of clinical investigation, have increasingly been awarded to trainees doing basic laboratory investigation. Whereas it is a time-honored tenet that major advances in medicine usually follow understanding of basic mechanisms, the application of laboratory insights to patient care is also an important step. Furthermore, diagnostic and therapeutic advances—echocardiography and coronary angioplasty, for example—often are initiated in the clinical arena and subsequently refined by studies in biology and physics; patient-based investigations, such as studies of angiography and surgery in acute myocardial infarction, often point the way to defining basic disease mechanisms such as thrombosis. Not surprisingly, many individuals have voiced concern that a significant imbalance is occurring between support for basic and clinical research.

Growing reliance on funds received from industry and patient care. Given the increasing difficulties in obtaining financial support for clinical research from the NIH and other granting agencies, clinical investigators have progressively turned to funds provided by medical industry and clinical income derived from patient care. Certainly the development, validation and definition of applications of new pharmaceutical agents and medical technology are prime areas for clinical investigation, and industry has been generous in supporting such endeavors. However, support from pharmaceutical and medical equipment sources is often limited to projects targeted toward the needs of the company. Furthermore, industry support creates the potential for bias in the generation and interpretation of scientific data. The increasing reliance on industry for funding represents an additional significant peril to clinical research.

A second major source of monies utilized for clinical research in recent years is income generated from patient care. However, the generation of research funding from clinical income has its own set of difficulties. The time required to cultivate a patient flow and render clinical services so that clinical income can be generated detracts from time available to perform good clinical research. Although it has been argued that faculty members dedicated to patient care and without an interest in investigation may alleviate this difficulty, physicians often see this role as second class citizenship, and the wide differences in financial compensation between private practice and academic medicine make it difficult to attract—and retain—outstanding individuals to academic practice. The generation of clinical income in academic institutions is further complicated by the fact that such centers often provide medical care for a large segment of the indigent population, a segment in which low collection rates mandate a greater work load for a given profit. The ability to use patient care income for clinical research is particularly compromised in cardiology because the profits generated by the delivery of services are customarily utilized to support the department of medicine. Accordingly, in an attempt to generate patient care income to support clinical research, cardiovascular faculty often expend enormous time and effort in the practice of medicine to yield sums of money that are largely utilized to support other activities within the institution. The generation of clinical income is, of course, dependent on an adequate flow of patients, a topic requiring the in-depth discussion to follow.

Competition for patients between academic centers and community hospitals. Assuming the existence of adequate time and equipment, the final requirement for clinical research is patient population. Outside of the United States the regionalization of health care often directs suitable numbers of patients to academic centers where clinical investigation is performed. Undoubtedly, this has played a role in the increased quantity of clinical research being performed abroad. However, in the United States, academic centers must compete with community hospitals for patients and are at a marked disadvantage in this competition. Academic institutions tend to be large and imposing and are often primarily responsible for the indigent care in their area, all of which may create a negative image in the eyes of private patients. The personal interests of physicians in teaching and research that lead them to join medical school faculty also often result in their tendency to show little interest in the amenities of practice and the marketing of services. The presence of medical students and trainees as part of the team of physicians caring for patients contributes to the impersonal air of the institution, as well as the sense that the patient may well be the subject of experimentation. Given these circumstances, it is not surprising that a substantial proportion of patients, particularly those with favorable insurance coverage, gravitate toward community hospitals. Accordingly, a mismatch often evolves in which community hospitals with little interest in investigation have the requisite quantity and type of patient material for clinical research, whereas academic institutions with the expertise and enthusiasm necessary for high quality clinical research suffer from a lack of optimal patient flow. This disjunction between clinical material and investigative expertise has profound implications for studying disease processes, evaluating new diagnostic modalities and assessing pharmaceutical and nonpharmaceutical therapeutic interventions.

Need for practitioners to participate in clinical research. One obvious potential remedy to solve any imbalance between clinical material and investigative expertise that may exist in community and academic hospitals would be active participation of private practitioners in clinical research. However, these physicians have recently shown an alarming trend toward withdrawal from clinical research that may be driven by traditional town-gown wariness, a growing atmosphere of competition, nonrecognition of significant unresolved medical issues, an inability to visualize an important role for themselves in research efforts or difficulties in undertaking the extra work, possible financial expenses and often onerous bookkeeping of the protocol. In a recent

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article in the *Washington Post*, the National Cancer Institute decried the lack of recruitment of cancer patients into investigative therapeutic protocols. Lawrence Friedman, MD, Acting Associate Director of the Clinical Applications and Prevention Program of the National Heart, Lung, and Blood Institute, has also commented on the difficulties encountered in enrolling patients from the private sector in several multicenter cardiovascular protocols currently underway. Although nonacademicians in community hospitals have played a significant role in several areas of clinical research, their efforts have often been limited to assessment of new technologies that served the additional purpose of enhancing the image of the physicians and their institutions in the eyes of the public. If the United States is to maintain its leadership position in clinical research, the interest and enthusiasm for inquiry must be rekindled in private practitioners, and the machinery must be put in place to facilitate their participation in investigative efforts.

Required actions. Given the many factors that threaten the future of clinical research in the United States, I believe a number of corrective actions are both readily apparent and essential. First, clinical research requires the unencumbered time of physician investigators, and granting agencies must recognize the necessity of financial support for this purpose. Specifically, I believe the NIH and other granting agencies must assess whether an inappropriate imbalance is occurring between the support available for basic laboratory studies and clinical research. Given the large number of basic scientists serving on existing study sections, some cardiovascular leaders have suggested the implementation of separate review panels staffed by clinical investigators to evaluate clinical research proposals. Second, to whatever degree that support for clinical research must be derived from funds for patient care, the generation of such funds should be facilitated and made as efficient as possible. Academic medical centers must become as attractive as possible as centers for patient care. Academic institutions, and departments of medicine in particular, must find alternate sources to subsidize activities incapable of generating independent support. Highly motivated clinical investigators willing to forego personal salary and deliver extensive patient care to fund clinical research will soon abandon their effort if the dollars are diverted to other areas within the institution. Third, support for clinical research from medical industry, currently an important basis of much investigation, should be acknowledged and increased. More importantly, mechanisms should be devised whereby at least some industry dollars can be applied to investigation that is not directly targeted to the marketing of a product and that enable data generated by virtue of industry contributions to be processed so as to avoid any potential bias. Finally, it must be acknowledged that large scale clinical trials addressing critical medical dilemmas will require the active and enthusiastic participation of the private practicing cardiovascular specialist. Steps must be taken to remove all unreasonable work and financial burdens from research protocols and to convince practicing physicians that they have an important role—and an obligation to participate—in the discovery of new medical knowledge. The failure of practitioners to join investigative efforts will not only imperil clinical research in the United States, but also result in the delay and possible failure to make important advances in the clinical care delivered to our patients.