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Presidential Address

Some Reflections on the Role of Basic Research and Service in Clinical Departments

DONALD W. SELDIN

I think it is fair to say that since the Second World War, the widespread application to biologic systems of the methods and theories of the generalizing sciences, physics and chemistry, has reshaped medicine. The most dramatic manifestations of this, perhaps, is the enormous increase in diagnostic and therapeutic tools available for the management of disease. Where previously he was largely a passive, though sympathetic, bystander, the physician could now actively intervene to fulfill the goals of medicine, the saving of life, the relief of pain, and the prevention of disability.

Perhaps even more important than these technologic triumphs was the growth of medical science itself. Powerful predictive and explanatory theories were elaborated. Whole new areas of medicine were developed. The critical methods of scientific inquiry became the common property of the clinical practitioner no less than the laboratory investigator. In a real sense, medicine was transformed from a crude empirical discipline into a scientific enterprise of formidable sophistication and power.

This transformation of medical science was paralleled by a similar transformation in medical schools. Before the War, with a few notable exceptions, most medical institutions were trade schools. Their faculties bore little resemblance to the association of scholars characteristic of the rest of the University. In clinical departments particularly, the educational program was developed by physicians who, however conscientious and competent, were occupied with the responsibilities of private medical practice, and who had neither the time nor the training to develop medical science or instill into students the habits of critical inquiry so necessary for scholarly growth. This situation has now been greatly altered. The clinical teacher is almost everywhere a medical scientist trained both as a clinician and an investigator.

It is precisely here, in defining the role of the clinical scholar, that serious problems begin to arise. The teaching of clinical medicine is mediated by a delicate triad consisting of a student, a patient, and the teacher, presumably a scholar, who articulates this rather fragile interaction. Can the clinical scholar devote sufficient time, is he sufficiently interested, to make of himself a

skillful clinician? Will small group teaching flourish if it must compete with the demands of clinical responsibilities and research work? If he succeeds as clinician and teacher, will he have sufficient time and energy to develop the type of fundamental basic research expected at the University?

We seem to have come the whole circle round. Having replaced the clinical practitioner with the clinical scholar in acknowledgment of the triumphs of medical science, we then raise the question as to whether it is possible to perform dignified basic research and at the same time remain a clinical teacher.

The issue is one of enormous practical as well as theoretical importance. It is already apparent that a number of institutions have concluded that the clinical scholar is unable to perform basic research and have developed various devices to compensate for this deficiency. Those medical schools which most of us would regard with pride and respect as embodying the noblest achievements of American intellectual life seem increasingly to recognize two classes of clinicians.

One group of clinicians is responsible for the clinical care of patients and the teaching of clinical medicine, where the term clinical medicine is used in a sharply restricted and crudely empirical sense. If the goal of a clinical discipline is the application of knowledge for the relief of pain, disability, and death in specific concrete patients, then these individuals are addressing themselves to the central issues that define a Department of Medicine. Yet because such responsibilities are enormously time consuming, because they require special aptitudes and skills, these clinicians are not expected—indeed they are often discouraged—from participating in serious investigation. In consequence, they maintain their status as clinicians but, however learned and conscientious, they cease to function as scholars. The clinician so regarded loses his moorings as a genuine member of the University faculty and becomes a kind of glorified technician, important to minister to patients, important to teach students their trade, but carefully isolated from those activities of creative inquiry which alone permit membership in the community of scholars that constitutes the University.

To fill the void in investigation thus created, a second

group of individuals are assembled. Their function is to foster research. Although they are members of the Department of Medicine and bear the titular designations applied to members of clinical departments—Assistant Professor of Medicine, Associate Professor of Medicine—they are in no meaningful sense of the term clinicians. They do not actively engage in clinical work; their activities and learning are not designed to heighten clinical skills. Yet they contribute—often brilliantly—to the scholarly activity, if not of a clinical department, then of the University as a whole.

It is my belief that this isolation of basic research from clinical activity is systematically undermining the structure of Departments of Medicine in a highly destructive manner. I want to challenge its wisdom in three distinct ways.

First, it is critical to recognize that research in a medical school subserves two functions. Investigation is by definition the search for truth, the discovery of new knowledge, the development of explanatory and predictive theories. If this were all, a University would be no different from a research institute. Clearly the University has the vital additional function of education. If investigation is progressively separated from clinical work and teaching, the educational process deteriorates. Only the investigator can inculcate the methods of critical inquiry acquired in research into the routine practice of medicine. Only he can bring physiology and biochemistry meaningfully to bear in the study and treatment of the sick. The practice of medicine, no matter how skillfully and responsibly conducted, becomes progressively removed from the science of medicine to the extent that the clinician is no longer simultaneously an investigator.

A second disadvantage to the isolation of research from clinical work results from the fact that the clinician is thereby degraded to second-class status. Research is performed by research specialists, quite irrespective of whether or not they have acquired in the past clinical degrees and training, now long dormant. The glamour of the department is monopolized by legendary names the students may never see in any relevant clinical context. Basic research becomes prized for the sophisticated tools and techniques utilized rather than for the penetration of the questions raised or the insight provided by the answers found. The Department of Medicine becomes a kind of repository for people—often of the greatest talent—who nevertheless may have no goals in harmony with those of a clinical discipline. The activity of the clinician is thus, by contrast, demeaned. At the same time, the value of research from a pedagogical point of view is perverted. Explanations involving elaborate pathways of synthetic reactions, the generation of high energy cofactors, the intricacies of DNA and RNA synthesis, often become a substitute for pertinent knowledge of explanatory power for the problem at hand. Behind the obfuscating facade of sophisticated biochemistry, the vital commonplace is obscured that Koplik's spots must be recognized to diagnose measles, and if this is the issue at hand, no discussion of energetics will constitute an adequate substitute.

COVERING LAW THEORY OF SCIENTIFIC EXPLANATION

- I. Event to be explained.
- II. Determining conditions.
- III. General laws establishing the determining conditions as the cause of the event with universal or statistical force.
- IV. *Explanation:* Event to be explained follows deductively from the premises.

FIG. 1.

Finally, the concern with basic research raises the pertinent question as to what is basic. Basic to what? All students of science agree that neither tools nor techniques by themselves confer upon scientific activity any special claim to fundamental status. It is also widely recognized that the term "basic" must be defined in terms of the frame of reference from which the problems emerge. In this light, what is "basic" for biochemistry may be crude or even irrelevant when the problems are posed by issues arising from a clinical context.

Logicians have long been interested in how the theories of a science may be ranked. In recent years the fundamental or basic character of a theory has come to be regarded as its explanatory power. Those theories which have broad explanatory power and consequently can organize vast amounts of discrete data into predictable sequences are regarded as basic. It may not be amiss, therefore, to examine the theory of explanation to ascertain what light it may throw on the kinds of laws that might be regarded as fundamental in a clinical discipline.

In Figure 1 a deductive model for scientific explanation as formulated in detail by Hempel (1, 2) is sketched. This has been termed the covering law theory by Dray (3) to emphasize that explanation is much more than a mere sequential chronicle of a series of events. The essential feature of scientific explanation, according to the covering law theory, is that the explanation is achieved by "subsuming what is to be explained under a general law" (3).

Consider the steps involved in the explanation of the edema of the nephrotic syndrome (event to be explained—Figure 1). Determining conditions would include the information that albumin losses exceeded the rate of albumin synthesis (thereby resulting in a reduction in total circulating albumin) and that the patient had access to dietary salt. Two general laws are required to explain edema, given the determining conditions. The first is some formulation of the Starling equilibrium, which permits the statement that a reduction in oncotic pressure, other things being constant, will result in transudation, thereby causing a contraction in effective blood volume. The second general statement asserts that a contraction in effective blood volume enhances the reabsorption of sodium salts in the proximal tubule of the kidney. Thus, the edema is explained by showing that it develops in accordance with certain laws when certain specified determining conditions are realized.

It is characteristic of the laws in medicine that they usually have this physiologic character. They organize vast amounts of data into broad generalizations that apply within an organ system or link together several organ systems. From the point of view of fundamental biochemistry, such laws may appear trivial because their explanatory force is not derived from a specification of discrete chemical events, but from the vantage point of clinical medicine they are enormously powerful. It is by virtue of physiologic laws of this type that normal and deranged regulatory functions are formulated. Such laws organize large amounts of otherwise discrete and unrelated facts and facilitate a rich insight into the deranged regulatory functions that define disease. From the point of view of clinical medicine, therefore, such laws are "basic," and investigation designed to discover them is, properly speaking, basic research.

The elaboration of physiologic laws pertinent to clinical medicine has come increasingly to depend on an appreciation and mastery of elaborate and highly technical tools and theories of biochemistry and biophysics. But so long as the aim is to elucidate issues pertinent to a clinical discipline, the value of the investigation is a function of the insight it provides in the clinical domain. The claim is sometimes advanced, however, that the theories of clinical medicine can in principle always be reduced to more fundamental disciplines. Psychiatry, so the argument goes, may be reduced, at least in theory, to neurology; neurology to neurophysiology; neurophysiology to physical chemistry and finally to physics. Why not, therefore, cultivate fundamental biochemical and biophysical investigation in a clinical department, even though it may be irrelevant to current clinical medicine, on the grounds that it may be the clinical medicine of the future?

This argument hinges on the thesis of reduction, the formal requirements for which have been elaborated by Nagel (4) and are summarized in Figure 2. Homogeneous reductions, which involve disciplines employing terms and concepts with the same meanings, pose less formidable

problems than do heterogeneous reductions, where the terms and concepts of the disciplines are different. Certainly, there can be no argument against the program that attempts to reduce previously established laws and theories to more fundamental levels, and recent successes in biochemistry have no doubt encouraged that hope. However, two serious dangers are inherent in a constant reductionist orientation.

In the first place, the objectives of research in a clinical department may be better served by the development of theories couched in terms of the clinical discipline. Attempts to reduce all problems to a very basic level may lead to investigations of a type which, whatever their technical sophistication, may be irrelevant from the point of view of clinical physiology and trivial from the point of view of basic biochemistry. Moreover, successful and important investigations from a biochemical vantage point may lure the clinical investigator in a direction progressively more remote from clinical medicine. The problems posed by patients no longer elicit curiosity. Deranged physiology becomes too complicated for the powerful but restricted tools of basic biochemistry. The net effect may be research not pertinent to any activity in a clinical department.

In the second place, an excessive reductionist emphasis may be doomed to failure because it is by no means certain that physiologic laws can, even in principle, be uniformly reduced to a more fundamental level. In physics it appears impossible to reduce electromagnetic theory to mechanics. Similarly, in clinical physiology, it may always be necessary to retain concepts and assert relations within and among organ systems that are neither defined in nor derived from basic biochemistry.

Because I do not believe that, in the nature of things, powerful explanations for macroscopic clinical problems will ever be available by a complete reduction to chemistry and physics, I feel it is essential, for this reason as well as others, to cultivate clinical investigation as a basic research activity of practicing clinicians and teachers.

If viewed in a formal way, basic research is only basic to a Department of Medicine if the research has explanatory value for medical issues. There is no reason to use basic postulates of biochemistry as an index of value of research in a medical department. It is we who determine, by the goals we choose, what is basic and what is superficial. In a moving and perceptive passage, Einstein (5) has emphasized the instrumental role of science:

"Whatever . . . [the scientific method] in the hand of man will produce depends entirely on the nature of the goals alive in mankind. Once these goals exist, the scientific method furnishes means to realize them. Yet it cannot furnish the very goals. The scientific method itself would not have led anywhere, it would not even have been born without a passionate striving for clear understanding."

Just as the University imposes on the clinical scholar the responsibility for basic research, so the community makes the demand for clinical service. The peculiar dilemma of the clinical department in meeting its academic

REDUCTION

The explanation of a theory in one area of inquiry by a theory from some other domain.

TYPES:

I. Homogeneous Reductions.

- A. The terms and concepts of the two disciplines have the same meanings.
- B. The more inclusive theory deductively incorporates the more restricted theory.

II. Heterogeneous Reductions.

- A. The restricted science employs terms and concepts not included in the more inclusive science.
- B. Heterogeneous reductions therefore require:
 1. Special laws of connectability.
 2. Special laws of derivability.

FIG. 2.

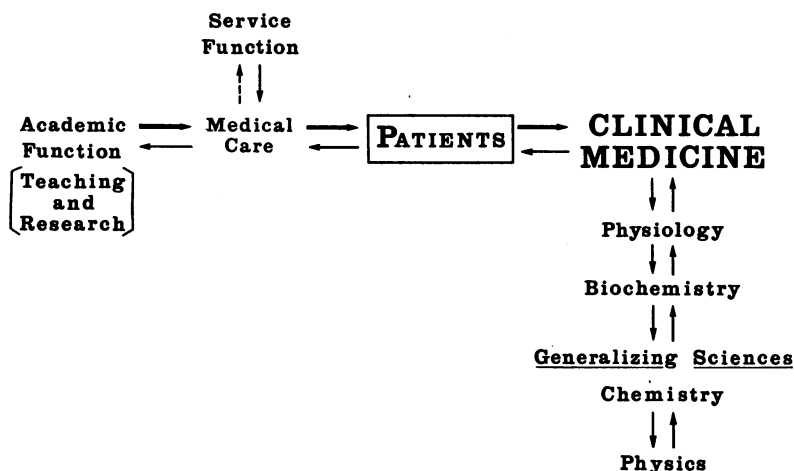


FIG. 3.

responsibilities is depicted in Figure 3. The responsibilities to the University have already been defined. These consist of teaching and research, based on the care of patients. The research should be as basic as possible, in the sense that there is a reciprocal and interacting movement down as well as up the chain of scientific disciplines, as indicated on the right side of Figure 3. The clinical setting imposes the requirement that the clinical scholar should not be marooned in a scientific discipline where the work has no relevance or interaction with clinical activity. In this formulation it should be emphasized that the magnitude of patient care should be delimited by the requirements of teaching and research.

We are now confronted from all quarters with the demand to undertake clinical service responsibilities far beyond what is required for academic purposes. The University is regarded, not as an institution of learning, but as the agency to solve the medical service needs of the community. These needs, to be sure, are pressing, and no responsible citizen can question the social value of legislation designed to bring the fruits of medical science to all people. However, for the University to become the prime agency for the solution of community service problems is a very grave step. The University is not a community service institution. Its prime function is the cultivation of learning. Once responsibility for broad patient care is assumed, this must, for moral reasons, take priority over every other activity. It is difficult to see how, under such circumstances, the qualities of academic life can be preserved. We hear much, in these days of regional medical centers and similar programs for broad medical care, of the need to "dismantle the barriers." But the University barriers are designed to preserve those functions unique to the University. The price for the

solution of community service requirements may be the inexorable erosion of academic activity.

The legitimate clinical responsibilities of a Department of Medicine are only those dictated by the requirements for teaching and research. Under these conditions, the clinical scholar, trained in both research and clinical medicine, can and has flourished. Such individuals, interested and alive to the activities and responsibilities of the Department, are in a position to raise questions and institute investigations basic to the study of disease and the care of the sick. At the same time, both clinical work and teaching are animated with the stimulation derived from critical inquiry. What is "basic" in research thus becomes intimately intertwined with the activities and goals of the Department. Only thus can the clinical scholar avoid a paralyzing schizophrenia and at the same time forge a healthy and inspiring climate for clinical work and investigation.

References

1. Hempel, C. G., and P. Oppenheim. Studies in the logic of explanation. *Philosophy of Science* 1948, **15**, 135.
2. Hempel, C. G. *Aspects of Scientific Explanation, and Other Essays in the Philosophy of Science*. New York, The Free Press, 1965.
3. Dray, W. *Laws and Explanation in History*. London, Oxford University Press, 1957.
4. Nagel, E. *The Structure of Science. Problems in the Logic of Scientific Explanation*. New York, Harcourt, Brace & World, 1961.
5. Einstein, A. *Out of My Later Years*. New York, Philosophical Library, 1950.