

of the innumerable capillary aneurysms that characterize diabetic retinopathy. Furthermore, the relationship of the aneurysms to the surrounding hemorrhages and exudates became apparent. Available for study in minute detail was the life history of the capillary aneurysm. In single specimens one could trace the development from a thin-walled dilatation to an onion-skin lamellated polysaccharide mass, which ultimately became hyalinized.

Friedenwald then undertook the study of the application of periodic-acid-fuchsin technic to other organs of diabetic patients. This resulted in the finding of similar staining and lamellation of the globular renal glomerular masses, previously described by Kimmelstiel and Wilson. In addition, serial sections of kidneys revealed true capillary aneurysms in the glomeruli of patients with retinopathy. A review of a large number of diabetics at autopsy revealed the occurrence of renal lesions only in those diabetics who had retinopathy. Thus were correlated for the first time the renal and retinal lesions of the diabetic, both as to appearance, staining characteristics, and occurrence in the same individuals.

Under the direction of Friedenwald, efforts were then concentrated on a comparison of the differences between diabetics with and without retinopathy. Thus was begun an intensive clinical and laboratory investigation in diverse directions and encompassing many related fields. Studies were undertaken of possible alterations in serum polysaccharides, plasma proteins, acetylating capacity, xanthurenic acid excretion following tryptophane administration, urinary vitamin B-12 output after parenteral administration, 17-hydroxysteroid excretion, eosinopenia following ACTH, etc. In addition, the studies of pathologic differences were continued and numerous attempts were made at experimental production in animals. From these extensive efforts the hypothesis which emerged that best accounted for the available clinical, histo-pathologic, and experimental data was that the adrenal cortex might play a role in the pathogenesis of diabetic retinopathy and nephropathy. Although this thesis remains unproved, subsequent studies and experiments have offered no outstanding evidence that negates the role of adrenocortical dysfunction in this disease process. This working hypothesis has provided a basis for various productive research projects. The perplexing problem of diabetic retinopathy remains unsolved, but there is every indication that its ultimate resolution will rest upon the solid foundation afforded by the brilliant work, the uncanny insight, and the stimulating suggestions of Jonas Friedenwald.

BERNARD BECKER, M.D.  
Saint Louis, Missouri

## MEDICAL RESEARCH: A MIDCENTURY SURVEY

The advent of two volumes under the above title invites editorial comment in appreciation and commendation of an invaluable critique of a half century of research in the medical sciences. A full awareness of the significance of these volumes requires a glance backward to the status of medical research in 1900.

At the turn of the century, scientific advance in the field of medicine proceeded at a snail's pace. What advances were being made were accomplished chiefly in the medical schools. The greatest experimental activities were in laboratories associated with departments of pathology. Here interest centered around morphology and the relations to basic sciences were either tenuous or nonexistent. Pharmacology was mainly materia medica and bacteriology was a new and essentially unexplored science which as yet had not penetrated appreciably into the medical schools. Clinical medicine was taught by busy practitioners and what experimental medicine they engaged in was largely confined to bedside observation, chiefly on the effects of therapeutic measures.

Now at the midcentury mark, the picture of the state of medical research is dramatic in its antithesis to that presented in 1900. Medical science is advancing at an ever accelerating rate. The basic sciences of chemistry, physics, and mathematics are assiduously mined for fundamental concepts which will lead to a better comprehension of the problems of disease. Not only in medical schools but also in independent foundations, large and small, and in the laboratories of innumerable pharmaceutical houses, research workers are pouring forth continually a torrent of literature on every aspect of medical science. The medical schools, both in the preclinical and clinical branches, are now staffed by men highly trained in many areas of the basic sciences. The lecture halls and clinics are flanked by numerous laboratories filled with elaborate and costly apparatus, manned by highly skilled technicians. These laboratories are constantly seeking to recruit to their staffs young men trained in basic sciences who are initiating careers in all areas of clinical medicine.

Financial support for medical research from government, private foundations, and from the public through the large national societies totals millions of dollars per year. Thousands of research projects directed by competent investigators are now supported by such foundations. Most individuals who have demonstrated reasonable competency in medical research can obtain adequate financial aid for investigative work in any direc-

tion which they believe will be rewarding. Fifty years of such activity has brought about enormous advances which have contributed immeasurably to our knowledge of disease.

The year 1950 afforded an appropriate time for a survey by competent persons of the many factors, scientific and otherwise, which contributed to these advances. This The American Foundation in *Medical Research: A Mid-century Survey*\* has done. In these volumes is presented an exposition of research progress in medical science for the past fifty years together with an evaluation of its significance. The magnitude of this task is indeed formidable, and it has been approached with vigor and understanding. For the accomplishment of the present task, the Foundation assembled a committee of consultants who are outstanding authorities in many fields associated with medical research. The members of this committee furnished the basic factual materials upon which the exposition and evaluations were made. But without coordination and integration, these reports would have lost much of their cogency and force. Miss Esther Everett Lape, the Foundation's "Member in Charge," and her staff have furnished these integrating and coordinating factors which make the *Survey* one of outstanding merit.

The first volume concerns itself with "American Medical Research in Principle and Practice." An introductory chapter outlines the scope of the "Survey." There follows an exposition of the relationship of the contributions of the fundamental sciences, chemistry, physics, and mathematics, to biological research. The rest of the volume expands a detailed discussion of the sociological, the financial, and the political factors which bear upon the manifold problems arising in the advancement of research in the medical sciences.

This volume, while perhaps more appealing to those concerned with administrative problems in medical education, medical research, medical care and other medical problems of public or quasi-public nature, is nevertheless highly informative and stimulating to those who are desirous of understanding the manifold factors which are involved in the administration of public policies in medical science.

Of particular interest to the practicing physician is the second volume, *Unsolved Clinical Problems in Biological Perspectives*, which presents a discussion of nine such problems. These are: cancer, infertility, arterio-

sclerosis, hypertension, the rheumatic syndrome, tuberculosis, the nature of virus and virus diseases, alcoholism, and schizophrenia. In these chapters, the advances of a half century of research in the respective fields together with an exposition of the current status of these problems are given in most succinct form without inclusion of distracting technical details or masses of experimental evidence. Indeed, as reviews of these complex subjects, they are examples of masterly thoroughness combined with unusual brevity.

The introductory chapter of this volume, "Current Metabolic Concepts Orienting Research in Biology and Medicine," is of particular interest to those concerned with diabetes or other clinical conditions involving metabolic concepts. Here the emphasis is upon basic principles: "Normal physiological functions are manifestations of the molecular changes that are metabolism; disease is a constellation of disturbances of finely integrated chemical mechanisms." The emphasis continually is that comprehension of symptoms and manifestations in disease must presuppose the understanding of molecular mechanisms which underlie biological activity. The role of enzymes and coenzymes is developed leading to discussion of the diversities of cellular metabolism. Cellular homeostasis is discussed in terms of these complex enzyme reactions. The relation of these reactions to the production of stored chemical energy as energy-rich phosphate compounds by oxidative phosphorylation is brought out. Finally the interrelation of the pancreatic islands, the pituitary, the adrenal, and other hormonal organs to these complex processes is outlined to the extent to which they are known. The chapter is illuminating in its discussion of how possible aberrations of these complex interrelationships of enzymes, coenzymes, and hormones leads to the development of diabetes mellitus. "The picture of diabetes as a syndrome involving defects in some aspect of nearly all phases of cellular metabolism and of the coordinating mechanisms of hormone interrelations is incomplete, suggesting many discrepancies. In nature there are no discrepancies and those that appear in tentative formulations therefore represent either erroneous observation or incomplete information. We may hope that, when all the facts are in, the apparent discrepancies will be resolved."

The chapter on alcoholism presents an analysis of a difficult problem in which many conflicting facts and opinions are placed in balanced perspective. In particular, the metabolic, endocrinologic, psychologic, and psychiatric aspects of this problem are discussed in the light of evidence both in humans and in animals which

\**Medical Research: A Midcentury Survey*, Volume I, 765 pp; Volume II, 740 pp. Boston, Little, Brown and Co., for The American Foundation.

have significant bearing on these facets of the problem. There is an illuminating discussion of the hypothesis that the compulsive drinker develops a conditioned pattern of tissue enzyme activity which forms the basis for his habituation. The craving for alcohol is explained "in terms of genetically conditioned individual biochemical differences that produce a relatively heightened need for vitamins or other elements." The evidence for this in the opinion of one authority is "clear-cut and unequivocal." In the opinion of another, however, the summation of the experimental evidence is "considered to be incompatible with any narrow concept of human alcoholism as due to nutritional or genotrophic defects." And another authority concludes that such a hypothesis is not applicable to "the intricate problem of human alcohol-

ism without a great many further fundamental investigations."

The remaining chapters of this volume are also treated with clarity and brevity. They comprise model reviews for the reader who wishes to keep abreast of these advancing fronts of medicine. Emphasis is constantly upon fundamentals, and metabolic aspects of these perplexing clinical problems come in for their share of emphasis. No one who aspires to the acquirement of some degree of scholarly purview of the entire field of medical science can afford not to possess and study these two books.

W. C. STADIE, M.D.  
UNIVERSITY OF PENNSYLVANIA  
PHILADELPHIA, PENNSYLVANIA

### *The Quality of Value*

No one has yet discovered a way of cultivating inventive genius. Psychologists who have been working on the problem for many years are not encouraged, in spite of the fact that some men have seemed to have an extraordinary capacity to inspire others to achievement. How do they do it? Perhaps this should be a prime target for pedagogic research, but a distinction should be made between originality and invention. Invention may be defined (for our purpose) as originality with a quality of value, whether applied to music, design, or science. It is a simple matter to teach originality if the quality of value is left out. Perhaps a starting point might be an attempt to develop men who regard their work as a fascinating adventure—a perpetual series of expeditions into the unknown. The conventional technologist has a different

viewpoint. He is skeptical of the very existence of the unknown, and he lacks the emotional drive to achievement of capital invention. Unless a man can be swayed by fancies he will stay with his facts and will never make the trips. We must try to develop imaginative men who can conceive of the unknown places, who have the naïveté to believe in their existence, the daring to start into the wilderness, and the stubborn determination to stay there until they can depart with some of its riches. If it is possible to teach genius, instead of merely hoping it will come along, the future will belong to the society that first discovers how.

From "Social Attitude Toward Invention"  
by Eugene Ayres in *American Scientist* 40:  
521-40, October 1955.

### *Psychological Factors in the Scientific Process*

It is commonplace to say that science depends on communication, that the invention of printing eventually advanced science enormously, that the publication of results is always essential, that the iron curtain and the secret classification of data are bad for science. All such obvious statements are concerned with whether or not the normal overt mechanisms of communications are working or blocked. On the other hand, there are covert influences that make up what has been called the climate of opinion, and by Goethe the *Zeitgeist*—the conventions of thought and the unquestioned assumptions that are implicit in the culture in general and in science in particular. These forces act as *vires inertiae*. They constrain originality and reinforce tradition, as well as limiting the irresponsibility

of the cranks who, excelling in originality, are deficient in critical wisdom. Conant has remarked that "a scientific discovery must fit the times . . . A well-established concept may prove a barrier to the acceptance of a new one. If a conceptual scheme is highly satisfactory to those who use it, neither a few old facts which cannot be reconciled nor a few new ones will cause the concept to be abandoned . . . Old concepts may be retained in spite of alleged facts to the contrary." The *horror vacui* that science cannot deny is the scientist's fear of being left without any theory at all. "It takes a new conceptual scheme to cause the abandonment of an old."

Edwin G. Boring in *American Scientist* 42:639-45, October 1954.