Solomon A. Berson

Jesse Roth, M.D., Bethesda

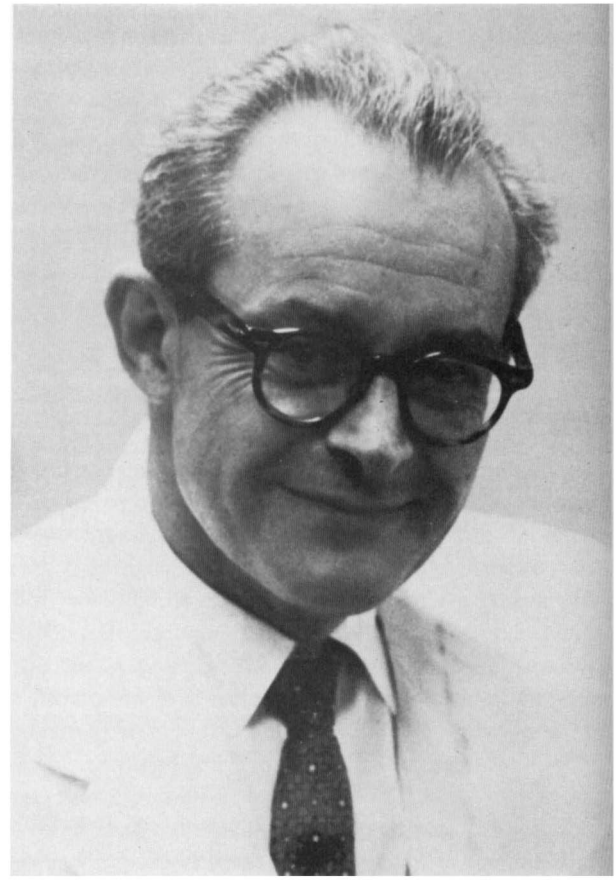
On April 11, 1972, the world lost one of its outstanding citizens—Dr. Solomon A. Berson died suddenly in Atlantic City, New Jersey, shortly before his fifty-fourth birthday.

Dr. Berson, together with Dr. Rosalyn S. Yalow, his long-standing partner in research, introduced the radioimmunoassay of plasma insulin in 1959. Over the next decade the method completely revolutionized the field of endocrinology, both technically and clinically. The revolution spread from polypeptide hormones to the steroid hormones and then, like other great revolutions, spread beyond the confines of endocrinology to involve clinical pharmacology, oncology, virology, and hematology. It is difficult to find a field of medicine or biology that has not been affected.

Dr. Berson was born and raised in New York City. He received the Bachelor of Science degree from the City College of New York in 1938, whereupon he entered the graduate schools of New York University. In 1939 he was awarded the Master of Science degree, and following three years in the Department of Anatomy, was enrolled in the School of Medicine, receiving the Doctor of Medicine degree in 1945.

In 1948, after having completed one year of internship at the Boston City Hospital, and two years in the U. S. Army Medical Corps, he moved to the Veterans Administration Hospital, Bronx, New York. In 1950, after completing his residency training in internal medicine, he was appointed to the staff of the Radioisotope Service, and became Chief of that unit in 1954. He became Senior Investigator in 1963, a title he held until his death. In 1968 he accepted appointment as Chairman and Murray M. Rosenberg Professor in the Department of Medicine of the Mt. Sinai School of Medicine and Director of the Department of Medicine of the Mt. Sinai Hospital in New York City.

In 1951 a paper appeared in Science (*114*:14) entitled "The use of K^{42}-tagged erythrocytes in blood volume determinations," by R. S. Yalow and S. A. Berson. This was the first of more than two hundred publications that were to appear in the scientific and medical literature over the next twenty years by these coauthors. Their research, which applied radioisotopes to the study of disease states in man, was focused (in the early 1950's) on red cell and plasma volumes, the fate of plasma proteins, especially albumin, the effects of irradiation on iodinated proteins, and the quantitative aspects of iodide metabolism.



DR. BERSON

These papers, which remain today as valid, exacting, very sophisticated, quantitative studies, are even more extraordinary when one recalls that Dr. Berson's research skills were essentially self-taught: He entered research directly from clinical medicine, without the years of research training that all contemporary investigators undergo.

In the mid-1950's Berson and Yalow turned their at-

tention to insulin. They labeled insulin with I-131 and showed that serum of all insulin-treated diabetics as well as insulin (shock)-treated mental patients contained insulin-binding antibodies which delayed the degradation of insulin in vivo. Antibodies were absent from diabetic and nondiabetic subjects that had never received insulin. These findings (very well documented) were published in 1956 in a paper by Berson, Yalow, Bauman, Rothschild and Newerly (J. Clin. Invest. *35*: 170) entitled "Insulin-I-131 metabolism in human subjects: Demonstration of insulin binding globulin in the circulation of insulin-treated subjects." The editors of the journal, at that time, were so disquieted by the notion that insulin was antigenic, that they agreed to publish the paper on the condition that the word "antibody" be removed from the title. Berson and co-workers did extensive studies over the next several years on the reaction of insulins from various species with insulin antibodies from different sources, including a systematic study that related clinical resistance to insulin in diabetics to the levels of circulating antibodies.

One finding, viz. guinea pig antibodies to porcine insulin reacted very strongly with human insulin, led them to devise the radioimmunoassay in which they used guinea pig antiporcine insulin serum and I-131-labeled porcine insulin to measure the concentration of endogenous insulin in human plasma (pure human insulin was not available at that time). These findings were published in their now-classic articles which describe the first successful radioimmunoassays (Nature *184*: 1648, 1959; J. Clin. Invest. *39*:1157, 1960; DIABETES *10*:339, 1961). Among their early, important findings was that diabetics with moderate glucose intolerance were not insulin deficient but in fact hyperinsulinemic, whereas more severe glucose intolerance was associated with insulin deficiency. They also showed that tolbutamide released insulin acutely, and that leucine, given to children with leucine-sensitive hypoglycemia, provoked a prompt burst of insulin release. They also showed how measurements of plasma insulin made possible the distinction between patients with insulinomas and those with other forms of fasting hypoglycemia.

They and others have extended these methods to virtually every protein hormone the chemists have been able to purify, and even to several hormones before they were purified. For the steroid hormones, the radioimmunoassay represented a great improvement of existing chemical methods, but for the peptide hormones, such as growth hormone, glucagon, and parathyroid hormone, the immunoassay represented the first and only direct measurement in blood. The result was a total revolution in endocrinology during the ten years that followed the introduction of the method.

They not only introduced the method but published extensive studies on the theoretical basis of the methodology and continued to pioneer new applications. They and workers in their laboratory published extensively on multiple aspects of the physiology, biochemistry and clinical pathology of growth hormone, parathyroid hormone, ACTH, and gastrin.

One of the early applications of this competitive binding methodology to a nonimmune, nonendocrine system came from their laboratory when intrinsic factor and radioactive vitamin B_{12} were used to measure vitamin B_{12}. Likewise they produced one of the most important nonendocrine applications of the radioimmunoassay: the specific and sensitive detection of Australia antigen and antibodies in screening the blood of donors for viral hepatitis. The impact of the competitive assay methodology that they introduced may be seen by the large percentage of papers at contemporary scientific meetings or in current journals that use these methods. These studies were recognized by many national and international awards and honors; those from the American Diabetes Association to Dr. Berson included the first Lilly Award in 1957, the Banting Memorial Lecture and Medal in 1965, and a special Insulin 50th Anniversary Commemorative Medallion in 1972.

In addition to doing research, Dr. Berson was a superbly lucid and vigorous lecturer and teacher. His quick, sharp questions and comments enlivened all meetings he attended or chaired. He was also one of the busiest referees of scientific manuscripts. Editors of several prominent journals called on him especially to referee works that contained complicated mathematics. Since Dr. Berson was a self-taught expert in both mathematics and physics, especially as applied to biological research, he was not discouraged by the mathematical complexities of some contemporary works.

As a teacher of research fellows, he was most zealous and energetic. Because the Veterans Hospital could not supply the formal classes of a vast graduate center, he himself often provided his fellows with formal didactic courses in mathematics, biochemistry and physics. In addition to being an excellent scientist and teacher, he was a superb physician: He had a large group of loyal and devoted patients who were given warm and attentive care at regular intervals. After moving to the Mt. Sinai School of Medicine, medical students and, even more prominently, interns and residents became his prin-

cipal students, and the bond between him and his house officers was very strong. His skill extended well beyond medicine and science, however; he was an accomplished violinist and chess player and was well read in history, philosophy, and art.

The tragedy of Dr. Berson's death was compounded several weeks later by the sudden death of his elder daughter, Wendy, at the age of twenty-four. He is survived by his wife, daughter, sister, and brother, and is mourned by co-workers, colleagues, students, and friends all over the world.

Editor's Note: Scientists and physicians throughout the world have paid homage to Dr. Berson by special ceremonies at scientific meetings, by contributions of papers to memorial issues of several journals (Metabolism; Israel Journal of Medical Sciences; Journal of the Mt. Sinai Hospital), *and by monetary contributions to the Solomon A. Berson Fund for Medical Research Inc., c/o Dr. L. J. Soffer, Mt. Sinai Hospital, New York, N.Y. 10029, which, if funds are sufficient, will honor Dr. Berson's memory by supporting the research training of young scientists of special promise.*

BOOK REVIEWS

JOSLIN'S DIABETES MELLITUS, *11th edition, edited by Alexander Marble, M.D., Priscilla White, M.D., Sc.D. (Hon.), Robert F. Bradley, M.D., and Leo P. Krall, M.D., with twenty-six contributors, $32.50, 884 pages, 122 illustrations, 2 color plates. Philadelphia, Lea & Febiger, 1971.*

Among the monumental medical publications of this century, *Joslin's Diabetes Mellitus* stands as a pylon. Considering the fifty years that have passed since insulin was discovered and revolutionized the care and prognosis of diabetic patients, the studious reader may note that Joslin first published his observations in 1916, in the still arid, woe-beset pre-insulin days on 1,000 patients. In 1916, 425 of these patients were known to have died after a duration of the disease averaging about five years.

The editors of the present work required the cooperative assistance of twenty-six authors to bring this edition up to date. Their job is exceedingly well done. This volume, while large, comprises, in 884 pages, thirty-two chapters. They range from a splendid introductory chapter on current concepts of diabetes by Marble, to an equally rewarding chapter on "Socioeconomic Considerations in the Life of the Diabetic" by Entmacher and Marks, the latter being the great veteran of statistical studies in this field.

All the contributing authors are or have been associated with the Joslin Diabetes Foundation.

Joslin's spirit pervades the book. In the foreword, the editors write "For purposes of practical therapy, we have chosen to regard diabetes as basically a disease in which there is a deficiency of available insulin." True to the Joslin view they write, "we believe that by meeting the insulin deficiency and maintaining the best control of diabetes practicable on a given patient, we may justifiably hope to prevent, or at least postpone and minimize the vascular complications of long-term diabetes."

This edition is beautifully set in bold type on glossy, firm paper. The traditional use of illustrations, figures and references is generous and up to date.

Controversial opinions are given due consideration and the reader may feel certain this is not a one-sided book with little attention to new, important leads in the effort to unravel the pathogenesis and nature of diabetes.

Although fifty years have passed since the discovery and introduction of insulin in the management of diabetes, its state in the circulating blood is still unclear. In the chapter "Insulin in Diabetes—Applied Physiology," Soeldner has provided a splendid survey of current and past knowledge including a comprehensive bibliography dealing with research into free, bound, atypical insulin, insulin resistance, and variations in metabolic states and disease.

The chapter by Stauffacher and Renold, "Pathophysiology of Diabetes Mellitus," is of special interest to students and other readers who would like a current biological view of the diabetic syndrome, from the mystery of lipoatrophic diabetes to the effects of cytotropic injurious agents on beta cells, allergic insulitis, and spontaneous diabetes in animals. These authors touch on all manner of factors affecting insulin secretion: metabolic effects of underproduction in all tissues, variants of ketotic and nonketotic acidosis, metabolic transport variations and disturbances and experimental diabetes. Their achievement is almost a monograph in itself and a guide for new as well as seasoned investigators. The chapter alone is followed by 727 references.

Of special interest to diabetologists and pathologists is a splendid chapter on "Glycoproteins and Diabetic Microangiopathy" by Robert Spiro—the single most persistent and authoritative investigator in this field. He has provided a lively summary of available knowledge and emphasizes the core problems related to abnormal glucose metabolism as a result of insulin deficiency which may lead to diabetic microangiopathy.

An up-to-date chapter on the "Pathology of Diabetes" is a must for the student and the interested physician—well illustrated and comprehensive in its inclusion of all related disorders with a diabetic character. Meissner and Legg have fulfilled their mission in a succinct but thorough summary which properly emphasizes recent new data.

A chapter entitled, "Onset, Course, Prognosis and Mortality