SOME RECOLLECTIONS OF MY TENURE AT MONTEFIORE HOSPITAL:

A HALF-LIFE WITH RADIOIODINE AND THE THYROID GLAND.

No history of the physiology and pathology of the thyroid gland can ignore the contributions and activities at Montefiore Hospital. Long before my arrival in 1948, the Hospital was an established center for research in these areas and for the care of patients afflicted with disorders to which the gland gives rise. Particularly notable were the prior accomplishments of David Marine and Emil Baumann at the Hospital in elucidating the roles played by dietary iodine in endemic goiter, much of which rested on the pioneering investigations conducted by Marine in Cleveland, Ohio on the etiology of endemic goiter associated with iodine-deficient regions. Over the years, the Hospital had become established as a celebrated facility for the care and treatment of the chronically sick, especially for its remarkable collection of neurological patients and for its care of tubercular and cancer patients, drawing to the institution a steady stream of scholars, students, and clinicians eager to study and to observe first-hand the natural history of rare disorders in patients being provided long-term custodial care. The "modern" era appears to have commenced with the appointment of Louis Leiter as Chief of the Medical Division, marking the transformation of the Hospital from a chronic disease home (reflected even today as its chartered name) to a comprehensive medical center, one stressing general care and clinical investigation.
As one of his first clinical appointments, Dr. Leiter brought to the Hospital Samuel M. Seidlin, an endocrinologist who had previously conducted research relating to thyrotropic hormone (TSH) and its inactivation by thyroxin. In the course of making his endocrine rounds at the Hospital in the early 1940's, Seidlin was intrigued in finding on the wards a severely thyrotoxic patient (Bernard Brunstein), who had multiple metastases of thyroidal origin, twenty years subsequent to undergoing a total thyroidectomy. Seidlin wondered whether Brunstein's metastases were "functioning" (that is, elaborating and secreting thyroid hormones) and, hence, responsible for the patient's thyrotoxicosis. Despite findings published in 1940 by Hamilton and colleagues indicating no localization of radiiodine by carcinomatous thyroids, Seidlin undertook to initiate studies of Brunstein with radiiodine, a heroic venture in those days: Medical research with radioisotopes was confined probably to two centers (Berkeley and Boston); obtaining radioisotopes in wartime was no trivial feat when their only source were cyclotrons heavily committed to atomic weapons; and the requisite specialized scientific and technical personnel, equipment, and facilities were not at hand. Applying his customary perseverance, ingenuity, and vision, Seidlin somehow persuaded L. D. Marinelli, an under-utilized physicist at Memorial Hospital, to collaborate with him and the MIT-Harvard cyclotron to squeeze in the production of the required radiiodine. The initial experiments and subsequent demonstrations at Montefiore Hospital were sensational: Brunstein's metastases proved highly functional, even making thus discernible a cerebral lesion prior to its subsequent visualization by x-rays, a consequence of Brunstein's own request to position "the machine", i.e., the Geiger counter, over the spot that pained him, "but not like a headache." Since thyroxin was found present in the patient's metastases and intramuscular injections
of thyroptropin did not result in detectable TSH in his urine, Seidlin concluded that it was the metastatic carcinoma that inactivated the TSH. He later used thiouracil to counteract the hyperthyroidism caused by Brunstien's functioning metastases. Two instances of acute myeloid leukemia developed in the series of 16 patients with metastatic thyroid carcinoma intensively treated with radiodine.

To explain why only some metastases of the thyroid gland were functional, Seidlin developed the hypothesis that TSH would induce function only after its inactivation was diminished by the total extirpation of the non-neoplastic gland, accomplished either surgically or by irradiation. He advocated, as the therapy of well-differentiated thyroidal metastases, the prior complete ablation of the gland followed by repeated doses of radiiodine until no further localization anywhere in the body of administered radiiodine tracers was demonstrable— a procedure essentially still in vogue today in the practice of nuclear medicine.

This was how the Medical Physics Laboratory came into being in the basement of the Van Cortlandt Pavillion, a tiny room next to the animal quarters, the first clinical radioisotope service in New York City and probably the third in the country. The research with radiiodine and metastatic thyroid carcinoma attracted widespread interest, so that we were always hosting colleagues from all over the world, eager to see the Laboratory, its techniques, and patients. I recall that frequent visitors in the late forties and early fifties were Paul C. Abersold, Marshall Brucer, John H. Lawrence, James Means, William G. Myers and Saul Hertz. I remember also that some residents and fellows then at the Hospital were destined to have futures linked to the thyroid gland: Isidore Edelman, Kenneth Sterling, and Bernard A. Sachs, and much later, Jack Oppenheimer. We were often
consulted by groups from all over when setting up their clinical radioisotope programs. Throughout the fifties, the Medical Physics Laboratory was the world's largest consumer of $^{131}$I, according to the late Dr. Abersold who maintained such records for the Atomic Energy Commission. It may be worth pointing out that Seidlin was an unsalaried member of the Hospital, responsible for raising financial support for the Laboratory's research; he surely devoted better than half-time to Montefiore Hospital as Chief of the Endocrine Service and of the Medical Physics Laboratory.

With Seidlin's death in 1955, I assumed an even greater role in the administration of the Laboratory, and expanded the number of diagnostic procedures and therapeutic procedures involving the internal administration of radioisotopes. An extraordinary feature of our operation was the over-all clinical responsibility assumed by the Radioisotope Board, comprised of representatives of the Hospital's major clinical services and chaired by Alter Weiss and, later, by Bernard Sachs, which evaluated patient findings, prescribed radioisotope therapy, and observed the patients' subsequent course for years. The entire Board met weekly, seeing the patients passing through the Laboratory and again as they returned for follow-up visits. These arrangements afforded our patients the benefits of the collective skills and wisdom of the various specialists while yielding us an invaluable fund of experience and knowledge, much of which found its way into remarkably complete and detailed records diligently maintained by the Laboratory. Among the Board members, I particularly recall Alter Weiss, Bernard A. Sachs, Jack Fried, Daniel Laszlo, Joseph Krakauer, Martin Nissel, Arthur Bauman, Frank A. Graig, Theodore Spaet, Stanley Kass, and Kenneth Rosenheck. Considered today, recalling their level of involvement, responsibility, and zeal, it is again remarkable that no members (except for me) of the Board
received any financial compensation for their participation.

Returning to thyroid research, the Laboratory after Seidlin's death continued to pursue a number of studies. One of these was the systematic examination of the thyroidal metabolism of group VII elements of the Periodic Table, a long-standing investigation initiated and directed by Emil Baumann; these experiments with laboratory animals entailed determining body distribution, especially by the thyroid gland, of radioactive bromine, rhenium, fluorine, and technetium. I believe the first metabolic studies of technetium were those reported from Montefiore; the radioisotope used for these experiments was $^{99}$Tc (half-life: $2 \times 10^5$ years), found to localize in, but not protein-bound by the thyroid gland—the basis for a current widely used scanning procedure.

Our comprehensive follow-up of patients and maintenance of detailed records of their clinical status and of radioiodine turnover, alluded to earlier, resulted in our being invited to participate in the national survey of the long-term effects of radiiodine sponsored by NIH, an undertaking that Bernard Sachs and I co-chaired until my departure in 1962. From this study of the fate of 603 patients treated with $^{131}$I (and followed from 1-17 years) we found, as the only untoward effect, the late onset of hypothyroidism, whose incidence correlated with the magnitude of the radiation delivered to the thyroid gland.

Another thyroidal investigation, jointly conducted by Bernard Sachs and me, concerned the in vitro localization of tagged iodinated compounds by the leucocytes of patients in relation to thyroidal status, anticipating that nucleated blood cells would prove very sensitive metabolic indicators.
We found that white cells localized much more NaI, T₃, and T₄ than did red cells, and that the uptake by WBC of labelled T₃ is significantly correlated with thyroidal status. (These in vitro studies at Montefiore led directly to those I initiated in 1962 with C. A. Tobias at the University of California (Berkeley), which demonstrated that cultured human kidney cells persist even in vitro in responding to the thyroidal hormones, and, furthermore, revealed by radioautography that these responsive cells localize tagged thyroxin in their nuclei, observations that bear on very directly on the Hospital's subsequent distinguished research pertaining to the existence and nature of nuclear thyroidal receptors.)

Subsequent to my departure from Montefiore, Bernard Sachs and I collaborated on a study of dietary iodine, as indicated by the content of the element in the breads of two geographic regions, and its influence on the uptake of radiiodine by the thyroid glands in patients residing, respectively, in The Bronx and Columbia, Missouri. We found that thyroidal radiiodine uptake levels for each locality differed, being indeed affected by the breads being consumed.

To keep this account within bounds, I have omitted many memorable incidents and anecdotes regarding events and individuals that I treasure. This being a personal account, I have necessarily limited inclusion of name and events judged appropriate for a brief sketch; the names of many other clinicians, scientists, and technicians who also contributed to the activities and achievements of the Laboratory should, of course, be made known. I am hoping that there will be occasions before long to be able to relate more fully this fascinating account. In the interim, the names
of some of these individuals appear as co-authors in the following abbreviated list of publications concerning the thyroid gland and the Medical Physics Laboratory:

AN ABBREVIATED LIST OF PUBLICATIONS BEARING ON THE THYROID GLAND AND THE MEDICAL PHYSICS LABORATORY.


S. M. Seidlin: Radiiodine in the Treatment of Metastatic Thyroid Carcinoma. Med. Clinics N. Amer. 36:663 (1952)

E. J. Baumann, N. Z. Searle, A. A. Yalow, E. Siegel, and S. M. Seidlin:
Behavior of the Thyroid toward Elements of the Seventh Periodic Group. Am. J. 
Physiol. 185: 71 (1956).

B. A. Sachs, E. Siegel, S. Kass, and M. Dolman: Radioiodine Therapy of Thyro-

B. A. Sachs, E. Siegel, B. N. Horwitt, and Elsie Siegel: Bread Iodine Content 
1972, pp.79.

E. Siegel and B. A. Sachs: The In Vitro Uptake of 125I Labeled Iodide, Triiodo-
thyronine, and Thyroxine by the Human Leukocyte in Relation to Thyroid 

E. Siegel and C. A. Tobias: End-Organ Effects of Thyroid Hormones: Subcellular 

E. Siegel and C. A. Tobias: Actions of Thyroid Hormones on Cultured Human 

May 25, 1984 Edward Siegel, Ph.D.