

## **Saul Hertz (1905-1950)**

### **and the Treatment of Hyperthyroidism with Radioiodine**

Saul Hertz was a bright, ambitious student. Born and raised in Cleveland, he went to relatively nearby Ann Arbor for his undergraduate work at the University of Michigan and then chose to further afield for his medical degree at Harvard which he received in 1929. After his internship and residency back in Cleveland, he returned to the Boston area in 1931 to take up further training at the Massachusetts General Hospital (MGH) under the nationally known professor of medicine, J. Howard Means. Means' forte was in thyroid function and disease and he had set up a thyroid clinic at the hospital. Hertz was so eager to be in this milieu that he agreed (and was able to) work without a salary. He did enough so that Means arranged for a fellowship with a modest salary after only three months. As there were no full-time positions of any sort at that time in the depths of the Great Depression, Means was able to keep Hertz on with periodic reappointments of two- to three-year terms. In 1934, Means named Hertz as the Director of the Thyroid Clinic, which in reality meant that he was in charge of the room where the basal metabolism tests were done. Hertz worked away at a number of projects as well as seeing patients with thyroid disease. He also was able to do fairly crude (at least to us today) bioassays. For example, with a bioassay based on thyroid histology, he and his colleagues were able to show that the urine of hypothyroid patients had something in it that stimulated the thyroid gland (note that thyrotropin or TSH had barely been recognized in the mid-1930s and it was not yet clear that it was in fact a separate hormone).

In 1939, Hertz attended a lecture with Means and two other colleagues from the Thyroid Clinic; the speaker was Karl Compton, the president of the Massachusetts Institute of Technology (MIT) and a practicing physicist. The talk mentioned a curious new idea: that one could artificially make radioactive isotopes of common elements. Hertz and Means wondered if there was such an isotope for iodine. The idea was clear: if there were such an isotope, one could do all sorts of studies on thyroid function that would be impossible otherwise. One might even be able to destroy by radiation enough of the thyroid gland in hyperthyroid patients to render them euthyroid. Compton was not sure of the answer but a few days later he wrote Hertz that it would indeed be possible to make radioiodine.

Hertz and his co-workers began with a home-made iodine radioisotope ( $^{128}\text{I}$ ) with such a short half-life (25 minutes) that experiments had to be done on the spot. First they did several studies in rabbits and showed that the thyroid gland took up the radioiodine avidly, that the rabbit thyroid took up even more of the radioiodine if TSH were injected first. But how could they use this isotope to treat hyperthyroid patients? The isotope lasted such a short time that there was no prospect of treating anyone.

The cyclotron had just been invented a few years before and was already being used to generate new isotopes. By 1940, Hertz and co-workers had two new radioiodine isotopes with much longer

half-lives:  $^{130}\text{I}$  (12.5 hr half-life) and  $^{131}\text{I}$  (8 day half-life). For a while they continued to do physiologic studies but now in man instead of rabbits, including some with Graves' disease. These last, as expected, had high thyroid uptake of the radioiodine. Finally, in early 1941, they began to treat hyperthyroid patients with radioiodine. It was then a major gamble, however obvious it may seem today. They had no way of knowing if the new therapy would work. They also had no idea how much to give but rather simply picked an arbitrary dose that more or less mimicked what they knew was taken up by the patients' thyroid glands. Although now it is hard to know exactly what they used as a dose, the average dose was probably about 4 mCi. They treated about one patient per month and had enough information to present their data to the annual meeting of the American Society for Clinical Investigation in May, 1942. Some patients had not recovered entirely but the majority had clearly improved. They had shown a new and nonsurgical treatment for hyperthyroidism.

Hertz continued with the work but in 1943 left to join the US Navy then, as was the rest of the United States, completely caught up in the Second World War. When he returned to Boston in 1945, still in the Navy, he was able to follow up his treated patients and write his classic paper on the radioiodine treatment of hyperthyroidism in 1946.

By this time, he was not alone: others at the MGH had treated hyperthyroidism with radioiodine while Hertz was away in the Navy and published simultaneously with him. Hertz unfortunately became embroiled in several personality conflicts and had to leave the MGH. He died at a tragically young age in 1945. His legacy is, however, clear: he was the principal author of a new and successful treatment for hyperthyroidism.