MGH News

MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MASSACHUSETTS Vol. 46 No. 6 September 1987

Remembering the Early Days of Nuclear Medicine

Long before the United States unleashed the awesome power of the atomic bomb to end World War II, scientists at the MGH and MIT pooled their talents and harnessed nuclear energy for another purpose—to battle disease.

This month marks the 50th anniversary of work that led to the first successful treatment of humans with an artificially radioactive material; specifically, radioactive iodine to treat an overactive thyroid gland (hyperthyroidism).

The collaboration between the MGH Thyroid Unit and the Radioactivity Center at the Massachusetts Institute of Technology helped to usher in the era of nuclear medicine.

Radioactive iodine and the technique by which it was first administered to MGH patients still hold an important place in the treatment of thyroid illnesses.

Knowledge of the relationship between iodine and the thyroid gland which regulates chemical changes in the body (metabolism) can be traced to ancient days. Enlarged thyroid glands (goiters) were treated then with seaweed and burnt sponge, both of which contain iodine.

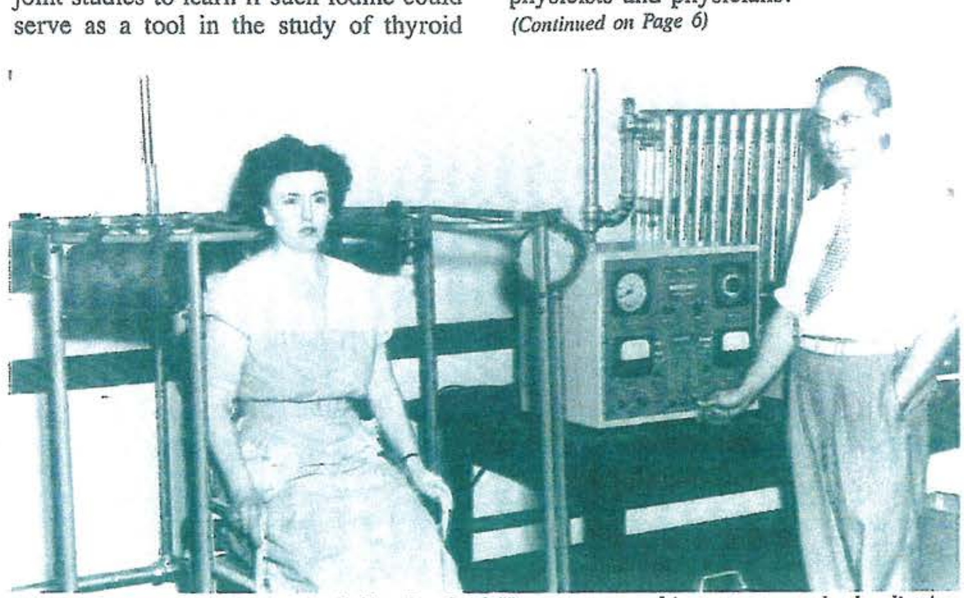
Scientific studies during the 1800s and early 1900s established that iodine is an essential ingredient of thyroid hormone and that in order to obtain iodine to produce the hormone the thyroid gland has developed a special avidity for the element.

It came as no surprise, therefore, in November of 1936 that Dr. Saul Hertz, Chief of the MGH Thyroid Unit, posed a question to MIT President Karl T. Compton at Harvard Medical School when Dr. Compton delivered a talk on "What Physics Can Do for Biology and Medicine." Dr. Hertz asked whether it was possible to produce a radioactive iodine.

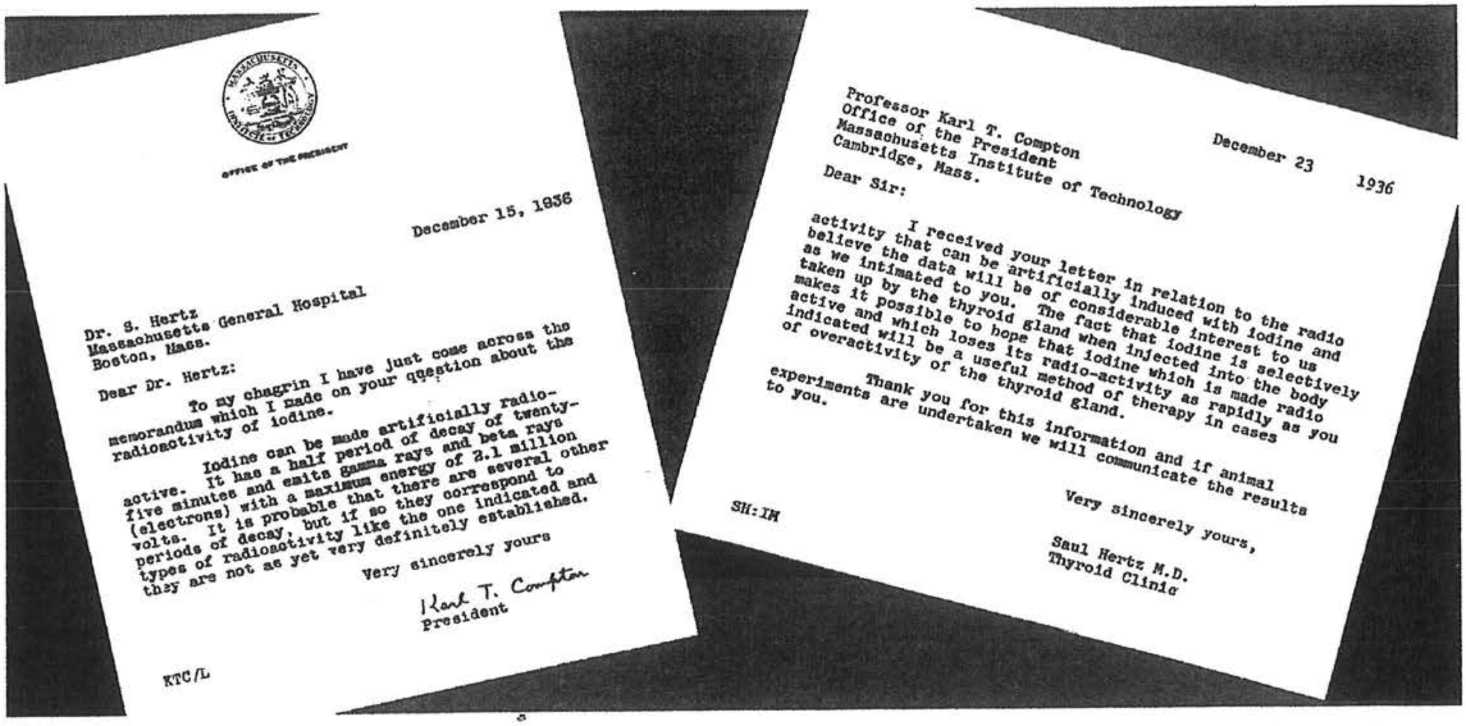
Dr. Compton did not know the answer immediately but promised to look into it. The following month he wrote Dr. Hertz to say that indeed iodine can be made artificially radioactive. This set in motion joint studies to learn if such iodine could serve as a tool in the study of thyroid physiology and possibly as an agent in the diagnosis and treatment of thyroid disease.

Prof. Robley D. Evans of MIT assumed charge of the physics phase of the program and retained the services of a young physicist, Arthur Roberts, Ph.D., for the project. Working under the general direction of Dr. James Howard Means, MGH Chief of Medical Services, Dr. Hertz collaborated with Dr. Roberts on the medical aspects. Dr. Means described the arrangement as a sound partnership of physicists and physicians.

(Continued on Page 6)



In this photo taken in the early 1940s, Dr. Saul Hertz uses a multicounter to study the distribution of radioactive iodine in a patient.



OFFICE OF THE PRESIDENT

December 15, 1936

Dr. S. Hertz
Massachusetts General Hospital
Boston, Mass.

Dear Dr. Hertz:

To my chagrin I have just come across the memorandum which I made on your question about the radioactivity of iodine.

Iodine can be made artificially radioactive. It has a half period of decay of twenty-five minutes and emits gamma rays and beta rays (electrons) with a maximum energy of 2.1 million volts. It is probable that there are several other periods of decay, but if so they correspond to types of radioactivity like the one indicated and they are not as yet very definitely established.

Very sincerely yours

Karl T. Compton
President

KTC/L

Professor Karl T. Compton
Office of the President
Massachusetts Institute of Technology
Cambridge, Mass.

December 23 1936

Dear Sir:

I received your letter in relation to the radio activity that can be artificially induced with iodine and believe the data will be of considerable interest to us as we intimated to you. The fact that iodine is selectively taken up by the thyroid gland when injected into the body makes it possible to hope that iodine which is made radio active and which loses its radio-activity as rapidly as you indicated will be a useful method of therapy in cases of overactivity of the thyroid gland.

Thank you for this information and if animal experiments are undertaken we will communicate the results to you.

Very sincerely yours,

Saul Hertz M.D.
Thyroid Clinic

SH:IM

Role for Radioactive Iodine Quickly Found

(Continued from Page 5)

The work was supported initially by the Milton Fund of Harvard University and later by help from the John and Mary R. Markle Fund.

The first task was to make radioactive iodine. Since there was as yet no cyclotron in Cambridge, a neutron source was prepared under Professor Evans' direction by mixing radium and beryllium. Dr. Roberts was then able to produce a form of radioactive iodine called I-128. It had only a 25-minute half-life (the time in which half of its atoms lose their radioactivity through disintegration).

This meant that after the I-128 was made Drs. Hertz and Roberts had only an hour or an hour and a half to anesthetize a test rabbit, inject the animal, remove its thyroid gland, and, using a Geiger counter, determine the amount of iodine taken up by the gland by measuring the radioactivity present.

"Actually, our very first experiments were aimed at finding out whether the iodine would be collected at all," said Dr. Roberts from his home in Illinois. "The total amount of iodine in a rabbit's thyroid is only about a milligram or so. Our work started in September of 1937 and by December we had already detected the iodine in the gland. It was a nice Christmas that year."

After lengthy studies with normal rabbits, the researchers began experimenting with rabbits which had stimulated thyroid glands (hyperplasia). A rabbit that was pregnant or put on a cabbage diet would develop hyperplasia. The condition could also be created through the administration of certain hormones.

"It turned out that these animals took up more iodine than the normal ones," Dr. Roberts said. "The tests showed that the physiology of the stimulated thyroid is such that it is literally hungry for iodine. That had not been realized in the past."

The promise shown by the early work with I-128 helped make it possible for MIT to obtain funds with which to build a cyclotron. When it went into operation in 1940 it supplied the thyroid investigators with a new isotope (I-130) with a half-life of 12.5 hours. This permitted a start of diagnostic experiments with humans.

By using tracer doses (small amounts for diagnostic purposes) of I-130 the researchers determined how much iodine the human thyroid took up. Soon after, one could calculate how much radioactive material was required for treatment.

The idea behind radioactive iodine as a therapy was that the abnormal thyroid's appetite for iodine would draw the radiation directly into the gland's abnormal cells. Beta rays created by the radioactivity would then destroy these cells. The short-distance nature of the beta activity assured protection for nearby healthy cells.

This therapeutic approach was clearly superior to the use of X ray since in order to reach the treatment site X ray would have to traverse many tissues which one does not want to irradiate.

When treatments began and the role of the physicist in the program became somewhat routine, Dr. Roberts left the project and joined the MIT Radiation Laboratory.

Dr. Hertz stayed on until 1943 when he joined the U.S. Navy. Upon entering the service, he invited Dr. Earle M. Chapman of the MGH Thyroid Unit to follow the hyperthyroid patients whom Dr. Hertz had treated.

In May of 1946, Drs. Hertz and Roberts reported in the *Journal of the American Medical Association* a three-to-five-year follow-up on 29 patients. The authors listed 20 as cured.

In a news interview Dr. Hertz was asked why there had been nine failures. He replied that in the early days of treatment the precise dose that a patient should receive was not always known. He said he felt sure that with this knowledge "we would have come up with 29 successes."

Dr. Hertz's pioneering work with radioactive isotopes ended in 1950 when the MGH endocrinologist and graduate of Harvard Medical School died suddenly at the age of 44.

But at the MGH and other major centers, in a silent tribute to scientists like Saul Hertz, radioactive iodine continues to serve as a useful tool in the diagnosis and treatment of thyroid disease.

Even Dr. Hertz's early practice of administering a dose of normal iodine after a radioactive one is still followed occasionally. The normal iodine produces a temporary but immediate desired drop in the patient's metabolic rate, thus relieving disease symptoms. This allows time for the radioactive iodine to impose a permanent therapeutic effect.

Dr. Gilbert Daniels of the MGH Thyroid Unit said that in coping with hyperthyroidism today an eight-day isotope called I-131 has proved to be "a simple, safe, and effective therapy."

"If the patient's entire gland is involved," he said, "the treatment in all likelihood will lead to hypothyroidism [an underactive thyroid], but this can be easily treated with pills.

"If the overactivity comes from only part of the gland—a lump, for instance—then only the abnormal portion will take up the iodine, and the gland will usually wind up functioning normally."

Well-differentiated thyroid cancer does not normally take up iodine but can be stimulated to do so. Suppose a patient had a thyroid cancer that had spread to the lungs. Making the patient hypothyroid would generate a release of more thyroid stimulating hormone (TSH) by the pituitary gland, which regulates thyroid activity much like a thermostat.

"The TSH would drive the tumor to take up the iodine in two thirds of such patients," Dr. Daniels said. "In this way, one could actually destroy metastatic thyroid cancer, particularly in young patients."■