A COMPARISON OF THE METABOLISM OF IODINE AND OF ELEMENT 85 (EKA-IODINE)*

BY JOSEPH G. HAMILTON AND MAYO H. SOLEY

RADIATION LABORATORY AND DIVISIONS OF MEDICINE AND PHARMACOLOGY AND THYROID CLINIC, UNIVERSITY OF CALIFORNIA

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One of the procedures employed for the identification of the recently discovered halogen, eka-iodine (element 85), demonstrated that this new element is accumulated in the thyroid gland in a manner similar to iodine.[1, 2, 3] The following report includes a description of the investigation of the comparative metabolism of iodine and element 85 in guinea pigs.

For many years attempts had been made to discover the missing member of the halogen group. All efforts to isolate element 85 were unsuccessful although extremely sensitive tests were available by which quantities of the order of 10^{-10} grams could be detected. Perrier and Segre in 1937[4] prepared and identified element 43 by the transmutation of molybdenum with the aid of the 37-inch Berkeley cyclotron. The amounts of element 43 obtained by this method were too minute to permit an investigation of its macroscopic chemical and physical properties. However, this artificially prepared element is radioactive and this characteristic made it possible to observe indirectly its chemical and physical properties and thereby to prove its identity. Pool and Quill[5] in 1938 stated that they had produced element 61 by the transmutation of neodynium in their cyclotron. These discoveries suggested that element 85 might be prepared in a similar manner. However, Oppenheimer[6] pointed out that to do so would require the transmutation of bismuth by alpha-particles (helium ions) possessing an energy in excess of 20,000,000 electron-volts. For this reason any attempts to produce element 85 had to await the availability of more energetic alpha-particles than could be obtained at the time when elements 43 and 61 were discovered. The recent completion of the 60-inch Berkeley cyclotron, which was designed and constructed by Lawrence and his associates, has made it possible to accelerate alpha-particles to energies exceeding 32,000,000 electron-volts. These extremely energetic nuclear particles were first successfully employed by Corson, MacKenzie and Segre[1] in the preparation of element 85. This new element is radioactive and has a half-life of 7.5 hours, but differs from all the other artificially produced radio-elements in that it emits alpha-particles.

Preparation of the Radio-Halogens.—Element 85 was produced by the bombardment of a water-cooled metallic bismuth target with 32,000,000 electron-volt alpha-particles. Approximately 200 mgm. of the irradiated bismuth were scraped from the surface of the target and placed in a small molybdenum boat which was heated to 400 degrees Centigrade in an evacuated bell jar. The volatized element 85 was collected upon a cold piece of glass suspended above the molten bismuth, dissolved in carbon tetrachloride and finally extracted with 10 cc. of 0.016 *N* sodium thiosulphate containing 4 mgm. of sodium carbonate.

Radio-iodine (I^{131}) was prepared by the bombardment of metallic tellurium with 16,000,000 electron-volt deuterons. Following the deuteron bombardment in the cyclotron, the tellurium was removed from the target and transferred to a distilling flask equipped with a long delivery tube. Thirty cubic centimeters of 6 *N* nitric acid were then added to the flask and the mixture was heated in order to distill the liberated radio-iodine into a receiver containing 60 cc. of carbon tetrachloride. After the tellurium had been completely dissolved, the carbon tetrachloride was washed twice to remove the nitric acid which had been distilled over with the radio-iodine. The radio-iodine was removed from the carbon tetrachloride by extraction with 10 cc. of 0.016 *N* sodium thiosulphate. These two radio-halogens were separated from the bismuth and tellurium without the use of a carrier. The approximate quantities prepared for each animal were: 5×10^{-12} grams of radio-iodine (1 microcurie)** and 10^{-13} grams of element 85 (0.2 microcurie).

Method of Study.—The animals used in these experiments were guinea pigs of both sexes from 4 to 5 weeks of age whose weights ranged from 170 to 240 grams and which had been raised under the same conditions. In order to facilitate the collection of excreta, the animals were kept in metabolism cages for the duration of the experiments. Two-thirds of the animals received daily injections of thyrotropic hormone for a week before the radio-halogens were administered. The thyrotropic hormone produced symptoms of thyrotoxicosis and marked hyperplasia of the thyroid gland.

The uptake into the thyroid glands and the rates of excretion of radio-iodine and element 85 were observed in groups of thyrotoxic animals and normal controls. Equal and known quantities of radio-iodine and element 85, which had previously been made isotonic by the addition of sodium chloride, were administered together by subcutaneous injection to six thyrotoxic animals and four normal controls. Four hours later three of the thyrotoxic animals and two of the normal controls were sacrificed. Aliquot fractions of the urine and aqueous extracts of the feces collected during the interval together with the thyroids and samples of muscle, blood, liver and lymph nodes, were obtained for measurement of their content of radio-iodine and of element 85. The remaining three thyrotoxic animals and two normal controls were sacrificed 18 hours after injection, and excreta and samples of tissue were obtained as before. The study was repeated without the measurement of urine and feces in nine thyrotoxic animals and six normal controls. These were sacrificed in groups of three thyrotoxic animals and two normal controls at the end of four, eighteen and sixty-five hours after administration of radio-iodine and element 85. The results of these experiments are shown in tables 1 and 2 and in figure 1.

The tissues and aliquot portions of the excreta were placed in flat ashing crucibles 4 cm. in diameter. One cubic centimeter of 0.1 *N* sodium hydroxide was added to each sample and the tissues were thoroughly macerated. The samples were then placed on a hot plate and evaporated to dryness at a temperature of 100 degrees Centigrade. This procedure made it possible to secure an even distribution of the material inside the crucibles. Aliquot fractions of the administered solutions of the two radio-halogens were measured out into these dishes together with 1 cc. of 0.1 *N* sodium hydroxide, and the mixture was evaporated to dryness. No corrections were made for the self-absorption by the tissues and excreta of the radiation emitted by the radio-iodine and element 85 since the dry weight of the samples was less than 2.5 mgm. cm.$^{-2}$. Corrections for the decay of radio-iodine and element 85 in the samples were not made since the standards and samples were measured at the same time.

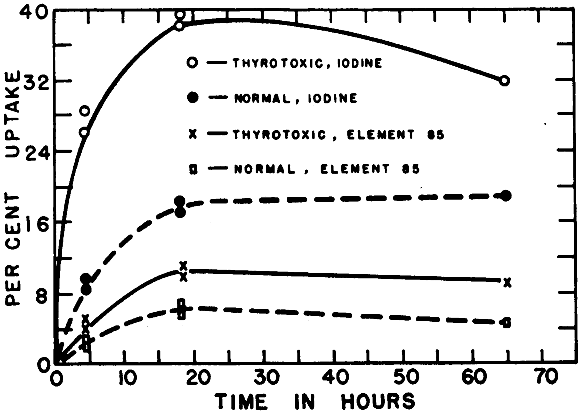

FIGURE 1

The uptake of radio-iodine and element 85 in the thyroid glands of normal and thyrotoxic guinea pigs.

The content of element 85 in the samples was determined by the use of a shallow ionization chamber which was connected to a linear amplifier and a mechanical recorder. This apparatus made it possible to measure quantitatively the number of alpha-particles emitted by the element 85 in the samples which also contained relatively large quantities of radio-iodine. Since the latter emits beta-particles, its radioactivity did not affect this type of ionization chamber. The radio-iodine in the samples was measured with a DuBridge type of vacuum tube electrometer several days later in order to allow the element 85 to decay to a negligible quantity. This technique, therefore, made it possible to determine the amount of element 85 and radio-iodine in each sample.

Results.—The results recorded in tables 1 and 2 show that element 85 is accumulated in the thyroid gland and excreted in a manner similar to iodine. The curves in figure 1 show that the variations of uptake of radio-iodine and of element 85 by the thyroid glands of the different groups of animals were similar in these experiments although the uptake of the latter was consistently less. The rates of excretion of radio-iodine and element 85 were almost identical and the kidneys apparently acted as the main channel of elimination. The proportion of the two elements excreted in the feces was probably due to contamination from the urine. The contents of the radio-iodine and of element 85 in the other tissues examined was found to be less than 1 per cent of their concentration in the thyroid gland.

TABLE 1

UPTAKE BY THE THYROID GLANDS AND URINARY AND FECAL EXCRETIONS OF RADIO-IODINE AND ELEMENT 85 IN NORMAL AND THYROTOXIC GUINEA PIGS

ANIMALS		HOURS AFTER ADMINISTRATION	UPTAKE BY THYROID		URINARY EXCRETION		FECAL EXCRETION	
NUMBER	TYPE		IODINE^{131}	ELEMENT 85	IODINE^{131}	ELEMENT 85	IODINE^{131}	ELEMENT 85
3	Thyrotoxic	4	26.1%	4.2%	13.0%	16.0%	1.0%	0.7%
2	Normal	4	8.5%	3.4%	12.4%	8.8%	0.8%	0.4%
3	Thyrotoxic	18	38.3%	10.7%	25.7%	34.0%	5.7%	8.7%
2	Normal	18	16.9%	5.4%	37.2%	36.0%	17.0%	13.0%

Discussion.—The thyroid gland is unique in that it possesses the ability to accumulate iodine selectively in relatively large quantities. This property is particularly striking because the iodine content of the blood averages less than one part in ten million while the thyroid gland normally contains approximately one part in a thousand. This indicates that the thyroid gland can concentrate the iodine it receives from the blood by a factor of ten thousand. Many organs of the body are capable of storing certain elements, such as phosphorus, magnesium and calcium in the bones, iron in the blood and the liver, and zinc in the pancreas. However, no organ in the body has the power of concentration and storage possessed by the thyroid gland.

A relationship between the periodicity of the chemical and the physical properties of the elements and their physiological action was discovered by James Blake and fully discussed by him in 1848.[7] He studied the effects of nearly all the elements known at that time on the circulation, respiration and the central nervous system of dogs. He was thus able to arrange the elements in groups on the basis of similarity of physiological action. Blake's observations have been confirmed by many investigators both for the elements available at the time of his experimental studies and for those which have been discovered subsequently.

Since element 85 is a halogen and iodine is its closest homologue, it was felt that further proof of its identity could be secured by a comparison of the biological properties of this new element with iodine. The results of the experiments described in this report show that element 85 shares with iodine the unique property of being selectively accumulated and stored in the thyroid gland. Further proof of the halogen character of this new element is demonstrated by the rapidity of its excretion while all the other heavy elements, such as radium, thorium, lead, bismuth and thallium, tend to be excreted slowly.

The fact that element 85 is retained in the thyroid suggests that it is probably held in firm chemical combination. Many years ago Marine[8] presented clinical data suggesting that once iodine is stored in the thyroid gland its release is very slow. We have recently confirmed his views by directly measuring the rates of uptake and storage of radio-iodine in the intact thyroid glands of normal human subjects and of patients suffering from various types of thyroid disease.[9, 10, 11] The relatively short half-life of element 85 makes it difficult to follow its metabolism in the thyroid for more than three days. However, the fact that no significant loss from the thyroid glands of either radio-iodine or element 85 was observed during this interval indicates that element 85 is held in thyroid tissue as firmly as iodine.

TABLE 2

UPTAKE OF RADIO-IODINE AND ELEMENT 85 BY THE THYROID GLANDS OF NORMAL AND THYROTOXIC GUINEA PIGS

ANIMALS		HOURS AFTER ADMINISTRATION	UPTAKE BY THYROID	
NUMBER	TYPE		IODINE^{131}	ELEMENT 85
3	Thyrotoxic	4	28.3%	4.3%
2	Normal	4	9.3%	2.9%
3	Thyrotoxic	18	39.8%	9.7%
2	Normal	18	18.5%	7.1%
3	Thyrotoxic	65	31.8%	8.8%
2	Normal	65	18.8%	4.5%

The increased accumulation of element 85 in the hyperplastic thyroid glands of guinea pigs suggests that this new element may be of potential value in the treatment of human thyroid disorders in which the functional activity of the thyroid gland is abnormally increased. An investigation of the relation between the microscopic anatomy of thyroid tissue and the deposition of radio-iodine has shown that this element is concentrated in the most actively functioning portions of the thyroid glands of goiterous patients.[12] If element 85 is found to behave in a manner similar to radio-iodine in the thyroid of patients with hyperthyroidism, then it should be superior to radio-iodine as a possible therapeutic agent. This is due to the fact that element 85 emits alpha-particles which have an average energy of 4,000,000 electron-volts, while the beta-rays from the radio-iodine (I^{131}) only have an average energy of approximately 200,000 electron-volts. Each alpha-particle gives up its energy in a material such as thyroid tissue within a distance of less than 50 microns, while the beta-rays from radio-iodine lost most of their energy in a distance of 500 microns. The density of ionization produced by these alpha-particles is over two hundred-fold greater than that resulting from the radio-iodine beta-rays. This means that, since the range of the alpha-particles is so short, the thyroid cells which accumulate element 85 in the largest quantities would suffer the brunt of its radiation. The action of radio-iodine in the thyroid gland would be much more diffuse because of the longer range of the beta-rays. Therefore there would be a considerable radiation effect upon the thyroid cells lying at a distance from those areas in which relatively large quantities of radio-iodine have been concentrated.

Summary.—A comparison of the metabolism of element 85 and that of iodine has demonstrated that these two halogens are stored in thyroid tissue and are excreted in a similar manner.

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** 1 microcurie is defined here as the quantity of radioactive material in which 3.7×10^4 atoms disintegrate per second.

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SURFACES OF MINIMAL CAPACITY

By G. C. Evans

Department of Mathematics, University of California

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It is asked whether, given a closed curve s in space, there exists among the surfaces of which s is the complete boundary, one for which the capacity is a minimum. This problem is investigated for the case of a closed curve which is itself of zero capacity and such that there exists a one-one continuous transformation ξ which carries a large sphere, containing s in its interior, into itself in such a way that s is equivalent to a circle σ, and the points of the surface of the sphere remain invariant. We may regard ξ as extended in the rest of space to be the identical transformation.

If S is a surface bounded by s, which except in the neighborhood of s is composed of a finite number of sufficiently smooth pieces, and $V(M)$ is the conductor potential for S it may be shown that a necessary condition for the capacity to be a minimum is the equality

$$\frac{dV(Q)}{dn+} = \frac{dV(Q)}{dn-}, \tag{1}$$

holding for all points Q on the smooth pieces which constitute S, $n+$ and $n-$ being oppositely directed normals at the point Q. A statement equivalent to (1) is the integral relation

$$\int_S\int \left(\frac{d}{dn_Q}\frac{1}{QP}\right) d\mu(e_P) = 0, \tag{2}$$

where $\mu(e)$ is the distribution of positive mass on S which generates the conductor potential.

The principal theorem is the following:

THEOREM. *There exists a unique surface S bounded by s which satisfies the equation* (1) *at all points of its smooth pieces; and except for nodal lines and points, this surface is analytic.*