Radio Iodine Uptake in Humans. V. Absolute Determination of Radio-iodine in the Thyroid. (17697)

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In the course of an investigation on the uptake of radio iodine in humans, it became apparent that a technique was needed which would permit reliable comparison of results obtained from many patients. The development of such a technique, based on basic principles of the behavior of radiation was undertaken. The result of the development was a method of measurement which permitted not only reliable intercomparison of results, but also led directly to the determination of the absolute amount of radio iodine in the thyroid gland at the time of measurement.

From previous work(1) in which radioactivity in the thyroid was measured by placing a Geiger counter directly over the gland, it was known that many errors existed, all of which were greatly exaggerated by the proximity of the gland and counter tube. These errors could be minimized by moving the counter tube some distance from the thyroid gland. but then, due to the high background caused by the radioiodine in the rest of the body of the subject, statistical accuracy of counting suffered. By enclosing the Geiger counter in a long lead tube which shielded it from all radiation except that originating in the thyroid gland area, the background was greatly reduced and statistical accuracy restored while retaining the improved geometric arrangement of source and counter tube.

It is the purpose of this paper to present (a) the counting technique as used for dogs and human subjects; (b) the utilization of these counts for the determination of the absolute radioiodine content of the thyroid; (c) a comparison of these results with those obtained by a direct measurement of thyroid radioiodine.

Method. On dogs, following intravenous injections of I^{131}, the radioactivity in the thyroid gland was counted at distances of 25 and 50 cm, the counter being shielded from all but thyroid radiation by means of a lead tube. Total thyroidectomies were done and the glands reduced to a suitable form for preparation of beta counting samples. The dogs weighed from 16 to 22 kg and were fed a standard stock diet. Forty-eight hours after intravenous injection of 75 to 100 microcuries of I^{131} in distilled water, they were anesthetized by drop ether and placed on their sides on a platform. One end of a specially constructed lead tube was placed against the thyroid gland; the correct localization of the gland was checked by palpation. The lead tube was about 60 cm long, rectangular in cross section, with internal dimensions 7.5 by 12.5 cm and wall thickness of 2.5 cm. It contained openings drilled transversely at 25 and 50 cm from the thyroid end of the tube for positioning of the counter tube. A cylindrical glass wall counter tube of active length 7.5 cm, and diameter about 2 cm was used. The tube was shielded from beta radiation by a brass sleeve 0.45 cm thick. An experimental check was made to determine the amount of scattered radiation reaching the Geiger counter from the walls of the lead tube. It was found that scatter increased the gamma ray intensity at the Geiger counter by approximately 1 to 2%, which was considered negligible for this experiment.

* The expense of this work was defrayed in part by grants from The Upjohn Co., Kalamazoo, the University of Michigan Phoenix Memorial Project, and the Committee on Growth of the National Research Council (American Cancer Society Grant).

1. Beierwaltes, W. H., Gomberg, H. J., and Lample, I., *Univ. Mich. Med. Bull.*, 1950, v16, No. 1.

Five and 10 minute counts were made at 25 and 50 cm respectively. At the completion of counting, total thyroidectomies were done by Dr. Philip Smith (John Harper Seeley Fellow, Department of Surgery). Complete removal was verified in each instance by inspection and by radioactivity check. The absolute radioiodine content of each thyroid gland was derived from the 5 and 10 minute counts described above by adjusting for the geometric system used in the experiment and utilizing previously determined absolute gamma sensitivity of the counter tube.

Adjustment for geometric correction was made by calculating the solid angle intercepted by the counter tube, treating the gland as a point source of radiation. With known radiation entering this solid angle, the total radiation from the gland was determined from the ratio of this solid angle to the solid angle of the sphere(2). Since the largest dimension of the gland was substantially smaller than the distance between the gland and counter tube, the assumption that the gland may be treated as a point source was justified. An experimental verification of this assumption was made and is described in a previous paper(1).

The absolute gamma sensitivity of the counter tube was determined as follows: a standard solution of I^{131} was prepared and activity verified by absolute beta determination (see below). An aliquot of this solution was pipetted into a Stender dish and evaporated at 60°C to dryness. This was treated as a calibrated source of beta and gamma radiation. By placing the Geiger tube at known distances from this source and using the geometric correction described above, the response of this tube to gamma radiation from I^{131} was determined. In this determination it was assumed that one gamma photon is emitted for each beta particle. An examination of the latest I^{131} decay scheme as determined by Metzger and Deutsch(2) justified this assumption for use within the detection range of our instruments. Typical sensitivity for a Radiation Counter Laboratory 10 A tube mounted in a Nuclear Instrument Corporation probe with beta shield in place is 0.002.

The method of radioactivity determination by absolute beta assay was as follows: The glands were weighed and placed in a Waring blender with a known weight of distilled water; then the blender was run for 10 minutes intermittently to avoid excessive temperatures. The mixture was removed and the blender cleared with a measured weight of distilled water. The mixture was checked by weighing to determine water loss by evaporation. Aliquots were weighed out in Stender dishes, and usually 3 samples of a given weight range and 4 different weight ranges were used. These were dried under partial vacuum in an oven at 70°. Radioactivity determinations by beta counting were made, using a thin mica window counter in a controlled geometric system. A self-absorption curve for these dried specimens of macerated thyroid tissue was obtained by plotting count per unit time against weight. By correcting for self-absorption of the specimen, window absorption, and geometric system, as well as other standard counting corrections(3), the absolute activity per g and total activity in the gland were determined. This absolute beta technic, properly adjusted, was used by us in the Iodine Intercomparison Surveys (No. 2 and No. 3) sponsored by the National Bureau of Standards. Since our determinations in these surveys agreed with the nationally accepted values within 5 and 10% respectively, we believe that this technic gives a reasonably accurate determination of the radioiodine content of the thyroid.

To date the opportunity to make similar observations in a human subject has presented itself only once. The patient was a female, 24 years old, with a moderately enlarged adenomatous gland. A dose of 505 microcuries of I^{131} was given by mouth 69 hours before counting. Counts were obtained with a lead tube designed for use with human sub-

2. Metzger, F., and Deutsch, M., *Physical Rev.*, 1948, v74, 1640.

3. Wilson, D., *et al.*, *Preparation and Measurement of Isotope Tracers: A Symposium Prepared for the Isotope Research Group*, J. W. Edwards, Ann Arbor, Mich., 1946.

TABLE I.
Values for I^{131} Content of Thyroid Gland as Determined by Direct Beta Assay and by *In Vivo* Distance Counting with Lead Tube.

		I^{131} content of thyroid					Direct assay minus *in vivo* counting			
			By *in vivo* counting							
			At 25 cm		At 50 cm		At 25 cm		At 50 cm	
Subject	I^{131} dosage, μc	By direct beta assay, μc	Mean, μc	Coeff. of variation,* %	Mean, μc	Coeff. of variation,* %	Absolute diff., μc	Diff. direct assay, %	Absolute diff., μc	Diff. direct assay, %
Dog 1	75 IV	4.08	3.88	12.0	†	†	+ .20	+ 4.9	†	†
2	75	3.74	3.21	6.7	†	†	+ .53	+14.2	†	†
3	100	7.83	7.41	5.9	8.44	20.0	+ .42	+ 5.4	— .61	— 7.8
4	100	14.30	13.70	1.9	12.33	5.2	+ .60	+ 4.2	+1.97	+16.0
5	100	7.09	5.59	3.8	6.15	11.3	+1.50	+21.2	+ .94	+13.3
Patient 1	505 *per os*	59.67	58.31	2.0	65.9	4.3	+1.36	+ 2.3	—6.23	—10.4

* Coefficient of variation equals standard deviation divided by mean, expressed as percent.
† These counts were so close to background counts that they were statistically unreliable.

jects and described previously in this series of studies(1). Total thyroidectomy was performed 1 hour after counting. The radio-iodine content of the gland was determined by the method of absolute beta assay described above.

Results. A summary of the pertinent information obtained in the experiments on 5 dogs and 1 patient is presented in Table I. All the radioactivity figures listed in this table are corrected for radioactive decay as of the time of administration. The quantity of I^{131} administered is indicated in the second column. At the left, under the heading "I^{131} Content of Thyroid," are seen the results in microcuries of absolute beta assay carried out after operative removal of the glands. At the right under this heading are seen the results of long distance measurement of gamma sensitivity. The I^{131} content of each gland as determined from measurements made at 25 cm from the thyroid is listed under the left side of this heading. Similar determinations made at 50 cm appear at the right. At the right of each of these columns is given the ratio of the standard deviation to the net total count, a measure of statistical validity of the counting known as the coefficient of variation. The statistical validity of the determinations at 50 cm for dogs No. 1 and 2 was so poor that they were discarded.

Under "Direct Assay Minus *In Vivo* Counting," the I^{131} content of the removed gland as determined by absolute beta assay was taken as the standard. The reliability of the results of long distance counting was determined by comparison with this standard. The differences between the standard values and the determinations from long distance counting are listed here both in microcuries and in percent. In 4 cases the agreement of the 25 cm determination with the standard was of the order of 5%. In the fifth case, agreement was within 14.2%, and in the sixth case, agreement only within 21.2% was obtained.

In general, the agreement of the determinations made at 50 cm with the standard was not as good as the agreement obtained between the 25 cm determinations and the standard, the range being 7.8 to 16.0%. As has been indicated above, the statistical validity of the 50 cm determinations was not as reliable as that obtained for the 25 cm counts.

Discussion. The method of determining the I^{131} content of the thyroid gland by long distance gamma counting as herein described is based on sound physical principles. To determine whether the application of these principles in this method is valid, an independent method of assay of thyroid I^{131} was used, namely, absolute beta counting. From the results, we believe that the validity of the analysis used in setting up our long distance counting technic is demonstrated. In the experimental data for the 25 cm counts, the maximal deviation from the standard was of the order of 20%, with the majority about 5%. At 50 cm, with its lower statistical reliability, the deviations ranged from 8 to 10%. For biological purposes, this method in its present stage of development can be considered quantitative and applicable whenever determinations of I^{131} content of the thyroid gland *in situ* are desired.

Statistical accuracy of *in vivo* measurements such as employed in this technic, can be improved upon by (a) an increase in counting time, (b) a decrease in background radiation, (c) an increase in dose of radioactive material, and (d) an increase in amount of radiation utilized in counting. In the experiments for each determination, a 20 minute counting period broken into 5 or 10 minute runs was used. It was found that a 500 second count was about the maximal time the patient could tolerate the relative immobility required. The reduction in background achieved by the lead shield tube appears maximal for this avenue of improvement. Because of potential radiation damage, increase in dose should be avoided. The most rewarding approach lies in increasing the utilization of available radiation. The absolute gamma sensitivity of the counters used in this work was about 0.002, which is typical of commercially available counter tubes of the Geiger type. However, the crystal type counter now in the process of development has an inherent gamma sensitivity of 0.25 or better, which would give a hundredfold increase in counts. When these high efficiency counters become available, the accuracy of the long distance counting technic can be greatly improved.

Summary. A method of counting at a distance over the thyroid was used in animal and human subjects. This method involves the shielding of the Geiger counter tube from all radiation except the thyroid gland, by enclosing the counter in a long lead tube opening over the thyroid. The statistical error inherent in long distance counting is thereby effectively reduced. Independent beta assays were done on the thyroids of 5 dogs and 1 human adult who were subjected to total thyroidectomy immediately after counting with the above technic. Comparison of radioactivity of these glands, as determined by beta assays and by long distance gamma counting, showed a maximal deviation of the order of 20%, with the majority agreeing within about 5%.

Suggestions are made regarding improvement of *in vivo* measurements such as employed in this technic.

Received February 9, 1950. P.S.E.B.M., 1950, v73.