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Monte A. Greer

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# CORRELATION OF THE 24-HOUR RADIOIODINE UPTAKE OF THE HUMAN THYROID GLAND WITH THE SIX- AND EIGHT-HOUR UPTAKES AND THE "ACCUMULATION GRADIENT"

By MONTE A. GREER<sup>1</sup>

(From the Robert Dawson Evans Memorial, Massachusetts Memorial Hospitals, and the Department of Medicine, Boston University School of Medicine, Boston, Mass.)

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Techniques for the determination of thyroid function have become increasingly refined since the demonstration of the relation of basal oxygen consumption to thyroid activity 50 years ago. Newer methods include the determination of serum protein-bound iodine and various procedures using radioactive iodine. The latter include direct measurements of the accumulation in the thyroid gland of an administered dose of radioactive iodine (1), studies of urinary excretion (2), and observations of the rate of formation of serum protein-bound radioiodine (3). All observers agree that there is an elevated rate of accumulation of radioactivity in the thyroid gland in hyperthyroid, a depressed rate in myxedematous, and an intermediate rate in euthyroid subjects. This is true whether the uptake is measured directly over the gland or indirectly by excretion curves.

There is no standardized procedure at present among various institutions using radioactive iodine, but the general preference seems to be for techniques measuring the accumulation of radioiodine directly over the thyroid rather than by excretion curves. Probably the measurement of radioactivity in the thyroid gland 24 hours following the administration of  $I^{131}$  (4) is most commonly used.

Astwood and Stanley (1) found that if the radioactivity in the thyroid is measured at frequent intervals following the administration of a tracer dose of  $I^{131}$ , the concentration in the thyroid is a linear function of the square root of time. The slope of the line expressing this linear relationship is constant for the first eight to 12 hours in euthyroid subjects and has been called the "accumulation gradient." By means of this technique it is pos-

sible to obtain rapidly an evaluation of thyroid function and it is quite valuable in determining the effect of various experimental procedures on the function of the thyroid gland. For example, if an antithyroid compound is administered following the initial determination of the gradient, the relative activity of the drug can be judged by the extent to which further accumulation of  $I^{131}$  is inhibited (5). Conversely, the effectiveness of an injection of thyrotrophin can be judged by the increase which it produces in the gradient (6).

Two important objections have been raised to using the accumulation gradient as an index of thyroid function, however. In the first place, no physiologic significance has yet been discovered for the finding that the early course of radioiodine accumulation follows a parabolic curve. Secondly, Astwood and Stanley described their technique during the early development of accurate counting devices and were limited to a small, shielded, Geiger-Mueller counter which was placed in direct contact with the skin overlying the thyroid. Consequently absolute determinations of radioactivity in the thyroid could not be made and the values were recorded only as "counts per second per 100 microcuries of administered  $I^{131}$ ." This made it impractical to utilize the observations of these investigators in other laboratories since the counting device would have to be duplicated exactly in order to obtain comparable data. Data expressing the radioactivity in the gland as a fraction of the administered dose can invalidate the second objection.

The present investigation was undertaken in an attempt to correlate the 24-hour uptake with other indices of thyroid function involving the use of  $I^{131}$ . All measurements were made with an adequately shielded Geiger-Mueller counter at a distance of 55 cm. from the neck. The absolute

<sup>1</sup> U. S. Public Health Service Fellow of the National Cancer Institute. Present address: Pratt Diagnostic Hospital, Boston, Mass.

values obtained can thus be compared with those of other investigators. The accumulation gradient, 6-hour, 8-hour, and 24-hour uptakes were determined in the same individual and the other three functions then correlated separately with the 24-hour uptake.

#### MATERIALS AND METHODS

All subjects were healthy, young, clinically euthyroid volunteers, predominantly female technicians. Separate determinations of all four indices were made in 75 instances using 38 subjects. Twenty-eight subjects were employed more than once, none more than three times. Those studied more than once were given oral desiccated thyroid following the initial determination.

A shielded Sylvania gamma counter (GG-306) was so arranged that only the region directly surrounding the thyroid would be counted when the apparatus was in position. A Tracerlab Autoscaler was used to total the counts. A device was employed which aligned the aperture of the shielding over the center of the thyroid gland and which could also be arranged to support a flask containing  $I^{131}$  at the same distance, when required. All counting was done at a distance of 55 cm. from the end of the Geiger-Mueller tube to the skin over the thyroid gland. Using the tube end-on the effective center of the counting volume is 6 cm. from the near end of the tube. The apparatus is to be described in detail in a future communication (7).

Approximately 50 microcuries of carrier-free  $I^{131}$  were pipetted into either a small 50 cc. glass beaker or Erlenmeyer flask, diluted with 15–20 cc. of tap water, and the absolute radioactivity determined at a distance of 55 cm. from the gamma counter to the near surface of the vessel. The subject was thereupon given the solution to drink. This was followed by a rinsing of another 15–20 cc. of tap water to facilitate removal of the radioactivity from the flask, mouth, and pharynx. A single rinsing was sufficient to remove 99 per cent of the radioactivity from the flask.

The thyroid region of the subject was then counted at approximately hourly intervals during the day. Correction was made for background radiation and extrathyroidal  $I^{131}$  by subtracting counts made over the lower thigh of the subject. The thigh count is somewhat less than the count contributed by the non-thyroidal tissues of the neck and this is therefore an undercorrection. The error thus introduced is not large, however, and is not significant except during the first hour or two after the tracer dose is given (8).

Since the counting was done at a distance of 61 cm. from the skin to the effective counting center of the Geiger-Mueller tube, small variations in the depth of the center of the thyroid gland from the skin would have little effect on the number of impulses reaching the tube. It seemed unnecessary, therefore, to make any correction for the estimated center of the thyroid gland since the radioactivity in the flask was also measured with its

TABLE I

x	Formula	S. D.	S. E.
Accumulation gradient	$y = 31.2x - 3.26x^2$	$\pm 0.141y$	$\pm 0.0164y$
6-hour uptake	$y = 1.67x$	$\pm 0.129y$	$\pm 0.0153y$
8-hour uptake	$y = 1.43x$	$\pm 0.134y$	$\pm 0.0160y$

near surface 61 cm. from the effective counting center of the tube. The calculated radioactivity in the gland was increased somewhat by back scatter from the cervical region, but this would seem to be far less (9) than that described by Myant, Honour, and Pochin (10).

The accumulation gradient was determined by plotting graphically the *per cent* of administered radioactivity present in the thyroid against the square root of the time in minutes following administration. The slope of this line was the numerical value of the accumulation gradient. The various gradients, 6-hour and 8-hour uptakes were then plotted, respectively, against the corresponding 24-hour uptakes.

#### RESULTS

A close correlation was found to exist between the 24-hour uptake and all other functions. In the case of the 6-hour and 8-hour uptakes, simple straight line formulae were found to fit the data quite well. Since the spread was greater with the higher uptakes, the standard deviation and standard error were calculated as a fraction of the calculated quantity rather than as absolute values. A straight line could not be fitted to the data correlating the accumulation gradient and the 24-hour uptake, but a parabolic curve having the formula  $y = 31.2x - 3.26x^2$  was found to fit quite pre-

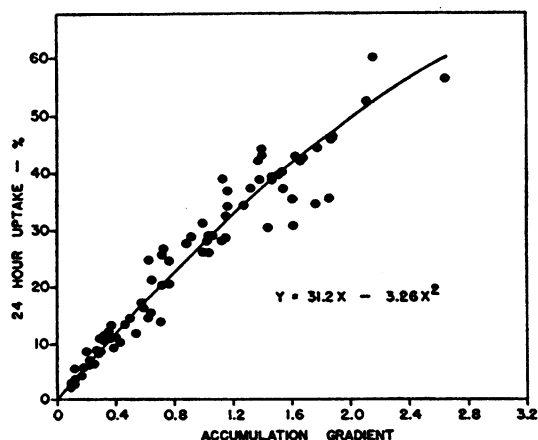


FIG. 1. RELATION OF ACCUMULATION GRADIENT TO 24-HOUR UPTAKE OF  $I^{131}$  BY THE THYROID

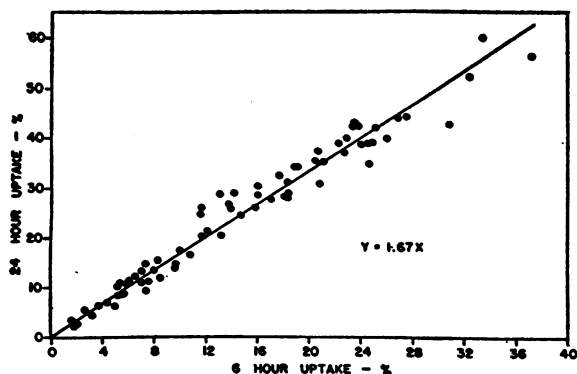


FIG. 2. RELATION OF 6-HOUR UPTAKE TO 24-HOUR UPTAKE OF  $I^{131}$  BY THE THYROID

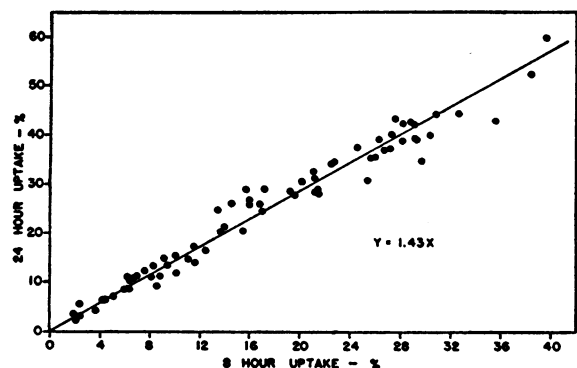


FIG. 3. RELATION OF 8-HOUR UPTAKE TO 24-HOUR UPTAKE OF  $I^{131}$  BY THE THYROID

cisely. The formulae for the various correlations with the 24-hour uptake are listed in Table I. In each instance  $y$  represents the 24-hour uptake plotted on the ordinate and  $x$  represents the other functions, respectively, plotted on the abscissa. The formula for the accumulation gradient was calculated by the method of least squares. (Figures 1-3).

#### DISCUSSION

The use of the data in this investigation makes possible the translation of the accumulation gradient, 6-hour, 8-hour, or 24-hour uptake in a euthyroid subject into comparable terms. Thus if a subject has an accumulation gradient of 1.6, using the formula  $y = 31.2x - 3.26x^2$ , the 24-hour uptake can be calculated to be  $41.7 \pm 6.9$  per cent. The standard deviation of  $\pm 6.9$  is obtained by taking 14.1 per cent of  $y$ , in this instance 41.7 per cent.

The 24-hour uptake can thus be transformed into the 6-hour or 8-hour uptake by dividing by 1.67 or 1.43, respectively.

Such translations are chiefly of value in observations of normal or hypothyroid subjects. It is unlikely that the values obtained in thyrotoxic subjects would exhibit the same degree of correlation since the rate of uptake is often so rapid that the parabolic curve is followed for only a short time, making the gradient inaccurate. Also, some hyperthyroid patients exhibit a significant loss of activity from the gland following the first two to three hours after administration of  $I^{131}$ . This is presumably because a hyperactive gland contains only a small store of thyroxin which therefore is of unusually high specific activity. The higher rate of discharge in thyrotoxicosis serves further to accentuate this loss of radioactivity from the gland. In euthyroid subjects this does not occur since the organically bound  $I^{131}$  serves to label a large "pool" of thyroxin and thyroglobulin in the colloid from which secretion takes place quite slowly. Consequently accurate predictions of the 24-hour counts from the accumulation gradients of thyrotoxic individuals are probably not possible.

The formula expressing the relation between the 24-hour uptake and the accumulation gradient is incorrect for the higher rates of accumulation seen in thyrotoxicosis. The parabola formed by this formula reaches a maximum at a gradient of 4.8. The corresponding 24-hour uptake is 75.8 per cent, obviously too low since many patients with severe hyperthyroidism have uptakes above 90 per cent.

The relatively large number of very low uptakes and gradients reported here for euthyroid subjects are due to the fact that these subjects had been given exogenous thyroid hormone as part of another study. It has been found that such therapy will produce a diminution in thyroid function, as measured by studies with  $I^{131}$ , to levels seen in myxedema (11). In every such instance, a previous uptake before thyroid medication had been instituted had shown a normally functioning gland. Although the activity of these thyroids was suppressed, no change was produced in the correlation of the various functions studied. It was of advantage to study subjects whose thyroid glands

were suppressed to various degrees by exogenous hormone since in this manner many points could be calculated between very low and high uptakes, otherwise a difficult task.

#### SUMMARY

The correlation of the accumulation gradient, 6-hour, and 8-hour uptake with the 24-hour uptake of radioactive iodine by the thyroid gland has been investigated in euthyroid human subjects. A close correlation has been found to exist between all four functions. If  $y$  is taken to represent the 24-hour uptake and  $x$  the various other functions, relatively precise formulae can be constructed by means of which the 24-hour uptake can be calculated from any of the other functions and vice versa. Thus,  $y = 31.2x - 3.26x^2 \pm 0.141y$  is the formula for the accumulation gradient,  $y = 1.67x \pm 0.129y$  is the formula for the 6-hour uptake, and  $y = 1.43x \pm 0.134y$  is the formula for the 8-hour uptake. These correlations hold even when the thyroid gland is suppressed by exogenous thyroid hormone. The data presented here may be of value in future investigations of thyroid physiology in euthyroid subjects. It is suggested that far less correlation would be expected in thyrotoxic subjects.

#### ACKNOWLEDGMENT

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