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The Estimation of Extra-Thyroid Neck Tissue Radioactivity During Thyroid Radioiodine Uptake Measurements.[1]

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INTRODUCTION

The accuracy of certain determinations of thyroid radioiodine content depends upon reliable estimation of the extra-thyroid neck tissue radioactivity counted simultaneously by the neck probe. This reliable estimate is required whenever measurements are made within a few hours after the administration of the radioiodine and is particularly important when determining plasma clearance of ^{131}I (or ^{132}I) by the thyroid or fractional thyroid uptake rate and when performing the perchlorate discharge test.

Direct measurement of extra-thyroid neck radioactivity is only possible when there is no thyroid uptake of iodine-131. There are two general methods of indirect estimation. In one, the extra-thyroid neck radioactivity is determined from the counting rate over the neck with a thick lead shield covering the thyroid gland (1, 2), or from the counting rate over the patient's thigh (3, 4). In the other, extra-thyroid neck radioactivity is estimated from the total neck counting rate shortly after the intravenous administration of the radioiodine (5, 6). However, for simplicity, Oddie *et al* (6) recommended the routine use of the mean value of extra-thyroid neck tissue radioactivity obtained in a group of patients using a standard neck counting arrangement. They claimed that this expedient is only justifiable when a high degree of accuracy is not required.

The investigations reported in this paper were designed to assess the reliability of Oddie's method of calculating extra-thyroid neck tissue radioactivity in individual patients and to determine if, when a standard counting arrangement is used, the values obtained in this manner are indeed more accurate than an estimate based upon the mean counting rate in a group of subjects with no thyroid ^{131}I uptake.

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METHODS

Patients were given approximately $15\mu Ci^{131}I$ by intravenous injection. The precise dose was determined from the difference between the counting rate of the dose vial before use and that of the vial and syringe after the injection had been made.

The counting rate over the neck was measured with a thallium activated sodium iodide scintillation crystal 4.5 cm in diameter, placed at 23 cm from the anterior surface of the neck. A heavy lead collimator 15 cm long with a minimum thickness of 1.4 cm and with an aperture 5.6 cm in diameter was used. With this arrangement, the whole counting face of the crystal can be "seen" by a circular area 6.2 cm in diameter on the frontal plane at the anterior surface of the neck and any point in a circular area 10.8 cm in diameter on this plane "sees" at least part of the crystal. Using focusing light beams, the probe was centered carefully on a skin mark placed over the thyroid isthmus. An appropriate correction factor derived from the counting rate of a standard dose in a "model" neck was applied so that the *in vivo* neck counting rate could be expressed as a fraction of the ^{131}I dose administered.

Total neck radioactivity was recorded for a three-minute period starting at 60 sec after the injection of the dose ($N_{2.5}$) and again for five-minute periods starting 27.5 and 57.5 min (N_{30} and N_{60}). In some subjects, five-minute counts were also recorded from 87.5 and 117.5 minutes (N_{90} and N_{120}).

The patients emptied their bladders at 34, 64, 94 and 124 minutes, i.e., four minutes after the mid-point of the neck counting periods. This time was chosen because we have noted that in ambulant persons who void naturally, significant amounts of radioactivity are regularly first detected in the urine about four minutes after intravenous administration of the ^{131}I dose. The urinary ^{131}I excretion during each time period was determined from the radioactivity of measured aliquots of the specimen and of a reference standard counted in a well-type scintillation counter.

Neck radioactivity (N) and cumulative urinary ^{131}I excretion (E) were always expressed as a fraction of the ^{131}I dose administered.

The proportion of the total body extra-thyroid radioiodine which is counted by the neck probe (Q) has been determined using two different methods. In patients with no thyroid uptake of ^{131}I, the extra-thyroid neck tissue radioactivity can be measured directly, and expressed as a fraction of total body ^{131}I by substitution in the formula:

$$Q = \frac{N}{1-E}$$

where 1–E represents the fraction of the dose retained within the body and Q the fraction of total body radioactivity counted by the neck probe. A value of Q obtained in this manner will be referred to as a directly measured value throughout this paper.

For patients in whom thyroid uptake of ^{131}I is proceeding, an estimate of extra-thyroid neck tissue radioactivity at any time (t) can be derived from neck counts recorded within the first few minutes after the intravenous injection of ^{131}I and those recorded at time t using the formula derived by Oddie *et al* (6). If early counts are measured in the period one to four minutes after the dose ($N_{2.5}$), Oddie's formula would be:

$$Q = \frac{\phi t \; N_{2.5} - 5.1 \; N_t}{.99 \; \phi t \; \dfrac{(Vn/V)_2}{Vn/V} - 5.1}$$

where ϕ is a correction factor for the mean extra-thyroid distribution space of ^{131}I during the time $0 - t$ min as defined and determined by Oddie *et al* (7).

For the observation times used in the present study, this formula resolves to:

$$Q_{30} = 1.05 \, N_{2.5} - .178 \, N_{30}$$
$$Q_{60} = .93 \, N_{2.5} - .093 \, N_{60}$$
$$Q_{90} = .87 \, N_{2.5} - .064 \, N_{90}$$
$$Q_{120} = .84 \, N_{2.5} - .049 \, N_{120}$$

Any value of Q obtained by using these equations will be referred to as a calculated value.

PATIENTS

The direct measurement of Q was made in three groups of patients with no thyroid uptake of iodine-131. The first group comprised 17 athyroid patients receiving thyroxine replacement therapy for previously established thyroid failure.

TABLE I

VALUES OF Q OBTAINED BY DIRECT MEASUREMENT (MEAN ± S.D.)

Patients	*t = 2.5′*		*t = 30′*		*t = 60′*		*t = 90′*		*t = 120′*	
	No.	*Q*	*No.*	*Q*	*No.*	*Q*	*No.*	*Q*	*No.*	*Q*
Athyroid	17	.0253 ±.0068	17	.0241 ±.0067	17	.0228 ±.0061	16	.0221 ±.0058	16	.0220 ±.0067
Euthyroid	17	.0245 ±.0048	17	.0243 ±.0056	17	.0244 ±.0062	17	.0252 ±.0066	17	.0258 ±.0073
Thyrotoxic	8	.0331 ±.0037	7	.0324 ±.0051	7	.0294 ±.0056	6	.0298 ±.0035	3	.0320 ±.0076
All Cases	42	.0265 ±.0063	41	.0256 ±.0066	41	.0246 ±.0063	39	.0246 ±.0064	36	.0246 ±.0075

The euthyroid group included 14 normal persons and three patients with non-toxic goitre in all of whom thyroid ^{131}I uptake had been blocked by the oral administration of 600 mg potassium perchlorate 20 minutes before the start of the test. The third group was comprised of eight patients with diffuse toxic goitre. These patients were given 1000 mg potassium perchlorate 20 minutes before the injection of iodine-131.

The calculated values of Q at 30 and 60 minutes were derived from a study of 34 normal persons, 12 patients with non-toxic goitre and 15 patients with diffuse toxic goitre. In eight normal subjects the observations were extended so that Q at 90 and 120 minutes could also be calculated. A second series of observations was made in nine of the normal subjects 24 hours after they had received 10 U TSH (Thytropar, Armour) by intramuscular injection.

In order to determine the correlation between the estimate of Q obtained by calculation and the measured value, 14 normal subjects were studied both when thyroid ^{131}I uptake was proceeding normally and again after uptake had been blocked with perchlorate.

RESULTS

The values of Q obtained by direct measurement 2.5, 30, 60, 90 and 120 minutes after the administration of the radioactive dose in 42 subjects in whom there was no ^{131}I uptake by the thyroid are summarized in Table I. The mean values for the athyroid patients were similar to those for the perchlorate blocked euthyroid subjects, but the perchlorate blocked patients with thyrotoxicosis gave slightly higher figures. There was a significant fall in the mean value of Q from .0253 to .0220 ($p < .01$) during the period of observation in the athyroid group, but in the other two groups Q appeared to increase slightly during the second hour. This fact suggests that despite the perchlorate block there was a slow uptake of ^{131}I by the thyroid in some of these subjects.

The mean calculated values of Q at 30 and 60 min in the three groups are shown in Table II. In normal persons the mean calculated Q, .0239 at 30 and .0236 at 60 minutes, was very similar to the mean value determined by direct

TABLE II

VALUES OF Q AT 30 AND 60 MIN OBTAINED BY CALCULATION (MEAN ± S.D.)

Patients	*No.*	*t = 30′*	*t = 60′*
Normal Subjects	34	.0239 ±.0087	.0236 ±.0085
Non-toxic Goitre	12	.0310 ±.0118	.0322 ±.0132
Diffuse Toxic Goitre	15	.0834 ±.0487	.0851 ±.0568

measurement in the athyroid subjects and perchlorate blocked euthyroid persons. However, dispersion of the calculated Q values about the mean was rather greater than that of the directly measured values (Figure 1). The mean calculated values of Q in patients with non-toxic goitre, .0310 and .0322 at 30 and 60 minutes respectively, were higher than the corresponding values for normals ($p < .05$) and those in patients with thyrotoxicosis were very considerably higher, the means being .0834 at 30 minutes and .0851 at 60 minutes ($p < .001$). In eight normal subjects Q was calculated serially every 30 minutes for 120 min. The mean value fell from .0241 at 30 minutes to .0236 at 60 minutes, .0231 at 90 minutes and .0229 at 120 minutes, but this change was not statistically significant.

The effect of TSH upon the 30 and 60 minute values of Q obtained by calculation was studied in nine normal persons. The mean thyroid uptake of ^{131}I was increased by the treatment from .051 to .155 at 30 minutes and from .076 to .224 at 60 minutes. The calculated value of Q also increased at both 30 and 60 minutes, from .0213 to .0308 and from .0213 to .0323 respectively ($p < .02$).

The individual values of Q at 30 minutes in all subjects, both those determined by direct measurement and those obtained by calculation, are illustrated in Figure 1.

The correlation between the measured and the calculated values of Q for 14 normal persons in whom this parameter was separately determined by both methods is shown in Table III. The mean values at both 30 and 60 minutes were very similar for measured and calculated Q and there was a significant degree of correlation between the two values.

DISCUSSION

Direct measurement of the proportion of the total body radioactivity counted by an external neck probe as extra-thyroid neck tissue radioactivity (Q) has been made in three groups of subjects in whom there was no thyroid uptake of iodine-131. The results obtained in this manner represent the best available estimate

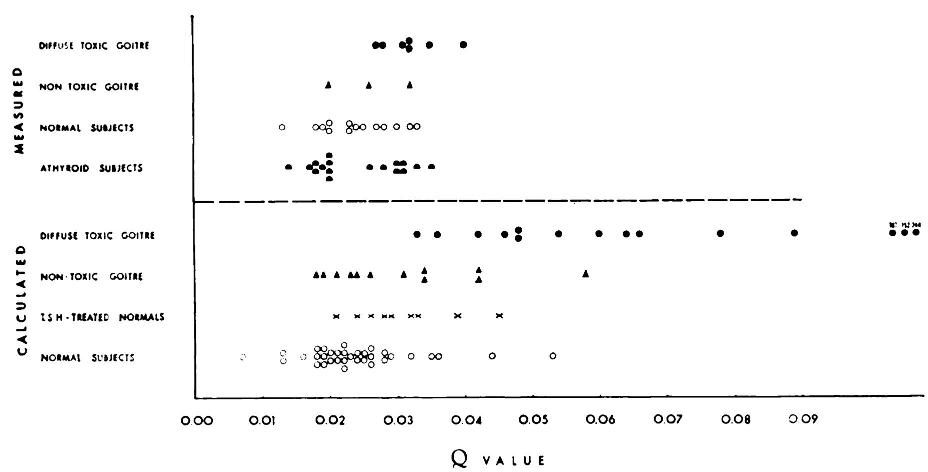

Fig. 1. Measured and calculated values of Q at 30 min after the administration of iodine-131.

of the true value of Q, as they are subject only to errors derived from variation in the position of the probe and the statistical errors of counting. The group means at 2.5 and 30 minutes for the euthyroid subjects in whom thyroid ^{131}I uptake had been blocked by potassium perchlorate were very similar to those for the patients with no functioning thyroid tissue. Thus, the presence of a functioning thyroid gland does not itself appear to alter the value of Q, but the rather higher values observed in patients with diffuse toxic goitre may be due to the increased vascularity of the gland in this condition. Amongst the athyroid patients there was a gradual and statistically significant fall in the mean value of Q from 2.5 to 120 minutes. This finding supports the suggestion by Oddie *et al* (7) that during the hours following iv administration of ^{131}I there occurs a greater expansion of the distribution space of the isotope in the body as a whole than in that part of the neck tissues "seen" by the external probe. However, the degree of fall was less than that noted by Oddie's group and it is possible that this condition is partly dependent upon the type of collimation used for the probe.

The validity of the method described by Oddie *et al* (6) for calculating Q in patients with thyroid glands actively concentrating ^{131}I, has been confirmed with respect to normal subjects by the comparison of calculated values with those obtained by direct measurement. In our group of 14 normal persons the mean results for both techniques were almost identical and there was a significant correlation between the two values obtained in each individual. However, the increase of the calculated Q values in normal subjects after TSH stimulation and the higher than normal mean calculated values in patients with non-toxic goitre and especially in those with diffuse toxic goitre does suggest that Oddie's method of calculation overestimates Q in persons with an avid thyroid gland. This impression is supported by a comparison of the calculated Q values with the measured values for patients with thyrotoxicosis (Figure 1). The reason for this tendency to overestimate Q by calculation in subjects with an avid thyroid is

TABLE III

THE CORRELATION BETWEEN VALUES OF Q OBTAINED BY DIRECT MEASUREMENT AND BY CALCULATION IN 14 NORMAL SUBJECTS.

	$t = 30'$ (*mean* ± *s.d.*)	$t = 60'$ (*mean* ± *s.d.*)
Measured Q (x)	.0239 ± .0057	.0240 ± .0064
Calculated Q (y)	.0235 ± .0058	.0231 ± .0061
Regression of y upon x	y = .662x + .077	y = .628x + .081
Correlation	r = +.646; t = 2.93; p < .02	r = +.661; t = 3.05; p < .02

not clear, but it could be caused by a diminishing net clearance of ^{131}I by these glands due to a significant secretion of organic ^{131}I or leak of inorganic ^{131}I during the early period after giving the radioactive dose (8).

Accordingly, the claim of Oddie *et al* (6) that the calculation of Q gives a better estimate of its true value than the mean value measured in a group of subjects with no thyroid uptake of ^{131}I is supported by our results only with respect to persons with a normal thyroid gland. The significant correlation between calculated and measured Q in normal subjects indicates that the estimate of Q in this group can be improved by the use of the calculated value. The maximum error reduction that may be achieved in this manner is 40-45% ($r^2 = .42$ and .44), and even this reduction can only be gained by the use of the regression equation of calculated Q (y) upon measured Q (x) (for our normal group: $y = .662x + .077$ at 30 minutes and $y = .628x + .081$ at 60 minutes) and not merely by the use of unmodified calculated values. On the other hand, the tendency to overestimate Q by calculation in patients with an avid thyroid gland potentially increases the error of the estimate by larger amounts than any erorr reduction expected from the use of such regression equations, which are any way only applicable to persons with normal thyroid function.

The results of this study therefore indicate that, except when thyroid function is known to be normal, the best estimate of Q is given by a constant value, which is the mean of those obtained by direct measurement in a group of persons in whom there is no thyroid uptake of iodine-131. The overall standard deviation of measured values from the grand mean in our subjects was .0065, so that the maximum expected error introduced by our use of this constant value would be $\pm$ .013. In actual practice the expected error would be smaller, because the range of true Q values would be less than the observed range of measured values, as the dispersion of these about their mean will have been increased by an unknown amount by counting and positioning errors. This error could be further reduced by applying a correction for the fall in Q with time and by using a higher Q value for patients with thyrotoxicosis.

It is particularly advantageous to use a constant value for Q when repeated measurements of thyroid ^{131}I content are being made in the same subjects, as for instance while performing the perchlorate discharge test or studying the effect of a pharmacological agent upon thyroid uptake of iodine. In these circumstances any error present in a constant Q will be minimized when the change in thyroid ^{131}I is calculated. On the other hand, the use of a separate counting rate over the shielded neck or the thigh to correct each measurement of thyroid uptake for extra-thyroid neck tissue radioactivity may mask important changes in thyroid ^{131}I content, because the errors in this type of correction factor tend to be magnified when comparative observations are made.

SUMMARY

Two methods of estimating the extra-thyroid tissue radioactivity, which is detected simultaneously by the neck probe during measurements of thyroid radioiodine content, have been assessed. In 42 subjects with no thyroid ^{131}I

uptake this extra-thyroid radioactivity was directly measured at 2.5, 30, 60, 90, and 120 minutes after the intravenous administration of the dose. The overall mean value was .025 of the total extra-thyroid radioactivity in the body, with a standard deviation of ± .0065. Slightly higher values were observed in patients with diffuse toxic goitre in whom thyroid uptake had been blocked by perchlorate, than in euthyroid persons.

In 61 subjects in whom there was unimpaired uptake of ^{131}I by the thyroid, the proportion of total extra-thyroid radioactivity in the neck tissues was determined by calculation using the method described by Oddie. In normal subjects, the overall mean value was similar to that obtained by direct measurement and there was a significant degree of correlation between the calculated and measured values separately obtained in 14 individuals. However, in TSH stimulated normals, in patients with non-toxic goitre and in thyrotoxic patients, the mean calculated values at both 30 and 60 minutes were significantly higher than those for normals.

Accordingly, although calculation provides a rather more exact estimate of the extra-thyroid neck tissue radioactivity in any normal individual, it is considered that the mean value obtained by direct measurement in a group of subjects should be used when studying patients with suspected abnormal thyroid function.

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