USE OF ^{123}I FOR THYROID UPTAKE MEASUREMENTS AND DEPRESSION OF ^{131}I THYROID UPTAKES BY INCOMPLETE DISSOLUTION OF CAPSULE FILLER

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Iodine-123 for thyroid iodine uptake measurements was evaluated by a method which allows simultaneous measurements of ^{131}I and ^{123}I. It was found that thyroid uptake measurements made with ^{131}I capsules from one commercial supplier gave consistently lower thyroid uptake values (in the order of 30% less) than simultaneous measurement of uptakes with ^{123}I capsules. The reason was traced to a delayed absorption of ^{131}I from capsules containing a Gelfoam filler.

The possibility of using ^{123}I for measurement of thyroid iodine uptake has been suggested by several authors (*1,2*) and ^{123}I has been shown to be useful as a thyroid imaging agent (*3*). Its principal mode of decay is by emission of a 159-keV gamma ray which is readily detected with scintillation crystals. As emphasized in the papers cited, this radionuclide has the attractive feature of delivering much less radiation to the patient as compared with that from ^{131}I, largely because it has no beta-particle emission. In the thyroid, the principal contribution to the radiation dose is from the K conversion electron.

The present studies were originally designed to evaluate the use of ^{123}I in thyroid iodine uptake studies by direct comparison with ^{131}I in the same patient, using commercially available radionuclides. Theoretically, the uptakes of ^{123}I and ^{131}I, expressed as percentages of the administered doses, should be identical within counting statistics when they are given simultaneously and by the same route. Any delay or decrease due to such factors as gastrointestinal absorption or urinary excretion is common to both isotopes and should have the same effect on both. However, for a while it appeared to be impossible to reconcile the results obtained with the two isotopes, the ^{123}I uptake being consistently higher than the ^{131}I uptake. Modification of the original experiment indicated that the basis of the discrepancy lay with the type of ^{131}I capsule used.

A difference between thyroid uptakes measured with ^{131}I in capsules and with ^{131}I in liquid form in the same patients has previously been reported by Halpern, et al (*4*); the two forms were administered about 2 weeks apart. These authors noted that when the ^{131}I capsules were used, there was both a lag in the onset of uptake and a decreased percentage uptake at 24 hr relative to the results obtained with ^{131}I in liquid form. This result has an important bearing on the question of the mechanism for the decrease in thyroid uptake of [^{131}I]NaI that has been noted recently (*5*). The effect of dietary iodide on radioiodine uptake is not questioned but this is not the only possible cause to consider.

The present study differs principally from that of Halpern, et al in that instead of comparing uptakes with ^{131}I in capsule and liquid forms given at different times, ^{123}I and ^{131}I were administered simultaneously to avoid the effect of day-to-day variations in thyroid uptake.

MATERIALS AND METHODS

Unselected patients with a wide range of thyroid disorders but generally free from gastrointestinal and kidney disorders who were referred for iodine up-

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takes were studied. Each was given a combination oral dose consisting of about 100 μCi of ^{123}I in a capsule (Medi+Physics, South Plainfield, N.J. and Emeryville, Calif.) and 2–5 μCi of ^{131}I (S) in a capsule (Squibb, New Brunswick, N.J.) (32 patients), 5 μCi of ^{131}I in aqueous solution (Squibb) (six patients), or 11–13 μCi of ^{131}I (M) in a capsule (Mallinckrodt, St. Louis, Mo.) (four patients). Activities were determined at 6 and 24 hr after administration with a lead-shielded 5.1-cm-diam NaI(Tl) crystal and photomultiplier tube, an amplifier, and either a two-channel or a multichannel pulse-height analyzer. The crystal-to-neck distance was 20 cm. A standard flat-field collimator (AEC) was used. In a few patients, uptakes were also measured at one or more additional times (½, 1, 2, or 4 hr after administration). A thigh count was used to approximate the neck nonthyroid background.

Data processing included the averaging of three 100-sec counts taken over the neck of each standard in an Abbott-ORINS Lucite neck phantom, correction for deadtime counting losses, subtraction of background, and correction for cross-talk between the ^{123}I 159-keV channel (140–180 keV) and the ^{131}I 364-keV channel (300–500 keV). The cross-talk correction involved use of the formula given by Belcher and Vetter (*6*). This is further discussed below.

Iodine-123, ^{131}I (S), and ^{131}I (M) were obtained as carrier-free NaI in capsules from commercial suppliers. The ^{123}I capsules were calibrated by the supplier to have 100 μCi/capsule as of noon of the date of delivery. Five capsules were received per shipment. Each of these was counted in the Lucite neck phantom with the same probe and other instrumentation and the same distance as used in counting the uptake in the thyroid. One ^{123}I capsule was saved as a running standard and each of the other four was administered to a patient along with a capsule of ^{131}I or followed immediately by the liquid ^{131}I. Similarly, one ^{131}I capsule was kept as a running standard. The ^{123}I capsules contained contaminating activity from other iodine isotopes (Table 1).

Deadtime corrections. At the time of calibration, the 100-μCi ^{123}I capsules had counting rates of the order of 600,000 counts/100 sec in the ^{123}I window. For these high counting rates the two-source deadtime loss formula for Method 2 of Adams and Zimmerman (*7*) was used. Although developed for use with an Anger camera, this formula is generally applicable and gives an exact solution, in contrast to the usual approximations.

Cross-talk corrections. Counting in the two windows corresponding to the photopeaks of the ^{123}I gamma ray (Channel A) and the ^{131}I gamma ray (Channel B) does not completely separate the two activities. In the system used, the ^{123}I counting rate in Channel B is approx 5% of its counting rate in Channel A, and the ^{131}I counting rate in Channel A is about 36% of its counting rate in Channel B. In the case of ^{131}I, the counting rate in Channel A is due principally to Compton scatter from the 364-keV gamma ray. However, the ^{123}I counts in Channel B are due to a mixture of causes including Compton scatter from the ^{123}I 530-keV gamma ray which occurs 2.3% as frequently as the 159-keV gamma ray and to photopeak or Compton contributions from the contaminating activities indicated in Table 1. Because of the presence of the contaminants, with half-lives different from that of ^{123}I, it is necessary to redetermine the Channel B-to-Channel A ratio for the standards each time that the patient is counted. The correction for cross-talk then follows the formulation given by Belcher and Vetter (*6*), modified to include corrections for the differences in the ratio of the counts in Channels A and B among the capsules in a given lot and as a function of time. Let j = counts in ^{123}I capsule per counts in ^{123}I standard in Channel A, k = counts in ^{123}I capsule per counts in ^{123}I standard in Channel B, m = counts in ^{131}I capsule per counts in ^{131}I standard in Channel A, n = counts in ^{131}I capsule per counts in ^{131}I standard in Channel B, p = (counts in Channel B × k)/(counts in Channel A × j) for the ^{123}I standard, q = (counts in Channel A × m)/(counts in Channel B × n) for the ^{131}I standard, A = observed thyroid counts in Channel A, B = observed thyroid counts in Channel B, x = corrected ^{123}I counts in Channel A, and y = corrected ^{131}I counts in Channel B. Then: $x = (A - qB)/(1 - pq)$, $y = (B - pA)/(1 - pq)$.

Finally, the percentage uptake is obtained by dividing the corrected ^{123}I counts in Channel A (x)

TABLE 1. RADIOISOTOPIC COMPOSITION OF ^{123}I CAPSULES AS OF NOON OF DATE OF ADMINISTRATION

Isotope	Half-life	Activity (μCi)*	Radiation to thyroid (rads)†
^{123}I	13.3 hr	100.0	2.0
^{124}I	4.2 days	1.0	1.3
^{126}I	13.1 days	1.0	2.0
^{130}I	12.3 hr	3.0	0.8
^{131}I	8.1 days	0.5	0.9
Total			7.0

* Maximum for non-^{123}I activities.
† Assuming 40% uptake in 20-gm thyroid. Calculations based on data from MIRD pamphlets No. 4, 5, and 6 (*8,9*).

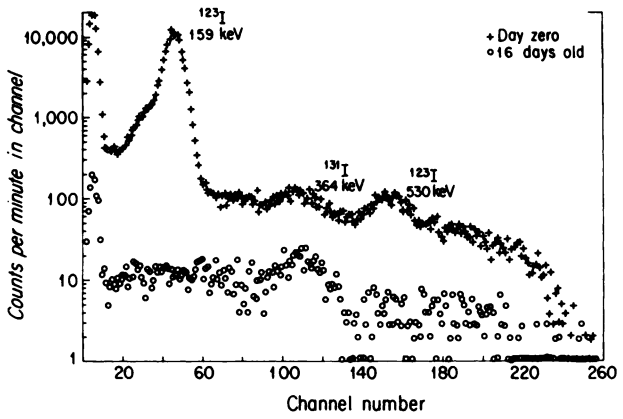

FIG. 1. Comparison of ^{123}I capsule spectra on Days 0 and 16; capsules were suspended in air (to decrease backscatter) on gauze 20 cm from crystal. In upper spectrum, 28- and 31-keV K-alpha and K-beta x-ray peaks are at left; ^{124}I 605-keV and ^{131}I 637-keV photopeaks are not clearly shown. Lower curve is essentially at background, except that ^{131}I peak is still present; decay studies show that peak also includes counts from ^{126}I 384-keV gamma rays.

by the ^{123}I standard counts in Channel A and dividing the corrected ^{131}I counts in Channel B (y) by the ^{131}I standard counts in Channel B. All of the calculations are readily achieved with a programmable desk calculator.

RESULTS

Because of the radioisotopic impurities, the spectrum of the ^{123}I capsule changed appreciably with age, as the isotopes with longer half-lives became more prominent (Fig. 1). When the combined ^{123}I and ^{131}I spectrum with both sources in the Lucite neck phantom is compared with the spectrum in a patient's neck at 6 hr after administration (Fig. 2), the general similarity of the two curves indicates that the neck phantom adequately simulates the attenuation and scatter conditions of the neck for both isotopes.

Figure 3 is a regression plot of the ^{123}I uptakes in the thyroid versus the ^{131}I uptakes, measured simultaneously in all 42 patients at 24 hr after administration of the dose. With one exception in the very low uptake region (0.5% and 0.6%), the ^{123}I uptakes are higher than the corresponding ^{131}I (S) uptakes. The least-squares line fitted to these data has the equation

$$Y = -0.35 + 1.28\,X$$

in which Y is the ^{123}I uptake and X is the ^{131}I (S) uptake. The correlation coefficient, r, is 0.994. In contrast, with the liquid form of ^{131}I, all the ^{123}I uptakes are slightly lower than the corresponding ^{131}I uptakes. The least-squares line fitted to the 10 points comprising the ^{131}I liquid and ^{131}I (M) trials has the equation

$$Y = -0.30 + 0.94\,X$$

and the correlation coefficient, r, is 0.995.

Similarly, for the 6-hr thyroid iodine uptakes, the corresponding regression lines are

$$Y = 0.45 + 1.27\,X$$

with $r = 0.992$ for ^{123}I versus ^{131}I (S) capsules, and

$$Y = -0.41 + 1.01\,X$$

with $r = 0.999$ for ^{123}I versus the combined ^{131}I liquid and ^{131}I (M) capsule data.

Table 2 presents the thyroid radioiodine uptake data for those patients in whom determinations were

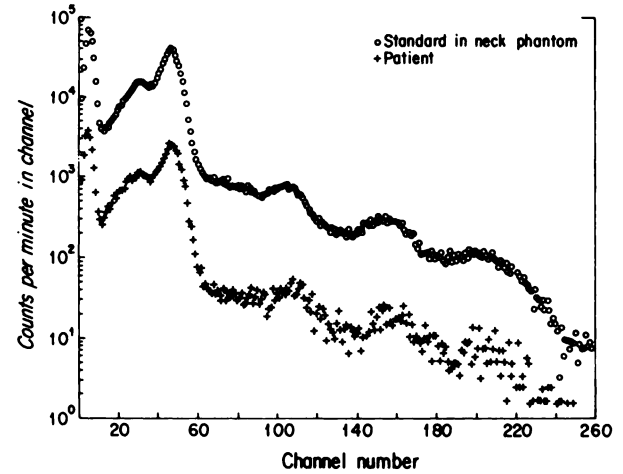

FIG. 2. Combined ^{123}I and ^{131}I spectrum counted with both sources in Lucite neck phantom and spectrum counted from patient's neck at 6 hr after administration of dose.

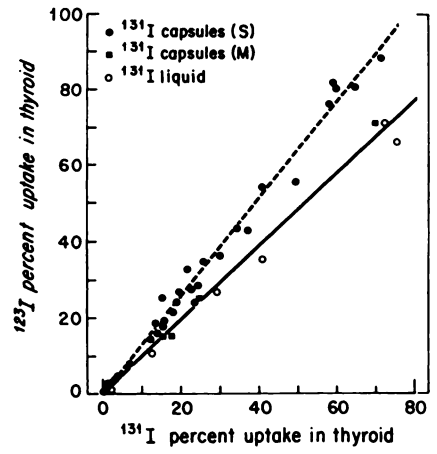

FIG. 3. Regression plots of simultaneously measured ^{123}I (in capsule form) thyroid uptakes versus ^{131}I (S) (N = 32), ^{131}I (M) (N = 4), and ^{131}I (liquid) (N = 6) uptakes.

TABLE 2. THYROID IODINE UPTAKES (PERCENT) IN PATIENTS WITH ADDITIONAL STUDIES

^{131}I form	Case	% Uptake at various times after dose, ^{123}I/^{131}I					
		½ hr	1 hr	2 hr	4 hr	6 hr	24 hr
Liquid	112			1.3/ 1.7		0.9/ 1.2	0.5/ 0.7
	255	18.3/18.5	32.1/29.5	45.2/42.5	58.1/55.8	69.9/67.5	71.4/72.3
	578			2.3/ 2.9		5.9/ 6.7	10.8/12.2
	711	2.8/ 3.8	3.8/ 4.8	4.4/ 6.3	7.1/ 8.1		26.9/29.5
	872	0.8/ 1.9		4.0/ 5.8			35.2/41.0
	991			27.3/23.8		53.0/55.0	66.2/75.6
Capsule (S)	223			0.9/ 1.1		1.1/ 1.2	1.0/ 1.0
	578			7.7/ 6.1		12.8/ 6.1	24.3/19.1
	818			9.5/ 0.6		14.2/ 6.7	25.1/15.0

made at one or more times in addition to the usual 6 and 24 hr.

DISCUSSION

The results strongly suggest that a systematic difference of about 30% exists between the ^{123}I method and the ^{131}I (S) capsule method, the latter giving the lower value. In borderline cases, this decrease could be an important item in establishing the diagnosis and, when the tracer uptake is used as a basis for determining the therapeutic dose to be used, the result could be seriously misleading. Halpern, et al (*4*) postulated that the difference found between the ^{131}I capsule method and the ^{131}I liquid method might be due to reactions involving the gelatin capsule. The present results indicate that, although there may be some such effect which would account for the small difference seen between ^{131}I liquid and ^{123}I capsules, it cannot explain the difference between the ^{131}I(S) capsules and the ^{123}I capsules because the same effect would be expected to apply to both. Instead, the difference appears to be attributable to the filler, Gelfoam, used in the ^{131}I (S) capsule. According to information obtained from the suppliers, the ^{123}I filler is sucrose and the ^{131}I (M) capsule filler is sodium phosphate.

Further evidence in support of this conclusion is available along several lines. It was found that the Gelfoam filler dissolved very slowly in 1 *N* HCl. This suggests that the delay observed in ^{131}I uptake (*4*) is associated with failure of dissolution of the ^{131}I (S) filler in the stomach. In other patients, scintiscans of the abdomen 24 hr after administration of larger doses (90 μCi) of ^{131}I (S) capsules showed distinct areas of activity in the colon whereas those taken after the same doses in liquid form or after ^{123}I capsules did not show such localization (Fig. 4). The scans suggest that some of the ^{131}I (S) is never absorbed although no such evidence was seen for ^{123}I.

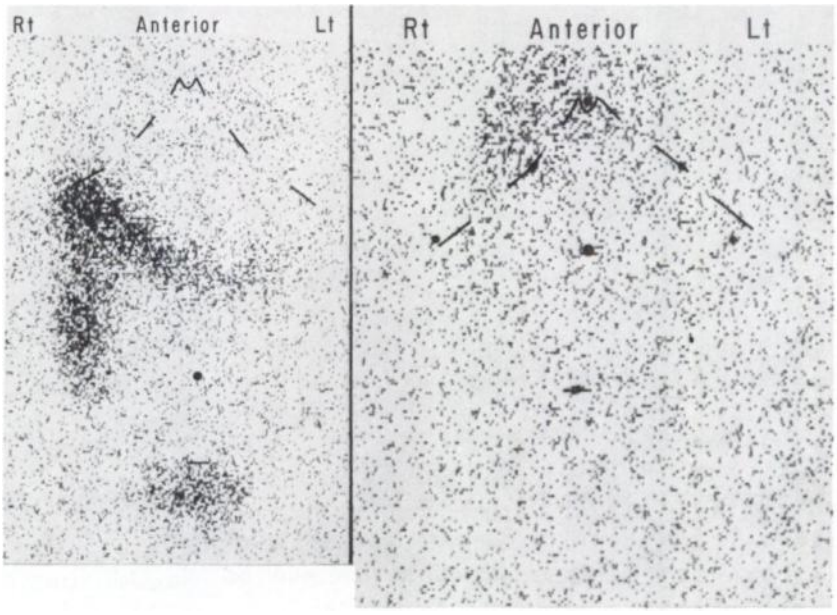

FIG. 4. Scintiscans of abdomen 24 hr after administration of dose. Left, with ^{131}I (S) capsule, there is localized activity in intestine. Right, with ^{131}I in liquid form, area of slightly increased activity in mid-upper region represents iodide secreted by stomach; otherwise, abdomen has no areas of localized activity.

At this institution, ^{131}I in aqueous solution was used for routine thyroid iodine uptake determinations until December 1972, at which time the use of ^{131}I (S) capsules was begun. Figure 5 shows the monthly means for all thyroid iodine uptake determinations made during the period 1971 through October 1973. Each point represents 39–80 determinations. For any given month the standard error (s.d./$\sqrt{N}$,) is about 15% of the mean. Although there is an appreciable spread of values on a month-by-month basis, the mean (±s.e.) for the 24-hr uptakes for the period December 1972 through October 1973 (20.4 ± 0.7%) is significantly different from the means for 1971 (28.3 ± 0.9%) and for 1972 excluding December (28.6 ± 0.9%). The downward trend from December 1971 through November 1972 is also statistically significant. There is no ready explanation for this decline. We are not aware of any change in our medical practice during this period that would change the spectrum of patients seen. Thus, although it appears that the relatively low mean value seen in 1973 is largely attributable to the use of ^{131}I capsules with Gelfoam fillers, the influence of other factors such as an increase of iodine in the diet is not absolutely excluded. We have made no effort to assess the role of the use of Gelfoam-filled capsules in the decreased thyroid iodine uptakes observed by others (*5*).

The good agreement of the ^{123}I uptakes with the ^{131}I liquid and ^{131}I (M) capsule uptakes and the high correlation with the ^{131}I (S) capsule uptakes indicate that ^{123}I is potentially useful for measurement of thyroid iodine uptake. However, a few disadvantages associated with the use of ^{123}I must be mentioned. Because of its relatively short half-life (13.3 hr), daily or every-other-day deliveries are necessary, and transportation delays may cause more serious problems than with the use of ^{131}I. The contaminating activities, although present to the extent of only a few percent, contribute significantly to the radiation dose delivered to the patient and weaken the arguments favoring ^{123}I for its low radiation dose. A 100-μCi dose of ^{123}I is unusually high for thyroid uptake measurements alone but it is anticipated that 100 μCi of ^{123}I would be used as a scanning dose and a thyroid uptake would be determined simultaneously. For uptake studies alone, 25 μCi would be adequate. However, this decreased level of activity cannot be reached by allowing the 100-μCi capsule activity to decay because the longer-lived activities would remain at almost their original strength. Instead, either a liquid ^{123}I form or 25-μCi capsules would have to be available. The method of dual isotope measurements described here may be useful for other studies of iodine metabolism.

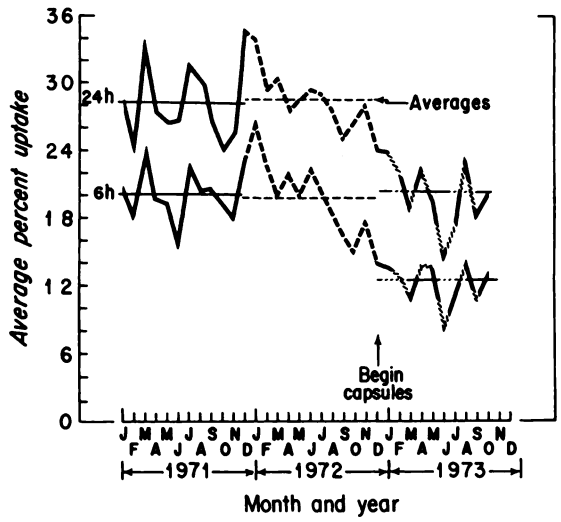

FIG. 5. Mayo Clinic experience with 6- and 24-hr thyroid ^{131}I uptakes, plotted as monthly means. Horizontal lines show means for the years indicated.

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