nm/PRELIMINARY NOTE

THE EFFECT OF CAPSULE CONTENT VARIATIONS ON THYROID UPTAKE RESULTS

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The customary method of measuring the thyroid uptake of iodide depends on the administration of a patient dose of the same strength as the standard which is to be used as the basis of comparison. It is generally assumed that all capsules in a given lot from a commercial radiopharmaceutical supplier contain equal amounts of radioactive iodide. Thus they may be used for either the patient or the standard. The purpose of this paper is to show that unexpected variations in capsule content do occur. The effects of these variations on thyroid uptake results can reach clinical significance.

MATERIALS AND METHODS

All thyroid uptake capsules included in this report were purchased from one radiopharmaceutical manufacturer. They are received in lots of 5 or 10 and are counted routinely before use. Each capsule of a specified lot is placed in a counting tube and inserted into the regular Lucite neck phantom. A Nuclear-Chicago pulse-height analyzer/scaler/timer is used with an International Atomic Energy Agency recommended thyroid collimator and a 2 × 2-in. NaI(Tl) crystal detector. With a crystal-to-capsule distance of 10 in., two 1-min counts (over 10,000 counts/min) are obtained for each capsule and averaged.

Evaluation of capsule tracer content for significant differences requires prior testing for significant instrument drift and inadvertent alterations in counting geometry. This is accomplished by recording a 1-min count on one capsule and then removing it from the Lucite phantom and counting tube. The same capsule is then reinserted in the tube and phantom in the same fashion as before, and another 1-min count is recorded. The procedure is repeated until 20 counts are recorded. A chi-square test on these 20 samples resulting in a probability between 0.1 and 0.9 indicates that variations among counts of the same capsule are most likely caused by the random nature of radioactivity rather than significant instrument drift or altered counting geometry. It is then assumed that these factors are insignificant causes of observed variations in counts of several capsules.

There are several ways in which variations among capsules in a lot can be expressed. The percent difference is used here to relate more closely the effect of capsule content variation to the individual patient test. This is calculated using the figures for counts per minute for the highest and lowest capsules in a lot (Table 1). If the result is within our acceptable range, the capsule lot can be used for patient uptake measurements. The mean capsule is designated as the standard.

To ascertain the potential effects of unacceptable differences among capsules in a lot, theoretical uptake values have been calculated based on actual patient results and several figures of percent difference encountered in the past 2 years. These values were calculated using

$$\frac{\text{Measured uptake} \times \text{C/M capsule assigned to patient}}{\text{C/M capsule assigned to standard}} = \text{Calculated uptake.}$$

Example: John M.

$$\frac{35\% \times 37749\ \text{C/M}}{28790\ \text{C/M}} = 46\%.$$

RESULTS

Observations were made on 108 lots of capsules received consecutively over a 2-year period. Differences per lot ranged from 0.2 to 55.4%. Five lots had values greater than 8% and these were returned to the manufacturer for replacement or were used for scan doses.

In Table 2 the counts per minute figures for high and low capsules in the same lot have been arbitrarily assigned to either the patient or the standard to evaluate the effects on the uptake results. Capsule differences of 8, 10, 20 and 55% have been applied to actual uptakes ranging from 10 to 50%. In the analysis presented in the third column of Table 2, new calculated uptakes are shown. These indicate what would have happened if the capsule with the

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highest tracer content had been assigned to the patient and the lowest to the standard. The next column demonstrates the effect if the reverse had taken place.

TABLE 1. CALCULATION OF DIFFERENCE IN CAPSULE CONTENT

	Capsule	Counting rate (cpm)
14.7 μCi/cap	A	16,603 (lowest)
	B	16,659
	C	16,771
	D	16,781 (highest)
	E	16,733 (mean used for standard)

$$\% \text{ difference} = \frac{16{,}781 - 16{,}603}{16{,}781} \times 100 = 1.1\%$$

TABLE 2. EFFECTS OF DIFFERENCES IN CAPSULE CONTENT ON THE THYROID UPTAKE

		Calculated uptake	
Measured uptake (%)	Capsule difference (%)	Patient assigned high capsule (%)	Patient assigned low capsule (%)
10	8	11	9
	10	11	9
	20	13	8
	55	22	5
15	8	16	14
	10	17	14
	20	19	12
	55	34	7
20	8	22	18
	10	22	18
	20	25	16
	55	45	9
25	8	27	23
	10	28	23
	20	31	20
	55	56	11
30	8	33	28
	10	33	27
	20	38	24
	55	67	13
35	8	38	32
	10	39	31
	20	44	28
	55	79	16
40	8	43	37
	10	44	36
	20	50	32
	55	90	18
45	8	49	41
	10	50	41
	20	56	36
	55	101	20
50	8	54	46
	10	56	45
	20	63	40
	55	112	22

With a 45% uptake (euthyroid-hyperthyroid overlap range) and a 20% capsule difference, the patient uptake could have been erroneously increased to 56% or decreased to 36%. A 55% difference in capsule content could have changed the actual 45% thyroid uptake to 101 or 20% values representing a possible spread of 81% in uptake values. Twenty percent capsule differences have potentially significant effects on all uptake ranges listed in Table 4 except for the 15 to 25% values. In the lowest uptake presented (10%) this 20% error would have caused a 13% uptake (euthyroid) on the one hand or 8% (hypothyroid) on the other. The effect of the same 20% capsule difference on an actual 35% uptake would change the result to 44% (overlap range) or 28% (euthyroid). Likewise the effect on a 40% uptake would cause an erroneous result of 50% (hyperthyroid) or one of 32% (euthyroid). The effects of 10% capsule lot differences are noted to be of borderline significance. Errors introduced by 8% differences appear to be insignificant for clinical purposes. Therefore, an 8% variation between the highest and lowest capsule counts in a lot represents the maximum acceptable range in this laboratory.

DISCUSSION

Brucer (*1*) has stated that "finally after many years of work by the commercial distributors these capsules are the most accurate method of purchasing and dispensing iodine 131 to patients." At present the manufacturers' specifications vary from company to company but all must conform to the maximum permissible limits of variation as set forth by the *United States Pharmacopeia.* In the 17th Revision (*2*), these limits were stated as "not less than 95% and not more than 105% of the labelled amount of I-131." These limits correspond approximately to a 10% difference in the method of expressing capsule differences used in this study. In the *Supplement* of May 15, 1967 (*3*), these limits were increased to 90% and 110%, thereby permitting a 20% variation in capsule label. Several of the larger manufacturers state their maximum variation as ±4% of the mean value of the lot. The observations on 108 lots reveal that serious discrepancies between capsules do occasionally occur.

As shown in Table 2, excessively wide difference in capsule content may result in a patient uptake exceeding 100%. This is of course an obvious error which would be recognized before reporting. Less obvious effects, however, would be unnoticed and these deserve special attention. The theoretical uptakes presented in Table 2 reveal that serious errors may creep into the uptake procedure if large dif-

ferences in tracer content in a capsule lot are not recognized by routine capsule counting. It is certainly feasible that capsules may be inadvertently assigned as described previously if a lot contains only 5–10 capsules (as is the case in our medium-size hospital laboratory).

As is any laboratory test if correctly performed, the thyroid uptake is very useful for clinical purposes. "With the use of standard sources and with a standard method of doing a thyroid uptake, it is possible to achieve an accuracy of ±5 percentage points with any machinery and any equipment" (*4*). Thus for an accurate evaluation of the thyroid status of any patient, one must be certain that the patient dose and the standard are reasonably alike. This can be ascertained by the precounting of all capsules as described in this report. The procedure takes little time and is easily adapted into the routine of even the busiest of laboratories.

CONCLUSION

Clinically important variations in capsule content of tracer have been found to occur on occasions. This is in spite of the diligent efforts of manufacturers to provide uniformity in every capsule lot.

The analysis of these observations indicates that significant errors in thyroid uptakes may occur if the percent capsule difference in a lot is greater than 8% or the deviation from the mean or label exceeds ±4%. Therefore it is strongly recommended that precounting of every lot of capsules be made a routine procedure in every nuclear medicine laboratory.

REFERENCES

1. Thyroid Radioiodine Uptake Measurement, Brucer, Marshall, ed., U.S. AEC Reports ORINS-19, Oak Ridge, 1959, p. 288.

2. The Pharmacopeia of the United States of America, 17th revision, U.S. Pharmacopeia Conventions, Inc., New York, 1965, p. 615.

3. The Pharmacopeia of the United States of America, Supplement No. 1, 17th revision, U.S. Pharmacopeia Conventions, Inc., New York, 1967, p. 24.

4. Thyroid Radioiodine Uptake Measurement, Brucer, Marshall, ed., U.S. AEC Reports ORINS-19, Oak Ridge, 1959, p. 309.