LETTERS TO THE EDITOR

Re: The Significance of I-131 Scan Doses in Patients with Thyroid Cancer: Determination of Ablation: Concise Communication

In the paper by Waxman et al. (*1*), two important variables in the assessment of the efficacy of I-131 scan doses were not addressed:

(1) If scan doses of 2 and 10 mCi are scanned at essentially the same scan speed with a rectilinear scanner, the larger dose is favored on purely statistical grounds: the fivefold increase in scan dose will produce a similar increase in recorded events per square centimeter in the resultant image. While the rationale of scanning for a fixed time is easily defended, it should be noted that the results obtained may well be on the basis of the statistical uncertainty with the smaller dose. It would have been helpful to reduce the scanning speed for a few 2-mCi doses to test this effect.

(2) The authors note that "scans were done 2–6 days after I-131 administration," but the precise time span is critical to the evaluation: many more lesions will be found at 3 days than at 2, and it is possible that a 6-day wait would enhance or degrade the lesion contrast (*2,3*). What was the effect of the time variable in this group of patients? More precisely, were the scanning intervals held constant for the 2- and 10-mCi doses for each patient? A 2-mCi dose scanned at 2 days cannot be compared with a 10-mCi dose scanned at 4 or 6 days. In reference to Table 2, comparing 10-mCi with 30-mCi doses, the statement ". . . the 10-mCi dose either gave a majority of the detected sites a higher target-to-nontarget ratio, or enabled formerly undetected sites to become visible" presumably should read "the *30*-mCi dose . . . ." Again, the 30-mCi doses were scanned at 7–10 days and were compared with 10-mCi doses scanned at 2–6 days.

Finally, Fig. 3 shows a positive 10-mCi scan followed *seven days later* by a negative 2-mCi scan. Has all the previous uptake from the 10-mCi dose really disappeared? If the time course is that rapid, Question No. 2 above becomes even more critical. The efficacy of therapy with I-131 becomes very problematical if turnover is truly that rapid. This turnover rate also raises questions about the decision to wait 7–10 days to scan the 30- and 100-mCi doses.

I do not take issue with the concepts of 10-mCi doses of I-131, endogenous TSH stimulation, and other parts of the protocol, which are very similar to those in use here for many years. The questions addressed in this paper are important to raise but are not really answered by the data presented.

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REFERENCES

1. WAXMAN A, RAMANNA L, CHAPMAN N, et al: The significance of I-131 scan dose in patients with thyroid cancer: determination of ablation: concise communication. *J Nucl Med* 22:861–865, 1981
2. PINSKY S, BEKERMAN C, HOFFER P: Total body imaging of thyroid cancer patients after total thyroidectomy. In *Thyroid Cancer*. Boca Raton, CRC Press, 1979
3. HENK JM, KIRMAN S, OWEN GM: Whole body scanning and ^{131}I therapy in the management of thyroid carcinoma. *Br J Radiol* 45:369–376, 1972

Reply

Dr. Thomas is correct in stating that two important variables in the determination of I-131 activity in the thyroid cancer patient are scan speed and time delay in performing the scan following I-131 administration.

On page 863, paragraph 2, we state that "a 10-mCi dose of I-131 represents a fivefold increase over 2 mCi. If one assumes the percentage uptake to be constant in a given region of iodine-trapping tissue, this should result in a fivefold increase in photon emission. If a 500-μCi dose is compared with a 10-mCi one, the latter would represent a twentyfold increase. Depending upon the sensitivity and resolution of the detection equipment used in making the scan, the fivefold or twentyfold increase in photon emission may be a critical factor in the visual detection of abnormalities."

It appears that we are in agreement with Dr. Thomas with respect to item 1. We note that in performing a rectilinear scan of the neck and chest at a scan speed of 36 cm/min, the total time required to perform the study is approximately 45–50 min. This protocol is generally followed in most laboratories using a rectilinear scanner. The point our paper makes is simply that a 45–50 min neck and chest scan, keeping all parameters the same except for dose, resulted in a significant difference in sensitivity as higher doses were used. Sensitivity increased most rapidly between the 2- and the 10-mCi dose levels.

The METHOD section in our paper stated that all patients in the study were scanned 2–6 days after I-131 administration. It was implied, but not clearly stated, that if the 2-mCi scan was done 3 days following I-131 administration, the 10-mCi scan was also done at 3 days. Thus, the scanning intervals were held constant for both the 2- and the 10-mCi dose.

Table 2 compares a 30-mCi scan dose with a 10-mCi one and shows the 30-mCi scan to have a higher sensitivity than the 10. On page 862, paragraph 4, the 10-mCi notation is incorrect and should read 30 mCi.

The 30-mCi doses were scanned with the same time interval as the 10; however, to ensure against high background activity obscuring abnormalities with the 30- or 100-mCi scan performed 2–4 days after I-131 administration, a *repeat* scan was performed 7–10 days after administration. Because the turnover rate of I-131 is variable, we attempted to minimize the time differences in performing scans. We also stated, in the METHOD section of our paper, that scans were done in *all* cases 2–6 days after I-131 administration and were *repeated* at 7–10 days when 30 or 100 mCi of I-131 were given for ablation. We are again in agreement with Dr. Thomas in that we felt it was important to minimize the time variable, not only for the 2- and 10-mCi doses but for higher doses as well.

We also agree that our Fig. 3 is of great interest. This figure shows a patient who had a positive 10-mCi I-131 scan followed 7 days later by a negative 2-mCi scan. Previous uptake from the 10-mCi dose was not detected despite the fact that an additional 2-mCi dose of I-131 was administered immediately following the 10-mCi scan and the combined doses showed no activity in the neck using a similar technique in rescanning the patient. Turnover of I-131 is important not only in calculating the radiation dose we can deliver to a differentiated thyroid carcinoma, but also may be important in detecting metastasis using I-131 if the scan is inappropriately delayed.

We again agree with Dr. Thomas in that the questions addressed in this paper are important. We are sure the data speak for them-

selves and clearly show that a 2-mCi scan was markedly less sensitive in detecting thyroid metastases or residual iodine-avid tissue than a comparable 10-mCi scan performed at similar intervals and using the same scanning techniques. We have also shown this to be the case using Anger scintiphotos.

In summary, the paper simply shows that there is a major difference in sensitivity in detecting iodine-avid tissue, and it is dose dependent. Institutions using 500 μCi–2 mCi of I-131 may expect a significantly reduced sensitivity compared with institutions using higher doses such as 10 mCi.

We also suggested that ablation be defined both visually and clinically. This is to say that visualization of residual iodine-avid tissue or metastasis by large doses of I-131 may not necessarily ensure a clinical response to I-131 therapy. Whether a 1-, 2-, or 5- to 10-mCi dose is most appropriate in evaluating the patient with differentiated thyroid carcinoma is not the key issue. A fundamental question to be answered is which patient to treat with high-dose I-131 therapy regimens based upon an arbitrary dose of I-131 used as a diagnostic scan.

We are in the final phases of evaluating our follow-up data on those patients who had negative 2- but positive 10-mCi I-131 scans and were subsequently treated with 100 mCi of I-131. We hope this information will add to our knowledge in determining which patients may be expected to have a beneficial response to I-131 therapy.

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Re: Reduction of Thyroid Uptake by Iodine Absorbed with Eye-Drop Therapy

It is well known that the administration of iodine for therapeutic or diagnostic use reduces the I-131 uptake by thyroid tissue as well as by functioning metastases of thyroid carcinoma. Recently we studied a 66-yr-old woman who had been treated with total thyroidectomy for papillary thyroid carcinoma. She had radiological evidence of widespread lung metastases, and her serum thyroglobulin levels were very high (9,800 ng/ml; normal range 1.5–30 ng/ml). No uptake was demonstrated by conventional whole-body scan performed 48–72 hr after administration of 5 mCi of I-131. The urinary excretion of stable iodine was elevated (2.550 μg/l). A careful clinical history revealed that for a long time the patient had been taking an anticataract collyrium containing NaI, KI, and RbI. Six months after withdrawal of eye-drop therapy, the urinary iodine was 103 μg/l and pulmonary uptake of I-131 could be observed clearly.

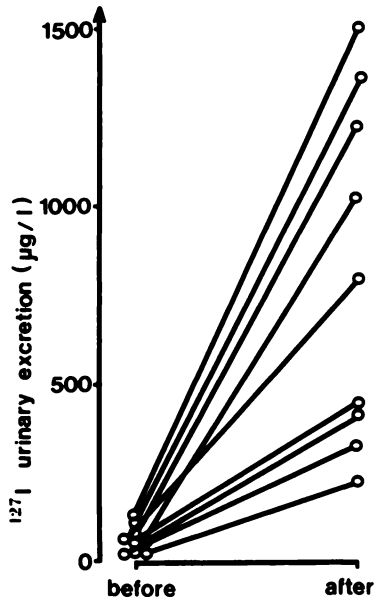

FIG. 1. Urinary excretion of I-127 in nine subjects before and 7 days after treatment with iodine-containing collyrium.

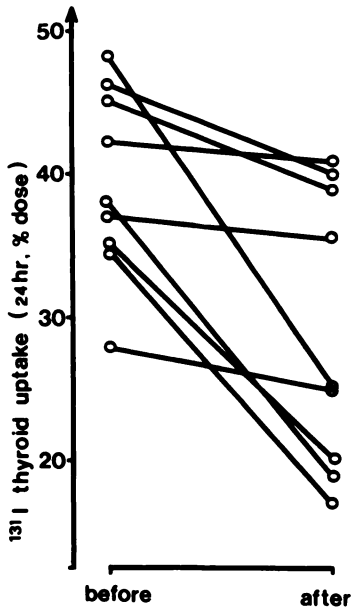

FIG. 2. Thyroid uptake of I-131 at 24 hr in nine subjects before and 7 days after treatment with iodine-containing collyrium.

To the best of our knowledge, no information is available on the possibility that the iodine may be absorbed after administration of eye drops. We therefore studied this problem, analyzing the urinary excretion of iodine and the I-131 thyroidal uptake in nine subjects (8 male, 1 female; age range 41–74 yr; none having thyroid or kidney disease) before and 7 days after administration of the iodine-containing collyrium. The dose was two drops/eye twice a day, corresponding 4 mg of stable iodine. The urinary iodine excretion increased in all subjects (Fig. 1): after treatment the mean value of 814 ± 153 μg/l (mean ± s.e.m.) was significantly higher than that observed before treatment (76.0 ± 13.2 μg/l; $p < 0.001$ by Student's t-test for paired samples). On the other hand, the 24-hr I-131 thyroidal uptake decreased in all subjects (Fig. 2), the mean values being 40.0 ± 2.1% before treatment and 28.1 ± 3.5% after ($p < 0.025$).

These data indicate that the iodine may be absorbed after administration of eye drops and therefore may interfere with thyroid uptake. Since iodine-containing collyria are widely used in Europe—though of dubious effectiveness in the medical treatment of cataract—their effects must be borne in mind during radioiodine studies of thyroid disease, and they should be avoided altogether in such studies of differentiated thyroid carcinoma.

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