RELATIONSHIP OF THE THYROID SCINTISCAN TO THE THERAPEUTIC EFFECTS OF ^{131}I IN HYPERTHYROIDISM WITH DIFFUSE GOITER

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Hypothyroidism following ^{131}I treatment for hyperthyroidism has been recognized as being the most common complication (*1–3*). It has been shown that lower doses of ^{131}I reduce the incidence of hypothyroidism during the first 2 years of followup (*4,5*). On the other hand, Skillman and associates (*6*) demonstrated no difference in the incidence of hypothyroidism following random doses of 132, 198, and 271 μCi ^{131}I/gm of thyroid tissue with an incidence of 50–60% in patients followed a minimum of 2½ years. In this latter study it was also shown that doses as low as 50 μCi/gm could produce hypothyroidism whereas doses as high as 300 μCi/gm were sometimes ineffective. These findings demonstrate a high degree of variability in individual response to treatment with radioactive iodine, and indicate that the result of therapy in each patient is unpredictable. Recently Philp (*7*) commented that besides the dose of treatment, biological factors of the sensitivity of the individual patient and the distribution in terms of ^{131}I in the thyroid gland (*8*) may play an important role in modifying the effect of radioactive iodine therapy.

The present study investigates the results of therapy in patients treated with ^{131}I at different dose levels and correlates the relationship between ^{131}I distribution within the gland as determined by thyroid scans and the response of patients to therapy.

METHODS

All patients with hyperthyroidism and diffuse goiters on physical examination treated with ^{131}I during the period between January 1967 and January 1969 were studied retrospectively. The hospital charts and records in the Department of Nuclear Medicine were reviewed, and questionnaires were sent to the attending physicians to obtain information regarding the latest condition of the patients. The followup period was calculated from the date of first ^{131}I treatment to the date the patient was last seen by the physician. The diagnosis of hyperthyroidism was made on clinical grounds and confirmed in all cases by the PBI, T_3 resin sponge uptake, and 24-hr ^{131}I uptake. On physical examination all patients had diffuse goiters without palpable nodules. A thyroid scintiscan was done on each patient prior to ^{131}I treatment. The scans were done on a 5-in. Ohio-Nuclear scanner using the gammagraphic technique first described by Christie (*9*). The initial weights of the glands were estimated by palpation and by thyroid scans. The treatment dose of ^{131}I in microcuries per gram of thyroid tissue was determined using the following formula:

$$\text{Treatment dose } (\mu\text{Ci/gm}) = \frac{\text{dose } (\mu\text{Ci}) \times 24 \text{ hr } ^{131}\text{I (uptake diagnostic)}}{\text{estimated weight of the gland (gm)}}.$$

For those patients who received multiple treatments, the dose was expressed as the sum of individual doses. No antithyroid medication was administered to any of the patients prior to ^{131}I therapy or for at least 2 weeks following treatment with ^{131}I.

The thyroid scans were classified into three categories on the basis of the distribution of radioactive iodine within the gland; namely homogeneous, intermediate, and irregular (Figs. 1–3). The scans were read independently by two interpreters. In cases of discrepancy in interpretation of the scans, a final decision was reached after discussion between the two interpreters. There was no difference in the physical examination of the thyroid glands of the three categories, and irregularities in distribution of radioactivity seen on scans could not be correlated with physical findings.

The post-therapeutic results were based on clinical data confirmed by laboratory testing. Based on the calculated initial dose the patients fell by chance into two groups: a lower dose group who received from 80 to 110 μCi/gm of thyroid tissue (mean 91.9 ± 8.7 μCi/gm) and a higher dose group who received

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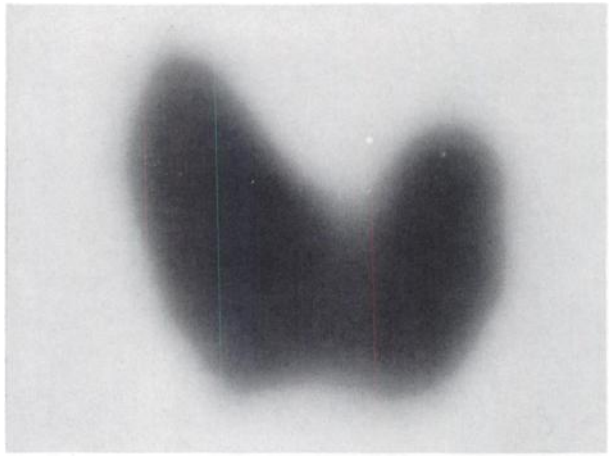

FIG. 1. Homogeneous scan. Radioactivity equally distributed within gland.

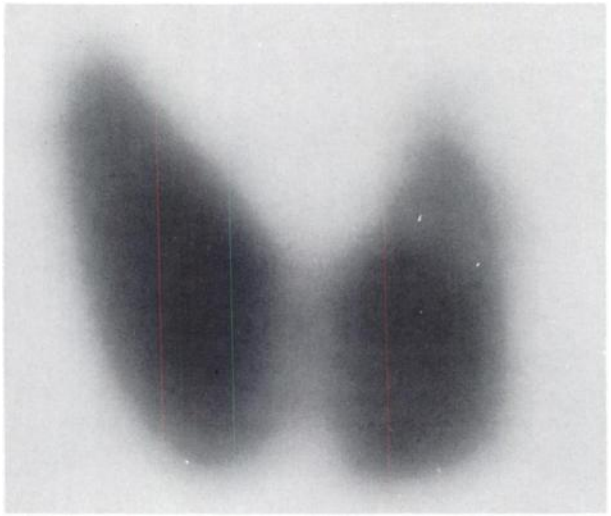

FIG. 2. Intermediate scan. Moderate variability in distribution of radioactivity.

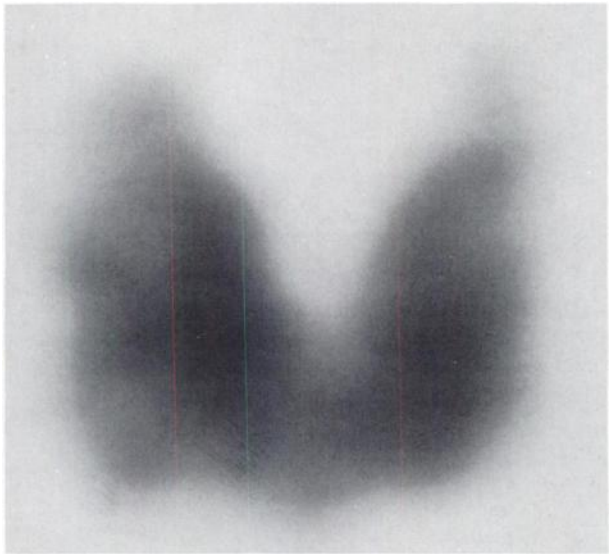

FIG. 3. Irregular scan. Marked variability in distribution of radioactivity.

135–190 μCi/gm (mean 155 ± 10.6 μCi/gm). The clinical features and response to the initial dose of ^{131}I of these two groups were compared. In addition, patients were divided into three groups on the basis of the character of the thyroid scan as described above and analyzed in terms of total dose received, initial weight of the gland, need for retreatment, and incidence of hypothyroidism.

RESULTS

There were 41 cases of hyperthyroidism with diffuse goiter. Three patients were lost to followup; one had thyroid surgery prior to ^{131}I treatment and one had multiple ^{131}I treatments in another hospital. These five cases were excluded, and the remaining 36 patients were the subjects of this study.

The sex ratio was 4 to 1 in favor of females. The mean age was 39 years with a range from 15 to 80 years. The longest followup period was 26 months, the shortest 9 months, and the mean followup period was 20 months. Seventy-five percent of the cases have been followed for more than 19 months.

The overall incidence of post-therapy hypothyroidism was 19.4% (7/36) at the end of the followup period. Figure 4 shows the cumulative incidence of post-therapy hypothyroidism. Six of the 7 patients developed hypothyroidism within 1 year after treatment.

Table 1 shows that the weights of the glands, ages of the patients, and followup periods were comparable between those who initially received 91.9 ± 8.7 μCi/gm (lower dose) and those receiving 155 ± 10.6 μCi/gm (higher dose). The incidence of post-therapy hypothyroidism was 28.5% in the higher dose group versus 13.8% in the lower dose group. The number of cases, however, does not allow this difference to be statistically significant. Eight out of 29 patients in the lower dose group required multiple treatments for control of hyperthyroidism, and one of these eight patients ultimately became hypothyroid (total dose 500 μCi/gm). No patient who received an initial higher dose treatment required retreatment.

The dose initially administered, the need for retreatment, and the patterns of thyroid scans are shown in Table 2. These data demonstrate that in the lower dose group there was a high proportion of homogeneous scans in patients requiring only a single treatment dose. In contrast, there was a high proportion of irregular thyroid scans in patients requiring retreatment.

Table 3 includes the total dose required to achieve control of hyperthyroidism. It also indicates the frequent requirement of repeated treatment in pa-

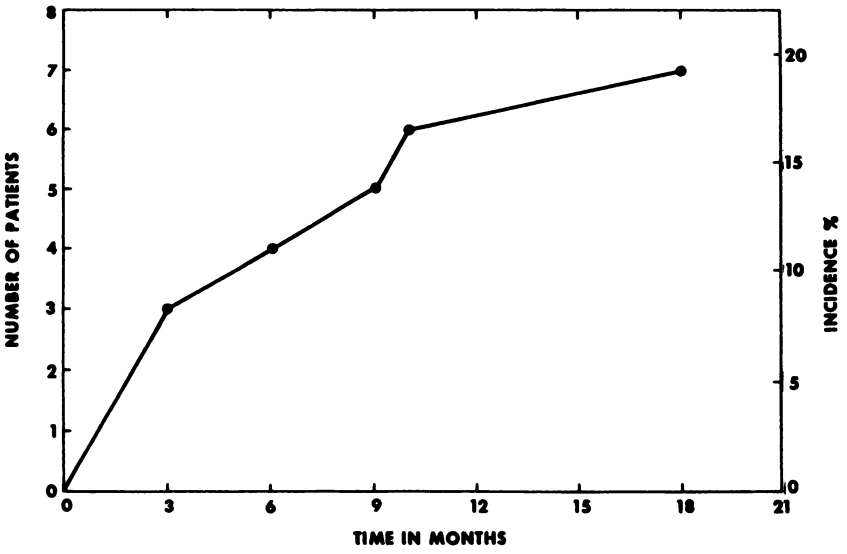

FIG. 4. Cumulative incidence of hypothyroidism.

TABLE 1. CHARACTERISTICS AND OUTCOME OF PATIENTS TREATED WITH HIGHER DOSE AND LOWER DOSE

Group	No. of patients	Initial dose* (μCi/gm)	Wt. of gland* (gm)	Age of patient*	Followup period*	Euthyroid	Hypothyroid	Repeated treatment
Higher dose	7	155.0 ± 10.6	46.9 ± 17.5	46.5 ± 19.3	18.5 ± 5.9	5/7 (71.5%)	2/7 (28.5%)	0
Lower dose	29	91.9 ± 8.7	38.5 ± 5.5 $p > 0.2$	37.7 ± 15.5 $p > 0.2$	20.3 ± 5.8 $p > 0.4$	17/29 (58.6%)	4/29 (13.8%) $p > 0.3$	8/29 (27.6%)

* Mean ± s.d.

TABLE 2. PATTERNS OF THYROID SCANS IN THREE DIFFERENT TREATED GROUPS

Group	No. of patients	Initial dose* (μCi/gm)	Homogeneous	Intermediate	Irregular
Initial lower dose Single treatment	21	91.6 ± 9.4	12 (4)	7	2
Initial higher dose Single treatment	7	155.0 ± 10.6	2 (1)	2 (1)	3
Initial lower dose and retreatment required	8	92.1 ± 8.0	1	2	5 (1)

* Mean ± s.d.
( ) Number of patients who became hypothyroid.

TABLE 3. CHARACTERISTICS AND OUTCOME OF PATIENTS WITH THREE DIFFERENT PATTERNS OF THYROID SCAN

	No. of patients	Total dose (μCi/gm)	Wt. of thyroid gland (gm)	Incidence of hypothyroidism	No. of treatments			
					one	two	three	four
Homogeneous scan	15	107.6 ± 30.6	39.6 ± 12.6	4/14 (26.6%)	14 (5)	1	0	0
Intermediate scan	11	122.2 ± 48.1	44.5 ± 11.0	2/11 (18.2%)	9 (1)	1	1	0
Irregular scan	10	*212.5 ± 141.8	55.0 ± 12.9	1/10 (10.0%)	5	2	2	1 (1)

* Includes three patients who received total dose of 325, 390, and 500 μCi/gm, respectively.
( ) Number of patients who became hypothyroid.

tients with irregular thyroid scans compared with those with homogeneous or intermediate scans. The need of retreatment is significantly higher in patients with irregular scans compared to those with homogeneous scans ($p < 0.02$). The incidence of post-therapy hypothyroidism is considerably lower, and the mean weights of the glands were considerably heavier in patients with irregular thyroid scans. Three patients with irregular thyroid scans received total doses as high as 500, 390, and 325 μCi/gm as the result of multiple treatments.

DISCUSSION

In those patients who received lower initial doses in the treatment of hyperthyroidism with diffuse goiter (92 μCi/gm) our series showed that the incidence of post-therapy hypothyroidism was 13.8% (4/29) at 20 months mean followup and the incidence of retreatment was 27.6%. The incidence of retreatment is similar to the 25% reported by Hagen and coworkers using low dosage treatment (80 μCi/gm) (*5*). The hypothyroidism of 13.8% is higher in comparison to the results reported by Smith and Hagen (5.4–6.0%) (*4,5*) but is comparable to the 16.6% (5/30) reported by Philp (*7*). In those patients who required only a single treatment (low dose) to control their hyperthyroidism there was a large population with homogeneous thyroid scans. In addition, all four patients who became hypothyroid in this group had homogeneous scans. This indicates that hypothyroidism in the single low-dose group patients occurred in patients with homogeneous thyroid scans. In contrast, among those who received repeated treatments (treated initially with low dose), there was a greater proportion of patients with irregular thyroid scans. Because the scans were more irregular, the requirement of retreatment was greater. These findings are consistent with the statement of Philp that "A homogeneous distribution of ^{131}I in therapeutic doses would affect all or most thyroid cells and would result in early hypothyroidism. A nonhomogeneous distribution on the other hand would spare areas of the gland in an unpredictable way so that persistent hyperthyroidism, recurrence of hyperthyroidism, or the euthyroid state would result" (*7*). We cannot explain the strikingly lower incidence of hypothyroidism observed in our series compared with that reported by Skillman and associates (*6*). We agree that an effective dose without complicating myxedema is difficult if not impossible to attain. However, an upper range dose of 130 μCi/gm as suggested by Skillman may well not be satisfactory in obtaining rapid control in a patient with an irregular scan.

SUMMARY

Thirty-six cases of hyperthyroidism with diffuse goiter treated with ^{131}I were studied retrospectively. The therapeutic doses and clinical results of the patients were correlated with the characteristics of thyroid scintiscans. Although the total number of patients in this study is somewhat small, the following conclusions may be reached: (A) Many patients with hyperthyroidism and diffuse goiter without palpable nodules by physical examination reveal marked irregularity of distribution of radioactive iodine within the glands as determined by the thyroid scintiscan. (B) Patients with an irregular distribution of radioactivity within the gland more often required multiple treatments and higher total dose for the control of hyperthyroidism compared with patients with homogeneous distribution of radioactivity within the glands. (C) The incidence of post-therapy hypothyroidism is lower in the patients with irregular distribution of radioactivity within the gland. (D) The pattern of radioactivity within the gland as determined by the thyroid scan is a good parameter in predicting the response to therapy, the likelihood of developing early hypothyroidism, and in determining the dose of ^{131}I to be used in treatment. (E) There is apparently no dose of ^{131}I presently used in treatment of hyperthyroidism which will completely eliminate post-therapy hypothyroidism.

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