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## The statistic study of radioactive iodine therapy for hyperthyroidism

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## 甲状腺機能亢進症における放射性ヨード治療の統計的研究

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甲状腺機能亢進症で  $^{131}\text{I}$  治療をおこなった738例に、適正吸収線量の決定に資するため追跡調査を実施、1年以上の経過観察ができた539例について検討した。

これらの症例について、 $^{131}\text{I}$  治療後の経年推移をみるとともに、吸収線量、 $^{131}\text{I}$  投与量、年齢、甲状腺重量、 $^{131}\text{I}$  摂取率、 $\text{RT}_3\text{U}$  別に、治癒率、甲状腺機能低下症の発生率、及び平均吸収線量について、統計的検討をおこなった。

$^{131}\text{I}$  治療後の甲状腺機能低下症の発生率は、5年目15.6%、10年目21.6%であった。

2年以上の経過観察例について、まとめてみると、吸収線量 6,000rad 以上では治癒率は70~76%、機能低下症の発生率も6,000ないし 8,000rad で10%前後と大差を認めなかった。甲状腺の放射

線感受性は年齢により異なることが推定され、30歳未満では5,000ないし 6,500rad で、30歳以上では 7,000rad で70%前後の治癒率を示した。

甲状腺重量が増加するにつれて、 $^{131}\text{I}$  投与量が少なめにする傾向がみられ、その結果、吸収線量も少なくなり、治癒率も低下したが、機能低下症の発生率は、特に減少する傾向は認められなかった。

$^{131}\text{I}$  摂取率別にみると、治癒率に大差を認めなかった。また、 $\text{RT}_3\text{U}$  が高値を示す程、吸収線量も少なくなり、治癒率も低下する傾向を示した。

以上のことより、甲状腺機能亢進症の  $^{131}\text{I}$  治療に際して、70%以上の治癒率を期待するためには、吸収線量6,500rad は必要と思われる。

Since the radioactive iodine therapy for hyperthyroidism was reported in 1942 by Hertz, it has been widely used because of its simplicity and great efficacy though there is a legal restriction in dealing with radioisotopes and hypothyroidism may occur as a side effect with the years.

There are many reports<sup>1)-4)7)11)</sup> which have stressed the occurrence of hypothyroidism.

In this study, in order to determine the proper dose of radioactive iodine ( $^{131}\text{I}$ ), a follow-up survey of patients who had undergone  $^{131}\text{I}$  therapy was made for statistical analysis.

## I. Subjects and Methods

Seven hundred and thirty-eight patients having hyperthyroidism underwent  $^{131}\text{I}$  therapy in the Department of Radiology of Kumamoto University Hospital for a period of 13 years (1965 to 1977). The subjects were 539 of these patients who could be followed up for more than one year. In addition, 398 of the 539 patients who could be followed up for more than two years and in whom  $^{131}\text{I}$  therapy was performed only once were regarded as those whose conditions were constant after the final diagnosis. The patients were divided into hyperthyroid, euthyroid, and hypothyroid conditions and the absorbed dose, the dose of  $^{131}\text{I}$ , and the patients' ages were examined.

The thyroid function is determined according to the patients' symptoms,  $\text{T}_3$  resin uptake ( $\text{RT}_3\text{U}$ ),  $^{131}\text{I}$  uptake rate of the thyroid gland, scintigraphic findings, BMR, and sero-biochemical findings. In addition,  $\text{T}_3$ ,  $\text{T}_4$ , and TSH by radioimmunoassay have been adopted for the diagnosis since 1974.

Efficacy of  $^{131}\text{I}$  therapy for hyperthyroidism depends on the assumed weight of the thyroid gland. We determined the assumed weight of the thyroid gland according to the Allen's and Okubo's methods in addition to our experiences. The dose of  $^{131}\text{I}$  was determined according to the formula of Quimby. The absorbed dose was 8000 rad/g of the thyroid gland before 1973 and has been 5000 rad/g of the thyroid gland since 1974. The doses increased or decreased according to the patients' ages.

## II. Results of Survey

### 1. Distribution of age and sex

Table 1 shows the distribution of age and sex in 539 patients. They ranged in ages between 8 and 68 years. Half of the male patients were in their twenties (25 patients) and in their thirties (38 patients). Seventy percent of the female patients were in their twenties (90 patients), in their thirties (95 patients), and in their forties (107 patients). The ratio of male patients to female patients in their thirties and forties was almost the same (133 female patients and 132 male patients). This number almost occupied a half of the total number of patients. The average age of the patients was 36.7 years. The ratio of male patients to female patients were approximately 1:4 (111 male patients to 428 female patients).

Table 1. Distribution of age and sex (%)

Age	Man	Female	Total
~19	7(10.9)	57(89.1)	64(11.9)
20~	25(21.7)	90(78.3)	115(21.3)
30~	38(28.6)	95(71.4)	133(24.7)
40~	25(18.9)	107(81.1)	132(24.5)
50~	13(15.5)	71(84.5)	84(15.6)
60~	3(27.3)	8(72.7)	11( 2.0)
Total	111(100)	428(100)	539(100)

Of the 539 patients, 43 had undergone more than two  $^{131}\text{I}$  therapies and 112 had received antithyroid drugs before  $^{131}\text{I}$  therapy. In addition, in 46 patients their family member had also been diagnosed as having hyperthyroidism and had been treated.

2. Serial changes in the thyroid function after <sup>131</sup>I therapy

Fig. 1 shows serial changes in the thyroid function after <sup>131</sup>I therapy.

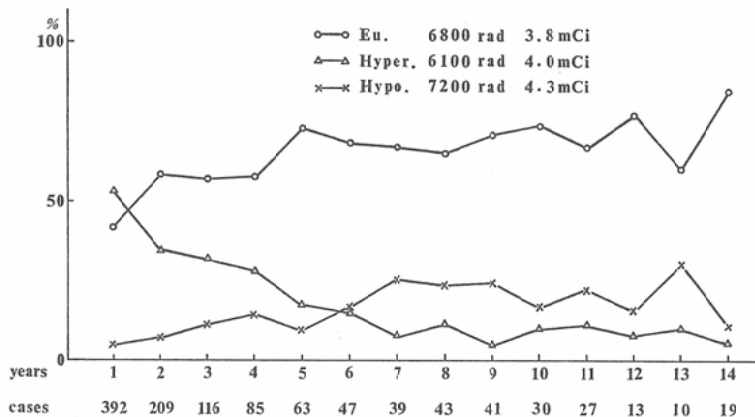


Fig. 1 Serial changes in the thyroid function after <sup>131</sup>I therapy

One year after the therapy, 208 of the 392 patients (53.1%) were still hyperthyroid. One hundred and sixty-four patients (41.8%) had become euthyroid. Twenty patients (5.1%) had become hypothyroid. Two years after the <sup>131</sup>I therapy, the number of hyperthyroid patients (209) decreased to 72 (34.4%). One hundred and twenty-two patients (58.4%) had become euthyroid. Fifteen patients (7.2%) had become hypothyroid. Furthermore, a follow-up survey for two more years revealed that 46 hyperthyroid or hypothyroid patients (22%) had become euthyroid and that the incidence of hypothyroidism increased by 1.5% (3 patients) (Table 2).

Table 2. Serial changes in the thyroid function after <sup>131</sup>I therapy

Years	No. of cases	Hyper →Eu	Hypo →Eu	Eu→Hyper	Eu→Hypo	Hyper →Hypo	Total
2	209(100)	39(18.7)	7(3.3)	1(0.5)	2(1.0)	1(0.5)	50(23.9)
3	116(100)	10( 8.6)	4(3.4)	1(0.9)	5(4.3)	1(0.9)	21(18.1)
4	85(100)	5( 5.9)	1(1.2)	3(3.5)	2(2.4)	2(2.4)	13(15.3)
5	63(100)	4( 6.3)	2(3.2)				6( 9.5)
6~	161(100)	3( 1.9)	1(0.6)	9(5.6)	6(3.7)		19(11.8)
Total	526(100)	61(11.6)	15(2.9)	14(2.7)	15(2.9)	4(0.8)	109(20.7)

The incidence of hyperthyroidism decreased with the years (17.8% 5 years after the therapy, 10% 10 years after the therapy, and 5.3% 14 years after the therapy). The incidence of euthyroidism increased with the years (73% 5 years after the therapy, 73.4% 10 years after the therapy, and 84.2% 14 years after the therapy). The incidence of hypothyroidism was 14.1% 4 years after the therapy and 24.4% 9 years after the therapy. In addition, a follow-up survey for two more years revealed that incidence of hypothyroidism increased by 5.2% and by 4.8%.

Two regression equations were prepared by regrading 7 years after <sup>131</sup>I therapy as a boundary (Fig. 1). The linear regression of hypothyroidism was  $y=0.6+3.0x$  (2 to 7 years) or  $y=32.7-1.1x$

(7 to 14 years); that of the hyperthyroidism was  $y=47.5-5.6x$  (2 to 7 years) or  $y=10.4-0.2x$  (7 to 14 years). According to the linear regression, the incidence of hypothyroidism was 15.6% and 21.6% 5 and 10 years after the therapy, respectively. The incidence of hyperthyroidism was 19.6% and 8.6% 5 and 10 years after the therapy. In addition, the incidence of euthyroidism was 64.7% and 69.8% 5 and 10 years after the therapy.

### 3. Distribution of the absorbed dose

Symptoms at the final diagnosis following  $^{131}\text{I}$  therapy was regarded as constant. The thyroid function was determined according to the absorbed dose of  $^{131}\text{I}$  (Fig. 2).

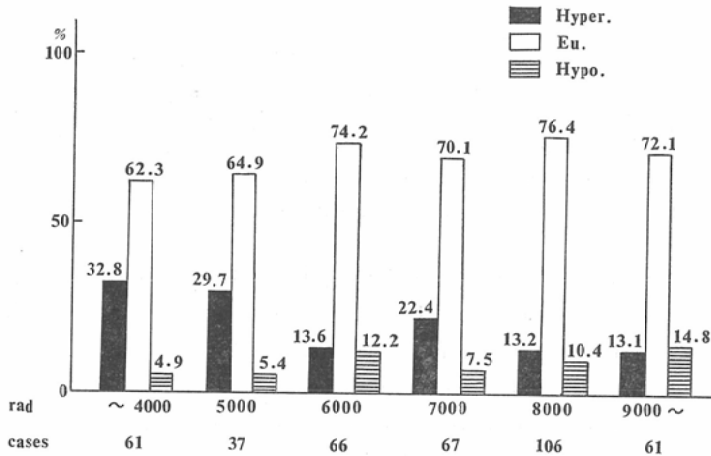


Fig. 2 Distribution of the absorbed dose

When the absorbed dose was less than 4000 rad or 5000 rad, the incidence of hypothyroidism was only approximately 5%, the incidence of hyperthyroidism was still 30%, and the incidence of euthyroidism was less than 65%.

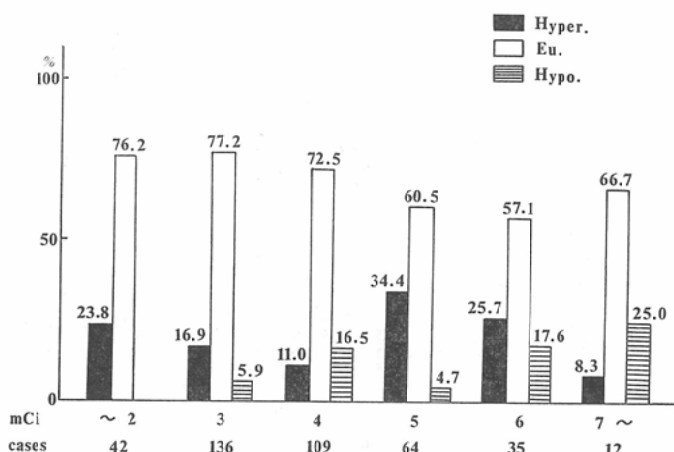
When it was 6000 rad, the incidences of euthyroidism, hypothyroidism and hyperthyroidism were 74.2%, 12.2%, and 13.6%, respectively. When it was 7000 rad, the incidences of euthyroidism, hypothyroidism, and hyperthyroidism were 70.1%, 7.5%, and 22.4%, respectively. When it was 8000 rad, the incidences of euthyroidism, hypothyroidism, and hyperthyroidism were 76.4%, 10.4%, and 13.2%, respectively. When it was more than 9000 rad, the incidences of euthyroidism, hypothyroidism, and hyperthyroidism were 72.1%, 14.8%, and 13.1%, respectively. These results revealed that there is not always relationship between an increase of the absorbed dose and the incidence of euthyroidism.

Of the 398 patients, 283 euthyroid patients (71.7%) had underwent an absorbed dose of 6800 rad on the average, 77 hyperthyroid patients (19.4%) had underwent 6700 rad, and 38 hypothyroid patients (9.5%) had underwent 7200 rad.

The absorbed dose given to the all patients was 6700 rad on the average.

### 4. Distribution of the dose of $^{131}\text{I}$

Fig. 3 shows the distribution of the dose of  $^{131}\text{I}$ . When a dose of  $^{131}\text{I}$  was less than 2 mCi, the

Fig. 3 Distribution of the dose of  $^{131}\text{I}$ 

incidences of euthyroidism and hyperthyroidism were 76.2% and 23.8%, respectively. No hypothyroidism occurred. When the dose was 3 mCi, the incidences of euthyroidism, hyperthyroidism, and hypothyroidism were 77.2%, 16.9%, and 5.9%, respectively. When it was 4 mCi, the incidences of euthyroidism, hyperthyroidism, and hypothyroidism were 72.5%, 11%, and 16.5%, respectively. When it was 5 mCi, the incidences of euthyroidism, hyperthyroidism, and hypothyroidism were 60.5%, 34.4%, and 4.7%, respectively. When it was 6 mCi, the incidences of euthyroidism, hyperthyroidism, and hypothyroidism were 57.1%, 25.7%, and 17.6%, respectively. When it was more than 7 mCi, the incidences of euthyroidism, hyperthyroidism, and hypothyroidism were 66.7%, 8.3%, and 25%, respectively.

Hyperthyroid and hypothyroid patients were divided into the group in which a dose of less than 4 mCi was given and the group in which a dose of more than 5 mCi was given. Both groups had the same tendency for the incidences of hyperthyroidism and hypothyroidism. That is, the incidence of hyperthyroidism decreased and the incidence of hypothyroidism increased.

In this study, the mean dose of  $^{131}\text{I}$  was 3.9 mCi.

##### 5. Mean absorbed dose according to the patients' ages

Fig. 4 shows the mean absorbed dose according to the patients' ages.

The mean absorbed dose was 5000 rad in euthyroid patients under the age of 19 (69.6%) and 3700 rad in hyperthyroid patients (30.4%). No patient under the age of 19 had not become hypothyroid. It was 6500 rad in euthyroid patients in their twenties (74.7%), 5800 rad in hyperthyroid patients (24%), and 6000 rad in hypothyroid patients (1.3%). It was 7400 rad in euthyroid patients in their thirties (66.7%), 7000 rad in hyperthyroid patients (24%), and 7200 rad in hypothyroid patients (12.5%). It was 7000 rad in euthyroid patients in their forties (71.7%), 6300 rad in hyperthyroid patients (13.1%), and 7300 rad in hypothyroid patients (15.2%). It was 7000 rad in euthyroid patients in their fifties (73.9%), 5000 rad in hyperthyroid patients (13%), and 7900 rad in hypothyroid patients (13.1%). It was 8200 rad in euthyroid patients in their sixties (66.7%), 7000 rad in hyperthyroid patients (22.2%), and 8000 rad in hypothyroid patients (11.1%).

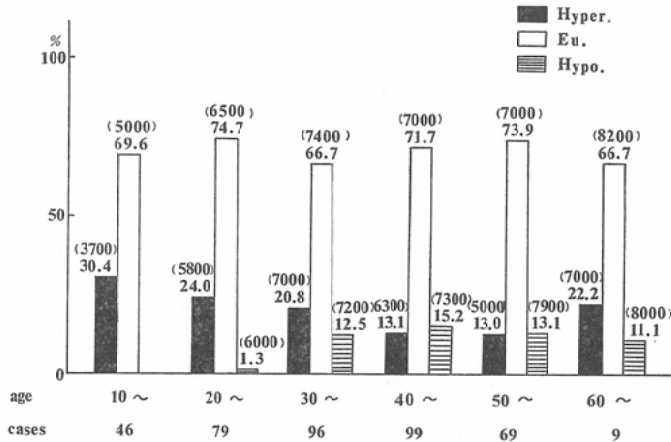


Fig. 4 Mean absorbed dose according to the patients' age  
( ) Absorbed dose: rad

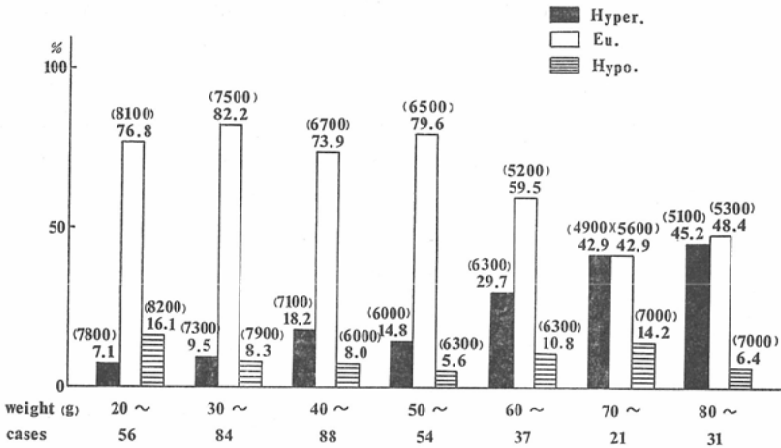


Fig. 5 Mean absorbed dose according to the weight of the thyroid gland  
( ) Absorbed dose: rad

The mean absorbed dose was higher in euthyroid patients in their twenties, thirties, and sixties than in hypothyroid patients in their twenties, thirties, and sixties. It was lower in hyperthyroid patients than in euthyroid and hypothyroid patients of each age.

6. Mean absorbed dose according to the weight of the thyroid gland

Fig. 5 shows the mean absorbed dose according to the weight of the thyroid gland.

When the weight of the thyroid gland was between 20 g and 29 g, the mean absorbed dose was 8100 rad in euthyroid patients (76.8%), 7800 rad in hyperthyroid patients (7.1%), and 8200 rad in hypothyroid patients (16.1%). When it was between 30 g and 39 g, it was 7500 rad in euthyroid patients (82.2%), 7300 rad in hyperthyroid patients (9.5%), and 7900 rad in hypothyroid patients (8.3%). When it was between 40 g and 49 g, it was 6700 rad in euthyroid patients (73.9%), 7100 rad in hyperthyroid patients (18.2%), and 6000 rad in hypothyroid patients (8.0%). When it was

between 50 g and 59 g, it was 6500 rad in euthyroid patients (79.6%), 6000 rad in hyperthyroid patients (14.8%), and 6300 rad in hypothyroid patients (5.6%). When it was between 60 g and 69 g, it was 5200 rad in euthyroid patients (59.5%), 6300 rad in hyperthyroid patients (29.7%), and 6300 rad in hypothyroid patients (10.8%). When it was between 70 g and 79 g, it was 5600 rad in euthyroid patients (42.9%), 4900 rad in hyperthyroid patients (42.9%), and 7000 rad in hypothyroid patients (14.2%). When it was more than 80 g, it was 5300 rad in euthyroid patients (48.4%), 5100 rad in hyperthyroid patients (45.2%), and 7000 rad in hypothyroid patients (6.4%).

In euthyroid patients, the absorbed dose decreased with an increase in the weight of the thyroid gland. The incidence of euthyroidism decreased with an increased incidence of hyperthyroidism. The absorbed doses varied in euthyroid, hyperthyroid, and hypothyroid patients when the weight of the thyroid gland was between 40 g and 49 g, between 50 g and 59 g, and between 60 g and 69 g.

7. Mean absorbed dose according to the <sup>131</sup>I uptake rate of the thyroid gland

Fig. 6 shows the mean absorbed dose according to the <sup>131</sup>I uptake rate of the thyroid gland.

When the <sup>131</sup>I uptake rate was between 40% and 49%, the mean absorbed dose was 6100 rad in euthyroid patients (81.8%), 6000 rad in hyperthyroid patients (13.6%), and 9000 rad in hypothyroid patients (4.5%). When it was between 50% and 59%, it was 6300 rad in euthyroid patients (66.0%), 6100 rad in hyperthyroid patients (19.1%), and 7100 rad in hypothyroid patients (14.9%). When it was between 60% and 69%, it was 6900 rad in euthyroid patients (73.1%), 6500 rad in hyperthyroid patients (16.7%), and 7000 rad in hypothyroid patients (10.2%). When it was between 70% and 79%, it was 6800 rad in euthyroid patients (69.4%), 5800 rad in hyperthyroid patients (22.5%), and 7100 rad in hypothyroid patients (8.1%). When it was more than 80%, it was 7400 rad in euthyroid patients (77.1%), 6300 rad in hyperthyroid patients (20.8%), and 5000 rad in hypothyroid patients (2.1%).

In conclusion, the absorbed dose increased with an increase in the weight of the thyroid gland in euthyroid patients. The absorbed dose was approximately 6000 rad in hyperthyroid patients and

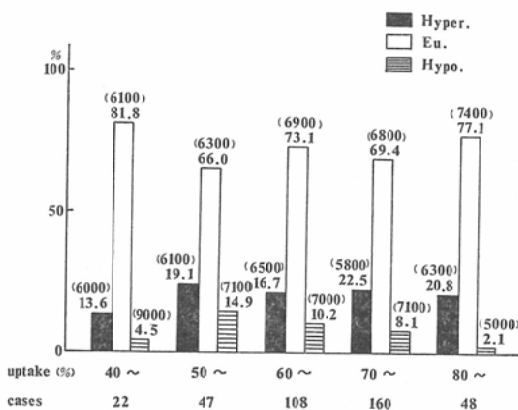


Fig. 6 Mean absorbed dose according to the <sup>131</sup>I uptake rate of the thyroid gland  
( ) Absorbed dose: rad

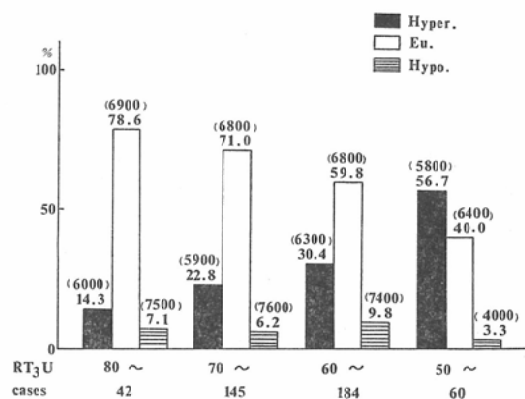


Fig. 7 Thyroid function according to the T<sub>3</sub>-resinu ptake (thyopac 3)  
( ) Absorbed dose: rad



approximately 7000 rad in hypothyroid patients, with the exception of cases in which the  $^{131}\text{I}$  uptake rate was between 40% and 49% or between 80% or 89%.

#### 8. Thyroid function according to the $\text{T}_3$ resin uptake (thyopac 3)

Fig. 7 shows  $\text{RT}_3\text{U}$  (thyopac 3), a thyroid function test with serum, and the mean absorbed dose.

The absorbed dose was 6900 rad in euthyroid patients with it's value of eighties (78.6%), 6000 rad in hyperthyroid patients (14.3%), and 7500 rad in hypothyroid patients (7.1%). It was 6800 rad in euthyroid patients with it's value of seventies (7.1%), 5900 rad in hyperthyroid patients (22.8%), and 7600 rad in hypothyroid patients (6.2%). It was 6800 rad in euthyroid patients with it's value of sixties (59.8%), 6300 rad in hyperthyroid patients (30.4%), and 7400 rad in hypothyroid patients (9.8%). It was 6400 rad in euthyroid patients with it's value of fifties (40.0%), 5800 rad in hyperthyroid patients (56.7%), and 4000 rad in hypothyroid patients (3.3%).

As clarified by the  $\text{RT}_3\text{U}$ , the thyroid function increased, the absorbed dose decreased and the incidence of euthyroidism decreased. The absorbed dose was approximately 6000 rad in hyperthyroid patients. As  $\text{RT}_3\text{U}$  increased, the incidence of euthyroidism decreased and the number of hyperthyroid patients increased. The absorbed dose was approximately 7500 rad in hypothyroid patients, with the exception of those in their fifties. There was no significant difference regarding the occurrence of hypothyroidism.

#### 9. Administration of an antithyroid drug before $^{131}\text{I}$ therapy

Table 3 shows the thyroid function in 112 patients who had received an antithyroid drug for more than one month before  $^{131}\text{I}$  therapy. An antithyroid drug was administered in 68 of the 283 euthyroid patients (24.0%), in 41 of the 77 hyperthyroid patients (53.2%), and in 3 of the 38 hypothyroid patients (7.9%).

Table 3. Administration of an antithyroid drug before  $^{131}\text{I}$  therapy

	Hyper.	Eu.	Hypo.	Total
Treated (T)	41	68	3	112
No. of cases (C)	77	283	38	398
T/C (%)	53.2	24.0	7.9	28.1

### III. Discussion

It is a matter of course that the assumed weight of the thyroid gland and an extremely small amount of the absorbed dose in the  $^{131}\text{I}$  therapy are great factors to cause euthyroidism or hypothyroidism.

As reported in the previous paper<sup>5)</sup>, the absorbed dose used in our department was 3000–8000 rad with a mean of 6000 rad before 1973. However, because hypothyroidism occurred in 4.4% of the patients who had undergone such radiotherapy, the absorbed dose has been 5000 rad since 1974.

However, as reported by many other investigators<sup>7)8)</sup>, the incidence of hypothyroidism tends to be increasing and the incidence of euthyroidism tends to be decreasing with the years though the absorbed dose is decreasing.

Although it is said that  $^{131}\text{I}$  therapy is simple and effective for hyperthyroidism, the fact that the

incidence of euthyroidism is decreasing is in question, as well as the fact that the incidence of hypothyroidism is increasing. In this study, in order to determine the proper absorbed dose, though it is unavoidable that hypothyroidism may some what occur, statistical studies were made.

The assumed dose of the thyroid gland and the rate of  $^{131}\text{I}$  uptake are greatly involved in the Quimby's formula used for calculation of the absorbed dose. Therefore, although only the absorbed dose seemed to be sufficient for study, the weight of the thyroid gland, the rate of  $^{131}\text{I}$  uptake, the ages of the patients and  $\text{RT}_3\text{U}$  were also taken into consideration for statistical analysis. Patients in whom  $^{131}\text{I}$  therapy had been performed within 1 year after the first therapy were excluded from this study.

#### Incidence of euthyroidism

Foreign reports<sup>2)3)8)</sup> have described that although the incidence of euthyroidism was more than 70% because a large dose of  $^{131}\text{I}$  was given, the incidence of hypothyroidism was also high (30–40%). This incidence of hypothyroidism seems to be higher than that in Japan. Our survey revealed a scattering 5 and 10 years after therapy because of the small number of patients for statistical analysis. According to the regression equation, the incidence of euthyroidism was 64.8% and 69.8% 5 and 10 years after therapy, respectively. On the other hand, the incidence of hypothyroidism was 15.6% and 21.6% 5 and 10 years after therapy, respectively. These results were almost the same as those reported by other investigators<sup>3)5)7)</sup>.

It seems that the incidence of hypothyroidism increased by 2% on the average every year.

#### The absorbed dose

When the absorbed dose was less than 5000 rad, although the incidence of hypothyroidism was only 5%, the incidence of euthyroidism was also low (less than 65%). When it was 6000 rad, the incidence of hypothyroidism was 12.2%. When it was 7000 rad, it was 7.5%. In both cases, the incidence of euthyroidism was more than 70%. The results with 8000 rad tended to be almost the same as those with 6000 rad. When it was more than 9000 rad, the incidence of hypothyroidism increased. That is, when 6000–8000 rad was given, there was no significant difference in the incidences of hypothyroidism and euthyroidism<sup>7)</sup>.

#### Dose of $^{131}\text{I}$

When the dose of  $^{131}\text{I}$  was less than 4 mCi, the incidence of euthyroidism was more than 70%. When it was more than 5 mCi, the incidence of euthyroidism was approximately 60%. However, the incidence of hypothyroidism markedly increased and the incidence of hyperthyroidism tended to be higher than that when less than 4 mCi was given.

In general, it seems that although the incidence of hyperthyroidism decreases with an increase of the dose of  $^{131}\text{I}$ , the incidence of hypothyroidism decreased. Therefore, it seems unnecessary to discuss the thyroid function according to the dose of  $^{131}\text{I}$ .

#### Absorbed dose according to the patients' ages

It seems that the  $^{131}\text{I}$  therapy is not performed positively in young people or women who have not yet delivered, condering radiation injury. There are some reports<sup>3)9)10)</sup> in which there is no relationship between radiosensitivities of  $^{131}\text{I}$  and the patients' ages.

When the absorbed dose was 5000 rad, the incidence of euthyroid patients under 20 years of age was

70% and no hypothyroid patient was observed. When it was 6500 rad, the incidence of euthyroid patients in their twenties was 75%. Because hyperthyroid patients were observed when 5800 rad was given, the absorbed dose of 6000 rad seems to be effective fully for the treatment. When 7000 rad to 7400 rad was given to the patients in their thirties, forties, fifties, or sixties, the incidence of euthyroidism was approximately 70%. When 7200 rad was given to these patients, the incidence of hypothyroidism was approximately 13%. The incidence of hyperthyroidism was high when 5000–6300 rad was given (with the exception of cases in which 7000 rad was given to the patients in their thirties). Therefore, the absorbed dose of 6500 rad seems to be sufficient for the treatment.

These results revealed that radiosensitivities vary according to the patients' ages.

#### Weight of the thyroid gland

The absorbed dose tended to increase as the weight of the thyroid gland decreased. Furthermore, euthyroidism and hypothyroidism tended to occur. The absorbed dose decreased with an increase of the weight of the thyroid gland. Furthermore, the incidence of euthyroidism tended to decrease and the incidence of hyperthyroidism tended to increase. Hypothyroidism was so-called in a slump and the incidence was the lowest when the weight of the thyroid gland was between 50 g and 59 g. These results correspond to the reports by other investigators in which the incidence of euthyroidism decreases with an increase of the weight of the thyroid gland<sup>3)4)7)</sup>. The dose of <sup>131</sup>I increases with an increase in the weight of the thyroid gland. Therefore, the dose was somewhat decreased in our department. Consequently, the absorbed dose was also decreased. The incidence of hypothyroidism was high when more than 7000 rad was given.

#### <sup>131</sup>I uptake rate of the thyroid gland

When the <sup>131</sup>I uptake was between 40% and 49% and when the absorbed dose was 6100 rad, the incidence of euthyroidism was high. In addition, when the absorbed dose was 6000 rad, the incidence of hyperthyroidism was low. Therefore, 6000 rad seems to be sufficient in treatment for hyperthyroidism. When the <sup>131</sup>I uptake rate was between 50% and 59% and when the absorbed dose was 6300 rad, the incidence of euthyroidism was low and the incidence of hyperthyroidism was high. In addition, because the incidence of hypothyroidism was high when the absorbed dose was 7100 rad, the absorbed dose of 6500 rad seemed necessary. When the <sup>131</sup>I uptake rate was more than 60% and when the absorbed dose was approximately 7000 rad, the incidence of euthyroidism was 70% and the incidence of hypothyroidism was less than 10%. Considering that the incidence of hyperthyroidism was high when the absorbed dose was 6500 rad, 6500–7000 rad seemed to be sufficient.

#### RT<sub>3</sub>U

According to the RT<sub>3</sub>U, as the capacity to combine the TBG was greater, the incidence of euthyroidism decreased and the incidence of hyperthyroidism increased. However, the incidence of hypothyroidism had no constant tendency. From measured values of thyopac 3, the absorbed dose was approximately 7000 rad in euthyroid patients in their fifties, approximately 6000 rad in hyperthyroid patients, and approximately 7500 rad in hypothyroid patients. Therefore, the proper absorbed dose seems to be 6500–7000 rad.

#### An antithyroid drug

In patients in whom antithyroid drugs had been administered before <sup>131</sup>I therapy, the incidence of

hypothyroidism was not so different from that in patients in whom only  $^{131}\text{I}$  therapy had been performed. However, the incidence of euthyroidism generally decreased.

The influences of  $^{131}\text{I}$  therapy upon the carcinogenesis, the incidence of leukemia, and upon offspring were studied<sup>4)12)13)</sup>. Of 539 patients, one patient had thyroid carcinoma 4 and 8 years after  $^{131}\text{I}$  therapy. However, this incidence was lower than that observed at the surgery for hyperthyroidism. Therefore, the incidence of thyroid carcinoma seems not to be due to  $^{131}\text{I}$ . Carcinomas other than thyroid carcinoma were observed in 6 patients. No leukemia was observed. The number of newborns whose mother or father had undergone  $^{131}\text{I}$  therapy was unknown. However, a girl's baby having Down syndrome whose 27 year-old father had undergone  $^{131}\text{I}$  therapy 2 years before was born.

When 5 mCi of  $^{131}\text{I}$  was given, the exposure dose to the whole body was less than 4 rad<sup>14)</sup>. As the gonad dose was to be much smaller, such a Down syndrome seemed not to be due to  $^{131}\text{I}$  therapy.

#### IV. Conclusion

Seven hundred and thirty-eight patients who had undergone  $^{131}\text{I}$  therapy for hyperthyroidism were surveyed and 539 patients who could be followed up for more than one year were selected as subjects for statistical analysis.

Five years after  $^{131}\text{I}$  therapy, the incidences of euthyroidism and hypothyroidism were 64.8% and 15.6%, respectively. Ten years after therapy, the incidences of euthyroidism and hypothyroidism were 69.8% and 21.6%, respectively.

The absorbed dose should increase or decrease according to the patients' ages. An absorbed dose of 6000 rad seemed to be sufficient in patients under 30 years of age and 6500 rad seemed to be sufficient in patients over 30 years of age.

The average age of the patients was 36.7 years. The mean absorbed dose was 6700 rad (3.9 mCi of  $^{131}\text{I}$ ). The duration of the follow-up survey was 5.3 years. The mean absorbed dose was 6800 rad in euthyroid patients, 6100 rad in hyperthyroid patients, and 7200 rad in hypothyroid patients.

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