Influence of Age, Sex, and Season upon Radioiodine Uptake by the Human Thyroid.* (18256)

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The uptake by the thyroid gland of tracer doses of radioiodine has been extensively investigated as an index of thyroid function (1-5). A wide range of values has been observed in euthyroid subjects, regardless of the tracer technique employed. As a consequence, there is an overlap between the range of uptake found in euthyroid and hyperthyroid or hypothyroid subjects. Any information relative to this overlap might be helpful. Age, sex, and season of the year have been reported as affecting thyroid function(6,7). Nevertheless, a recent review(8) has led to the conclusion that there is little evidence that serum iodine levels are affected by these factors. It has been suggested(6) that tracer uptake may reflect the effect of age without corresponding change in serum iodine. Accordingly, a survey has been made of the tracer tests performed in this laboratory during the past three years, to provide further information about the role of age, sex and season of the year in conditioning the spread of uptake values in euthyroid individuals.

Method. Thyroid uptake of radioiodine has been determined from measurement of activity over thyroid, by a well-shielded Geiger counter in a fixed position 15 cm from the skin over the thyroid isthmus, as described in detail elsewhere(9). Uptake values were established 24 hours after the administration of a tracer dose of I-131, given without carrier. The dosage used for the first six months of the program was 100 μc, and subsequently 40 μc.† A detailed discussion of tracer methods, sources of error, significance of results obtained, and comparison with other tests of thyroid function, has been presented elsewhere(5). The patient material comprises a clinic and in-patient population. Completely accurate information as to diagnosis is available in practically all patients reviewed herein. Values from patients with disorders known to derange the thyroid, whether primary in the gland or secondary to disease elsewhere, have been excluded from this study, as have been values obtained from euthyroid subjects with a history of recent medication with agents known to suppress iodine uptake, such as stable iodine in the form of iodides or gall-bladder dye, thyroid, etc.(5). A few individuals with either hypo- or hyperthyroidism, or treated with the medications just mentioned, have doubtless been included; they are so few as not to invalidate any conclusions drawn, in view of the large series.

Results. Up to May 1, 1950, tracer tests were performed on 1,403 patients; a considerable number of these had more than one test. The total has been reduced to 952 patients (1,050 tests) considered available for

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† The value of the μc is that agreed upon by the New York City Hospital Physicists' Group, and generally called the "New York μc". It is 1.15 times the present Oak Ridge value. That is, 40 New York μc = 46 Oak Ridge μc.

TABLE I. Effect of Age on Average Uptake in Euthyroid Subjects.

Age	No. of cases	Avg	Stand. dev.	Stand. error of mean
<20	49	27.3	10.4	1.43
20-29	195	26.9	7.4	0.53
30-39	228	26.1	8.3	0.55
40-49	191	24.6	8.5	0.61
50-59	150	23.7	8.7	0.71
60-69	88	22.1	8.0	0.85
70-86	51	23.2	9.1	1.28

TABLE II. Effect of Season on Average Uptake in Euthyroid Subjects.

Month	No. of cases	Avg	Stand. dev.	Stand. error of mean
Jan.	101	25.8	8.6	0.86
Feb.	89	25.0	9.4	1.00
Mar.	106	24.0	8.2	0.79
April	100	25.6	9.8	0.98
May	108	24.3	9.8	0.94
June	87	23.8	9.2	0.99
July	62	23.9	8.0	1.02
Aug.	45	23.5	8.5	1.26
Sept.	60	25.3	7.3	0.94
Oct.	98	25.8	7.8	0.79
Nov.	99	25.5	8.7	0.87
Dec.	95	25.2	8.8	0.90

the present study for the reasons mentioned under "Methods." Of the 1,050 tests thus analyzed, 989 fell into the 10-40% range of uptake of I-131 at 24 hours, 20 in the less than 10%, and 41 in the 40-51% range. No uptake value in excess of 51% at 24 hours was observed in the euthyroid group. Information as to time of year is available for all tests (Table II). Results of measurement for every month over a 3-year period are available. Age and sex are known for 952 of the 1,050 tests (Table III). There was a ratio of males to females of 1 to 2.3. Ages ranged from 16 to 86.

Effect of Sex. In the entire data there were 284 tests in men and 668 in females for which adequate sex and age information was available (Tables I and III). The overall uptake average for the former was 23.5% at 24 hours, and for the latter 25.8% (Table III). The standard error of the mean was 0.42 and 0.31, respectively. The slightly higher uptake for women over men is still seen if the data are rearranged to express both decades of age and sex. The observed difference in uptake, while statistically significant for these large series, is not of a degree to be clinically significant.

Effect of age. Results of analysis by age decades (both sexes together) are shown in Table I. The progressive decrease toward old age is statistically significant, although probably not enough to be clinically important. The slight but steady decrease in uptake with each decade of advancing age is also seen when the data are broken down according to both decades and sex.

Seasonal Variation. Average monthly uptakes (both sexes and all ages) are given in Table II. The apparent decrease toward midsummer is not statistically significant.

Factors Considered Separately. In order to make sure that, in studying any one of the 3 factors under discussion, variations due to the other 2 were not introducing errors, the entire set of data was tabulated to show variations for sex and age, winter and summer. (Winter was arbitrarily set as November to April, inclusive; Summer as May to October). This is shown in Table III. The separate factors may now be examined independently. Considering men and women in winter, in the different age groups, it is seen that the average uptake by women is always a little higher. The difference is not so evident in summer. However, many of the subgroups are so small that sampling fluctuations may be large. A detailed statistical analysis has not been deemed necessary. Similarly, the trend toward lower values in old age is not so evident when the sub-groups are examined.

A further check on possible influence of seasonal variation was found in examining the tests which had been repeated in a small group of the individuals without thyroid dysfunction. There were 38 subjects on whom two or more tests had been performed at different seasons. If seasons are divided into the usual 4—winter: Dec., Jan., Feb.; spring: Mar., Apr., May; summer: June, July, August; autumn: Sept., Oct., Nov., the findings were as follows: 16 patients, no change from season to season.‡ 10 patients,

‡ By "no change" is meant a shift of less than 10% of a value, *e.g.*, a shift from 28 to 30% uptake.

TABLE III. Analysis of Euthyroid Data by Age, Sex, and Season.

	Men						Women					
	Winter			Summer			Winter			Summer		
Age	No.	Avg	Stand. dev.	No.	Avg	Stand. dev.	No.	Avg	Stand. dev.	No.	Avg	Stand. dev.
<20	9	27.9	9.2	8	26.1	10.0	20	27.8	12.2	12	26.8	9.2
20-29	19	24.5	6.7	11	30.3	5.7	77	28.0	7.9	88	26.2	7.7
30-39	28	24.7	8.5	14	23.4	7.6	111	27.5	8.3	75	25.1	8.5
40-49	52	22.5	7.8	21	24.0	8.6	67	26.0	9.3	51	25.2	8.4
50-59	41	23.4	6.0	25	21.7	7.2	51	25.2	9.5	33	23.3	10.8
60-69	21	21.3	7.6	13	21.5	6.6	32	23.2	8.5	22	21.7	8.4
70-86	16	20.9	7.6	6	27.8	6.9	17	22.7	7.8	12	24.6	14

Totals	No.	Avg	Stand. dev.	Stand. error of means
All men	284	23.5	7.6	0.42
All women	668	25.8	8.5	0.31
All winter	561	25.4	8.4	0.35
All summer	391	24.8	8.4	0.43

lower reading in warmer season. 6 patients, lower reading in colder season. 6 patients, indeterminate. (In each of these, there were 3 tests, and shifts occurred in both directions). Accordingly, the results in this small group with repeated determinations are in accord with the statistical findings of the entire series, in that no significant seasonal variation was found.

Discussion and Conclusions. The uptake of radioiodine by the normal thyroid is a reflection, in general, of the level of secretory activity. This relationship may be disrupted by a number of influences not usually present in an unselected population, such as the administration of stable iodine or anti-thyroid drugs. In the present study, such extraneous influences have been excluded, granting an inevitable small error. Three findings emerge from the data. The level of thyroid activity in the euthyroid individual as determined from the radioactivity of the thyroid gland 24 hours after a dose of 40 to 100 μc I-131 is unaffected by season of the year. Uptake appears to decrease progressively, though slightly, with age. Uptake is a little higher in women than in men at all ages.

Perlmutter and Riggs(6) have called attention to a progressive decrease with age in rate of radioiodine uptake early after administration, of a very marked degree. They employed the "accumulation gradient" as a criterion, determined during the first four hours after the ingestion of I-131. In a limited sampling of their patients tested chemically for serum precipitable iodine, as well as with radioiodine, they found no corresponding variation in the serum iodine levels. This led the authors to postulate a decreasing utilization of thyroid hormone at the periphery, with advancing age, rather than any intrinsic diminution in thyroid activity.

The findings of the present study also show a stepwise decline in the uptake of I-131 as measured at 24 hours, but of an entirely different range of magnitude than that reported for the "accumulation gradient." It is generally agreed that the 24 hour determination is a more reliable index of overall thyroid function than the gradient which may be influenced by absorptive and circulatory factors. Since the degree of decrease in 24-hour uptake is only questionably significant clinically, unlike the decline in gradient with advancing age, it is likely that a corresponding change in serum precipitable iodine level might be concealed by a small sampling in euthyroid subjects. Thus a far larger series of patients would have to be studied in this regard than was examined by Perlmutter and Riggs. It therefore still appears to be open to question whether thyroid function decreases gradually with age, whether peripheral

utilization of thyroid hormone is diminished with age, or whether the slight degree of decline in radioiodine uptake represents some extraneous mechanism which affects the rate of iodine accumulation but which does not influence the overall secretory activity of the gland.

The persistently higher radioiodine uptake by women over men raises the same question of biological versus statistical significance. The higher uptake by women does not correspond with the lower basal metabolic rate found in this sex compared to men of the same age. No ready explanation for the uptake difference is at hand, but the data serve to emphasize that other factors influence basal metabolic rate(10) besides the level of thyroid hormone secretion.

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Summary. 1. The percentage of a tracer dose of radioactive iodine deposited in the thyroid gland at the end of 24 hours was determined by measurement of radio-activity directly over the gland in 1,050 tests in 1952 apparently euthyroid individuals. 2. It is concluded that, within the New York area, there is statistically no effect of season, on the average uptake of radioiodine by the thyroid gland of the euthyroid individual. 3. The 24-hour uptake of radioiodine decreases progressively but slightly with each decade of age. The extent of fall is statistically, but not clinically, significant. 4. Women in all age groups show a slightly higher average uptake than men. The difference is not clinically significant.

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Protective Action of N-Allyl-Normorphine Against Respiratory Depression Produced by Some Compounds Related to Morphine.*† (18257)

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Some of the pharmacological properties of N-allyl-normorphine have previously been investigated by Unna(1) and Hart and McCawley(2). These studies demonstrated that N-allyl-normorphine prevents, or abolishes, certain actions of morphine, *i.e.*, the respiratory depression, the excitatory action in cats, and increased the lethal dose. No information seems to be available showing whether the protection of the respiratory center afforded by N-allyl-normorphine against morphine extends to other narcotics, therefore, data on this point were collected for the following: codeine (methylmorphine), Dilaudid (dihydromorphinone), Demerol (ethyl 1-methyl-4-carboxylate-hydrochloride), Metopon (methyl-dihydromorphine), and Methadon (6-dimethylamino-4, 4-diphenyl-3-heptanone hydrochloride).

Methods. The dogs were anesthetized with sodium barbital 250 mg/kg and a sound passed down the left carotid into the aorta for the registration of blood pressure with a Hamilton manometer(3). Respiratory rate was recorded by attaching a chest plethysmograph to a Hamilton manometer. Two pro-

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