

lected among the patients of the Veterans Administration Hospital and normal medical students and staff. A brief history was obtained, the chart was examined if the subject was a patient (about two thirds of the subjects), and the subject was examined to exclude thyroid disease, serious cardiac, renal or hepatic disease and exposure to x-ray contrast mediums or other known sources of iodine or drugs that might alter thyroid function. The subject was then given an oral dose of about 1 to 5 μCi of ^{131}I , and the 24-hour thyroidal radioiodine uptake was measured.

In 1967 we began making several changes in the procedure. However, in the process of setting up the new procedure we also redetermined the uptake in euthyroid subjects with the use of the old phantom and procedure, and all results given in this paper are from this older method.

Fifty-three subjects were studied in 1967-68. We attempted to select them in exactly the same manner as in the 1959 study and, in addition, obtained determinations of serum protein-bound iodine (PBI) on all except one to help confirm the euthyroid status. All were normal (individual values are given in the report referred to above¹). In this study the patients were required to fast after midnight, and the oral dose of ^{131}I was given between 8 and 9 a.m. Frequent counts were then obtained throughout that day and less frequently during the following day. Otherwise, the same procedure and apparatus were used as in the 1959 study.

When it became apparent that lower values were being obtained in 1967-68, we evaluated the wooden phantom to see whether its drying could change the counting rate of the standard. However, making fresh wooden phantoms of the same dimensions or soaking older phantoms in water for prolonged periods did not appreciably alter the counting rate of the standard.

In 30 of the 53 subjects, additional indexes of iodine metabolism were determined by the methods of Wayne, Koutras and Alexander.² The clearances were measured from two to five hours after approximately 20 μCi of ^{125}I given intravenously.

We made determinations of dietary iodine content in 30 meals by obtaining trays of food identical to those sent to the patients, removing the food from the trays and homogenizing it in a Waring blender. Chemical iodine determinations were done on aliquots, with special precautions to obtain representative, well mixed samples. Fifteen meals were obtained from the Veterans Administration Hospital — breakfast, lunch and supper for five days, and 15 from the University of Alabama at Birmingham Hospital. In the latter case three meals from each day were pooled for homogenization and sampling. The salt from the trays was not included. All chemical iodine determinations were carried out by Bio-Science Laboratories, Van Nuys, California.

Bread and bread constituents for analysis were obtained from a local bakery.

RESULTS

The mean 24-hour uptake in 1959 was 28.6 per cent, with a standard deviation of 6.5 per cent. Thus, inclusion of plus-or-minus two standard deviations would give a normal uptake of about 16 to 42 per cent. This value is in keeping with normal values commonly cited in the literature,^{3,4} which approximate 15 to 45 per cent. The frequency distribution of the uptakes determined in 1959 is shown in Figure 1. This distribution shows the skew to the left also noted in other studies.⁵ The uptake in

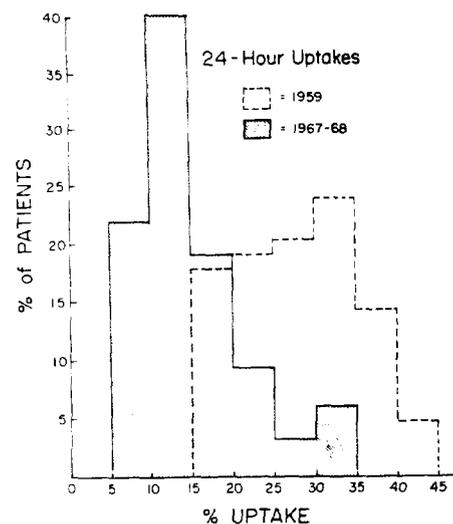


FIGURE 1. Frequency Distribution of the Uptakes Measured in 1959 and 1967-68.

the 1967-68 series was 15.4 ± 6.8 per cent (mean and S.D.), also shown in the figure.

Values for the serum PBI and several aspects of iodine kinetics are given in Table 1. It is apparent that there is not only an abundance but a surfeit of iodine in our subjects.

Results of analyses of diets served in the Veterans Administration and University of Alabama at Birmingham hospitals (Table 2) indicate that these are sources of large amounts of iodine. Since all the table salt used in our Veterans Administration Hospital must be iodized, inclusion of the six packet

TABLE 1. Iodine Metabolism in Central Alabama Subjects.⁸

PBI	C_r	C_t	PII_{SA}	PII_{CHEM}	E
$\mu\text{g}/100 \text{ ml}$	ml/min	$\mu\text{g}/100 \text{ ml}$	$\mu\text{g}/100 \text{ ml}$	$\mu\text{g}/\text{day}$	$\mu\text{g}/\text{day}$
5.3 ± 0.2	30.3 ± 2.3	6.6 ± 0.6	1.87 ± 0.21	1.9 ± 0.2	680 ± 70
(4.9-5.9)	(1.35-4.1)	(2.2-11.7)	(0.17-0.55)		(44-171)†

*Values are for 53 subjects & are means \pm standard deviations. Normal value given in parentheses are from Wayne et al.² as means \pm standard error of mean or as range.†

C_r indicates renal clearance of iodide. C_t thyroidal glandular iodide clearance. PII_{SA} plasma inorganic iodide concentration by specific activity, PII_{CHEM} = PBI - chemical difference between PBI & total serum iodine, & E 24-hour urinary excretion of iodine.

TABLE 2. Iodine Content of Representative Hospital Diets.*

ANALYSIS		TOTAL CONTENT μg
Daily (3-meal total)	UAB	533 \pm 82 (274-842)
	VA	677 \pm 19 (595-713)
By meals (VA only)	Breakfast	186 \pm 25
	Lunch	204 \pm 26
	Supper	287 \pm 21

*Per portion shows total quantities of iodine contained in the meals for 1 day (mean \pm SD, with range in parentheses below) at University of Alabama at Birmingham Hospital (UAB) & Birmingham Veterans Administration Hospital (VA). 15 meals from each hospital were included in analyses (see "Methods"). Breakdown by meals, 5 analyses each for breakfast, lunch & supper, given in lower portion (mean \pm SD).

of salt, about 1.3 gm each, served daily with the meals would have added several hundred micrograms of iodine to the estimated intake.*

Analyses of the white bread used in the hospitals showed that each slice contained 150 μg of iodine (Table 3), confirming the findings of London, Vought and Brown.⁶ Discussion of the bread-making proc-

TABLE 3. Total Iodine Content of Bread.*

VARIETY	TOTAL CONTENT μg
Bread:	
White, sandwich — 1 slice 100 gm	150 \pm 11.2 884
Frankfurter bun:	
1 bun 100 gm	99 \pm 9.8 246
Cornbread:	
Square 100 gm	17.4 \pm 0.6 61

*6 samples of each variety of bread analyzed, & results given as total iodine (common unit used (mean \pm SD) & for each 100 gm of such bread).

ess with local bakeries revealed that a new "continuous-mix" process was initiated in this area in 1961 and came into common use over the subsequent several years.

Fourteen bread constituents were obtained from a local bakery and their iodine contents determined. Calculations based on the iodine content of each constituent and the quantity of that constituent added to the final amount of dough showed that large quantities of iodine are contributed by the yeast food, flour, a nonfat milk substitute and other components, including calcium iodate tablets. On the basis of these calculations the total iodine per slice should

be 122 μg , in reasonable agreement with the quantity found.

DISCUSSION

In 1959 normal values in our laboratory were quite consistent with those from the literature — approximately 15 to 45 per cent. However, values determined in 1967-68 were about half the 1959 figure, with the use of the same instrumentation and subjects from apparently the same population.

Evaluation of several aspects of iodine kinetics in 30 of our euthyroid subjects revealed them to be heavily loaded with iodine. We had anticipated that local subjects probably ingested liberal quantities of iodine, but we had not expected to find such high values as 680 μg per day for the urinary iodine excretion or 1.9 μg per 100 ml for the plasma inorganic iodide concentration (PII). These values are far in excess of most in the literature^{2,7} and approach those found in groups ingesting diets unusually rich in iodine.⁸ The thyroïdal iodine clearance in such people is depressed, offsetting in part the high PII and tending to maintain thyroïdal ¹²⁷I uptake at a relatively low level despite the large quantity of iodine presented to the gland by the blood.^{7,9} A second thyroïdal mechanism for maintaining hormonal secretion at a normal rate despite the availability of excess iodine is leakage of iodide-like material from the gland.⁷

The above results could explain the present low thyroïdal radioiodine uptake by simple dilution of the radioiodine by ¹²⁷I, and the dietary iodine determinations confirmed food as the source of this ¹²⁷I. However, the change that occurred between 1959 and 1967 was not explained by these findings. The high iodine content of bread, previously noted by London, Vought and Brown,⁶ was confirmed by measurements of iodine in local bread (Table 3). The finding that the new continuous-mix process had been introduced into the Birmingham area in 1961 and had come into more general use over the subsequent several years appears to explain the change. More than a dozen ingredients are added during the continuous-mix process, and many of these contain iodine. London et al. were struck by the addition of iodate to bread during this process, as we were. However, direct analyses indicate that other constituents (to which iodine is separately added) may contribute a greater proportion of the total iodine. The function of the iodine in many of these is to "stabilize" the bread during the new process. The continuous-mix process was first used in 1955 in New Bedford, Connecticut, and currently accounts for about 43 per cent of the white pan bread made in the entire United States and about 65 per cent of that made in the Southeast.¹⁰ Thus, bread made by this process probably contributes large quantities of iodine to the diet of a large proportion of the population in the United States. That the distribution is irregular is indicated by higher

*On January 11, 1952, the Marketing Division of the Supply Division of the United States Veterans Administration, based on Federal specification SS-31d, made it mandatory that Veterans Administration depots issue only iodized salt. Since Veterans Administration hospitals are ordinarily required to purchase from such depots, virtually all the salt used in the United States Veterans Administration system is iodized. It is likely that salt used by other governmental agencies is also iodized.

uptakes seen in some euthyroid patients traveling to Birmingham from other cities in this area.

There is no assurance that this situation will continue unchanged. Bread makers are using a new organic agent, azodicarbonamide, to an increasing extent to replace the halogens.¹¹ If this trend continues, dietary iodine from this source may fall to low levels. Other uses of iodine make it difficult to predict what the iodine intake may be in the future. It is likely that values in other regions of the United States, and perhaps elsewhere, are presently lower than the traditionally stated 15 to 45 per cent. The currently accepted normal range for the 24-hour thyroidal radioiodine uptake at the National Institutes of Health Clinical Center is 9 to 32 per cent (95 per cent range for 30 euthyroid adults; median 17.5 per cent),¹² and the uptake in Sydney, Australia, in 1967 was 62.5 per cent of the 1965 value.¹³

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ARGININE-INITIATED RELEASE OF HUMAN GROWTH HORMONE*

Factors Modifying the Response in Normal Man

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Abstract To improve the usefulness of testing pituitary function by the response of human growth hormone (HGH) to I.V. arginine loads, arginine infusions were given under a variety of conditions to healthy subjects aged 17 to 35. The minimum effective arginine load causing release of HGH was 1/6 gm per pound of body weight in men and 1/12 gm per pound of body weight in women. At each of three dosage schedules used, women responded with greater increases in plasma HGH

than men. Treatment of men with diethylstilbestrol augmented their HGH response to arginine, whereas methyltestosterone pretreatment did not decrease the response in women. The HGH response to arginine was not abolished by acute hyperglycemia but was attenuated or delayed by a previous stimulus for HGH release.

In the use of this test of pituitary function, it is necessary to use a proper dose of arginine, to avoid other stimuli of HGH release, and to pretreat men with estrogens

ARISE in the plasma concentration of human growth hormone (HGH) in adult female sub-

jects follows either the oral ingestion of protein or the intravenous administration of several amino acids.¹⁻³ After our initial report of arginine-initiated HGH release, we reported, in a preliminary form, several conditions modifying the HGH response to arginine in intact man.^{4,5} A more complete characterization of the HGH response to arginine is the subject of the present report. HGH secretion was compared in males and females after infusion of graded doses of arginine. The effects of stilbestrol pretreatment, methyltestosterone pretreatment and accompanying hyperglycemia on the HGH response to arginine are examined. Double-infusion studies

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