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48 hr uptakes—
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# Uptake of Radioactive Iodine by the Normal and Disordered Thyroid Gland in Children

A Preliminary Report

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STUDIES OF THE uptake of radioactive iodine by the normal and hyperfunctioning thyroid gland in adults have been published by Hamilton and Soley, Hertz, Roberts and Salter, (1, 2) and others. Hamilton, Soley, Reilly, and Eichorn have reported on iodine studies in a small series of cases of childhood hypothyroidism, including some with goiter (3). Most of their tests were made with eight-day iodine containing an appreciable admixture of stable iodine; with such material the apparent uptake is always much less than with a "carrier-free" preparation in which all the iodine is radioactive.

Since the search for an unambiguous indicator of thyroid function in children, particularly in infants, still continues, the present study was undertaken in the hope of achieving this goal..

Eight-day radioactive iodine ($I^{131}$), carrier-free, was obtained from the cyclotron laboratory of the Massachusetts Institute of Technology in dilute solution of sodium iodide. The amount of the latter was so small as to be considered physiologically negligible. The material was administered quantitatively by mouth, a stomach tube being used in the case of infants and uncooperative small children. The subjects were not fasted. The doses varied from 20 to 40 microcuries (containing not more than 2 micrograms of iodine) in about 20 c.c. of solution. Smaller amounts were given to babies than to older children, but they were not calculated accurately on a weight basis.

The relative quantities of the iodine concentrated in the thyroid glands were determined by measurements with a shielded Geiger counter placed in a fixed position over the front of the neck. These were related to the administered doses by measurements in the laboratory with a "phantom" set-up approximating the geometrical relationships with the patient. Whenever possible, all urine was collected for two successive 24-hour periods for measurement of the amount of iodine excreted.

Pathological cases were selected chiefly on the basis of medical interest; this resulted in the study of infants and children of from three weeks to fourteen years. To eliminate differences in uptake due to possible variations in the material received from the cyclotron, an effort was made to study a control child of the same age and of approximately the same size simultaneously with each patient. The controls all came from the hospital population. While none showed features which justified the suspicion of "glandular" disorder, no matter how vague, only a few were strictly well children. The majority were suffering from, or in convalescence after, various illnesses, such as infection, diarrhea, or nutritional disorder, which can certainly be conceived to have affected temporarily the state of activity of the thyroid gland. The precaution of studying a control at the same time as the patient proved unnecessary, since significant variations in the quality of the test material were not detected.

Fifty-four subjects are included in this report; two or three tests were done on a few. Twelve were infants under one year. Of these, 11 were controls; the other had

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TABLE I. PER CENT OF RADIOACTIVE IODINE IN THYROID GLAND IN CONTROLS AT 48 HOURS AFTER ORAL ADMINISTRATION

| Infants to 1 year | | Children 1–4 years | | Children 5–14 years | |
|---|---|---|---|---|---|
| Name | Per Cent | Name | Per Cent | Name | Per Cent |
| [redacted] | 10 | E. G. | 10 | [redacted] (adult) | 10 |
| [redacted] | 7 | P. M. | 4 | [redacted] | 15 |
| | 15 | D. A. | 7 | | 9 |
| | 15 | R. H. | 11 | | 18 |
| | 10 | J. G. | 12 | | 15 |
| | 11 | G. M. | 15 | | 13 |
| | 9 | E. S. | 10 | | 12 |
| | 12 | | — | | 20 |
| | 9 | Average | 9.9 | | 15 |
| | 20 | $\sigma$ = | 3.3 | | 13 |
| | 17 | | | | 11 |
| | — | | | | 12 |
| Average | 12.3 | | | | 17 |
| $\sigma$ = | 3.7 | | | | 12 |
| | | | | | 12 |
| | | | | | — |
| | | | | Average | 13.5 |
| | | | | $\sigma$ = | 2.9 |

Total mean 12.0 $\sigma$ = 3.6

been recognized as a cretin at the age of three weeks. Fifteen were between one and four years of age; 7 were controls as defined above; 2 were classical cretins; 1 showed some features of hypothyroidism which were not modified by treatment; 2 were dwarfs; in 1 the diagnosis was "gargoylism"; 1 was suspected of progeria, a disorder associated with some of the features of hypothyroidism, and the last exhibited features of moderate sexual precocity. Twenty-seven were more than four but less than fifteen years of age. Of these 2 had unmistakable hypothyroidism, 2 Graves' disease, 1 questionable hyperthyroidism. Four were dwarfs; of these, 1 showed debatable signs of reduced thyroid function. One had a colloid goiter of small dimensions and showed no evidence of alteration of thyroid function. One had an adrenal pheochromocytoma, and 1 idiopathic hypoparathyroidism without evidence of hypothyroidism. Fifteen served as controls—again in the sense already defined.

Measurements on a few children were started shortly after administration of the material and carried out at intervals through the day for several days thereafter. Others were measured only daily for a few days and then at longer intervals. It was found that the values are substantially constant from the first through the fourth day, when correction is made for radioactive decay. Therefore, for convenience of comparison, the 48-hour reading was arbitrarily selected. These 48-hour readings for the controls are given in Table I, with averages and standard deviations.

Measurements of excretion were possible in only the five- to fourteen-year group and not in all of these. Some specimens were frequently lost. The available data for controls are given in Table II. It appears that excretion is rapid and that the totals are fairly constant but would not be satisfactory as an index of uptake.

Table III presents the data relating to the concentration of iodine in the neck region of the hypothyroid and hyperthyroid individuals and of those who had, or for one reason or another may be considered suspect of, some endocrine disorder.

The few observations that were made on the excretion of iodine in the urine of these individuals appear in Table IV.

## DISCUSSION

In view of the preliminary character of this communication and the limited nature of the data, it does not appear warranted to discuss them in great detail.

As regards the controls, the mean value for uptake is 12.0 per cent with a standard deviation of 3.6.

One feature stands out in the group of abnormal subjects, namely, the extremely small retention in the case of the individuals with indisputable hypothyroidism. [redacted] suffered from complete athyreosis occasioned by the inadvertent removal of a small, spherical mid-line undescended thyroid gland which was erroneously taken to be a thyroglossal duct cyst. Her uptake was essentially zero. The cretins, although their defect of glandular substance appeared to be complete on clinical grounds, concentrated enough iodine to suggest that traces of the gland were present, thus confirming a common anatomical observation in cretinism.

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TABLE II: URINARY EXCRETION OF RADIOACTIVE IODINE IN CONTROLS
(Per Cent of Oral Dose)

| Case | 0–8 Hours | 8–16 Hours | 16–24 Hours | 24–48 Hours | Total |
|---|---|---|---|---|---|
| [redacted] | 44 | 28 | 4 | 3 | 79 |
| | 33 | 19 | 13 | 4 | 69 |
| | 25 | 25 | 8 | 9 | 77 |
| | 7 | 21 | 10 | 7 | Incomplete |
| | 13 | 35 | 5 | 13 | 66 |
| | 25 | 9 | No specimen | 12 | Probably incomplete |
| | Two days' specimens assembled | | | | 68 |
| | 44 | 8 | Incomplete | 0 | Incomplete |
| | 49 | 0 | 11 | 2 | 62 |
| | Lost | 25 | 11 | 19 | Incomplete |

TABLE III: PER CENT OF RADIOACTIVE IODINE IN THYROID GLANDS OF ABNORMAL SUBJECTS

| Case | Diagnosis | Age | Per Cent Uptake, 48 hr. | Per Cent Excretion, 48 hr. |
|---|---|---|---|---|
| Known Thyroid Disorder | | | | |
| [redacted] | Sporadic cretinism | 2 mo. | Less than 1 | |
| | Sporadic cretinism | 16 mo. | Less than 1 | |
| | Sporadic cretinism | 2 yr. | Less than 1 | |
| | Sporadic cretinism | 14 yr. | Less than 1 | |
| | Surgical myxedema | 12 yr. | Less than 1 | 70 |
| | Graves' disease | 9 yr. | 60 | Less than 10 |
| | Graves' disease | 10 yr. | 34 | |
| | * Slightly enlarged thyroid | 14 yr. | 20 | 49 |
| | Probably diffuse colloid goiter | | | |
| | Colloid adenoma of thyroid | 12 yr. | 3 | |
| | No evidence of hypothyroidism | | | |
| | Repeated test | | 3 | 71 |
| Other Abnormals | | | | |
| [redacted] | Dwarfism | 7 mo. | 6 | |
| | Dwarfism; extremely questionable hypothyroidism, non-responsive to treatment | 2 yr. | 8 | |
| | Dwarfism | 2 yr. | 6 | |
| | Dwarfism; questionable hypothyroidism | 7 yr. | 5 | |
| | Dwarfism | 8 yr. | 21 | 54 |
| | Dwarfism; nutritional difficulty | 9 yr. | 17 | 44 |
| | Dwarfism | 12 yr. | 0.5 | 87 |
| | Progeria (?) | 16 mo. | 30 | |
| | After 2 months on thiouracil | | 11 | |
| | Four months after stopping thiouracil | | 21 | |
| | Gargoylism | 2 yr. | 9 | |
| | Slight sexual precocity | 3 yr. | 21 | |
| | Adrenal-cortical tumor (?) | | | |
| | Hypoparathyroidism (idiopathic) | 10 yr. | 6 | |
| | No evidence of hypothyroidism | | | |
| | Pheochromocytoma of adrenal | 12 yr. | 13 | 64 |

* This patient had been on iodine therapy for six months; it had not been discontinued prior to the test. Her basal metabolic rate, cholesterol, and blood iodine were all normal. She was suspected of hyperthyroidism but could not be expected to show an elevated radio-iodine uptake under these circumstances.

With the exception of the patient mentioned in the previous paragraph, only patients with clear-cut hypothyroidism had values so low. However, *quite* low concentrations were observed not only in those individuals who presented unequivocal evidence of hypothyroidism but also in some who failed entirely to suggest this possibility. Attention may be drawn to [redacted], a white boy of twelve years whose stature was about that of a six-year-old. The history, physical features, and laboratory evidence pointed to non-endocrine dwarfism or, at most, to dwarfism due to unique deficiency of the growth-promoting secretion of the hypophysis. The low re-

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TABLE IV. EXCRETION OF RADIOACTIVE IODINE IN THE URINE OF ABNORMAL SUBJECTS
(Per Cent of Dose)

| Name | 0–8 Hours | 8–16 Hours | 16–24 Hours | 2d Day | 3d Day | Total |
|---|---|---|---|---|---|---|
| [redacted] | First 24 hours..... | | 32 | 32 | 6 | 70 |
| | First 24 hours..... | | 30 | 19 | .. | 49 |
| | 8 | Less than 1 | Less than 1 | Less than 1 | .. | Less than 10 |
| | 50 | 3 | 20 | 14 | .. | 87 |
| | 30 | 4 | 14 | 6 | .. | 54 |
| | Lost | 25 | 11 | 12 | .. | Incomplete |
| Repeat | 35 | 15 | 16 | 5 | .. | 71 |
| [redacted] | 9 | 16 | 11 | 8 | .. | 64 |
| | .. | .. | 39 | 5 | .. | 44 |

tention and rapid excretion of iodine can certainly not be ascribed to hypothyroidism of any recognizable variety or degree. Since the boy came from a part of the country where iodized table salt is commonly used, saturation of the gland is a possible explanation, but the history failed to reveal information on this point. His basal metabolic rate, calculated by three standards, was −60. However, this is doubtless wrong. It should be pointed out that there are no satisfactory standards for dwarfs. [redacted] had a small colloid adenoma of her gland but was normal in all other respects. The idiopathic or cryptogenic hypoparathyroidism which [redacted] exhibited was not accompanied by any signs whatever of reduced function of the thyroid gland.

A second but somewhat less impressive feature in the group of abnormal subjects is the high value in the two cases of Graves' disease and the elevated retention in the single case of what is probably progeria.

As was stated in the introduction, the excretion of iodine in the urine was confirmatory of the uptake by the gland. Discrepant results should serve to call attention to the possibility of technical error in one or the other of the measurements or to the loss of specimens of urine. Since in young children the need to collect urine quantitatively over a considerable period of time imposes a serious restriction on the feasibility of any test, this part of the study has not been pursued with great zeal.

## CONCLUSIONS

The administration to infants and children, by the oral route, of carrier-free radioactive iodine in doses of from 20 to 40 microcuries is followed by concentration and retention within the thyroid gland of amounts which vary from about 12 per cent in those without evident thyroid disorder, upward to severalfold this value in hyperthyroidism and downward to less than 1 per cent in those who are typically hypothyroid. Values considerably below the mean, and occasionally as low as those in unmistakable hypothyroidism, are found not only in individuals who are only dubiously hypothyroid but also in some whose thyroid function is quite beyond clinical suspicion of insufficiency. These limitations to interpretation doubtless depend in part on the fact that hyperthyroidism and hypothyroidism are both relative states and show variability of degree. However, non-numerical examination of the data suggests that sharper results could be obtained by more careful standardization of the test with respect, among other things, to the patient's previous intake of iodine and the state of his health at the time of the observation.

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## REFERENCES

1. HAMILTON, J. G., AND SOLEY, M. H.: Studies in Iodine Metabolism of the Thyroid Gland in Situ by the Use of Radioiodine in Normal Subjects and in Patients with Various Types of Goiter. Am. J. Physiol. 131: 135–143, November 1940.

2. HERTZ, S., ROBERTS, A., AND SALTER, W. T.: Radioactive Iodine as an Indicator in Thyroid Physiology. IV. The Metabolism of Iodine in Graves' Disease. J. Clin. Investigation 21: 25–29, January 1942.

3. HAMILTON, J. G., SOLEY, M. H., REILLY, W. A. AND EICHORN, K. B.: Radioactive Iodine Studies in Childhood Hypothyroidism. Am. J. Dis. Child. 66: 495–502, November 1943.

SUMARIO

Absorción de Yodo Radioactivo por el Tiroides de los Niños

La administración a los niños, incluso lactantes, de yodo radioactivo, sin portador, por vía bucal, a dosis de 20 a 40 milicuries va seguida de concentración y retención en el tiroides de cantidades que varían de aproximadamente 12 por ciento en personas sin distiroidia manifiesta a varias veces dicha cifra en el hipertiroidismo y menos de 1 por ciento en los hipotiroideos típicos. Encuéntranse cifras considerablemente inferiores al promedio, y de cuando en cuando tan bajas como las del hipotiroidismo indudable, no sólo en individuos dudosamente hipotiroideos sino también en algunos cuya función tiroidea queda más allá de toda sospecha clínica de insuficiencia. Estas limitaciones de la interpretación dependen sin duda en parte de que tanto el hipertiroidismo como el hipotiroidismo son estados relativos de intensidad variable. Sin embargo, el estudio no numérico de los datos disponibles indica que cabría obtener resultados más netos mediante una estandardización más cuidadosa de la prueba con respecto, entre otras cosas, a la previa ingestión de yodo por el enfermo y el estado de su salud en la fecha de la observación.

(*For discussion of this paper, see page 229*)

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