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RADIOISOTOPE STUDY OF THYROID FUNCTION IN 21 MONGOLOID SUBJECTS, INCLUDING OBSERVATIONS IN 7 PARENTS

G. S. KURLAND, M.D., J. FISHMAN, M.D.†, M. W. HAMOLSKY, M.D. AND A. S. FREEDBERG, M.D.

The Department of Medicine, Harvard University Medical School, Boston, and the Medical Service and Medical Research Department of the Yamins Research Laboratories of the Beth Israel Hospital, Boston, Massachusetts

MONGOLISM, a common clinical entity (1) of unknown etiology is believed to result from deceleration of normal growth during the fetal period (2). A possible relationship between abnormalities in development and function of the thyroid gland and the fetal growth process in mongolism is suggested by anatomic evidence of pathologic alterations in the thyroids of mongoloid children (1, 3), and the reported frequency of abnormal thyroid function in their mothers (4).

Although data are available concerning isolated phases of thyroid function in mongolism, a detailed investigation of the various aspects had not, at the time of our studies, been carried out. This report presents the results of an investigation of the thyroid gland in mongolism, utilizing a variety of recently available techniques.

METHOD

Twenty-eight subjects were studied.[1] Twenty-one were mongoloid patients in residence at the Walter E. Fernald State School (Massachusetts Department of Health). Their ages ranged from 5 to 26 years. The remaining 7 were healthy parents (5 mothers and 2 fathers) of mongoloids. Sixty-four euthyroid subjects ranging in age from 10 to 65 years served as controls (5).

In the mongoloid subjects, a dose of 70 microcuries of carrier-free radioactive iodine (I^{131}) was administered orally after an overnight fast. In the parents and in the control subjects, the tracer dose was 100 microcuries.

The thyroidal uptake of the tracer dose was measured by the four-tube G-M method previously described from this laboratory (5), modified by a correction factor for scatter

Received July 14, 1956.

• This investigation was supported in part by research grant No. A-140, National Institute of Arthritis and Metabolic Diseases, Public Health Service, and under a contract with the Atomic Energy Commission No. AT-(30-1)-916.

† Present address: 2499 Channing Road, University Heights 18, Ohio.

[1] Made available through the cooperation of Dr. C. E. Benda, Director of Research, Walter E. Fernald State School.

The Journal of Clinical Endocrinology and Metabolism, Volume 17, No. 4 April 1957

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and absorption which was obtained in each patient by counting a suitable mock-up containing I^{131} in air, and against the patient's neck. Measurements were made twenty-four hours after the tracer dose and on two or more occasions during the subsequent three to five days. The thyroidal turnover of I^{131} reported as the effective half-life (EHL) was calculated according to a previously described method (5, 6). The urinary I^{131} excretion for the first twenty-four hours following the tracer dose was measured by the four-tube method (7).

The plasma butanol-extractable I^{131} (8, 9) (thyroxine-like material) was measured in duplicate at 24-hour intervals for three days following the administration of the tracer dose. The results are reported in per cent as the ratio of radioactivity in the butanol-extractable fraction to the total radioactivity per cubic centimeter of plasma.

Thyroxine metabolism was studied in 2 mongoloids by following the rate of disappearance from the plasma of intravenously infused I^{131}-labeled thyroxine and by measuring the appearance of radioactivity in the thyroid gland after the infusion. The infusion was made with 1.5 micrograms of *l*-thyroxine[2] containing 55 microcuries of I^{131}. Samples of venous blood were obtained daily for ten days. The plasma was separated and 1-ml. aliquots (in triplicate) were counted in a well-type scintillation counter. A standard was prepared from the same shipment of thyroxine-I^{131} and was similarly counted. The plasma radioactivity was plotted daily as a percentage of the administered dose per liter of plasma. After distribution had been achieved, a straight line was drawn which best fitted the data and the half-time of disappearance was calculated. The percentage turnover per day was calculated from the formula: Turnover $= \ln 2/t_{\frac{1}{2}}$. The collection of urine and feces by such patients was not sufficiently reliable to permit more detailed calculations of the rate of synthesis and peripheral degradation of thyroxine (10).

Previous studies from our laboratory (11) had shown that the plasma-thyroid hormone interrelation could be investigated by an *in vitro* system in which the uptake by erythrocytes of I^{131}-*l*-triiodothyronine from whole blood was measured.

Tracer amounts of I^{131}-*l*-triiodothyronine were added to aliquots of whole blood, which were then incubated in a water bath with agitation at 37° C. Following incubation, the erythrocytes were separated, washed, and their radioactive content determined as a percentage of total blood radioactivity, corrected to 100 hematocrit. To assess the respective roles of the plasma and the erythrocytes, "criss-cross" experiments were carried out in which we determined the uptake of I^{131}-*l*-triiodothyronine by mixtures comprising: 1) erythrocytes of mongoloids in compatible plasma of euthyroid subjects, and 2) erythrocytes of euthyroid subjects in compatible plasma of mongoloids.

Labelled thyroxine and triiodothyronine were also added to serum and plasma and the distribution of radioactivity was determined after filter-paper electrophoresis in a Durrum-type[3] cell, using veronal buffer at pH 8.6 and 0.05 u for sixteen hours at 5 milliamperes. After drying in air in an oven for thirty minutes, the strip was scanned for radioactivity by rotating it slowly before a suitable shielded end-window G-M tube (2.4 mg./sq.cm., mica window). Protein was located by staining with bromphenol blue.

RESULTS

Thyroidal 24-hour I^{131} uptake

In the 21 mongoloid subjects, the 24-hour thyroidal uptake (Table 1)

[2] Abbott Laboratories.

[3] Spinco Model R, Spinco Division, Beckman Instruments, Inc.

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TABLE 1. DATA ON 21 MONGOLOID PATIENTS

No.	Patient	Age & Sex	Thyroidal 24-hr. I^{131} uptake (%)	Urinary 24-hr. I^{131} excretion (%)	I^{131} half-life (days)	Conversion ratios (%)			PBI, μg./100 ml.	Serum cholesterol (mg./100 ml.)
						24-hr.	48-hr.	72-hr.		
1		16 M	17	53	3.6	32	31	69	5.4	175
2		16 M	25	49	3.3	38	84	89	5.5	245
3		17 M	25	49	8.0	40	67	84	5.4	230
4		20 M	30	49	—	38	62	84	7.2	185
5		18 M	20	57	2.4	31	50	58	5.1	235
6		21 M	25	48	4.2	35	56	68	6.5	195
7		25 M	30	45	3.6	51	76	83	6.3	195
8		— F	26	22	6.0	43	56	80		—
9		18 F	15	28	—	47	62	67	6.2	220
10		16 F	12	59	—	35	50	73	4.9	230
11		19 F	20	53	6.7	55	84	85	6.5	295
12		20 F	31	27	—	—	—	—	6.2	215
13		16 F	22	50	7.4	—	—	—	4.7	235
14		16 F	25	53	5.7	—	—	—	5.3	230
15		27 F	32	41	8.0	—	—	—	8.4	215
16		— F	22	42	5.6	13	40	58	—	—
17		22 F	26	58	6.3	26	58	67	6.6	205
18		— F	30	38	7.5	26	66	63	—	—
19		— F	21	52	3.1	16	39	62	—	—
20		5 F	26	—	5.8	—	—	—	—	—
21		13 F	44	—	6.2	—	—	—	—	—

ranged from 12.0 to 44.0 per cent, with an average of 25.0 per cent (S.E. 1.5; S.D. 6.7).

The mean uptake of the entire group was lower than observed in our previously reported observations of euthyroid subjects (5).

Since the average age of the euthyroid control subjects was higher than that of the mongoloids, another group of 23 euthyroid subjects of an age comparable to that of the mongoloid subjects was studied. The thyroidal uptake values (average, 27.5 per cent; S.E. 1.5; S.D. 7.0) obtained in this group did not differ significantly from those obtained in the larger group of controls ($t=0.9$). When the mean thyroidal 24-hour I^{131} uptake of the younger group of euthyroid subjests was compared with that of the group of mongoloids, the t value[4] was 1.1—not statistically significant (Table 3).

The thyroidal I^{131} uptake in the 7 parents (5 mothers and 2 fathers) of mongoloid children ranged from 21.0 to 41.5 per cent, with an average of

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TABLE 2. THYROIDAL 24-HOUR I^{131} UPTAKE AND TURNOVER IN PARENTS OF MONGOLOIDS

Parent	Age of parent at birth of mongol	Age at time of study	Sex	Thyroidal 24-hr. I^{131} uptake (%)	I^{131} half-life (days)
	26	27	F	41.5	6.0
	28–30	31	F	28.4	
	35	35	F	26.2	7.0
	46	51	M	26.0	7.5
	46	51	F	21.0	
	45	58	F	38.0	4.5
	42	55	M	35.0	6.2

30.9 per cent (S.E. 2.6; S.D. 6.0). Comparison with data on the group of euthyroid subjects previously reported revealed no significant difference; $t = 0.7$ (Tables 2 and 3).

Effective half-life of thyroidal I^{131} (EHL)

The effective half-life of thyroidal I^{131} was measured in 18 mongoloid subjects. The values ranged from 2.4 to 8.0 days, and averaged 5.4 days (S.D. 1.7; S.E. 0.4). In 6 of the 18 patients the EHL was 2.4 to 4.2 days; in the remainder it was 5.6 to 8.0 days. The EHL or thyroidal turnover of I^{131} in mongoloids (Table 3) was significantly faster than in the euthyroid control group ($t = 4.0$). No significant difference from the normal ($t = 1.9$) was observed in the parents of mongoloids, the EHL ranging from 4.5 to 7.4 days, with an average of 6.2 days (S.E. 0.5; S.D. 1.0).

Urinary 24-hour I^{131} excretion

The 24-hour urinary excretion of I^{131} in the mongoloid subjects ranged from 22 to 59 per cent of the tracer dose. All but 4 values were between 41 and 59 per cent. The average excretion for the entire group was 46 per cent. The urinary excretion of I^{131} in this group of mongoloids did not differ significantly ($t = 1.7$) from that of euthyroid controls (Table 3).

Plasma butanol-extractable I^{131} (conversion ratio)

The conversion ratios in the mongoloid subjects (Table 1) ranged from 13 to 51 per cent. Comparable values were obtained in our laboratory in euthyroid subjects (9).

[4] $t = \frac{\text{Difference between the means}}{\text{Standard error of difference between means}}$ and is used as a measure of the statistical significance of the difference between two means. A value of 3.0 or greater is considered significant.

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TABLE 3. THYROIDAL 24-HOUR THYROIDAL UPTAKE, TURNOVER, AND I^{131} URINARY EXCRETION IN MONGOLISM

	Mean 24-hr. thyroidal I^{131} uptake			t		Effective half-life			t	Mean 24-hr. urinary I^{131} excretion			t
	%	S.E.	S.D.	A	B	Days	S.E.	S.D.	A	%	S.E.	S.D.	A
A. Euthyroid controls	29.0	0.6	5.1			7.1	0.1	0.8		52		11.0	
B. Mongoloid subjects	25.0	1.5	6.7	2.5		5.4	0.4	1.7	4.0	46		9.9	1.7
C. Euthyroid controls (young adults)	27.5	1.5	7.0	0.9	1.1								
D. Parents of mongoloid subjects	30.0	2.6	6.9	0.7		6.2	0.5	1.0	1.9				

Hormone transport and metabolism

In mongoloid patients, filter-paper electrophoresis was carried out on plasma to which I^{131} thyroxine had been added *in vitro*. In 2 patients, a single peak of radioactivity was found to have migrated with the alpha-2 globulin—an observation comparable to the findings in normal controls. However, the *in vitro* uptake of labelled triiodothyronine by red blood cells was increased. In 9 mongoloids, the uptake ranged from 14.6 to 20.9 per cent and averaged 17.3 per cent. The average value for euthyroid female subjects in our laboratory is 13.0 per cent. In a series of "criss-cross" experiments, the increased uptake was shown to be due to a plasma factor, since erythrocytes from mongoloids had a normal uptake in normal plasma whereas normal erythrocytes had an increased uptake in plasma from mongoloid patients.

Following intravenous infusion of I^{131}-labelled thyroxine in 2 mongoloids, the plasma radioactivity (measured daily for ten days) decreased at the rate of 7.6 per cent and 10 per cent per day, respectively. Similar values have been reported in euthyroid patients (10, 12).

DISCUSSION

The present studies demonstrate the necessity of measurement of multiple parameters in the investigation of thyroid function. Our studies indicate no difference in the 24-hour thyroidal I^{131} uptake, conversion into butanol-extractable material, and urinary I^{131} excretion in mongoloids as compared with euthyroid non-mongoloid subjects of the same age group. Determinations of the serum protein-bound iodine and cholesterol levels (obtained in many of these subjects by Dr. Clemens Benda) (Table 1) were within the range of normal. Isolated studies of thyroid function in mongoloid children found in a review of the literature also revealed no abnormality. One study (13) reported the 24-hour thyroidal I^{131} uptake in a 1-month mongoloid infant to be lower than normal; a second reported a

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t	Mean 24-hr. urinary I^{131} excretion			t
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mongoloid infant (14) with a normal thyroidal 24-hour I^{131} uptake as well as normal values for I^{131} excretion, conversion ratio (TCA precipitation method), and serum protein-bound iodine concentration. Others have found "no significant difference" in serum protein-bound iodine levels between mongoloid children 5 to 15 years old and children of the same age with "undifferentiated mental deficiency" (15). In a recent report of a rare case of thyrotoxicosis in a mongoloid patient, data on 3 other euthyroid mongoloids indicated normal thyroid function (16). Cottino *et al.* (17) found "no endocrine basis for mongolism" after a radioisotope study of 14 patients.

In contrast to these normal findings, the EHL or thyroidal I^{131} turnover was found to be significantly faster in mongoloid subjects than in euthyroid controls. Since the observation of an increased thyroidal I^{131} turnover rate and a normal 24-hour I^{131} uptake might be explained by the assumption that significant turnover and loss of I^{131} by the thyroid had occurred before the 24-hour measurement, we studied 3 mongoloid patients at five and at twenty-four hours after a tracer dose of I^{131}. In these 3 patients, the 5-hour uptake averaged 17 per cent, and the 24-hour uptake averaged 35 per cent. However, since none of these subjects exhibited a rapid turnover, further studies are required.

The apparent discrepancy between rapid thyroidal I^{131} turnover rate and normal serum protein-bound iodine concentration has also not been resolved. If peripheral utilization of thyroid hormone were increased in the same degree as thyroid hormonal release, an equilibrium would be established maintaining the amount of hormone in the blood at a normal level. The normal turnover time of plasma thyroxine observed in 2 mongoloid children does not support the hypothesis of altered peripheral utilization. Since neither of these subjects showed an increased thyroidal turnover of iodide, additional data are needed.

These findings of an increased thyroidal turnover of iodide and a normal plasma protein-bound iodine concentration are consistent with the hypothesis that thyroid function in such individuals resides in only a small portion of the gland working at an increased rate, with consequent normal total iodine uptake, a more rapid turnover, and the effective maintenance of a normal level of serum hormone.[5]

[5] The diet served to the institutionalized mongoloid patients was obviously not the same as that consumed by our controls. However, the diet was in all respects adequate. Moreover, in New England, with its proximity to the Atlantic, a low-iodine diet is very difficult to achieve. We conceive that the physiologic observation, related to the anatomic abnormalities described by Benda, is an increased turnover rate, so that the total hormonal output by the thyroid remains normal. Further studies would be necessary to prove this point.

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Results of anatomic studies (1, 2) of the thyroid gland in mongolism are consistent; the gland is hypoplastic and often below normal weight. Histologic studies reveal additional marked abnormalities. Benda, in a study of 48 mongoloids (1) found only 1 case in which the thyroid gland appeared normal. The main pathologic conditions are described as: 1) resting colloid goiter (most frequent), 2) fetal-type gland with developmental arrest or retardation, 3) replacement fibrosis, and 4) colloid goiter with scattered areas of hyperplasia. It should be emphasized that group 4 represented 21 per cent of the thyroid glands examined.

The other abnormality of thyroid function observed in this study was an increased erythrocytic uptake of triiodothyronine (average 17.3 per cent). Such elevated values have previously been found in thyrotoxicosis. None of these patients had any of the stigmata of hyperthyroidism and, with the exception of thyroidal I^{131} turnover, other parameters of thyroid function were normal. Two additional mentally deficient patients from the same school as the mongoloids (one possibly a cretin) were studied and the erythrocytic uptakes were found to be 11.2 and 9.8 per cent, respectively. Further studies are necessary to clarify the significance of the observation in mongolism, which may indicate an alteration of the plasma protein-thyroid hormone complex or a plasma factor(s) affecting the tissue uptake of thyroid hormone.

Detailed studies of thyroid function in parents of mongoloids are not available. Myers (18) emphasized the significance of thyroid deficiency in the mother. He observed an increase (2:1) in the proportion of mongoloid children born in a geographic area with a high incidence of thyroid disorders as compared to an area with a low incidence. He also reported a markedly higher incidence (9:1 by history) of thyroid disorders in mothers who had given birth to mongoloids as compared to that in mothers of only normal children. By the methods employed, we were unable to detect any abnormality of thyroid function in 7 parents of mongoloid children in our study. However, our studies were made from six months to thirteen years after the birth of the mongoloid offspring and permit no estimation of the maternal thyroid hormonal response to the stress of pregnancy.

SUMMARY

A study of thyroid function in mongolism, utilizing radioisotopic methods of investigation, is reported.

1. In 21 mongoloid subjects, the values for 24-hour thyroidal I^{131} uptake and urinary excretion were in the low-normal range and did not differ significantly from values in a group of euthyroid controls of the same age group.

2. In mongolism, the effective half-life or turnover rate of I^{131} by the

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thyroid was significantly faster than in a euthyroid control group. The possible significance of this observation is discussed.

3. The conversion ratio, or the ratio of plasma butanol-extractable I^{131} to total plasma I^{131}, in mongoloid subjects was comparable to that in euthyroid controls.

4. The turnover rate of labelled thyroxine was normal in 2 mongoloid children.

5. Serum cholesterol and serum protein-bound iodine levels were normal.

6. A possible abnormality of the plasma protein-thyroid hormone complex was suggested by the elevated *in vitro* erythrocytic uptake of labelled triiodothyronine in mongolism.

7. No significant abnormality was observed in thyroidal 24-hour I^{131} uptake and turnover or in urinary I^{131} excretion in 7 parents studied six months to thirteen years following the birth of a mongoloid child.

REFERENCES

1. Benda, C. E.: Mongolism and Cretinism, ed. 2. New York, Grune and Stratton, 1949.
2. Benda, C. E.: What is mongolism? *Internat. Rec. Med.* 165: 75, 1952.
3. Benda, C. E.; Dayton, N. A., and Prouty, R. A.: On the etiology and prevention of mongolism, *Am. J. Psychiat.* 99: 822, 1943.
4. Benda, C. E.: Prenatal factors in mongolism, *J.A.M.A.* 139: 979 ,1949.
5. Freedberg, A. S.; Chamovitz, D. L., and Kurland, G. S.: Thyroid function in normal and pathological states as revealed by radioactive iodine studies. I. Thyroid I^{131} uptake and turnover in euthyroid, hyperthyroid and hypothyroid subjects, *Metabolism* 1: 26, 1952.
6. Freedberg, A. S.; Chamovitz, D. L., and Kurland, G. S.: II. Factors influencing the uptake and turnover of I^{131} by the thyroid gland, *Metabolism* 1: 36, 1952.
7. Freedberg, A. S.; Ureles, A. L.; VanDilla, M., and McManus, M. J.: A new simple method for accurate measurement of urinary I^{131} after tracer and therapeutic doses, *J. Clin. Endocrinol.* 10: 437, 1950.
8. Clarke, D. E.; Moe, R. H., and Adams, E. E.: The rate of conversion of administered inorganic radioactive iodine into protein bound iodine of plasma as an aid in the evaluation of thyroid function, *Surgery* 26: 331, 1949.
9. Hamolsky, M. W., and Freedberg, A. S.: Unpublished data.
10. Ingbar, S. H., and Freinkel, N.: Simultaneous estimation of rates of thyroxine degradation and thyroid hormone synthesis, *J. Clin. Invest.* 34: 808, 1955.
11. Hamolsky, M. W.: The plasma protein-thyroid hormone complex in thyrotoxicosis vs. euthyroidism in man, *J. Clin. Invest.* 34: 914, 1955.
12. Sterling, K.; Lashof, J. C., and Man, E. B.: Disappearances from serum of I^{131} labelled L-thyroxine and L-triiodothyronine in euthyroid subjects, *J. Clin. Invest.* 33: 1031, 1954.
13. Lowry, G. H.; Beierwaltes, W. H.; Lampe, I., and Gomber, H. J.: Radioiodine uptake curve in humans. II. Studies in children, *Pediatrics* 4: 627, 1949.
14. Kearns, J. E., and Hutson, W. F.: The use of radioactive iodine studies in congenital thyroid aplasia, *Quart. Bull. Northwestern Med. School* 25: 270, 1951.

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08/29/95 TUE 11:38 FAX 202 254 5041 OHRE, DOE 022

15. Simon, A.; Ludwig, C.; Gofman, J. W., and Crook, G. H.: Metabolic studies in mongolism, *Am. J. Psychiat.* 111: 139, 1954.
16. McGirr, E. M., and Murray, I. P. C.: Thyrotoxicosis in a mongol (Letter to the Editor), *J. Clin. Endocrinol. & Metab.* 16: 160, 1956.
17. Cottino, F.; Ferraris, G. M., and Coda, G.: Thyroidal function in mongolism (Letter to the Editor), *J. Clin. Endocrinol. & Metab.* 16: 830, 1956.
18. Myers, C. R.: An application of the control group method to the problem of the etiology of mongolism, *Proc. Am. A. Mental Defic.* 62: 142, 1938.

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The Journal of

CLINICAL ENDOCRINOLOGY and METABOLISM

VOLUME 17 NUMBER 4

APRIL 1957

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