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Iodine Metabolism in a Region of Endemic Goiter. (22364)

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The great avidity for iodine exhibited by the thyroid gland of subjects living in certain regions where endemic goiter is prevalent has been demonstrated by Stanbury *et al.*(1,2) and by Roche *et al.*(3). It appeared to us of interest to carry out further measurements on different aspects of iodine metabolism in the regions previously studied by us. Results of thyroid and renal radioiodine clearance, conversion ratios, protein-bound I^{131}, stable iodine urinary excretion, rate of hormonal iodine formation and salivary radioactivity are reported in the present article.

Material and methods. All subjects were apparently healthy and euthyroid adults. One group (cases 1 to 14) came from the region of Bailadores, where previous studies had been carried out(3), and the other group (cases 15 to 21) from the region of Tabay, near the city of Mérida. Both regions lie within the Venezuelan Andes, at an altitude above 4,500 feet. For the study of thyroid I^{131} uptake, subjects were chosen whose thyroid was either barely palpable, or palpable but not readily visible. Radioiodine was supplied by Abbott Laboratories at Oak Ridge. External thyroid measurements were carried out with a Nuclear (Model DS-1) scintillation counter, placed 40 cm away from the thyroid cartilage. The resulting activity was multiplied by 0.85(1), and the activity measured 40 cm from the thigh was subtracted from the resulting value. The result was expressed as % of the administered dose, as measured 40 cm away from a 250 cc beaker (when the dose was given orally) or in a 20 cc syringe (when the dose was given intravenously). The beaker was thoroughly washed and the washings given to the patients. The syringe was counted before and after intravenous administration of the dose, and the second count was subtracted from the first. Measurements of plasma, saliva and urine radioactivity were performed in a well-type scintillation counter (Nuclear, Model 3037 B) and compared with the activity of suitably prepared standards.

Measurements of thyroid and renal clearances were carried out as follows: 50 μc of I^{131} in 10 cc of saline solution were injected intravenously. The thyroid was counted at 2 and 29 minutes during 2 consecutive minutes. The results, properly corrected, were taken to represent neck activity at 3 and 30 minutes respectively, and were expressed in terms of % of the administered dose. Blood was obtained at 5, 10 and 30 minutes and radioactivity of 3 cc of plasma was counted, compared with a standard and expressed in terms of % of the administered dose per liter of plasma. The patient was asked to urinate at 35 minutes and urine radioactivity was measured and compared with the standard. Thyroid clearance was calculated from a formula given by Kretchmar(4), modified from the method of Berson *et al.*(5):

$$T_c = \frac{N_{30} - \left[\left(\frac{P_{30}}{P_3} \times N_3\right) \div 0.88\right]}{\mu}$$

Where T_c = Thyroid clearance, N_{30} = Neck activity at 30 min., N_3 = Neck activity at 3 min., P_{30} = Plasma activity at 30 min., P_3 = Plasma activity at 3 min., calculated from curve constructed with the 5, 10 and 30 minute values and μ = Average plasma level, as measured planimetrically from the plasma radioactivity curve. The factor 0.88 was taken from Oddie(6). Renal clearance was calculated by dividing average plasma dose by urine concentration. Conversion ratio was established by counting radioactivity in 3 cc of plasma, precipitating with 6 cc 10% trichloracetic acid, washing twice with the same substance, and redissolving the precipitate in 3 cc 1 N NaOH. Saliva was obtained without stimulation, and the radioactivity was counted in the deep well scintillator. Urinary I^{127} concentration was determined chemically (7). The urines were collected in the usual way, their volume was measured and an aliquot was alkalinised, placed in glass-stoppered bottles, kept in the ice box and taken directly by plane within three weeks to the Boston Medical Laboratory where the determinations were performed. Rate of hormonal iodine secretion was calculated from the formula given by Stanbury *et al.*(2).

TABLE II. Conversion Ratios and Protein-Bound I^{131} in Subjects from Endemic Goiter Region.

Patient	Sex	Type of goiter*	Conversion ratio (%)	24 hr protein-bound I^{131} (% dose/L of plasma)
8	♂	D 1	96	.017
9	♂	D 2	97	.021
10	♂	N 2	100	.019
11	♂	D 2	42	.011
12	♀	N 2	52	.020
13	♂	D 2	90	.012
15	♂	D 2	51	.048
17	♀	N 3	75	.112
18	♀	N 3	90	.084
19	♀	N 3	64	.045
20	♀	D 1	87	.522
21	♂	N 3	87	.056
		Avg	78	.081
		Range	42–100	.011–.522

* N = Nodular; D = Diffuse. 1 = Barely palpable; 2 = Definitely enlarged, but not yet visible; 3 = Enlarged and visible.

Results. In Table I are shown results of thyroid uptake and clearance, renal 24 hr excretion and clearance of I^{131}, 24 hour I^{127} urinary excretion and daily rate of hormonal iodine secretion. All the patients in this table came from the region of Bailadores.

In Table II are listed the results of conversion ratios and 24 hour protein-bound I^{131}. In Table III we may see the results of sali-

TABLE I. Studies in Iodine Metabolism in Subjects from a Region of Endemic Goiter.

Patient No.	Type of goiter	Sex	24 hr thyroid I^{131} uptake (% of dose)	24 hr urinary I^{131} (% of dose)	Thyroid I^{131} clearance (ml/m)	Renal I^{131} clearance (ml/m)	Urinary I^{127} excretion (μg/d)	Rate of hormonal iodine secretion (μg/d)
1	No	♂	49.0	31.8	118.5	58.0	21.8	20.9
2	No	♂	54.8	25.9	124.4	43.7	19.8	24.0
3	N 2	♂	56.2	—	—	—	—	—
4	D 2	♂	52.0	33.2	82.6	35.7	9.6	10.4
5	D 1	♂	54.6	39.7	135.4	35.8	26.7	32.1
6	D 2	♂	55.3	15.3	130.5	42.7	19.8	24.5
7	D 2	♀	—	—	168.2	21.8	—	—
8	D 1	♂	43.2	13.2	86.2	51.5	21.1	16.0
9	D 3	♂	59.0	18.3	131.0	8.0	19.2	27.6
10	N 2	♂	53.0	22.7	110.3	18.8	20.0	22.6
11	D 2	♂	41.5	52.2	87.2	26.8	40.0	28.3
12	N 2	♀	36.1	79.5	38.5	35.3	35.4	20.0
13	D 2	♂	57.6	30.1	125.5	72.0	27.3	37.1
14	D 1	♂	43.1	12.5	70.7	32.0	9.0	6.8
Avg			50.4	31.2	108.4	37.1	22.5	22.5
Range			36.1–59.0	12.5–79.5	38.5–168.2	8.0–72.0	9.0–40.0	6.8–37.1

TABLE III. Saliva Radioactivity 24 Hr after Administration of 50 μc of I^{131}.

Patient No.	Saliva radioactivity (c/m/3 cc)
1	1262
2	713
3	1410
4	730
5	657
6	792
8	1412
9	727
10	961
11	1246
12	4670
13	654
14	2539
15	1604
16	640
17	2930
18	256
19	690
20	2819
21	91
Avg	1341
Range	91–4670

vary radioactivity measurements.

Discussion. The I^{131} studies are in accord with previous reports(2,3) and may be explained by a high iodine extracting efficiency of the thyroid. Thyroid clearance in these cases is generally well above the normal limits of 8-38 ml/m (mean 16) given by Myant *et al.*(8), of 26.3 $\pm$ 5.2 (standard error) given by Oddie *et al.*(6), and of 12.0-68.0 (mean 33.0 ml/m) given by Berson *et al.* (5). Although the 24 hour thyroid I^{131} uptake is not greatly elevated, and in some of the cases is even normal, a study of the thyroid clearance shows clearly that thyroid avidity for iodine is markedly increased in this region. In individuals with larger goiters, one would expect this avidity to be even higher. The only case who shows nearly normal values (case No. 12) was a woman who had lived for 15 years in Caracas, the capital, where thyroid uptake has been shown to be normal(9), and had lived in Bailadores for the last 3 years. Her diet was plentiful as compared to that of the other subjects in this study whose diet was almost exclusively of local vegetal origin(11).

Renal I^{131} excretion is somewhat reduced, but clearance is normal, showing that in these regions individuals do not develop the ability to conserve iodine through renal mechanisms. Normal renal iodine clearance is given by various authors as 11-44 ml/m, with a mean of 31 ml/m(8), 31.0-76.0 ml/m with mean 53.9(5) and 33.3 $\pm$ 3.1 (standard error)(10). Stanbury *et al.*, in Mendoza, in 3 subjects, found renal clearance values of 25, 29 and 44 ml/m respectively, all within normal limits also(2).

In cases 6, 8 and 14, the very low I^{131} excretion is suspicious, since total recovery of I^{131} was low; loss of urine is probable. Individual urine volumes in these cases were 1,100, 1,320 and 900 cc.

The 24 hour stable iodine excretion is quite low, confirming further the probability that the finding of increased thyroid avidity for iodine in this region is conditioned by iodine deficiency in food and water. Compensation for this iodine deficiency appears to be adequate in the cases studied, as evidenced by the clinical status and by the normal, although low, daily hormonal iodine secretion. A similarly low I^{127} excretion (17 μg/day average) had been found previously by De Venanzi *et al.* in individuals from a region nearby (13).

Saliva radioactivity has not been previously reported in a region of endemic goiter. In our cases, it was generally low, and corresponded approximately to the values one would expect in hyperthyroid patients with similar thyroid uptakes(12).

Conversion ratios are unusually high, and there seems to be an increased quantity of protein-bound I^{131} at 24 hours in the plasma. Here again, the findings resemble those of hyperthyroidism and are compatible with the idea that in the endemic goiter found in this region, as in the Mendoza goiter, there is increased extraction of iodine by the thyroid, a faster rate of iodine turnover, with an adequate quantity of hormonal iodine being synthesized.

Summary. Studies carried out in the Venezuelan Andes show that in this region there is an increase in thyroid clearance of iodine, thyroid uptake, conversion ratios and 24 hour protein-bound I^{131}. Renal clearance

of I^{131} is normal and urinary and salivary I^{131} low. Urinary I^{127} is low. It is concluded that in this region there exists a state of iodine deficiency, leading to compensatory thyroid avidity for iodine. There is no compensatory renal conservation of iodine.

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