Iodine balance studies in protein-calorie malnutrition

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Ingenbleek, Y., and Malvaux, P. (1974). *Archives of Disease in Childhood*, **49**, 305. **Iodine balance studies in protein-calorie malnutrition.** In 12 malnourished Senegalese children iodine intake and excretion were measured on admission for 4 consecutive days. All subjects were in negative iodine balance, averaging $-20.5 \mu\text{g}$ iodine/day. One month later, after nutritional rehabilitation, 7 children re-submitted to comparative balance study showed a strongly positive balance of $+19.3 \mu\text{g}$ iodine/day.

Protein-calorie malnutrition is characterized by a continuous impoverishment of the thyroid's iodine content, while clinical recovery is accompanied by a progressive restoration.

The consequences of protein depletion on the thyroid gland of various animals have been extensively surveyed (Aschkenasy *et al.*, 1962; Srebniak, Evans, and Rosenberg, 1963; Ramalingaswami *et al.*, 1965; Cowan and Margossian, 1966; Platt and Stewart, 1967; Florsheim *et al.*, 1970). In the human, attempts to define thyroid function in protein-calorie malnutrition are sparse. Low levels of protein-bound iodine and BEI have been found in the serum of malnourished children associated with a reduced basal metabolic rate (Gómez, Ramos-Galvan, and Cravioto, 1955; Valledor *et al.*, 1959; Montgomery, 1962; Lifshitz *et al.*, 1962; Mönckeberg *et al.*, 1964; Beas *et al.*, 1966).

Poor food intake and malabsorption being part of the protein-calorie malnutrition syndrome, a disturbance of iodine metabolism, i.e. iodine intake and/or iodine malabsorption, may be suspected. By means of iodine balance studies we have investigated the iodine intake and excretion in children before and after recovery from uncomplicated protein-calorie malnutrition.

Patients and methods

Twelve Senegalese children, aged from 18 to 30 months, were studied. They presented all the clinical signs of uncomplicated kwashiorkor, i.e. failure of weight and height gain, hair discoloration, diarrhoea, and oedema. The 4-day balance study was started 24 hours after admission. 24-hour stools and 24-hour urine specimens

were collected separately under careful nursing supervision, the patients being kept in an air-conditioned metabolic ward to avoid severe sweating, which may cause an iodine loss of 2 to 9% of the urinary excretion (Harden and Alexander, 1963; Consolazio *et al.*, 1966).

Dietary therapy was composed of increasing quantities of semiskimmed milk (Nido, Nestle) and of a commercial mixture of oligopeptides and amino acids (Nesmida, Nestle). In case of profuse diarrhoea only the latter proteolytic suspension without lactose was given. No drugs or vitamins were added. All the children improved, and after clinical recovery one month later a 4-day balance study was again performed on 7 of them in the same conditions of nutrition and sampling.

Iodine in foods, urine, and faeces was measured by the process described by Benotti *et al.* (1965) with reagents provided by Dade Inc. (Miami, Florida, U.S.A.). Dietary iodine was measured on each can. The iodine content of 15 cans of semiskimmed milk (Nido) was $35.7 \pm 6.0 \mu\text{g}/100 \text{ g}$ of edible powder (range 25 to 45 μg). Iodine content of 4 cans of Nesmida was $41.2 \pm 7.1 \mu\text{g}/100 \text{ g}$ of edible powder (range 33 to 50 μg). Results are given in absolute value and in μg iodine $\pm$ SD.

Results

The individual and mean values of iodine determination collected in 12 malnourished children during the first 4 days of admission are given in Table I. After clinical recovery, 7 out of the 12 children were reinvestigated during a 4-day period; individual and mean values are given in Table II.

On admission, according to the actual needs of the children with protein-calorie malnutrition, the food

tein-calorie malnutrition on admission

Dy 4	Total for 4 dy (µg)	Faecal iodine (µg/dy)					Iodine balance* (µg/4 dy)
		Dy 1	Dy 2	Dy 3	Dy 4	Total for 4 dy (µg)	
7.3	52.5	9.0	8.1	1.4	2.8	21.3	-38.9
24.4	91.6	6.9	5.2	7.4	6.0	25.5	-51.4
32.6	167.3	14.3	8.6	7.9	6.8	37.6	-128.6
22.6	70.1	32.2	7.9	19.1	17.0	76.2	-109.5
23.0	102.5	21.1	11.7	10.4	20.2	63.4	-121.8
15.9	54.7	4.3	0.7	2.1	2.8	9.9	-32.4
27.3	149.4	1.3	7.0	5.6	6.3	20.2	-118.4
12.6	53.4	13.1	12.8	13.1	9.0	48.0	-23.4
32.0	113.5	7.5	12.9	13.7	20.5	54.6	-98.0
14.6	95.0	10.7	13.4	16.5	9.4	50.0	-45.0
15.5	84.7	11.6	9.5	28.0	8.3	57.4	-90.1
17.9	110.7	26.6	18.6	14.3	12.9	72.4	-131.1
20.4	95.4 ±36.5	13.2	9.7	11.6	10.1	44.7 ±21.7	-82.3 ±41.1

nutrition after nutritional rehabilitation

Dy 4	Total for 4 dy (µg)	Faecal iodine (µg/dy)					Iodine balance* (µg/4 dy)
		Dy 1	Dy 2	Dy 3	Dy 4	Total for 4 dy (µg)	
24.4	91.5	5.6	26.8	10.9	25.3	68.6	+81.3
29.4	110.7	6.9	5.2	7.4	6.0	25.5	+117.8
43.2	176.0	7.2	3.6	7.3	6.9	25.0	+35.2
39.8	164.9	3.0	15.1	15.2	11.2	44.5	+45.1
28.7	135.3	5.0	6.4	7.0	16.1	34.5	+103.6
36.6	142.1	16.6	9.2	8.5	7.3	41.6	+65.3
37.3	144.5	9.2	6.7	7.2	8.5	31.6	+93.9
34.2	137.8 ±29.2	7.6	10.4	9.0	11.6	38.7 ±15.0	+77.4 ±30.4

value of 9.6 µg/day did not differ from the mean faecal iodine value found during the first balance study. However, the percentage of faecal excretion calculated at discharge was 15.2% of intake. Nutritional rehabilitation was characterized in all patients by a positive retention of iodine reaching the mean value of 19.3 µg/day and 77.4 µg for the 4-day period (Fig. 2).

Both Fig. 1 and 2 agree with the recommendations of Reifstein, Albright, and Wells (1945).

Discussion

It is generally accepted that in euthyroid subjects over a long period of time there exists a good correlation between iodine intake and urinary output. In our study there is no such correlation

($r = 0.33$). Urinary excretion generally exceeds intake and is usually within the normal range (25 to 35 µg/day in 2-year-old healthy Senegalese children). Urinary iodine, therefore, may not be useful as an index of iodine depletion. Moreover, faecal loss of iodine represents on admission an appreciable amount of the low dietary iodine (77.4%). Malnutrition seems to be characterized by a continuous impoverishment of the intrathyroidal pool of iodine, and the depletion is estimated to be -20.5 µg/day.

The importance of faecal loss of iodine is obvious in all malnourished children, but is less marked in patients suffering from recently contracted acute kwashiorkor (Cases 1, 2, 6, 7, and 10) than in prolonged starvation where faecal iodine is higher and the negative balance more pronounced (Cases 3, 4, 5, 8, and 12). Cases 9 and 11 represent clinically

FIG. 1.—Quantitative aspects of negative iodine balance on admission. The height of each rectangle below the base-line gives the mean daily iodine intake. The length of each black rectangle represents the mean faecal iodine and the length of each stippled rectangle the mean urinary iodine. The height of the rectangles above the base-line gives the average daily iodine loss.

intermediate stages of medium severity. This is consistent with the observation that intestinal malabsorption of iodine is a well-established feature in protein-calorie malnutrition. A tracer dose of oral $\text{Na-}^{131}\text{I}$ reveals 15.5% radioactivity in the stools, and this faecal quantity is significantly increased by comparison with the same radioisotope given intravenously, thus excluding an endogenous origin (Ingenbleek and Beckers, 1973). The iodine malabsorption appears to be partly a functional consequence of histological changes in jejunal mucosa (Stanfield, Hutt, and Tunnicliffe, 1965) and is negatively correlated with the thyroidal avidity for iodine, substantiated by the maximal radioiodine uptake (Ingenbleek and Beckers, 1973). In early malnutrition, the maximal radioiodine uptake is subnormal, iodine malabsorption is moderate, and iodine balance is slightly negative. In long-term protein deficiency, the maximal radioiodine uptake is lowered, iodine malabsorption is more severe, and negative balance is aggravated. There is known to be depression of the jejunal mitotic index (Brunser *et al.*, 1966) and extensive interstitial fibrosis of the thyroid gland (Scrimshaw *et al.*, 1955). After nutritional rehabilitation, all the children presented a reversed strongly positive iodine balance with a mean value of $+19.3 \mu\text{g/day}$. On discharge, the faecal loss of iodine was only 15.2% of the dietary intake.

In Senegal no evidence occurs for decreased

FIG. 2.—Quantitative aspects of positive iodine balance on discharge. The height of each rectangle below the base-line represents the mean daily iodine intake. The length of each black rectangle represents the mean faecal iodine and the length of each stippled rectangle the mean urinary iodine. The amount of iodine retained per day is represented by the height of the white rectangle.

thyroidal function in healthy patients (Y. Ingenbleek, unpublished data) as reported in Jamaica (Harland, Richards, and Goldberg, 1971). No description has been made concerning the iodine content of the thyroid gland of children living in the tropics. Widdowson and Spray (1951) claimed that in 2-year-old Caucasian infants, the total amount of intrathyroidal halide averages $500 \mu\text{g}$ and may reach $1000 \mu\text{g}$. If this statement is valid for Senegalese children as well, and if the elimination of iodine in children with protein-calorie malnutrition persists at the rate of $-20.5 \mu\text{g/day}$, then the thyroidal stores would be depleted within a period of 25 to 50 days. The mean quantity of $19.3 \mu\text{g}$ iodine retained daily during recovery is not significantly different ($t = 0.87$; $0.3 < P < 0.4$) from the amount lost per day on admission. This fact suggests that the rate of depletion of intrathyroidal iodine content corresponds to the rate of restoration on discharge, and that the iodine recovery period must be of similar duration to the elimination period. The iodine retention period might be maintained beyond the clinical rehabilitation.

There is no necessary correlation between the iodine accumulation and thyroxine secretion by the thyroid gland (Feinberg, Hoffman, and Owen, 1959; Koutras *et al.*, 1961; Fisher and Oddie, 1964). But iodine constitutes the primary element indispensable

to the hormonal biosynthesis. Therefore, it is our opinion that continuous depletion of intrathyroidal iodine content leads to reduced thyroxine secretion.

The technical assistance of Miss J. Hennaux is gratefully acknowledged.

REFERENCES

- Aschkenasy, A., Nataf, B., Piette, C., and Sfez, M. (1962). Le fonctionnement thyroïdien chez le rat carencé en protéines. *Annales d'Endocrinologie*, **23**, 311.
- Beas, F., Mönckeberg, F., Horwitz, I., and Figueroa, M. (1966). The response of the thyroid gland to thyroid-stimulating hormone (TSH) in infants with malnutrition. *Pediatrics*, **38**, 1003.
- Benotti, J., Benotti, N., Pino, S., and Gardyna, H. (1965). Determination of total iodine in urine, stool, diets, and tissue. *Clinical Chemistry*, **11**, 932.
- Brunser, O., Reid, A., Mönckeberg, F., Maccioni, A., and Contreras, I. (1966). Jejunal biopsies in infant malnutrition: with special references to mitotic index. *Pediatrics*, **38**, 605.
- Consolazio, C. F., Matoush, L. O., Nelson, R. A., Isaac, G. J., and Canham, J. E. (1966). Comparison of nitrogen, calcium, and iodine excretion in arm and total body sweat. *American Journal of Clinical Nutrition*, **18**, 443.
- Cowan, J. W., and Margossian, S. (1966). Thyroid function in female rats severely depleted of body protein. *Endocrinology*, **79**, 1023.
- Feinberg, W. D., Hoffman, D. L., and Owen, C. A. (1959). The effects of varying amounts of stable iodide on the function of the human thyroid. *Journal of Clinical Endocrinology and Metabolism*, **19**, 567.
- Fisher, D. A., and Oddie, T. H. (1964). Comparison of thyroidal iodide accumulation and thyroxine secretion in euthyroid subjects. *Journal of Clinical Endocrinology and Metabolism*, **24**, 1143.
- Florsheim, W. H., Suhr, B. Z., Mirise, R. T., and Williams, A. D. (1970). Thyroid function in protein-depleted rats. *Journal of Endocrinology*, **46**, 93.
- Gómez, F., Ramos-Galvan, R., and Cravioto, T. (1955). Determinación de yodo unido a la proteína en niños desnutridos y durante su recuperación. *Revista Mexicana de Pediatría*, **24**, 94.
- Harden, R. M., and Alexander, W. D. (1963). Quantitative aspects of iodide excretion in human thermal sweat. *Clinical Science*, **25**, 79.
- Harland, W. A., Richards, R., and Goldberg, I. J. L. (1971). Reduced thyroid activity in Jamaicans. *Journal of Endocrinology*, **49**, 537.
- Ingenbleek, Y., and Beckers, C. (1973). Evidence for intestinal malabsorption of iodine in protein-calorie malnutrition. *American Journal of Clinical Nutrition*, **26**, 1323.
- Koutras, D. A., Alexander, W. D., Buchanan, W. W., Crooks, J., and Wayne, E. J. (1961). Studies of stable iodine metabolism as a guide to the interpretation of radioiodine tests. *Acta Endocrinologica*, **37**, 597.
- Lifshitz, F., Chavarria, C., Cravioto, J., Frenk, S., and Morales, M. (1962). Yodo hormonal en la desnutrición avanzada del niño. *Boletín Médico del Hospital Infantil (México)*, **19**, 319.
- Mönckeberg, F., Beas, F., Horwitz, I., Dabancens, A., and González, M. (1964). Oxygen consumption in infant malnutrition. *Pediatrics*, **33**, 554.
- Montgomery, R. D. (1962). Changes in the basal metabolic rate of the malnourished infant and their relation to body composition. *Journal of Clinical Investigation*, **41**, 1653.
- Platt, B. S., and Stewart, R. J. C. (1967). Experimental protein-calorie deficiency: histological changes in the endocrine glands of pigs. *Journal of Endocrinology*, **38**, 121.
- Ramalingaswami, V., Vickery, A. L., Jr., Stanbury, J. B., and Hegsted, D. M. (1965). Some effects of protein deficiency on the rat thyroid. *Endocrinology*, **77**, 87.
- Reifenstein, E. C., Jr., Albright, F., and Wells, S. L. (1945). The accumulation, interpretation, and presentation of data pertaining to metabolic balances, notably those of calcium, phosphorus, and nitrogen. *Journal of Clinical Endocrinology*, **5**, 367.
- Scrimshaw, N. S., Béhar, M., Perez, C., and Viteri, F. (1955). Nutritional problems of children in Central America and Panama. *Pediatrics*, **16**, 378.
- Srebnik, H. H., Evans, E. S., and Rosenberg, L. L. (1963). Thyroid function in female rats maintained on a protein-free diet. *Endocrinology*, **73**, 267.
- Stanfield, J. P., Hutt, M. S. R., and Tunnicliffe, R. (1965). Intestinal biopsy in kwashiorkor. *Lancet*, **2**, 519.
- Valledor, T., Lavernia, F., Borbolla, L., Satonowsky, C., Costales, F., Prieto, E., and Bardelas, A. (1959). Thyroid function disturbances in malnourished infants and small children. *Revista Cubana de Pediatría*, **31**, 533.
- Widdowson, E. M., and Spray, C. M. (1951). Chemical development in utero. *Archives of Disease in Childhood*, **26**, 205.

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