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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 μg iodine/day. One month later, after nutritional rehabilitation, 7 children resubmitted to comparative balance study showed a strongly positive balance of +19·3 μg 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; Srebnik, 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±6·0 μg/100 g of edible powder (range 25 to 45 μg). Iodine content of 4 cans of Nesmida was 41·2±7·1 μg/100 g of edible powder (range 33 to 50 μg). Results are given in absolute value and in μg iodine±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

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TABL

Iodine balance study in children wi

Case no.	Dietary iodine (μg/dy)					Urinary iodi (μg/dy)		
	Dy 1	Dy 2	Dy 3	Dy 4	Total for 4 dy (μg)	Dy 1	Dy 2	Dy 3
1	3·3	15·8	7·9	7·9	34·9	19·9	18·9	6·4
2	3·3	10·8	23·3	28·3	65·7	32·8	13·7	20·7
3	16·6	19·9	19·9	19·9	76·3	58·9	50·9	24·9
4	9·2	9·2	9·2	9·2	36·8	22·6	10·6	14·3
5	4·9	7·9	13·9	17·4	44·1	29·8	29·9	19·8
6	3·3	3·3	3·3	22·3	32·2	14·8	12·9	11·1
7	3·3	3·3	22·3	22·3	51·2	60·7	31·8	29·6
8	19·5	19·5	19·5	19·5	78·0	8·3	18·9	13·6
9	17·3	17·3	18·5	17·0	70·1	23·4	25·4	32·7
10	25·0	25·0	25·0	25·0	100·0	35·7	24·9	19·8
11	13·0	13·0	13·0	13·0	52·0	15·7	28·6	24·9
12	13·0	13·0	13·0	13·0	52·0	46·6	30·6	15·6
Mean ±SD	10·9	13·1	15·7	17·9	57·7 ±20·5	30·7	24·7	19·4

*Dietary iodine – (urinary iodine + faecal iodine).

TABI

Iodine balance study in children with protein-calo

Case no.	Dietary iodine (μg/dy)					Urinary iodi (μg/dy)		
	Dy 1	Dy 2	Dy 3	Dy 4	Total for 4 dy (μg)	Dy 1	Dy 2	Dy 3
1	54·4	68·0	59·0	60·0	241·4	32·8	13·6	20·7
2	56·0	66·0	66·0	66·0	254·0	38·8	18·6	23·9
3	53·2	57·0	63·0	63·0	236·2	44·8	52·2	35·8
6	43·0	85·5	63·0	63·0	254·5	43·0	41·7	40·4
8	72·0	72·0	72·0	57·4	273·4	43·7	35·2	27·7
9	60·0	60·0	63·0	66·0	249·0	46·6	30·6	28·3
11	63·0	63·0	72·0	72·0	270·0	38·7	35·6	32·9
Mean ±SD	57·3	67·3	65·4	63·9	254·0 ±13·8	41·2	32·5	29·9

*Dietary iodine – (urinary iodine + faecal iodine).

intake was poor and the daily iodine intake was low, ranging from 3·3 to 28·3 μg/day with a mean of 14·4 μg/day and 57·7 μg for the 4-day period.

The progressive increase from day 1–4 for many of the patients is due to the fact that the diet was not imposed on the children but was adapted to their digestive capacities, the food intake being increased rapidly for some patients, while remaining low for others.

Urinary iodine excretion ranged from 6·4 to 60·7 μg/day with a mean value of 23·8 μg/day. There was a poor correlation between urinary iodine excretion and intake ($r = 0{\cdot}33$) and this correlation is not improved by excluding the first day of the balance study ($r = 0{\cdot}39$). The faecal iodine represents an important percentage (77·4%) of the dietary iodine; there was no correlation between intake and faecal excretion ($r = 0{\cdot}11$). The mean faecal value was 11·2 μg/day with extreme values ranging from 0·7 to 32·2 μg/day. Iodine balances were negative in all children; the mean loss was 20·5 μg/day and 82·3 μg during the 4-day period (Fig. 1).

After clinical rehabilitation, the 7 children who were investigated again received about 150 g semiskimmed milk daily, which brought an iodine intake ranging from 43 to 85·5 μg/day with a mean value of 63·5 μg/day and of 254 μg for the 4-day balance study. This considerable increase of iodine intake during the recovery period was accompanied by a small rise in the urinary iodine, which amounted to 34·4 μg/day. Nevertheless, there was no correlation between intake and urinary excretion. The range of faecal iodine was again extremely wide, from 3 to 26·8 μg/day, and the mean faecal iodine *tein-calorie malnutrition on admission*

		Faecal iodine (µg/dy)					Iodine balance* (µg/4 dy)
Dy 4	Total for 4 dy (µg)	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

lnutrition after nutritional rehabilitation

		Faecal iodine (µg/dy)					Iodine balance* (µg/4 dy)
Dy 4	Total for 4 dy (µg)	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 Reifenstein, 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

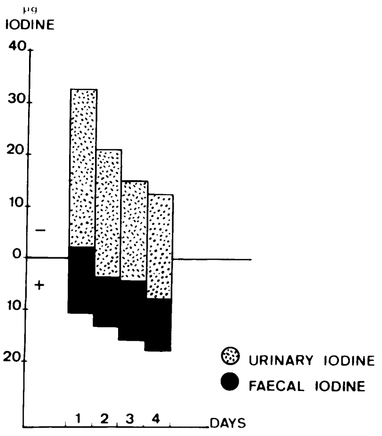

FIG. 1.—*Quantitative aspects of negative iodine balance on admission. The height of each rectangle below the base-line gives the mean daily iodine intake. The length of each black rectangle represents the mean faecal iodine and the length of each stippled rectangle the mean urinary iodine. The height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

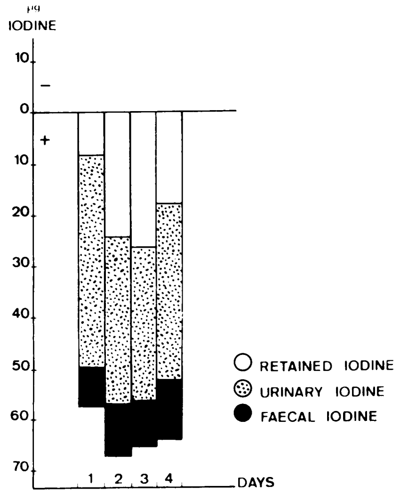

FIG. 2.— *Quantitative aspects of positive iodine balance on discharge. The height of each rectangle below the base-line represents the mean daily iodine intake. The length of each black rectangle represents the mean faecal iodine and the length of each stippled rectangle the mean urinary iodine. The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

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 Na-^{131}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 μg/day. On discharge, the faecal loss of iodine was only 15·2% of the dietary intake.

In Senegal no evidence occurs for decreased 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 μg and may reach 1000 μg. 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 μg/day, then the thyroidal stores would be depleted within a period of 25 to 50 days. The mean quantity of 19·3 μg 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.

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