

Increased risk of iodine deficiency with vegetarian nutrition

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Observational studies primarily based on diet questionnaires or food records have reported that vegetarians can have a very low I intake. However, analytically ascertained data on the possible degree of I deficiency with this form of diet is lacking. Six healthy adult volunteers participated in the present controlled experimental diet study carried out in four separate 5 d diet periods. The study diets, normal, protein-rich, lactovegetarian, and repeat of the initial normal diet, were almost isoenergetic and contained no fish, sea food, iodized salt or processed foods fortified with I. During the last 48 h of each diet period two 24 h urine samples were obtained from each subject. I analyses were performed in the urine samples and in representative samples taken from all ingested diets. Urinary I excretion was significantly lower with the lactovegetarian diet (36.6 (SD 8.8) $\mu\text{g/d}$) than with the normal and the protein-rich diets (50.2 (SD 14.0) and 61.0 (SD 8.0) $\mu\text{g/d}$ respectively). Accordingly, a markedly reduced I intake was confirmed analytically for the lactovegetarian diet (15.6 $\mu\text{g/d}$ v. 35.2 and 44.5 $\mu\text{g/d}$ respectively). Our results provide experimental confirmation of literature findings indicating that I supply is higher with non-vegetarian than with vegetarian diets. Specifically, the extremely low intake and urinary output of I as analytically determined for one exemplary vegetarian diet, demonstrate that dietary I may be limiting when strict forms of vegetarian dietary practices (no iodized salt, no I supplements) are followed. The present study is, therefore, the first diet-experiment-based pointer to the potential danger of I deficiency disorders due to strict forms of vegetarian nutrition, especially when fruits and vegetables grown in soils with low I levels are ingested.

Iodine: Vegetarians: Micronutrients

Elimination of I deficiency is a global health priority (Maberly *et al.* 1994). More than one billion people worldwide consume inadequate daily amounts of I (International Council for Control of Iodine Deficiency Disorders, 1997) and are at risk of I deficiency disorders. Apart from enlargement of the thyroid (goitre) a wide spectrum of mental, psychomotor and growth abnormalities (Delange, 1994) as well as increased infant mortality (Cobra *et al.* 1997; DeLong *et al.* 1997) can result from I deficiency.

In industrialized countries with markedly less I deficiency than in developing countries, such health risks make it necessary to identify, particularly, those groups of people who still are at increased risk of I deficiency disorders despite universal access to iodized foods.

Literature findings indicate that vegans not consuming I supplements, seaweed and/or related products have inadequate intakes of dietary I (Draper *et al.* 1993; Rauma *et al.* 1994; Lightowler & Davies, 1996). In many countries the I content of plant foods is very low due to an extremely low I concentration in the soil. On the other hand animal products such as eggs, cheese, milk, meat, fish, and poultry are important contributors to total I intake (Park *et al.* 1981).

In industrialized countries most animal feeds are supplemented with I.

However, reliable analytical data directly comparing the I status of subjects on vegetarian and non-vegetarian diets have hitherto been lacking. To address this issue directly, both dietary I intake and urinary I output were investigated in an experimental diet study. An exemplary lactovegetarian diet was compared with two non-vegetarian, almost isoenergetic diets in the same subjects. A lactovegetarian diet was chosen instead of a pure vegetarian (vegan) diet to ensure at least a minimum I supply with dairy products.

Subjects and methods

Six healthy adult volunteers (three females aged 24–25 years and three males aged 31–49 years, no palpable goitre) were selected. Because a repeated-measure design was used in the present study (with each individual being his or her own control) the age difference between the males and females was not expected to have any effect on the results of the dietary manipulations. Along with this, the repeated-measure design is a powerful tool to detect, even with a

Abbreviations: L, lactovegetarian diet; N, normal (moderately protein-rich) diet; P, protein-rich diet.

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small sample size of *n* 6 individuals, moderate changes of about 20% in biological variables such as adrenal androgens (Remer *et al.* 1995, 1996a) known to be relatively unresponsive to certain endocrine and dietary treatments (Remer *et al.* 1995, 1996b).

Mean BMI values were 22.5 (SD 2.3) and 24.4 (SD 2.4) kg/m² for females and males respectively. The study protocol was approved by the institutional review board of the Dortmund Research Institute of Child Nutrition. All subjects gave written informed consent after the experimental protocol was explained to them in detail.

The initial aim of the present study was to investigate whether it is possible to estimate reliably the renal net acid excretion produced by different natural food diets. The underlying study protocol allowed us also to investigate the dietary impact on individual I status. There was no danger of interfering with the initial study aim after the following additional adjustments for the I issue had been introduced: no fish, no sea food, and no iodized salt at all were ingested during the different experimental diet periods. In addition, the only beverage allowed was an I-free water (Volvic; Puy-De-Dome, France) with a very low mineral content. However, its use was intended *per se* in order to ensure that the minerals originating from the beverage (which was available *ad libitum*) did not affect acid–base metabolism. Furthermore, none of the processed foods (bread, cheese etc.) given with the experimental diets was enriched with I or contained iodized salt.

Since the results on diet-dependent renal net acid excretion have already been published along with a detailed description of methods (Remer & Manz, 1994a), the methods are briefly summarized here.

This investigation, a controlled experimental diet study, was a repeated-measure design and was carried out in four consecutive diet periods during which all subjects received the respective diets in the same chronological order. Each diet period lasted 5 d. In the initial period, a normal (N) moderately protein-rich diet was fed. This was followed by a protein-rich (P) diet, a lactovegetarian (L) diet, and a repetition of the initial diet N. The repeat diet N was slightly modified in that 20 mmol (3.0 g) L-methionine (Acimethin, Gry-Pharma, Kirchzarten, Germany) was additionally administered daily specifically to increase renal net acid load.

Protein, carbohydrate, fat, and energy contents of the diets are given in Table 1. A description of the composition of the diets according to major food groups is given in Table 2. The diet periods P, L, and repeat N were each separated by a 9 d interval without dietary restrictions (except for the recommendation to use iodized table salt and to eat I-rich foods). A 2 d interval without strict diet regulations was set between the initial (N) and the second (P) period.

Dietary intervention periods of 5 d duration were chosen to clearly identify physiologically relevant short-term (not acute) effects on I metabolism and to assure full dietary compliance. Acute changes in I intake can be observed in 24 h urine samples within 1–2 d (Wahl *et al.* 1998), whereas long-term changes in urinary I output with full adaptation of thyroid metabolism takes at least 4 months (Höhler *et al.* 1990).

Table 1. Macronutrient compositions of the normal (N; moderately protein-rich), protein-rich (P), and lactovegetarian (L) diets

	Diet		
	N	P	L
Energy (kJ/70 kg per d)*	8263	8439	8171
Fat (g/70 kg per d)	73	87	82
Carbohydrate (g/70 kg per d)*	245	195	267
Protein (g/d)†	95	120	49

* Additional energy (335–670 kJ) was ingested in individually constant daily amounts during all diet periods as carbohydrates (Dextro Energen (dextrose and maltodextrin); Maizena GmbH, Heilbronn, Germany) according to individual preference.

† The protein content of the diet was kept nearly constant for all subjects receiving the same diet, irrespective of sex and weight.

All foods and meals prepared for the diets were weighed and/or measured precisely and the apportioned meals were completely ingested. Cooking losses of electrolytes and minerals were virtually completely avoided, e.g. by including the total amount of cooking water (used for the preparation of vegetables and potatoes) in the final meals. On one day of each diet period exactly 20% of each meal was collected (from the respective meals prepared in appropriate excess) and the portions were combined for subsequent homogenization, lyophilization, and I analysis. During the last 2 d of each diet period, timed 24 h urine samples were collected and immediately stored at below –20°. External I contaminations (Neubert & Remer, 1996) were carefully avoided. Quantification of urinary I was carried out by a modified Sandell–Kolthoff method after wet ashing of the samples (Wawschinek *et al.* 1985). For each diet four portions of the homogenized and lyophilized total menus were subjected to alkaline ashing before the determination of I by the Sandell–Kolthoff reaction (Aumont & Tressol, 1986). Single measurements were performed for each of

Table 2. Compositions of the normal (N; moderately protein-rich), protein-rich (P), and lactovegetarian (L) diets according to major food groups

	Diet		
	N	P	L
Meat, meat products (g/d)	190	220	0
1st Breakfast	50	–	–
2nd Breakfast	10	–	–
Lunch	120	200	–
Snack	–	–	–
Dinner	10	20	–
Cheese and eggs (g/d)	60	340	0
1st Breakfast	20	80	–
2nd Breakfast	–	100	–
Lunch	–	40	–
Snack	–	20	–
Dinner	40	100	–
Fruits and vegetables (g/d)	700	230	1610
1st Breakfast	–	–	100
2nd Breakfast	–	100	120
Lunch	550	80	680
Snack	100	–	150
Dinner	50	50	560

the 'total menu portions' (n 4 measurements per diet). Two-way ANOVA for repeated measurements and t test for paired observations were applied for statistical evaluation (significance level: $P = 0.05$). Significance was adjusted for multiple comparisons by the Bonferroni procedure (three two-way comparisons, adjusted significance level: $P = 0.017$).

Results

A clear influence of diet on daily urinary I excretion was observed. Individual I excretion values with the diets are shown in Fig. 1. Renal 24 h I output was lowest with the lactovegetarian diet and significantly higher with the omnivorous diets N and P (Fig. 1; F value for the factor diet: 12.4, $P = 0.001$; initial diet N *v.* diet L, $P = 0.01$; diet P *v.* diet L, $P = 0.001$). Mean daily I excretion with the initial and the repeat diet N did not differ significantly (Fig. 1; $P = 0.51$) and both diet periods (N and repeat N) are therefore referred to in the following as diet N without further differentiation. The average daily urinary I excretion over all experimental diet periods was found to be 50.7 (SD 13.2) $\mu\text{g}/\text{d}$.

In accord with the I excretion data a markedly reduced I intake was confirmed analytically for diet L compared with diets N and P. With the latter diets the analysed daily I intakes were more than twice as high as the lactovegetarian diet. However, urinary I output clearly exceeded measured I intake with all three diets (Fig. 2). The average difference between measured I intake and measured urinary I excretion ranged from 15.0 to 21.0 $\mu\text{g}/\text{d}$. The I content as estimated from food composition tables (Souci *et al.* 1994) and the analysed I content were found to be nearly identical for diet

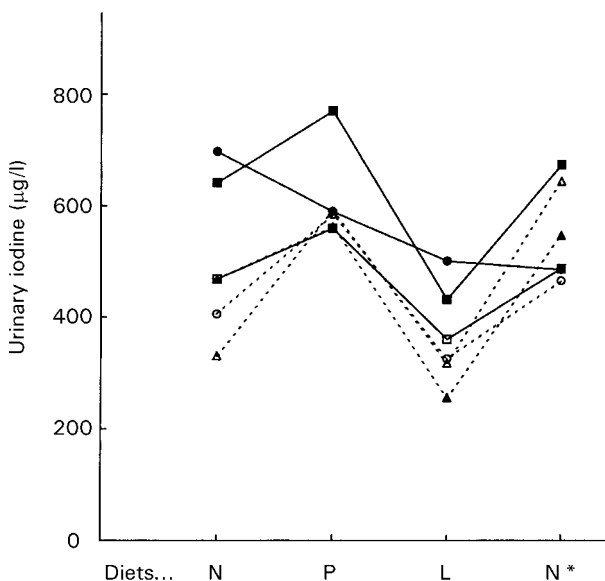


Fig. 1. Individual average 24 h iodine excretion rates for male (—) and female (---) subjects consuming different diets: normal (N; moderately protein-rich), protein-rich (P), lactovegetarian (L) and a repeat of the normal diet (N*). The average 24 h iodine excretion was obtained for each subject from the mean urinary output of the two 24 h specimens collected successively on days 4 and 5 of each diet period. For details of procedures, see p. 46.

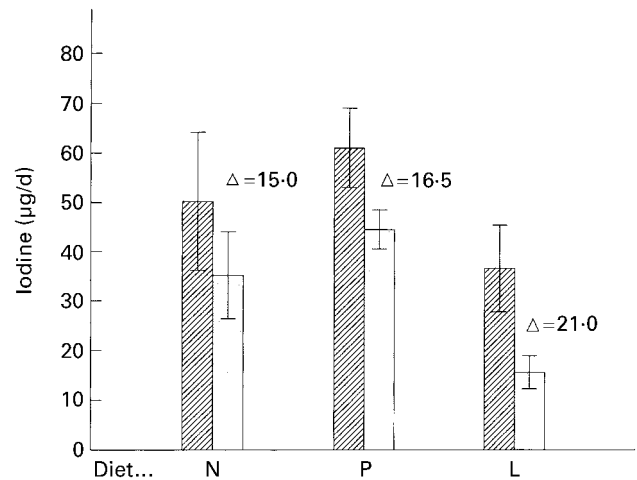


Fig. 2. Comparison of mean analysed iodine intake (▨; from four single measurements of separate representative samples of the total menus) and mean analysed urinary iodine excretion (▤) by six subjects consuming different diets: normal (N; moderately protein-rich), protein-rich (P) and lactovegetarian (L). Values are means with standard deviations represented by vertical bars. (Δ), Difference ($\mu\text{g}/\text{d}$) between mean iodine intake and mean iodine excretion. For details of diets, see Tables 1 and 2.

P, but for diets N and L clearly higher I levels were estimated from food tables than were measured analytically (results not shown).

Discussion

Indirect evidence of greater deficiency problems with vegetarian diets compared with meat-containing mixed diets might be seen in the fact that I deficiency is usually most prevalent in rural populations (Sullivan *et al.* 1997) which primarily consume plant foods. However, a low I concentration in the soil of the region affects the I concentrations of both plant and animal products. In industrialized countries I replacement in soil, but not in animal feed, is uncommon. In accord with this are the results of an American diet study in which the foods of typical market basket samples were analysed for their I content. The food groups potatoes, leafy vegetables, legume vegetables, root and miscellaneous vegetables, and fruits contributed only about 10 $\mu\text{g}/\text{d}$ to total I intake (Park *et al.* 1981). These data correspond with the very low I intake (16 $\mu\text{g}/\text{d}$) that was analytically determined for diet L (fruits and vegetables 1610 g/d) of the present study.

The use of food tables for the calculation of I intakes yielded a marked overestimation for diets N and L, i.e. for diets with high contents of fruits and vegetables. This overestimation of I content in the vegetable and fruit groups seems to be a particular problem related to those food tables (Holland *et al.* 1991; Souci *et al.* 1994) which contain I data at a relatively high level (as is appropriate for plants from regions with a high I content in the soil). Recently, Rauma *et al.* (1994) using regional Finnish food tables, calculated an average daily I intake in vegans of only 29 $\mu\text{g}/\text{d}$, whereas Draper *et al.* (1993) (using British tables) reported a nearly 3-fold higher I intake in vegans. Such discrepancies underline the importance of clearly

defined, analytically verified (experimental) data on I intake and excretion with different forms of nourishment in order to clarify whether certain vegetarian dietary practices might bear a health risk.

The average I excretion (calculated over all diet periods) was found to be low (i.e. about 50 µg/d). This low level is only, in part, attributable to the switch from a pre-experimental state of regular consumption of iodized table salt and occasional ingestion of sea fish (and/or sea food) to the experimental situation without consumption of any of these foodstuffs. However, the low average I excretion is primarily caused by the fact that none of the processed foods eaten by the participants with the experimental or the pre-experimental diets were enriched with I or contained iodized salt. This is due to the very restrictive German food legislation on iodization of foods which was in force until recently. In addition to this, the I content of German drinking water is very low (on average 5 µg/l; Manz, 1992), and German milk produced during the summer months contains less than 70 µg I/l as measured in our laboratory in exemplary samples collected in 1997.

The low overall urinary I output in our diet experiment is in accord with the results of large cross-sectional studies performed in Germany during recent years showing that until the mid 1990s Germany has been a classical I-deficient country with average urinary I excretion levels of 70 µg I/g creatinine in adults (Hampel *et al.* 1996) and 60 µg/d per 1.73 m² (standardized to the adult body surface area of 1.73 m²) in children (Remer & Manz, 1994b). Endemic goitre has been scientifically documented for decades and is still present in Germany (Delange *et al.* 1997; Hampel *et al.* 1997).

In the present diet experiment with its temporary cessation of sea fish and iodized salt consumption, a metabolic steady state (with a quantitatively balanced I intake and excretion) could not be achieved within each of the four experimental periods. This is clearly reflected in 24 h I excretion values exceeding the analysed daily I intake in all dietary periods. Obviously, during none of the short-term diet periods could absolute thyroid I uptake increase appropriately to compensate for the experimentally reduced I intake. Consequently thyroid I losses must have contributed to 24 h urinary I excretion and the actual dietary I deficit was more severe than reflected by urinary excretion data alone.

The measured average I intakes of 35 and 45 µg/d with diets N and P respectively, fell below the biological minimum requirements of healthy adults assumed to range between 50 and 80 µg/d (Meng, 1992). These findings again confirm that dietary practices which specifically exclude the use of iodized table salt and the consumption of fish, sea food, and processed I-enriched foods, put great pressure on thyroidal management of I balance. However, this pressure further increases if, apart from the previously mentioned foodstuffs, meat and meat products are also avoided (diet L, measured I intake < 20 µg/d). Among the various vegetarian regimens, followers of vegan and total vegetarian diets frequently adopt dietary practices which are comparable to the nutritional situation with diet L (except for the consumption of dairy products with the latter). Vegans (or total vegetarians) not only reject all animal products and processed foods but often reject iodized salt

as a processed product as well. Sea salt (containing virtually no I) is used as a 'natural product' instead.

Our results experimentally confirm literature findings (primarily based on food table-derived estimates) indicating that I supply is higher with non-vegetarian than with vegetarian diets. Specifically, the extremely low intake and urinary output of I as analytically determined for diet L, clearly demonstrate how unacceptably limiting the I supply can become when stricter forms of vegetarian dietary practices are followed. As long as alternative methods of I supplementation based on I replacement in soil are used only sporadically (Cao *et al.* 1994; DeLong *et al.* 1997) the I contents of fruits and vegetables will remain extremely low in most regions worldwide. Nutritionists and physicians should consider that strict vegetarians are possibly at risk of developing I deficiency disorders especially if anamnesis reveals that neither iodized salt nor iodine supplements (including seaweed preparations) are taken. In a group of North American total vegetarians who used only uniodized sea salt, significantly reduced serum I concentrations and clearly elevated thyroid stimulating hormone levels were detected with a prevalence of 25 %, and 12 % of the total group developed hypothyroidism (Crane *et al.* 1992). Further studies specifically investigating biochemical and clinical indicators of I status in strict vegetarians appear to be necessary.

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