Long-Term Consumption of a Raw Food Diet Is Associated with Favorable Serum LDL Cholesterol and Triglycerides but Also with Elevated Plasma Homocysteine and Low Serum HDL Cholesterol in Humans[1,2]

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ABSTRACT High consumption of vegetables and fruits is associated with reduced risk for cardiovascular disease. However, little information is available about diets based predominantly on consumption of fruits and their health consequences. We investigated the effects of an extremely high dietary intake of raw vegetables and fruits (70–100% raw food) on serum lipids and plasma vitamin B-12, folate, and total homocysteine (tHcy). In a cross-sectional study, the lipid, folate, vitamin B-12, and tHcy status of 201 adherents to a raw food diet (94 men and 107 women) were examined. The participants consumed ~1500–1800 g raw food of plant origin/d mainly as vegetables or fruits. Of the participants, 14% had high serum LDL cholesterol concentrations, 46% had low serum HDL cholesterol, and none had high triglycerides. Of raw food consumers, 38% were vitamin B-12 deficient, whereas 12% had an increased mean corpuscular volume (MCV). Plasma tHcy concentrations were correlated with plasma vitamin B-12 concentrations ($r = -0.450$, $P < 0.001$), but not with plasma folate. Plasma tHcy and MCV concentrations were higher in those in the lowest quintile of consumption of food of animal origin ($P_{trend} < 0.001$). This study indicates that consumption of a strict raw food diet lowers plasma total cholesterol and triglyceride concentrations, but also lowers serum HDL cholesterol and increases tHcy concentrations due to vitamin B-12 deficiency. J. Nutr. 135: 2372–2378, 2005.

KEY WORDS: • *raw food diet* • *vegetarian diets* • *vitamin B-12*

Dietary guidelines recommend a high intake of vegetables and fruits and a low intake of SFAs and cholesterol to reduce cardiovascular morbidity (1). In this context, a large body of evidence indicates that predominantly plant-based diets (vegetarian) can effectively contribute to the prevention of cardiovascular disease (CVD)[3] (2–5).

Vegetarian diets vary in the types of foods included. Semi- or partial vegetarians include small amounts of fish and chicken; ovo-lacto-vegetarians include milk, dairy products and eggs; lacto-vegetarians include milk and dairy products; and strict vegetarians (vegans) completely omit all foods of animal origin (6).

A further type of regimen, the so-called raw food diet, is even more restricted in food selection (7). The raw food movement originated in the Natural Hygiene movement in the United States (8,9). Many variants of these diets exist and there is no general definition (7). In all variants of the raw food diet, food is consumed predominantly or exclusively as uncooked and unprocessed raw food; the main components of the diet are fruits, nuts, seeds, and sprouted grains and beans (10). In the most popular variants of raw food diets in Germany, cereals and dairy products are completely omitted, and usually only a single food is eaten within the same meal, i.e., not mixed with other foods. Raw food diets can be practiced in several versions: ovo-lacto-vegetarian, vegan, or omnivorous (mixed raw food diets, including raw meat and fish) (11,12). Raw food diets are intended by the adherents to achieve better health and to prevent diseases such as cancer and CVD, although they have also been related to low bone mass (8,9,13,14). However, deficiencies of essential nutrients such as vitamin B-12, vitamin D, and iron may arise depending on the strictness of the regimen (11,12,15). In a recent meta-analysis of prospective studies, a higher mortality from coronary heart disease was observed in vegans than in ovo-lacto-vegetarians (16). Furthermore, results of several studies suggest that strict vegetarians have a high prevalence of elevated plasma total homocysteine (tHcy), which is considered to be an independent risk factor for CVD (17–24). Hyperhomocys-

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[3] Abbreviations used: ATP, Adult Treatment Panel; CVD, cardiovascular disease; MCV, mean corpuscular volume; tHcy, total homocysteine.

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teinemia is associated with endothelial dysfunction resulting from a reduced bioavailability of nitric oxide (NO), the major mediator of endothelium-dependent relaxation (25–28), which could provide one mechanistic explanation for the higher mortality from coronary heart disease in vegans.

Little information is available on the long-term effects of raw food diets on lipid profiles, vitamin B-12 status, and homocysteine concentrations, or on the effect of the degree of strictness of these diets on the respective nutritional variables. The "Giessen Raw Food Study" was designed to investigate the effect of diets in which 70–100% of all food is consumed as raw foods on several variables of nutritional status. The aim of the present study was to investigate the effect of varying types of vegetarianism (vegan, ovo-lacto-vegetarian, and mixed raw food diet including meat) on lipid profiles, vitamin B-12, and folate status and plasma tHcy as indicators of cardiovascular risk in raw food diets.

SUBJECTS AND METHODS

Study design and subjects. The study had a cross-sectional design. Dieters living in Germany who followed a raw food diet were recruited by advertisements in magazines, at congresses, and lectures as well as via self-help groups within the Natural Hygiene and raw food movement. Subjects were eligible if they were between 25 and 64 y of age, consumed at least 70% of total food intake as raw food, and had adhered to the raw food diet for at least 24 mo at the time of blood sampling. Smokers and subjects suffering from gastrointestinal diseases were excluded. The study was approved by the Ethics Committee of the Division of Human Medicine, University of Giessen, Germany. All participants gave written informed consent.

Baseline information and dietary intake. A detailed questionnaire was used to obtain baseline information (age, sex) and dietary habits (food preferences and avoidances, self-estimated amount of raw food consumed, and duration of raw food diet). In addition, before the blood sampling, dietary intake was assessed using a 7-d estimated and self-administered food record designed and validated for the present study. The food record included 236 food items subdivided into 12 food groups. Additionally, a table was provided in which nonlisted foods could be filled in by participants, to be subsequently relocated to the concerned food groups by the staff. Typical household measures and the corresponding portion size (in grams) were provided for every food item. Vegetable and fruit items discriminated between cooked and uncooked foods. The food record also assessed general information about the use of drugs and dietary supplements. To increase reporting accuracy and unambiguous classification of certain food items, the food record also provided colored photographs and detailed descriptions of portion sizes. Detailed oral and written instructions were given on how to complete the food record. The estimated food record was validated against a weighed food record in 72 raw food diet adherents who did not participate in the main study. The mean difference between estimated and weighed food record was between 2 and 10% for all nutrients; the correlation coefficients were 0.71–0.77 for macronutrients, and 0.48–0.82 for vitamins and minerals. For all nutrients, 63% of the participants were classified into the same tertiles. However, the calculated intake of energy and nutrients was slightly higher with the estimated than with the weighed food record.

Nutrient intake was calculated based on the German Food Code and Nutrition Data Base BLS II.2 (29), complemented with information from producers. Participants were classified according to: *1*) estimated proportion of raw food eaten (70–79, 80–89, 90–99, and 100% of total food consumption), and *2*) the type of animal foods omitted from their diet (mixed, ovo-lacto-vegetarian, and vegan raw food diet).

Blood analyses and BMI. Body weight was determined using an electronic calibrated scale to the nearest of 0.1 kg (Soehnle). Height was assessed with a GPM anthropometer to the nearest of 0.1 cm (Siber & Hegner). BMI was calculated as body weight (kg)/body height (m^2).

Venous blood was drawn from fasting subjects into both trace element–free vacutainers without anticoagulant and EDTA-containing vacutainers (Becton-Dickinson). Plasma and serum were separated from cells by centrifugation (2000 × *g* for 15 min) within 2 min of venipuncture and stored at −80°C until analyzed. Hemoglobin and erythrocyte indices [mean corpuscular volume (MCV) and RBC count] were determined using a Coulter Counter STKS (Beckman Coulter). Between-run CVs were 0.6% for MCV, and 1.1% for RBC count.

Plasma tHcy was measured using a reverse-phase HPLC method (30,31); for quantification, the samples were analyzed with and without the addition of a standard amount of tHcy, and the average response factors for the added tHcy were used to calculate the original concentration of endogenous tHcy in each sample. Recoveries in individual samples deviating >10% from the mean were rejected, and the measurement was repeated. The between-run CV for plasma tHcy was 4%. Plasma vitamin B-12 and plasma folate concentrations were determined using a commercial chemoluminescence assay kit (ACS 180, Bayer Vital). The between-run CV for plasma vitamin B-12 and plasma folate was 7.9%.

Serum lipids were analyzed by enzymatic photometric assays (CHOD-PAP method for cholesterol and GPO-PAP method for triglycerides) using a Hitachi 917 analyzer (Roche Diagnostics). HDL and LDL cholesterol were determined in the serum supernatant using homogeneous enzymatic colorimetric assays (Roche Diagnostics). The between-run CV was 1.5% for total cholesterol, 2.1% for LDL cholesterol and 2.6% for HDL cholesterol. LDL cholesterol was determined according to the Friedewald formula (32), and the ratio of LDL cholesterol to HDL cholesterol was calculated. Serum triglycerides were analyzed after hydrolysis of glycerol and fatty acids by the GPO-PAP method (ADVIA Trig, Bayer Healthcare). The between-run CV for triglycerides was 1.4%.

Statistical methods. Statistical analyses were performed using SPSS for Windows 12.0. Data are presented as medians with 25th and 75th percentiles in parentheses; differences with $P < 0.05$ were considered significant. Subgroups of raw food diet adherents were compared using the χ^2 test and ANOVA models. Linear trend tests were performed to estimate the effect of different proportions of raw food, as well as of foods of animal origin (mixed, ovo-lacto-vegetarian, and vegan diet). For associations between plasma vitamin B-12 and plasma tHcy, partial correlations adjusted for plasma folate are given. To determine the relation between consumption of food groups, intake of nutrients, and plasma lipid profiles and other biomarkers, multiple linear regression models were fitted with quintiles of intake as independent variables. Plasma vitamin B-12, plasma folate, and tHcy were log-transformed before analysis.

Blood lipids were classified according to the Adult Treatment Panel (ATP) III classification (33,34): total cholesterol levels < 5.2 mmol/L were considered as desirable, 5.2–6.2 mmol/L as borderline high and >6.2 mmol/L as high; LDL cholesterol levels < 2.6 mmol/L were classified as optimal, 2.6–3.4 mmol/L as near optimal, 3.4–4.1 mmol/L as borderline high, 4.2–4.9 mmol/L as high and >4.9 mmol/L as very high. Low HDL cholesterol levels were defined as <1.1 mmol/L for men and <1.3 mmol/L for women. Elevated triglyceride levels were defined as >1.7 mmol/L.

For plasma vitamin B-12, the following cutoff points were applied (35–37): vitamin B-12 concentrations < 150 pmol/L were defined as deficient, between 150 and 250 pmol/L as marginal, and >250 pmol/L as adequate. Elevated tHcy concentrations were defined as >16 pmol/L (38), and low plasma folate concentrations as <7 nmol/L (39).

RESULTS

Description of study population. A total of 1328 subjects expressed their interest in participating in the study and were sent a screening questionnaire by mail. Of 865 returned questionnaires, 293 were incomplete; of the remaining 572 subjects, 288 subjects consumed >70% of total food as raw food and were thus considered eligible for the study. Of these, 58 subjects were not interested in participating in the entire study, leaving 236 subjects who started the study; 35 subjects with incomplete data sets (missing food record and/or blood

sample) were excluded from the analysis, leaving 201 participants who completed the study.

Baseline characteristics and food consumption. The mean ± SD age of raw food dieters was 46 ± 11 y and mean BMI was 20.8 ± 2.5 kg/m^2. The median time of practicing a raw food diet was 3.5 y (minimum 2.2 y, maximum 38 y). Participants adhered to different variants of the raw food diet (**Table 1**). The majority consumed a mixed raw food diet including raw meat and fish (58%), 21% were ovo-lacto-vegetarians, and 21% consumed a vegan raw food diet. In terms of the proportion of raw food consumed, the majority of participants (75%) adhered to a strictly raw food diet, defined as >90% of total amount of food consumed raw.

Subjects consuming a mixed raw food diet consumed meat and fish in quite small amounts, and mostly uncooked (**Table 2**). By definition, ovo-lacto-vegetarian raw food diet adherents completely omitted meat and fish from their diet, whereas vegan raw food diet adherents also omitted milk, dairy products, and eggs. In the above groups combined, 95% of food was eaten raw, and 97% of all foods eaten were of plant origin. Fruits (1029–1313 g/d) but not vegetables (411–457 g/d) were the major food group consumed by all of the participants. The intake of bread, cereals, rice, legumes, and dairy products was negligible. Consequently, the raw food diet was low in energy and high in dietary fiber (~60 g/d). More than half of energy intake was derived from carbohydrates (~60%), ~30% from fat, and ~10% from protein. Fat was consumed mainly as PUFAs (58% of total energy) with only small amounts of SFAs (17% of total energy; **Table 2**). Dietary vitamin B-12 intake was <2.0 μg/d in 84% of subjects of all groups combined, in 72% of the mixed raw food dieters, 98% of the ovo-lacto-vegetarians, and all vegans (mixed vs. other: $P < 0.001$). Dietary folate intake was >400 μg/d in 72%, and <200 μg/d in 3% of all groups combined. Folate intake (>400 μg/d) did not differ among the groups.

TABLE 1

Baseline characteristics of raw food diet adherents[1]

Characteristic	Subjects
	n (%)
Age distribution, *y*	
25–34	46 (23)
35–44	46 (23)
45–54	54 (27)
55–64	55 (27)
BMI, *kg/m^2*	
<19	46 (23)
19–24	133 (66)
>24	22 (11)
Gender	
Male	94 (47)
Female	107 (53)
Proportion of food consumed raw,[2] %	
70–79	12 (6)
80–89	37 (19)
90–99	95 (47)
100	57 (28)
Type of raw food diet	
Mixed	115 (57)
Ovo-lacto-vegetarian	43 (21)
Vegan	
Smokers	0 (0)

[1] Based on $n = 201$.
[2] Proportion of weight of food.

Blood lipids. According to the ATP III (33,34) classification, 90% of participants had desirable total cholesterol concentrations, 10% were classified as being borderline high, and 1% as having high total cholesterol concentrations. LDL cholesterol concentrations were optimal in 52% of the participants, near-optimal in 34%, borderline high in 12%, and high in 2% of the participants. None of the participants had very high LDL cholesterol concentrations. HDL cholesterol concentrations were low in 46% of participants. None of the participants had elevated triglyceride levels. With an increasing proportion of raw food, a significant negative linear trend was observed for total and LDL cholesterol, but also for HDL cholesterol (**Table 3**). The ratios of total:HDL and LDL:HDL cholesterol as well as triglyceride levels did not differ among the groups with different amounts of total food consumed as raw food. Total, HDL, and LDL cholesterol, as well as ratios of total:HDL and LDL:HDL cholesterol and triglycerides did not differ among raw food diet adherents following a mixed, ovo-lacto-vegetarian, or vegan raw food diet (data not shown). Lipid profiles were optimal (LDL < 2.59 mmol/L, triglycerides < 1.69 mmol/L) in 50% of the participants. The proportions of subjects with optimal lipid profiles were similarly distributed among groups consuming different amounts of total food as raw food, as well as among mixed, ovo-lacto-vegetarian, and vegan raw food diet adherents. There was no association between the presence of optimal lipid profiles and the intake of single food groups or nutrients.

Plasma vitamin B-12, folate, and homocysteine. Three participants were also excluded from this analysis due to hyperhomocysteinemia (plasma tHcy > 100 μmol/L) of unknown origin; inclusion or exclusion of these subjects did not affect the results. In raw food diet adherents not using vitamin B-12 supplements, plasma vitamin B-12 and tHcy concentrations and MCV decreased according to the type of raw food diet, whereas plasma folate, hemoglobin, and hematocrit did not differ (**Table 4**).

Plasma vitamin B-12 concentrations were low in 41%, marginal in 38%, and adequate in 21% of the participants. Plasma tHcy concentrations were elevated in 51% of the participants. Vitamin B-12 deficiency, defined as low plasma vitamin B-12 and elevated plasma tHcy, occurred in 38% and MCV > 96 fl in 12% of participants. None of the participants had low plasma folate concentrations.

Vitamin B-12 supplements were used on a regular basis by 12 participants (data not included in Table 4). Plasma vitamin B-12 was higher and plasma tHcy was lower in subjects taking vitamin B-12 supplements than in participants not taking supplements. The plasma concentrations were 403.3 (257.9–1285.8) pmol/L for vitamin B-12, 39.4 (29.2–43.6) nmol/L for folate, and 12.9 (9.6–16.5) μmol/L for tHcy ($P < 0.001$).

The odds ratio for having vitamin B-12 deficiency (low plasma vitamin B-12 with elevated plasma tHcy concentration) was 5.4 (95% CI 2.1–13.8) for vegan and 3.1 (95% CI 1.4–6.9) for ovo-lacto-vegetarian raw food diet adherents, with mixed raw food diet adherents as the reference. The frequency of vitamin B-12 deficiency was independent of the proportion of food consumed raw (data not shown).

The main predictor of plasma tHcy was the dietary intake of vitamin B-12. No correlation was observed between plasma tHcy and folate intake. In a multiple linear regression analysis, plasma tHcy was correlated with plasma vitamin B-12 concentrations (partial $r = -0.450$, $P < 0.001$) (**Fig. 1**), but not with plasma folate (partial $r = -0.076$, $P = 0.295$). MCV was not related to plasma vitamin B-12, even after adjustment for plasma folate, serum ferritin, and transferrin.

A lower quintile of consumption of foods of animal origin

TABLE 2

Food consumption and nutrient intake in subjects according to the type of raw food consumed[1]

	Type of raw food diet			
	Mixed (n = 115)	Ovo-lacto-vegetarian (n = 43)	Vegan (n = 43)	P-value[2]
Food consumption, *g/d*				
Bread, cereal, rice, pasta	28 (0–88)	21 (0–21)	0 (0–13)	<0.001
Vegetables	411 (291–618)	427 (245–575)	457 (199–737)	0.827
Potatoes	0 (0–29)	0 (0–29)	0 (0–0)	0.001
Fruits	1313 (1031–1717)	1029 (749–1542)	1349 (918–2035)	0.391
Juice (fruit, vegetable)	0 (0–60)	29 (0–393)	0 (0–43)	0.720
Milk, yoghurt, cheese	4 (0–39)	6 (0–39)	0 (0–0)	<0.001
Meat, fish, eggs	11 (0–43)	0 (0–0)	0 (0–0)	<0.001
Raw meat, fish, eggs	0 (0–31)	0 (0–0)	0 (0–0)	<0.001
Total consumption	1974 (1599–2564)	1667 (1231–2050)	1851 (1372–2684)	0.298
Raw food consumption	1868 (1474–2335)	1514 (1136–2032)	1816 (1408–2665)	0.400
of plant food origin	1948 (1572–2354)	1632 (1228–1951)	1851 (1372–2684)	0.287
of animal origin	47 (22–96)	13 (5–47)	0 (0–0)	<0.001
Nutrient intake				
Energy, *MJ/d*	8.6 (6.7–10.7)	7.5 (5.4–9.2)	7.9 (5.8–10.0)	0.028
Carbohydrates, *g/d*	280.2 (200.5–362.7)	220.1 (160.2–291.2)	259.7 (174.1–337.1)	0.075
Total energy, %	56.2 (49.6–62.3)	53.1 (46.7–62.0)	58.9 (45.8–68.4)	0.266
Protein, *g/d*	30.0 (35.7–63.7)	36.8 (27.7–52.0)	39.0 (26.9–47.8)	<0.001
Total energy, %	8.8 (7.8–10.1)	8.4 (7.0–9.8)	8.2 (6.3–8.7)	<0.001
Fat, *g/d*	65.0 (48.9–84.6)	56.9 (42.2–76.5)	57.6 (26.2–101.3)	0.507
SFA, *g/d*	11.9 (8.6–17.3)	10.3 (7.4–14.2)	7.3 (3.5–13.7)	<0.001
MUFA,[3] *g/d*	15.8 (10.7–21.4)	13.5 (8.5–20.4)	14.2 (4.3–21.2)	0.444
PUFA, *g/d*	34.1 (24.7–46.6)	32.5 (23.0–46.2)	36.2 (18.4–58.1)	0.696
Total energy, %	30.9 (24.8–38.2)	35.2 (25.8–40.4)	30.3 (19.4–45.2)	0.624
Dietary cholesterol, *mg/d*	61.1 (31.0–102.2)	9.2 (1.7–29.9)	0.0 (0.0–0.0)	<0.001
Dietary fiber, *g/d*	58.1 (45.2–79.1)	59.5 (38.4–70.5)	59.0 (46.7–72.8)	0.943
Soluble	21.8 (16.0–26.6)	18.2 (14.1–23.2)	20.4 (16.2–29.2)	0.894
Nonsoluble	37.7 (30.8–51.0)	33.1 (25.2–40.6)	41.2 (30.0–54.0)	0.624
Vitamin B-12, *μg/d*	0.4 (0.0–1.2)	0.2 (0.0–0.7)	0.2 (0.0–0.6)	0.117
Folate, *μg/d*	476.7 (407.1–609.4)	457.7 (338.6–593.5)	518.4 (391.2–671.8)	0.602
Vitamin B-6, *mg/d*	3.0 (2.4–4.3)	3.0 (2.1–4.0)	3.3 (2.3–4.5)	0.354

[1] Values are medians (25th–75th percentiles).
[2] P for trend was calculated for the types of raw food diet.
[3] MUFA, monounsaturated fatty acids.

was associated with lower plasma vitamin B-12 ($P_{trend} < 0.001$) and higher plasma tHcy and MCV ($P_{trend} < 0.001$). For single food groups such as dairy products or meat and fish, there were no associations with plasma vitamin B-12, plasma tHcy, and MCV.

DISCUSSION

In Western and transitional societies, the increase in the prevalence of nutrition-related diseases such as the metabolic syndrome and CVD is a major health problem. Dietary factors are clearly linked to disturbances of lipoprotein metabolism (elevated LDL, elevated triglycerides, and low HDL cholesterol) leading to atherosclerosis, which is the main cause of CVD (40). Furthermore, elevated plasma tHcy and decreased plasma folate and vitamin B-12 are considered independent risk factors for CVD (22,34,41). To help prevent CVD, dietary recommendations focus on an increase in the daily consump-

TABLE 3

Serum lipids concentrations in subjects grouped by the proportion of raw food consumed[1]

	Proportion of raw food				
	70–79% (n = 12)	80–89% (n = 37)	90–99% (n = 95)	100% (n = 57)	P-value[2]
Total cholesterol, *mmol/L*	4.4 (3.9–5.1)	4.2 (3.8–4.7)	4.2 (3.5–4.8)	4.0 (3.5–4.4)	0.009
LDL cholesterol, *mmol/L*	2.7 (2.1–3.4)	2.7 (2.3–3.1)	2.6 (2.1–3.1)	2.4 (1.9–2.8)	0.031
HDL cholesterol, *mmol/L*	1.5 (1.2–1.6)	1.2 (1.1–1.4)	1.2 (0.9–1.5)	1.2 (0.9–1.4)	0.018
Triglycerides, *mmol/L*	0.6 (0.6–1.0)	0.7 (0.5–1.0)	0.7 (0.6–1.0)	0.8 (0.6–0.9)	0.181
Total:HDL cholesterol	3.2 (2.5–3.7)	3.2 (2.9–4.1)	3.5 (2.8–4.3)	3.6 (2.7–4.3)	0.159
LDL:HDL cholesterol	1.9 (1.3–2.5)	1.9 (1.7–2.6)	2.1 (1.6–2.9)	2.1 (1.5–2.7)	0.326

[1] Values are medians (25th–75th percentiles).
[2] P for trend was calculated for the proportion of raw food.

TABLE 4

Plasma vitamin B-12 status and related variables in subjects according to type of raw food consumed[1,2]

	Type of raw food diet			
	Mixed (n = 109)	Ovo-lacto-vegetarian (n = 38)	Vegan (n = 39)	P-value[3]
Plasma vitamin B-12, *pmol/L*	174.5 (142.2–249.8)	143.2 (121.2–175.9)	126.2 (87.8–182.3)	<0.001
Plasma folate, *nmol/L*	34.8 (24.0–46.4)	35.7 (26.1–46.4)	40.5 (28.5–46.4)	0.032
Plasma tHcy, *μmol/L*	14.7 (11.9–18.3)	17.1 (13.1–20.2)	18.5 (13.5–28.9)	<0.001
Hemoglobin, *g/L*	137 (131–144)	137 (129–144)	134.5 (130–144.7)	0.622
Hematocrit	0.41 (0.39–0.43)	0.41 (0.39–0.43)	0.41 (0.39–0.44)	0.906
MCV, *fL*	91.0 (89.0–94.0)	90.0 (87.5–93.0)	93 (90.7–98.0)	0.001

[1] Participants not using vitamin B-12 supplements (n = 186).
[2] Values are medians (25th–75th percentiles).
[3] P for trend was calculated for the types of raw food diet.

tion of vegetables and fruits to at least 400 g or 5 portions (1). Epidemiologic prospective studies suggest that an increase of 1 portion of vegetables/fruits each day is associated with a 6% lower risk or ischemic stroke (42). However, there is little information about the effect of an extensive consumption of fruits and vegetables on dietary risk factors of CVD. To obtain more information, we examined the effects of a diet with raw fruits and vegetables as the major constituents (1500–1800 g/d or 18–22 portions/d) on blood lipids, plasma tHcy, folate, and vitamin B-12.

Raw food diets are extreme dietary regimens that have not been investigated extensively (11,43–46). To our knowledge, the Giessen Raw Food Study is the only study worldwide to date that examined a relatively large number of individuals following a strict raw food diet for a prolonged period of time (11). Two earlier reports examined the vitamin B-12 status of a small cohort (n = 49) of individuals following the so-called "Hallelujah diet," a strict vegan diet composed mainly of raw fruits and vegetables (46), and the lipid and hematological profile of 12 subjects following a "living food diet," a strict uncooked vegan diet (47). According to dietary guidelines for the general population and as adapted for vegetarians, foods rich in complex carbohydrates such as cereals and potatoes, and fat from vegetable oils and nuts, should provide the main dietary sources of energy (48–52). However, these foods were almost completely omitted by the raw food dieters and replaced by fruits and vegetables. Interestingly, despite this discrepancy, the macronutrient ratio of the different raw food diets (~58 energy% carbohydrates, 9 energy% protein, and 33 energy% fat) was remarkably close to the dietary recommendations (>50 energy% carbohydrates, 8–10 energy% protein, and 30 energy% fat) (51). Fat intake in raw food dieters was markedly lower than in the average Western diet, and slightly lower than that reported in other strict vegans in the UK (53) and Finland (47).

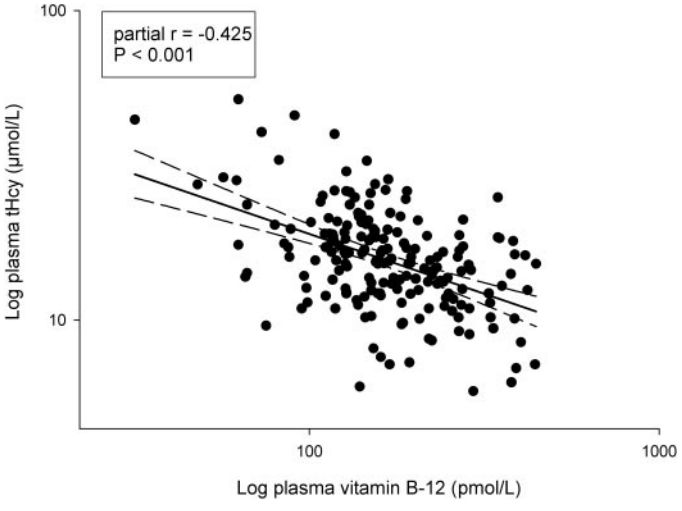

FIGURE 1 Relation between plasma vitamin B-12 and plasma tHcy in raw food diet adherents (n = 186). The partial correlation coefficient adjusted for plasma folate is shown.

The dietary cholesterol intake in our study population was also low in all variants of the raw food diet. The low triglyceride and total cholesterol levels in serum may reflect the low fat intake and the low BMI of these raw food diet adherents. Several studies with lacto-vegetarians reported favorable lipid profiles compared with individuals following conventional diets (3,54,55). However, to our knowledge, there have been no other reports of such extremely low triglyceride and total cholesterol levels. Nevertheless, despite the negative trend for total and LDL cholesterol with increasing proportions of raw food, the total:HDL and LDL:HDL cholesterol ratios and the triglyceride levels were not associated with the amount of raw food consumed or the variant of the raw food diet. Thus, consumption of greater amounts of raw food did not improve the LDL:HDL cholesterol ratio. These results indicate that an extremely high consumption of raw food does not positively affect lipid profiles. Moreover, 46% of raw food dieters had low HDL cholesterol; in fact, those concentrations were lowest in the group of participants who ate the greatest amount of raw food.

When the cardioprotective effects of HDL cholesterol are attributed to its role in reverse cholesterol transport, this finding is less relevant for raw food diet adherents, considering the overall low health risk and the low total cholesterol concentrations in this specific population. Nevertheless, there is increasing evidence that the severity of the formation of atherosclerotic lesions in humans is inversely related to HDL cholesterol concentrations (56). HDL particles stimulate endothelial nitric oxide synthase. In this process, the presence of apolipoprotein A-I and the scavenger receptor, class B, type I is also essential (57). The endothelium-derived NO is a key mediator of vasomotor tone and an important protective molecule, which also modulates platelet and leukocyte adherence to the endothelium as well as endothelial cell proliferation and

migration (58,59). Therefore, the very low HDL cholesterol observed in the present study may be of special importance considering the accompanying high concentrations of tHcy observed in the raw food diet adherents.

The vitamin B-12 supply is a critical point in strict plant-based diets due to the complete avoidance of animal products. Low plasma vitamin B-12 concentrations together with increased plasma tHcy concentrations and MCV, and low hemoglobin concentrations are classified as stage III of vitamin B-12 deficiency (60). Low plasma vitamin B-12 combined with elevated plasma tHcy was reported in studies of strict vegetarians (21,37) and in ethnic groups consuming mainly plant-based diets (19,20). In our study, the type of raw food diet was related to plasma vitamin B-12 and plasma tHcy levels, with the lowest vitamin B-12 and the highest tHcy concentrations present in the vegan raw food diet adherents. Nearly half of all raw food diet followers had a functional vitamin B-12 deficiency defined as low plasma vitamin B-12 in combination with elevated plasma tHcy. This observation was accompanied by elevated MCV in vegan raw food diet adherents. Although elevated MCV and tHcy concentrations can be due to vitamin B-12, folate, or vitamin B-6 deficiency, the folate and vitamin B-6 intake of the raw food diet adherents in our study (532 μg/d folate and 3.3 mg/d vitamin B-6) by far exceeded the recommended dietary reference intakes for folate of 400 μg/d and for vitamin B-6 of 1.6 mg/d (39), indicating that the increased MCV and tHcy concentrations were due exclusively to vitamin B-12 deficiency.

This was confirmed by multivariate analyses, which showed that plasma tHcy concentrations were explained solely by plasma vitamin B-12, and not by plasma folate concentrations. In addition, the subgroup of raw food diet adherents who used vitamin B-12 supplements on a regular basis had higher plasma vitamin B-12 and lower plasma tHcy concentrations than nonusers. Achieving an adequate folate intake with conventional diets or even in well-balanced plant food diets may be difficult (61), but as observed in our study, strict raw food diets contain adequate amounts of dietary folate due to an exceptional high consumption of fruits and vegetables. Nevertheless, the present study suggests that a strict raw food diet is accompanied by a high risk of elevated tHcy due to functional vitamin B-12 deficiency. Recent studies suggest that even a mild elevation of plasma tHcy to concentrations between 10 and 15 μmol/L is associated with an increased risk of CVD and stroke (24).

The vitamin B-12–dependent enzyme methionine synthase catalyzes the major pathway for homocysteine remethylation. This reaction is also folate dependent. In experimental hyperhomocysteinemia, an impaired vasodilation mediated by the endothelium-derived NO was observed (25). Furthermore, several other complex factors such as asymmetric dimethylarginine, oxidative damage, cytokine release, and an increased prothrombotic environment may contribute to hyperhomocysteinemia (62,63).

The results of the present study have to be interpreted with some caution because of the cross-sectional design of the study. Although it might be interesting from a scientific point of view to confirm the presented results in a large prospective study, it would appear ethically impermissible to perform such a study in view of the present quite alarming results.

In conclusion, the present study indicates that a strict raw food diet may result in remarkably low serum total cholesterol and triglyceride concentrations. However, the elevated tHcy as well as the low HDL cholesterol concentrations in participants in this study could provide a mechanistic explanation of the higher mortality from coronary heart disease in vegans compared with ovo-lacto-vegetarians, which was reported in a recent meta-analysis of prospective studies (16). A high tHcy concentration accompanied by a low HDL level may result in endothelial dysfunction via impaired bioavailability of NO. In contrast, studies of moderate ovo-lacto-vegetarian diets suggest that well-planned vegan and other types of vegetarian diets are appropriate for all stages of the life-cycle including during pregnancy, lactation, infancy, childhood, and adolescence and reduce risk for diseases (49). Changing the ratio of raw food intake toward an extreme regimen with a very low intake of vitamin B-12 may be harmful in the prevention of coronary heart disease rather than providing additional benefits as occurs with milder dietary regimens.

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