

UNCOOKED, LACTOBACILLI-RICH, VEGAN FOOD AND RHEUMATOID ARTHRITIS

M. T. NENONEN, T. A. HELVE,* A.-L. RAUMA and O. O. HÄNNINEN

Department of Physiology, University of Kuopio and *Kivelä Hospital, Helsinki, Finland

SUMMARY

We tested the effects of an uncooked vegan diet, rich in lactobacilli, in rheumatoid patients randomized into diet and control groups. The intervention group experienced subjective relief of rheumatic symptoms during intervention. A return to an omnivorous diet aggravated symptoms. Half of the patients experienced adverse effects (nausea, diarrhoea) during the diet and stopped the experiment prematurely. Indicators of rheumatic disease activity did not differ statistically between groups. The positive subjective effect experienced by the patients was not discernible in the more objective measures of disease activity (Health Assessment Questionnaire, duration of morning stiffness, pain at rest and pain on movement). However, a composite index showed a higher number of patients with 3–5 improved disease activity measures in the intervention group. Stepwise regression analysis associated a decrease in the disease activity (measured as change in the Disease Activity Score, DAS) with lactobacilli-rich and chlorophyll-rich drinks, increase in fibre intake, and no need for gold, methotrexate or steroid medication ($R^2 = 0.48$, $P = 0.02$). The results showed that an uncooked vegan diet, rich in lactobacilli, decreased subjective symptoms of rheumatoid arthritis. Large amounts of living lactobacilli consumed daily may also have positive effects on objective measures of rheumatoid arthritis.

KEY WORDS: Rheumatoid arthritis, Vegan food, Activity index, Vitamin B12, Sodium excretion, Lactobacilli.

PATIENTS with rheumatoid arthritis (RA) often claim that their symptoms are alleviated by a special diet or by simple elimination of certain constituents from their free-choice diet. Foods most often linked with worsened symptoms are red meat, spices, flour products, citrus fruits, chocolate and alcohol [1]. Improving symptoms have been reported with vegetables, oils and fish [1]. True food allergy seems uncommon in patients with RA [2]. Fasting is an effective treatment of the symptoms of RA, but most patients relapse on reintroduction of food [3, 4].

Haugen *et al.* [5] have collected data from patients suggesting that extreme vegan diets have alleviated their rheumatic symptoms. 'Living food' teachers and consumers have also reported beneficial effects of the diet [6–8]. 'Living food' is an uncooked vegan diet, rich in lactobacilli, which contains no animal products, raffinated substances or added salt. A detailed description of the diet is presented by Hänninen *et al.* [7]. The majority of food items are soaked and sprouted (seeds and grains), and many are fermented. Some items are blended and dehydrated (bread). Fermented products contain high amounts of various lactobacilli [9]. Fermentation and mechanical processing distinguish this diet from other vegan diets.

Finnish RA patients often consume a deficient diet. Rauma *et al.* [10] have found that their calculated intakes for energy, iron, zinc and niacin were lower than those in healthy persons. Shifting to a 'living food' diet in the present study significantly increased the daily intakes of energy (6.6 MJ to 8.9 MJ, $n = 13$). The calculated daily intakes of iron (13 mg to

26 mg, $n = 13$), zinc (9 mg to 18 mg, $n = 13$) and niacin (11 mg to 19 mg, $n = 13$) increased during the intervention. There was also an increase in the intakes of vitamins C and E [10].

Kjeldsen-Kragh *et al.* [11] have reported positive effects of fasting and 1 yr of a vegetarian diet in RA. Their patients were mainly in functional group II and had only mild medication. In their study, there was a high drop-out rate (35%), most (22%) due to flare-up of arthritis symptoms. Kjeldsen-Kragh [12] summarizes the studies of the group, stating that the beneficial effect of the dietary treatment was perhaps not related to the diet *per se*, but was caused by alterations in the microflora secondary to changes in the diet.

Alterations of intestinal bacterial flora may play a role in RA. The composition of the intestinal flora of patients with RA seems to differ from that of healthy subjects [13]. Uncooked vegan food increases the counts of faecal lactobacilli in the healthy population [14] and in rheumatoid patients [9]. Peltonen *et al.* [15] have shown that a change in the faecal microflora was connected with decreasing activity of RA in the above-mentioned 1 yr intervention with vegan and vegetarian diets [11].

Our previous studies [7, 8] have shown anecdotal evidence of positive effects of the extreme, uncooked, vegan diet ('living food') in RA. The aim of the present study was to investigate subjective and objective effects of this diet on chronic RA, and to select possible therapeutic components of the diet for further studies.

SUBJECTS AND METHODS

Subjects

Forty-three consecutive adults with diagnosed (ARA criteria; [16]), chronic and active RA (Steinbrocker's functional class II–III; [17]) visiting the Rheumatic

Submitted 23 October 1996; revised version accepted 2 July 1997.
Correspondence to: M. Nenonen, National Research and Development Centre for Welfare and Health, PO Box 220, FIN-00531 Helsinki, Finland.

Outpatient Clinic at the Kivelä Hospital, Helsinki, Finland, were selected for the study. There were no refusals. All selected patients had active joint symptoms (more than three swollen or five tender joints) and elevated inflammatory parameters [erythrocyte sedimentation rate (ESR) > 20 mm/h, or C-reactive protein (CRP) > 10 mg/l]. Patients were randomized into two groups. The intervention group started the experimental diet and the control group continued their previous omnivorous diet. Three intervention patients could not eat all of their diet, and two of them refused to continue in the study after a few weeks; one stopped later. One suffered abdominal pains and distension. One patient from the control group stopped the study for personal reasons, and one died of a heart attack just after the 3 month follow-up period had ended. Their data are used where adequate, no extrapolations were made.

One intervention subject with high sodium excretion (diet non-compliance) and one patient from the control group (because of medication-induced hepatic toxicity) were excluded from analyses of interfering variables. None were hospitalized and all patients continued their previous medication at the beginning. The medication was modified when necessary on clinical grounds (by rheumatologist TAH). Caffeine-containing drinks, chocolate, alcohol and tobacco smoking were prohibited in both groups.

The duration of the intervention was planned to be 3 months, but eight patients had to stop their intervention diet after 2 months because of nausea, diarrhoea ($n = 3$) or difficulties with the taste of some food items. The controls stopping the follow-up after 2 months were selected to match these intervention subjects by age, sex, disease activity and body mass index. There were no differences between the 2 and 3 month intervention groups, and the duration of the intervention had no effects on the clinical outcome. The basic data of the subjects are presented in Table 1.

Diet

The 7 day dietary records were collected by a qualified dietitian three times: the first before the intervention, the second in the middle, and the third at the end of the intervention. Subjects in the dietary intervention group received all the components of their daily diet from a specialized 'living food' kitchen in packed form. The kitchen weighed the components, and the subjects recorded items they did not consume and the amount of extra food. Subjects were supervised and tutored daily by the teacher of the 'living food' diet. The patients in the control group prepared their omnivorous meals at their homes without tutoring.

The nutrient contents of the diets were calculated with UNIDAP (Unilever Dietary Analysis Program, Paasivaara Ltd, Finland), and the results have been published separately [10]. The dietary compliance of the intervention group was followed by daily interviews, dietary records and by analysing their

daily urinary sodium excretion. Accurate use of the intervention diet [7] causes a decrease in urinary sodium excretion to less than one-third part.

Clinical follow-up

One rheumatologist (TAH) carried out the clinical evaluation blindly. The patients filled in questionnaires recording their subjective experiences and gastrointestinal functions on the 0–10 scale at the beginning, in the middle, and at the end of the dietary intervention. This questionnaire has been modified from the questionnaires used in our previous studies [7]. It is a modification of a visual analogue scale (VAS) with a numbered scale. Patients were interviewed after the study, and their experiences were collected by a structured discussion. Three months after the study period, their impressions about the effects were recorded again with the 0–10 scale.

Laboratory analyses

Fasting blood, daily urine and faecal samples were collected according to normal laboratory practice. Samples for the intervention period were collected: (1) before the dietary intervention (weeks -1 and 0); (2) after the first month (weeks 4–5); (3) at the end of the intervention period (weeks 8–9 or 12–13); and (4) 3 months after the intervention period. Most of the analyses were carried out immediately. The samples analysed later were stored at -20°C . The analyses were carried out with normal laboratory methods used in the hospital.

Statistical methods

The normality of interval variables was checked by calculating the Shapiro–Wilk statistic W , and data were scrutinized for outliers. The data for C-reactive protein (S-CRP) and the duration of morning stiffness deviated intolerably from the normal distribution, and normal scores calculated from the ranks [18] were used in statistical analysis. Analyses were performed with MANOVA for repeated measurements [19] using different combinations of independent variables and change in weight as a percentage as covariate.

The overall changes in the disease activity were analysed with a composite index described by Paulus *et al.* [20]. The index was calculated from the changes in the following six variables: ESR, number of swollen joints, number of tender joints, rheumatic pains on a VAS, HAQ and global patient estimate. A decrease or increase of 20% or more was estimated as significant and the number of significantly changed variables was calculated for each patient. Changes in ESR within normal values and <5 mm/h were judged as non-significant. Zero values as divisor were replaced by 0.01, and the clinical relevance and significance of the change in percentage was checked individually in these events. Separate indices were calculated for improved and deteriorated variables. The percentage of each

TABLE I

Test statistics (A), anthropometric data (B), history (C) and medication (D) of rheumatic disease and compliance with the diet of the intervention and control groups (E) in the 2 to 3 month intervention study with an extreme vegan diet, 'living food'. Interval data are given as means and s.d.

	Intervention group		Control group		Difference Intervention vs control
	Mean or number	s.d.	Mean or number	s.d.	
A. Test statistics					
Randomized for study	22		21		
Started the study	22		20		
Completed the study	19		20		
Follow-up after study	19		19		
Duration of test (2/3 months)	8/11		8/12		n.s.*
B. Anthropometric data					
Sex: male/female	1/18		1/19		n.s.*
Age (yr)	49.1	7.1	55.6	10.8	$P = 0.02$ †
Height (cm)	163.4	5.0	164.3	7.4	n.s.†
Weight (kg)	68.0	10.4	63.6	11.8	n.s.†
Body mass index (kg/m ²)	25.5	4.1	23.5	3.5	n.s.†
On pension	6		12		n.s. ($P = 0.06$)*
C. History of rheumatic disease					
Rheumatic disease (yr)	12.6	10.3	16.1	13.6	n.s.†
Seropositive disease	15		14		n.s.*
D. Medication					
Gold (i.m. or p.o.)	4		6		n.s.*
Methotrexate	10		5		n.s.*
Sulphapyridine	2		3		n.s.*
Steroids	10		9		n.s.*
Non-steroidal anti-inflammatory drugs	16		18		n.s.*
E. Dietary compliance					
Strict dietary compliance	10				
Use of fermented wheat drink daily	6	(500–1000 ml/day) (only 5 patients used the fermented wheat drink daily and had a strict compliance with other food items)			

*Fisher's exact test.

†*t*-test.

number of variables within the intervention and control groups was compared with Fisher's exact test.

The Disease Activity Score (DAS) was calculated as described by the European League against Rheumatism (EULAR; [21]). The stepwise regression analysis was used to build models explaining the changes in disease activity described by DAS. Maximum R^2 improvement, minimum R^2 improvement, stepwise and backward elimination methods were used. Medication, diet, disease history and anthropometric data served as independent variables.

The power of significance of the tests was calculated from the nomogram presented by Altman [22]. For a 30% change in most variables, the statistical power was >0.5 at a significance level of 0.05. On pains at rest, HAQ, morning stiffness, Ritchie indices, ESR, alanine (ALAT) and γ -glutamyl (γ -GT) transferases, this power was achieved for 50% changes. The variation in CRP was so high that the power to detect a 50% change was only 0.25. The subjective estimates of patients were analysed by Mann-Whitney *U*-test.

RESULTS

Patients

The randomization divided subjects into intervention and control groups with no difference in height, weight, body mass index, duration of rheumatic disease, seropositivity and medication. Yet the intervention group was younger (49 vs 56 yr, $P = 0.02$) (Table I). The dietary compliance in the intervention group was good, as shown by the urinary excretion of sodium. Only one patient lacked a clear decrease. However, only six of the 19 subjects used all their fermented wheat drink (Rejuvelac) daily (recommended amount 500–1000 ml). According to the daily records, nine patients had minor deviations from the diet. The diet of the control group remained stable during the intervention period. However, some started to use minor amounts of 'living food' items. The patients could keep the secret and the clinical observer (TAH) remained blinded during the follow-up. All were on stable medication and continued with least possible changes (decrease of medication for six patients in the interven-

tion and for three patients in the control group, increase of medication for one control patient).

The intervention group lost weight, ~9%, during the intervention, while the controls gained ~1% of weight. The difference in the weight changes between the groups was significant ($P = 0.0001$) and was not explained by medication when tested separately for methotrexate, gold and steroids (Fig. 1).

Laboratory values

Serum alkaline phosphatase ($P = 0.01$) and alanine aminotransferase (0.002) decreased in the intervention group. The change in weight as covariate abolished the significance of these changes. Serum protein values in the intervention group were significantly lower at the end of the intervention than before it ($P = 0.04$). The decrease in protein levels was seen in patients on methotrexate treatment ($P = 0.05$) independently of the diet. Albumin levels decreased in both groups with no effect of diet ($P = 0.005$).

Serum vitamin B12 levels decreased in the intervention group ($P = 0.0006$). Values already differed after 4–5 weeks ($P = 0.02$). This decrease was strongest in the most compliant diet subgroup (used the diet with no aberrations and consumed all the fermented wheat drink daily). Their values decreased from 308 to 179 pmol/l (P for combined effect of accuracy of diet and use of drink = 0.05). Serum calcium (corrected for serum protein) decreased in both groups ($P = 0.0001$). Serum sodium ($P = 0.0001$) levels decreased in both groups in the first half of the intervention. Daily excretion of sodium decreased ($P = 0.0001$) to one-fourth of the pre-test level in the dietary intervention group, whereas excretion of potassium increased ($P = 0.02$).

Subjective effects

Most patients in the dietary intervention group experienced positive subjective changes during the intervention diet in rheumatic pains, rheumatic joint swelling, morning stiffness and general impression (Table II). Most of the control group experienced no change. The difference was statistically significant (Mann–Whitney U -test, $P < 0.03$). When the intervention was over, the majority of intervention patients reported either no change or a negative change in the above-mentioned parameters ($P < 0.01$), except the ability to move. Correlation analysis showed that the subjective estimates of disease activity were mainly dependent on the number of tender joints (Pearson correlation coefficients 0.41–0.6, $P = 0.02$ –0.0001).

Activity measures of rheumatoid arthritis

CRP, ESR, B-haemoglobin, B-thrombocyte count, Ritchie index, HAQ, morning stiffness, VAS for pains at rest and on movement did not behave statistically differently in the intervention and control groups. The steroid users in both groups had an 18% lower number of tender joints ($P = 0.02$) with a decrease at the end of the study and 40% lower swollen joint numbers ($P = 0.002$). The CRP values of the intervention group

had a rising tendency at 3–6 months after intervention ($P = 0.15$) (Fig. 1). ESR increased during the intervention period in both groups. This rise was seen in methotrexate users (40%, $P = 0.03$), and it was independent of the intervention diet.

Composite indices

The composite index, after Paulus [20], for changes in disease activity showed in the intervention group an improvement of 20% or more in 2.9 variables (s.d. 1.7). In the control group, only 2.0 variables improved (s.d. 1.3, $F = 3.79$, $P = 0.059$, ANOVA). There were no differences in the mean amounts of deteriorated variables (1.4 vs 1.6). The percentage of patients with three ($P = 0.025$), four ($P = 0.076$) and five ($P = 0.05$) improved variables was greater in the intervention group (Fig. 2). This difference was nearly significant ($P = 0.056$ –0.1) even when the data were analysed according to the intention to treat principle. The percentage of patients with one or two deteriorated variables was not higher in the intervention group.

A decrease in disease activity, as measured as a change in the DAS [21], during the intervention was associated in a stepwise regression model ($R^2 = 0.48$, $P = 0.02$) with increasing daily amounts of wheat grass drink and fermented wheat drink, increased intake of dietary fibre, and decreased intake of iron during the intervention, and no need for gold, methotrexate or steroid medication at entry (Table III). In the intervention group as a whole, the changes in DAS were not statistically significant (given as mean/95% confidence interval at the beginning, in the middle, at the end and 3 months after: 3.26/2.88–3.63, 3.12/2.73–3.50, 3.01/2.54–3.48 and 3.13/2.70–3.57 in the intervention group, and 3.44/2.94–3.94, 3.45/3.00–3.90, 3.46/3.02–3.90 and –3.56/3.18–3.94 in the control group, respectively; $P = 0.7$, MANOVA for repeated measures).

DISCUSSION

This study showed that an uncooked vegan diet rich in lactobacilli, 'living food', caused subjective improvement in the symptoms of RA. The objective measures of disease activity did not change when analysed separately. Two indices describing the activity of RA were used to analyse the results (composite index by Paulus, DAS by van der Heijde). Both indices showed a therapeutic effect of the dietary intervention with 'living food' or an effect of some of its components on the symptoms of RA.

The following group of dietary factors was partially (48%) responsible for the observed decrease in the disease activity index: fermented wheat drink, wheat grass drink, dietary fibre and iron. These factors are indicators of compliance with the 'living food' diet. Fermented wheat drink (Rejuvelac, [6]), the water phase of germinated wheat seeds and water (1:3) mixture (fermented for 48 h with freshly cut wheat

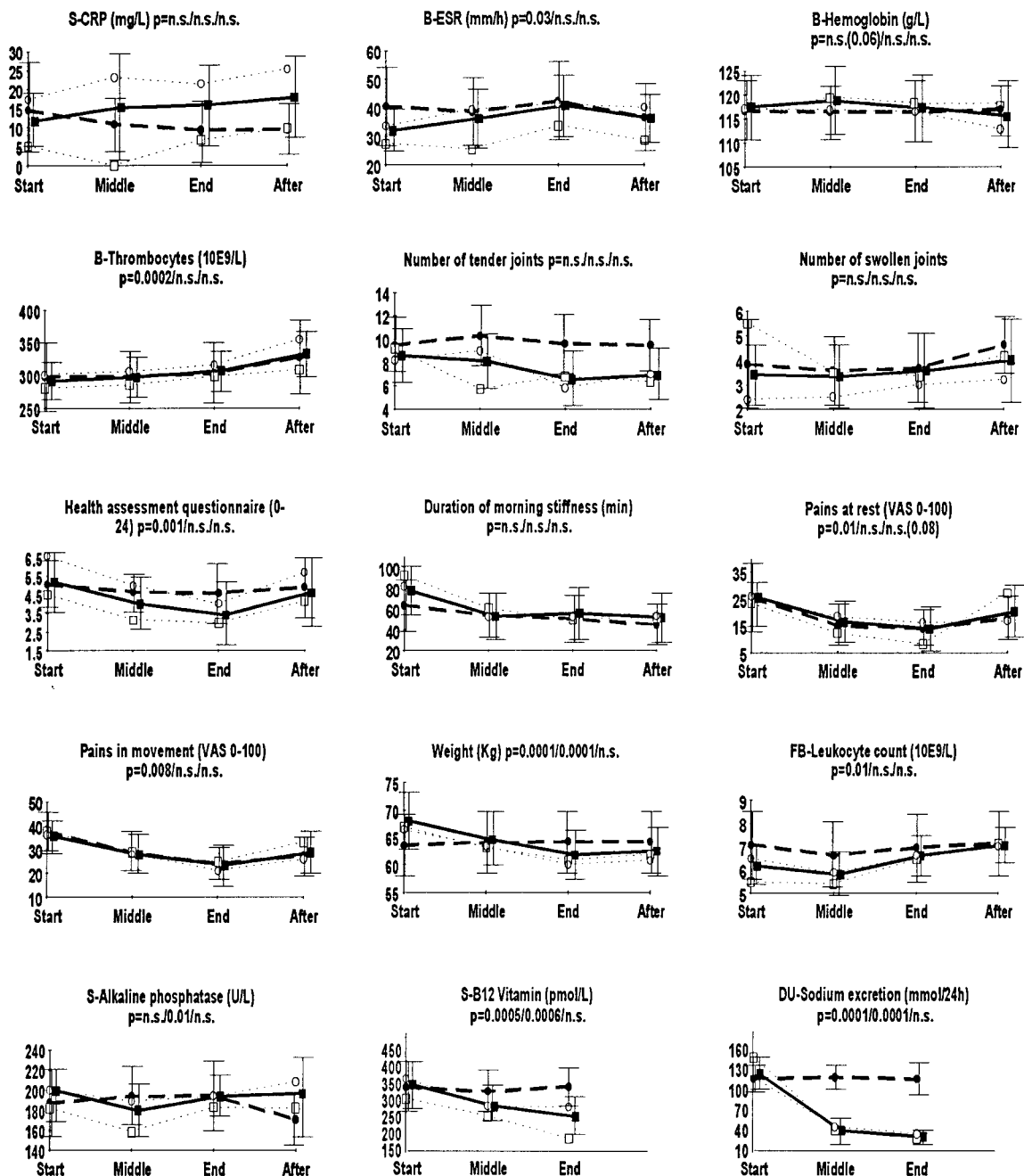


FIG. 1.—The results of the clinical and laboratory follow-up of the intervention and control groups in the 2 to 3 month intervention study in rheumatoid arthritis patients ($N = 39$) randomized to either intervention group starting an extreme vegan diet, 'living food', for 2–3 months and omnivorous controls. Data were collected during and 3 months after the dietary intervention. Periods used in the figures are: Start, at the beginning of the intervention; Middle, in the middle of the intervention; End, at the end of intervention (2 to 3 months); After, 3 months after the intervention. Data are given as means and 95% confidence interval (95% CI). Intervention group, —■—; control group, --●--; regular use of fermented wheat drink, ...□...; no regular use of fermented drink, ...○... Statistical significance (MANOVA for repeated measurements) is given as P values for the effects of time alone/effects of division to intervention vs control groups/effects of consuming fermented wheat drink.

grass), gives large amounts ($2.4-4.5 \times 10^{10}$ /day) of viable *Lactobacillus plantarum* and *L. brevis* strains [9], and it modifies the intestinal microflora. The counts of faecal lactobacilli were higher in the intervention group [9] and their faecal β -glucuronidase activity decreased during the study ($P = 0.04$, MANOVA for repeated measurements). Lactobacilli have many

effects on other bacteria in the gut and regulate their number [23–25]. The role of lactobacilli is further supported by the findings of Peltonen *et al.* [15] and Eerola *et al.* [26]. They found that in both the study of Kjeldsen-Kragh [11] and in this intervention, the positive clinical effect was associated with a change in the colonic microflora.

TABLE II

The subjective estimates of the rheumatoid patients about their disease symptoms during and after dietary intervention (uncooked, lactobacilli-rich, vegan food in the test group). Data were collected immediately and 3 months after completion of the study on 0–10 scales (5 = no change). Significant difference between groups was tested with the Mann–Whitney *U*-test (from the original 0–10 scale material)

	Intervention group				Control group				Total	Difference
	Positive change	No change	Negative change	No answer*	Positive change	No change	Negative change	No answer†		
During the intervention period										
Rheumatic pains	14	2	3	3	4	12	1	3	42	<i>P</i> = 0.03
Swelling of joints	15	5	0	2	4	11	2	3	42	<i>P</i> = 0.003
Morning stiffness	16	4	0	2	3	13	1	3	42	<i>P</i> = 0.0008
Ability to move	11	5	4	2	4	13	0	3	42	n.s.
General impression	14	3	3	2	5	13	0	2	42	<i>P</i> = 0.03
After the intervention period										
Rheumatic pains	2	8	8	4	4	14	0	2	42	<i>P</i> = 0.007
Swelling of joints	3	7	9	3	4	14	0	2	42	<i>P</i> = 0.004
Morning stiffness	3	7	9	3	3	15	0	2	42	<i>P</i> = 0.005
Ability to move	2	11	6	3	2	13	1	4	42	n.s.
General impression	5	5	9	3	4	13	1	2	42	<i>P</i> = 0.07 n.s.

*Two patients stopped the diet after a few weeks, one later; some patients left some questions unanswered.

†One patient stopped the study for personal reasons and one died just after the intervention period. Some patients left some questions unanswered.

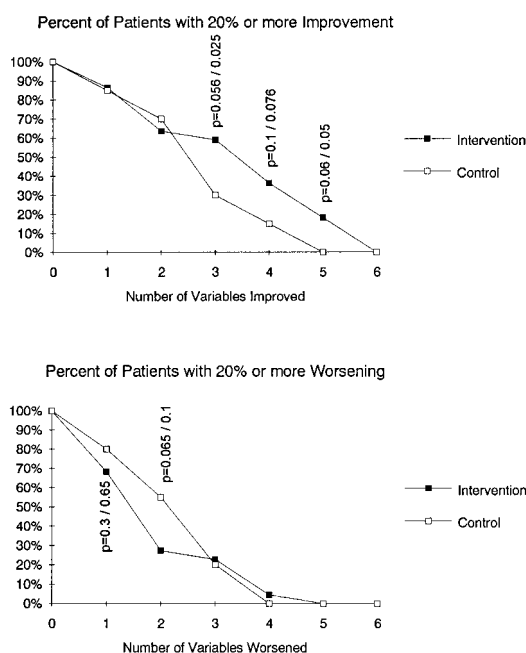


FIG. 2.—The 2 to 3 month intervention study in rheumatoid arthritis patients (*N* = 39) randomized to either intervention group starting an extreme vegan diet, ‘living food’, for 2–3 months and omnivorous controls. Percentage of patients in the intervention and control groups with at least 20% improvement or worsening in 0–6 of the following variables: ESR, number of swollen and tender joints, rheumatic pains (VAS), HAQ and global patient estimate. Statistical significance is calculated with Fisher’s exact test and the results are given as *P* values for all randomized patients (intention to treat analysis of 42 patients) and for the patients completing the 2 to 3 month intervention (*N* = 39).

TABLE III

Stepwise regression analysis of the disease activity score (DAS) for the change in the rheumatic disease activity during the 2 to 3 month intervention period (maximum *R*² improvement method, d.f. = 8) in a group (*N* = 39) of rheumatoid arthritis patients randomized to either an uncooked vegan or omnivorous diet

<i>R</i> ² for the model	0.48
<i>F</i>	2.92
Prob > <i>F</i>	0.02

Variable	Parameter estimate	<i>F</i>	Prob > <i>F</i>
Intercept	−0.8498	7.10	0.013
Gold (p.o. or i.m.)	0.2949	1.30	0.266
Fermented wheat drink (ml/day)	−0.0004	0.80	0.378
Wheat grass juice (ml/day)	−0.0088	3.99	0.057
Methotrexate	0.5450	4.74	0.039
Steroids	0.2886	1.70	0.204
Change of fibre intake (%)	−0.0074	3.98	0.057
Change of iron intake (%)	0.0094	7.75	0.010
Daily urinary sodium excretion at the start (mmol/24 h)	0.0032	1.92	0.178

The other drink, wheat grass drink, is consumed at 50–150 ml/day. It is pressed from fresh wheat grass and presumably contains high amounts of chlorophyll and coumarin [27]. Its effects are unknown. The daily intake of dietary fibre increased 2- to 4-fold when shifting to the intervention diet [10]. This may have contributed to the changes in colonic microflora [28] by shortening the intestinal transit time [29]. In this study, shifting to uncooked vegan food increased the calculated daily intake of iron by 98% [10]. The haemoglobin levels remained unchanged, however. The absorption of iron was probably impaired. There is

evidence about alterations in iron metabolism in RA [30], and Haugen *et al.* [31] have shown a negative correlation between serum iron and ESR.

The calculated energy intake of this experimental diet was not hypocaloric, but it caused a decrease in body weight of 9%. This may be due to the low biological availability of the energy-yielding nutrients that was caused by the insufficient food processing and the high fibre content of the diet (42 g/day; [10]). It could also result from the difficulties experienced with the diet (nausea, etc.). The loss of weight could have influenced the immune response and explained part of the results. On the other hand, the multivariate analysis of variance does not support this. The calculated content of the experimental diet covered most of the recommended daily requirements [10]. The calculated daily protein intakes in the intervention group increased from 58 to 80 g/day; in the control group, the intake was stable (57–59 g/day; [10]). These values are near to those measured in long-term users of this diet (48 g/day; [32]). The lowered serum albumin values were found in both groups and were not solely associated with the intervention diet. Achieving this kind of daily intake demands that all food items are consumed in recommended amounts. This is not always possible because of the unfamiliar taste and the strenuous and time-consuming processing of some items. It must also be remembered that the intervention diet corrected many deficiencies in the diet of the RA patients studied by Rauma *et al.* [10]. This alone may have had positive effects on the patients in the intervention group. The results of regression analyses did not, however, support this hypothesis. The stepwise regression analyses did not include changes in the problematic nutrients in the models explaining positive responses.

Half of the patients experienced adverse effects (nausea, diarrhoea) during the diet and stopped the experiment prematurely, three during the first days or weeks and eight after 2 months. There were no severe side-effects caused by the diet, but the high premature cessation rate shows that extreme diets are not good for every patient. Caution and sound rationing is needed both from the patient and the doctor.

The indicators of disease activity behaved as expected. The changes were not statistically significant as in the Kjeldsen-Kragh *et al.* [11] study. Exclusion of the unfavourable patients in their study may have caused this difference. The patients in the present study also had a more severe disease history and used more medications. When the same kind of composite index [20] was used in both studies, the proportions of patients with at least 20% improvement in at least five variables were 30.6% [11, 15] and 21.1% (the present study). The difference in these percentages was not significant (difference 9.5%, 95% CI –35 to 16%).

The discrepancy between the subjective experiences of the patients and the more 'objective' measures of basically the same phenomena (HAQ, duration of morning stiffness, pain at rest and pain on movement) deserves a mention. The patients seemed to link their

subjective experiences mainly with the number of tender joints. Thus, their estimates may have been influenced by even small variation in their status and strengthened by the great expectations caused by the strange and 'mystic' diet.

When the results of this study are compared with those of the minocycline intervention studies [33, 34], the most striking difference is the almost total lack of subjective improvement in the subjective variables during the antibiotic treatment. However, both types of interventions probably caused changes in the intestinal microflora. One explanation for this discrepancy could be either less placebo effect in the double-blind antibiotic intervention or differences in the gastrointestinal effects of these studies (selection of bacteria?).

Many recorded parameters behaved differently in patients with different medications (methotrexate, steroids, etc.). Many of these effects probably have no real significance because of the small number of patients in each group. The effect of dietary manipulation might be better studied without drugs, but this was considered unethical. The association of decreasing disease activity with no need for arthritis-specific drugs may denote a better effect of the diet in less active disease.

This study showed that subjective relief of the symptoms of the RA could be achieved with a radical dietary manipulation (uncooked extreme, lactobacillirich vegan diet, 'living food'). There were, however, no significant effects on the separate objective disease markers (CRP, ESR, joint counts, etc.). The activity index calculated from four disease activity indicators did, however, find a statistically significant connection between compliance with the tested diet and the decrease in disease activity.

ACKNOWLEDGEMENTS

The authors thank all their brave and patient patients, Dr E. Leskinen (Kivelä Hospital), J. Laakso and I. Ruokonen (MILA Ltd) for laboratory analyses, Mrs M. Svennevig (Green-Way restaurant) for providing the diet and tutoring the intervention group, Mrs L. Pajanne (Kivelä Hospital) for the practical arrangements in the rheumatology out-patient clinic, Mrs A. Rokka for her help in the dietary analyses, and Dr H. Lenzner (University of Tartu) for analysis of the faecal bacteria. This study was supported by the Juho Vainio Foundation.

REFERENCES

1. Garrett SL, Kennedy LG, Calin A. Patients' perceptions of disease modulation by diet in inflammatory (rheumatoid arthritis/ankylosing spondylitis) and degenerative arthropathies. *Br J Rheumatol* 1993;32(suppl. 2):43.
2. van de Laar MAFJ, van der Korst JK. Rheumatoid arthritis, food, and allergy. *Semin Arthritis Rheum* 1991;21:12–23.
3. Sköldstam L, Larsson L, Lindström FD. Effects of fasting and lactovegetarian diet on rheumatoid arthritis. *Scand J Rheumatol* 1979;8:249–55.
4. Hafström I, Ringertz B, Gyllenhammar H, Palmblad J, Harms-Ringdahl M. Effects of fasting in disease activity, neutrophil function, fatty acid composition, and leukotri-

- ene biosynthesis in patients with rheumatoid arthritis. *Arthritis Rheum* 1988;31:585–92.
5. Haugen M, Kjeldsen-Kragh J, Nordvåg BY, Förre Ö. Diet and disease symptoms in rheumatic disease—Results of a questionnaire based survey. *Clin Rheumatol* 1991;10:401–8.
 6. Wigmore A. *Recipes for longer life*, 1st edn. Wayne, NJ: Avery Publishing Group Inc., 1980.
 7. Hänninen O, Nenonen M, Ling WH, Li DS, Sihvonen L. Effects of eating an uncooked vegetable diet for one week. *Appetite* 1992;19:243–54.
 8. Nenonen M. Vegan diet, rich in lactobacilli ('Living food'): metabolic and subjective responses in healthy subjects and in patients with rheumatoid arthritis. Dissertation, University of Kuopio, Finland, 1995.
 9. Ryhänen E-L, Mantere-Alhonen S, Nenonen M, Hänninen O. Modification of faecal flora in rheumatoid arthritis patients by lactobacilli rich vegan diet. *Milchwissenschaft* 1993;48:255–9.
 10. Rauma A-L, Nenonen M, Helve T, Hänninen O. Effect of a strict vegan diet on energy and nutrient intakes by Finnish rheumatoid patients. *Eur J Clin Nutr* 1993;47:747–9.
 11. Kjeldsen-Kragh J, Haugen M, Borchgrevink CF *et al.* Controlled trial of fasting and one-year vegetarian diet in rheumatoid arthritis [see comments]. *Lancet* 1991;338:899–902.
 12. Kjeldsen-Kragh J. Dietary treatment of rheumatoid arthritis. Dissertation, Department of General Practice, University of Oslo, Norway, 1995, 29 pp.
 13. Severijnen AJ, Kool A, Swaak AJG, Hazenberg MP. Intestinal flora of patients with rheumatoid arthritis: Induction of chronic arthritis in rats by cell wall fragments from isolated *Eubacterium aerofaciens* strains. *Br J Rheumatol* 1990;29:433–9.
 14. Peltonen R, Ling WH, Hänninen O, Eerola E. An uncooked vegan diet shifts the profile of human fecal microflora: computerized analysis of direct stool sample gas-liquid chromatography profiles of bacterial cellular fatty acids. *Appl Environ Microbiol* 1992;58:3660–6.
 15. Peltonen R, Kjeldsen-Kragh J, Haugen M *et al.* Changes of faecal flora in rheumatoid arthritis during fasting and one-year vegetarian diet. *Br J Rheumatol* 1994;33:638–43.
 16. Arnett FC, Edworthy SM, Bloch DA *et al.* The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. *Arthritis Rheum* 1988;31:315–24.
 17. WHO Workgroup. *International classification of impairments, disabilities and handicaps*. Geneva: WHO, 1980.
 18. Blom G. *Statistical estimates and transformed beta variables*. New York: John Wiley & Sons, 1958.
 19. SAS Institute Inc. *The GLM procedure*. In: *SAS user's guide: statistics*, Version 5, 1st edn. Cary, NC: SAS Institute Inc., 1985:433–506.
 20. Paulus HE, Egger MJ, Ward JR, Williams HJ, Cooperative Systematic Studies of Rheumatic Diseases Group. Analysis of improvement in individual rheumatoid arthritis patients treated with disease-modifying anti-rheumatic drugs, based on the findings in patients treated with placebo. *Arthritis Rheum* 1990;33:477–84.
 21. Scott DL, van Riel PL, van der Heijde D, Studnicka Bence A (eds) *Assessing disease activity in rheumatoid arthritis*. The EULAR handbook of standard methods, 1st edn. London: EULAR, 1993.
 22. Altman DG. How large a sample? In: Altman GA, Gore SM, eds. *Statistics in practice*, 1st edn. London: British Medical Association, 1989:6–8.
 23. Juven BJ, Meinersmann RJ, Stern NJ. Antagonistic effects of lactobacilli and pediococci to control intestinal colonization by human enteropathogens in live poultry. *J Appl Bacteriol* 1991;70:95–103.
 24. Lindgren SE, Dobrogosz WJ. Antagonistic activities of lactic acid bacteria in food and feed fermentations. *FEMS Microbiol Rev* 1990;87:149–64.
 25. Mehta AM, Patel KA, Dave PJ. Purification and properties of the inhibitory protein isolated from *Lactobacillus acidophilus* AC1. *Microbios* 1983;38:73–81.
 26. Eerola E, Peltonen R, Nenonen M, Helve T, Hänninen O, Toivanen P. Intestinal flora and disease activity in rheumatoid arthritis during vegan diet. Abstract submitted for XIIIth European Congress of Rheumatology, Amsterdam, The Netherlands, 18–23 June 1995.
 27. Rauma AL. *Nutrition and biotransformation in strict vegans*. Dissertation, University of Kuopio, Finland, 1996, 114 pp. (Kuopio University Publications D. Medical Sciences 102).
 28. Benno Y, Endo K, Mizutani T, Namba Y, Komori T, Mitsuoka T. Comparison of fecal microflora of elderly persons in rural and urban areas of Japan. *Appl Environ Microbiol* 1989;55:1100–5.
 29. Davies GJ, Crowder M, Reid B, Dickerson JW. Bowel function measurements of individuals with different eating patterns. *Gut* 1986;27:164–9.
 30. de Jong G, van Noort WL, Feelders RA, de Jeu Jaspars CM, van Eijk HG. Adaptation of transferrin protein and glycan synthesis. *Clin Chim Acta* 1992;212:27–45.
 31. Haugen MA, Höyeraal HM, Larsen S, Gilboe I-M, Trygg K. Nutrient intake and nutritional status in children with juvenile chronic arthritis. *Scand J Rheumatol* 1992;21:165–70.
 32. Orlov SN, Ågren JJ, Hänninen OO *et al.* Univalent cation fluxes in human erythrocytes from individuals with low or normal sodium intake. *J Cardiovasc Risk* 1994;1:249–54.
 33. Kloppenburg M, Breedveld FC, Terweil JP, Mallee C, Dijkmans BAC. Minocycline in active rheumatoid arthritis. A double-blind, placebo-controlled trial. *Arthritis Rheum* 1994;37:629–36.
 34. Tilley BC, Alarcon GS, Heyse SP *et al.* Minocycline in rheumatoid arthritis. A 48-week, double-blind, placebo-controlled trial. *Ann Intern Med* 1995;122:81–9.