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Haruo Ito
Teikyo University

Tadashi Kotake
Teikyo University

Naoto Miura
Teikyo University

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EVALUATION AND MANAGEMENT OF DIETARY HABITS IN JAPANESE RENAL STONE FORMERS

Haruo Ito*, Tadashi Kotake, Naoto Miura

Department of Urology, Teikyo University School of Medicine, Ichihara Hospital
3426-3 Anesaki, Ichihara, Chiba 299-01, Japan

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Abstract

To elucidate the relationship between the formation of kidney stones and diet, we carried out a dietary investigation in patients with urinary tract stones. Dietary intakes were estimated for 36 patients (24 men, 12 women) with calcium stones, and compared with the official dietary requirements for the Japanese.

Total protein intake, animal protein intake and animal protein ratio were significantly higher for patients with stones in both men and women. Dietary salt intake was significantly higher for male patients and the total group. Dietary calcium and carbohydrate intakes were significantly lower for patients with stones in men and the total group, and tended to be lower for female patients.

As a result of dietary guidance, the intakes of total protein, animal protein and salt were markedly reduced. The animal protein ratio was also lowered. Caloric intake and the dietary intakes of carbohydrate, fat and salt were reduced, too. However, the dietary calcium intake did not change. Chemical analysis of 24 hour-urine revealed that the excretion of urea nitrogen was reduced, which reflected the decrease in protein intake produced by the dietary regimen. The excretions of urate and oxalate also tended to decrease.

Key Words: Kidney stone, calcium oxalate, dietary habits, dietary management, calcium intake, protein intake, salt intake, urinary calcium, urinary oxalate, urinary urate.

*Address for Correspondence:

Haruo Ito
Department of Urology,
Teikyo University School of Medicine,
Ichihara Hospital,
3426-3 Anesaki,
Ichihara, Chiba 299-01, Japan

Telephone No.: 81-436-62-1211 ext. 2824

FAX No.: 81-436-61-4773

Introduction

The incidence of renal stones rapidly rose after the second world war in western countries [22], and slightly later, in Japan too [20], where the incidence of nephrolithiasis has increased approximately 3 times compared to that before the war. Even in the recent 10 years, from 1975 to 1985, the 35% increase had been observed in the risk of suffering from urolithiasis at some time in one's life. But the incidence is still half of that in the U.S.A. [27]. The change of life-style, especially that of dietary habit, has been suggested as the causative factor of the upsurge in the incidence of nephrolithiasis [25]. However, according to Fellström *et al.* [6], there seem to be only marginally different dietary habits between stone formers and carefully matched control subjects. To elucidate the significance of diet in the formation of renal stones, we investigated the effects of the types of food taken by patients with calcium stones, and studied the potential effect of dietary counseling.

Subjects and Methods

A total of 36 patients (24 men, 12 women) participated in the study, who had calcium stones without apparent predisposing conditions such as primary hyperparathyroidism and renal tubular acidosis. Patients with renal failure or urinary tract infection were excluded. Men were 20 to 78 years of age (mean 44 years; standard deviation, SD: 13 years), and women were 20 to 67 years (mean 39 years; SD: 13 years), with the mean and SD for the total group at 42 years and 13 years, respectively. Patients in their 20s to 40s accounted for 79% of the males and 83% of the females.

Stones were removed by extracorporeal shock wave lithotripsy (ESWL; EDAP LT-01) on an outpatient basis in most patients. In these cases, the patients were studied after 1 month or later when they were restored to ordinary daily life. When patients were hospitalized or underwent an open operation, the study was performed after 3 months or later. Urine was collected on a 24-hour basis, and the dietary intake was investigated by the staff of the nutrition department of our institute.

Table 1. Dietary intake of various nutrients by calcium stone patients and nutrient requirements of Japanese.

	Male		Female		Total	
	Stone patient (n = 24)	Daily nutrient requirement	Stone patient (n = 12)	Daily nutrient requirement	Stone patient (n = 36)	Daily nutrient requirement
Calories (kcal)	2235 ± 362 ⁺	2313 ± 290	1816 ± 235	1679 ± 145	2095 ± 380	2101 ± 390
Carbohydrate (g)	300 ± 54	346 ± 44**	232 ± 39	252 ± 23	277 ± 59	314 ± 59**
Fat (g)	58 ± 13	61 ± 13	59 ± 15	42 ± 4**	58 ± 14	55 ± 14
Total Protein (g)	84 ± 16	73 ± 5**	78 ± 13	60 ± 1***	82 ± 15	69 ± 8****
Animal Protein (g)	46 ± 14	33 ± 2****	42 ± 13	27 ± 1***	45 ± 14	31 ± 3****
Animal Protein Ratio	54 ± 9	45 ± 0***	54 ± 8	45 ± 0**	54 ± 9	45 ± 0****
Calcium (mg)	539 ± 206	610 ± 35*	566 ± 146	575 ± 32	548 ± 189	599 ± 38*
Sodium chloride (g)	13 ± 3	10 ± 0****	11 ± 3	10 ± 0	12 ± 3	10 ± 0***

⁺ mean ± S.D.; * p < 0.05; ** p < 0.005; *** p < 0.0005; **** p < 0.0001.

Table 2. Change of dietary intake of various nutrients under nutrimental guidance in calcium stone patients.

	Male (n = 16)		Female (n = 11)		Total (n = 27)	
	Before	After	Before	After	Before	After
Calories (kcal)	2143 ± 419	1937 ± 289	1809 ± 333	1567 ± 412	2007 ± 415	1786 ± 384*
Fat (g)	486 ± 50	265 ± 40	242 ± 56	213 ± 53	268 ± 56	244 ± 51
Total protein (g)	86 ± 17	76 ± 15*	78 ± 17	64 ± 22	83 ± 17	71 ± 19**
Animal protein (g)	48 ± 13	39 ± 12*	43 ± 14	33 ± 17	46 ± 14	37 ± 14**
Ann. protein ratio (%)	56 ± 7	52 ± 10*	54 ± 8	48 ± 1	55 ± 7	50 ± 13*
Calcium (mg)	461 ± 138	503 ± 190	529 ± 186	410 ± 158	488 ± 160	466 ± 181
Sodium chloride (g)	13.0 ± 4.0	9.7 ± 3.0*	11.4 ± 3.7	8.6 ± 3.0*	12.2 ± 4.0	9.3 ± 3.0**

* p < 0.05

** p < 0.005

Table 3. Total and animal protein intakes in patients with hypercalciuria and hyperuricosuria.

	n	Total Protein	Animal Protein
Hypercalciuria	7	73.1 ± 12.0*	46.9 ± 14.7
Normocalciuria	28	84.7 ± 15.9	46.7 ± 14.5
Hyperuricosuria	4	101.0 ± 18.9	60.2 ± 17.5
Normouricosuria	32	80.0 ± 13.7	42.9 ± 13.0

* mean ± S.D.

The values of nutrients shown here represent the mean of 3-day measurements. Dietary requirements were calculated from the 4th version of "Recommended Dietary Allowances for the Japanese" [9] for the subjects on the basis of their sex, age, height and physical activity. The animal protein ratio was placed at 45% in consideration of the recommended value, which was 40 to 45% [1]. This was followed by dietary counseling for 16 men (41 ± 10 years) and 11 women (43 ± 16 years), a total of 27 subjects (42 ± 12 years). The patients were instructed to use the Recommended Dietary Allowances for the Japanese as their goal. The contents of their diet were re-investigated 2 months after the completion of dietary counseling and 24-hour-urine was collected from 19 of the subjects.

The collection of 24-hour-urine was done at the outpatient clinic. For the measurement of calcium and

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Table 4. Change of urinary excretion under nutrimental guidance in calcium stone patients.

	Male (n = 11)		Female (n = 8)		Total (n = 19)	
	Before	After	Before	After	Before	After
Urea nitrogen (g)	11.0 ± 2.3 (n = 10)	9.3 ± 1.8	9.0 ± 2.0 (n = 7)	8.6 ± 1.7	10.0 ± 2.0 (n = 17)	9.0 ± 1.7*
Creatinine (mg)	1342 ± 139	1330 ± 130	851 ± 270	876 ± 148	1136 ± 319	1141 ± 268
Uric acid (mg)	675 ± 175 (n = 8)	605 ± 249	467 ± 103 (n = 6)	385 ± 149	586 ± 179 (n = 14)	510 ± 234
Na (mg)	5312 ± 1749	5084 ± 1531	4367 ± 1403	4439 ± 1150	4914 ± 1642	4822 ± 1389
Ca (mg)	247 ± 80	289 ± 65	175 ± 76	126 ± 61	219 ± 84	225 ± 103
P (mg)	860 ± 258	909 ± 130	773 ± 232	678 ± 196	823 ± 245	812 ± 195
Mg (mg)	86 ± 44 (n = 10)	91 ± 15	85 ± 34 (n = 7)	79 ± 39	85 ± 39 (n = 17)	86 ± 27
Oxalate (mg)	49 ± 24 (n = 7)	34 ± 31	31 ± 18 (n = 3)	12 ± 5	44 ± 23 (n = 10)	27 ± 27

* p < 0.05.

oxalate, urine was collected in a vessel containing 100 ml of 1.2 N hydrochloric acid. For the measurement of other components, urine was collected in a vessel not containing preservatives. Urea nitrogen, creatinine, calcium, magnesium, phosphorus, uric acid, and sodium and potassium in the urine were measured with an auto-analyzer (Hitachi Model 705, Tokyo, Japan). The excretion of ≥ 300 mg calcium/day for men or ≥ 250 mg calcium/day for women was defined as hypercalciuria [5]. The excretion of ≥ 800 mg uric acid/day for men or ≥ 750 mg uric acid/day for women was defined as hyperuricosuria [26]. Oxalate was determined according to the method of Frazer *et al.* [10]. Briefly, 20 ml urine, centrifuged to remove the solid matter, was adjusted to pH 4.5 with NH_4OH solution. To this urine, 0.4 ml of 2mg/ml $\text{Na}_2\text{C}_2\text{O}_4$ solution and 0.4 ml of 100 mg/ml CaCl_2 solution were added. This mixture was heated to 100°C, then cooled to room temperature, and its pH was readjusted to 4.5 with a solution of NH_4OH or H_2SO_4 . It was then centrifuged. The precipitate was washed 3 times with 6 ml saturated solution of CaC_2O_4 in water, and dissolved in 1 ml of 1 N H_2SO_4 by heating at 60°C, for 5 minutes. Subsequently, 4.0 ml distilled water was added to this solution, then the solution was further diluted 25 times with water, and its calcium content was determined with atomic absorption spectrophotometer.

Results

Comparison of the dietary intakes of calcium stone patients with the dietary requirements for the Japanese (Table 1) revealed that total protein intake, animal protein intake, and animal protein ratio were markedly higher for patients with calcium stones in men, women or the total group. Dietary salt intake was significantly

higher for male patients and the total group, and tended to be higher for female patients. Dietary carbohydrate and calcium intakes were lower for male patients and the total group, and a similar tendency was detected in women. Dietary fat intake was higher for female patients, but not for male patients.

Fig. 1 shows the total protein intake of individual patients as compared with the dietary requirements for the Japanese. In nearly all patients, the intake exceeded the requirements.

The dietary calcium intake, which is of particular interest, was significantly lower than the requirement in the total group and in men, and a similar tendency was noted in women (Fig. 2). Table 2 shows the dietary intakes before and after dietary counseling. As a result of the counseling, total protein, animal protein and salt intakes were markedly reduced. The animal protein ratio was also reduced. In addition, calorie, carbohydrate, and fat intakes, were reduced as well, but no change was observed in calcium intake.

Fig. 3 shows changes in individual total protein intake. Dietary protein intake was reduced as a result of the dietary counseling in men, women and the total group.

Total and animal protein intakes in patients with hypercalciuria and hyperuricosuria are shown in Table 3. Total protein intake tended to be higher in normocalciuric group than hypercalciuric group, and animal protein intake was almost same in the 2 groups.

Table 4 shows the urinary excretions of calculi-related substances. The excretion of urea nitrogen was reduced as a result of dietary counseling. The uric acid and oxalate excretions also tended to, but did not significantly, decrease. The calcium and phosphorus excretions did not change.

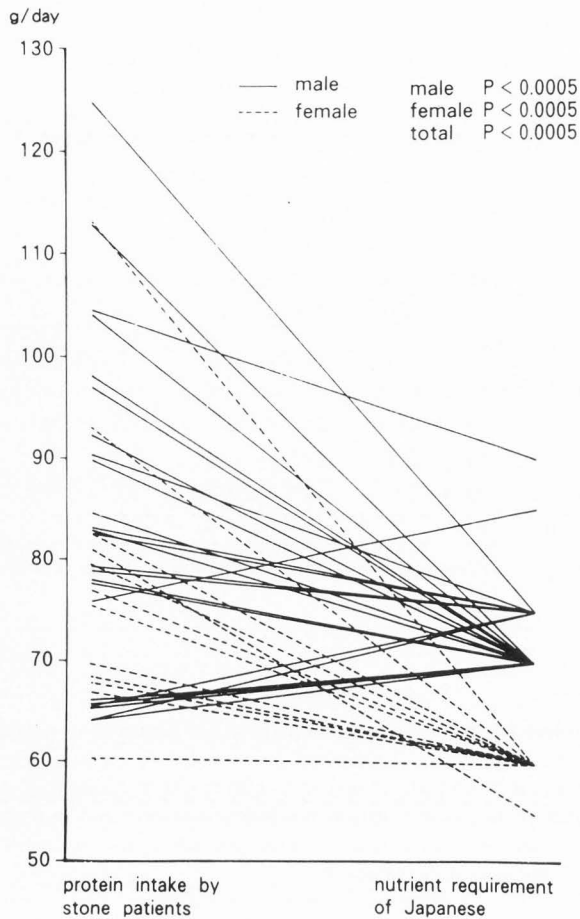


Figure 1. Comparison of total protein intake by stone patients and nutrient requirements of Japanese.

Fig. 4 shows the individual urinary excretion of uric acid before and after dietary counseling. It tended to decrease after counseling.

Discussion

Unlike struvite or cystine stones [16], it is well known that the formation of calcium stones is related to diet. Particularly, evidence from both long-term [28] and short-term [24] studies shows that an increase in animal protein intake leads to a rise in the incidence of renal stones. Meanwhile, in the comparison of protein intake between patients with stones and the control matched for socioeconomic status, no difference was detected between groups as to intake [6]. The present study confirmed the contention of former group by revealing that patients with calcium stones ingested more total as well as animal protein. The total protein intake, animal protein intake, and animal protein ratio in patients with stones, whether male or female, were well above the requirements for the Japanese. Urinary citrate, a low molecular weight inhibitor, is known to be involved in the physicochemistry of stone formation and

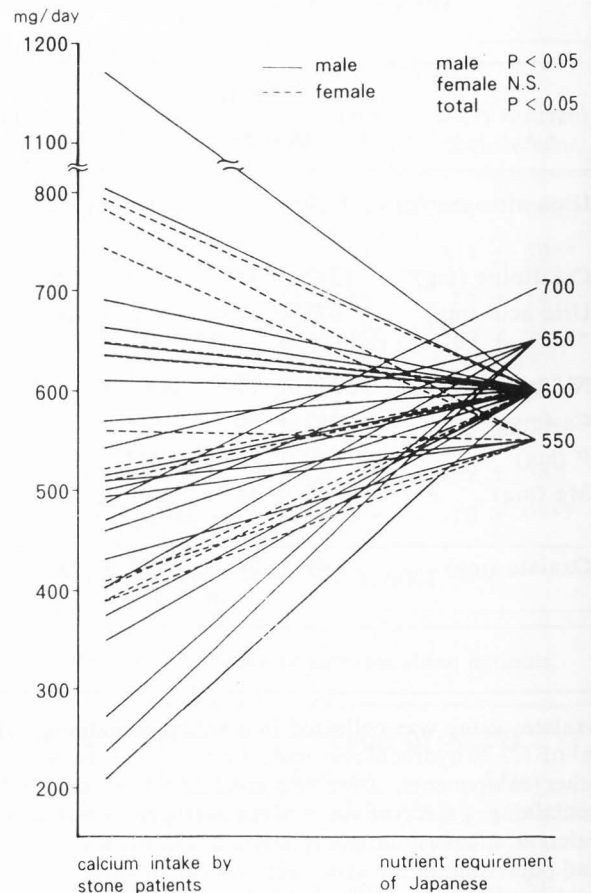


Figure 2. Comparison of calcium intake by stone patients and nutrient requirements of Japanese.

known to be affected by diet. In our investigation, neither urinary citrate nor high molecular weight inhibitors were measured.

Urinary calcium is certainly related to the formation of stones. In the present study, however, when patients with stones were divided into hypercalciuric and normocalciuric groups, and the two groups were compared with respect to protein intake, the total protein intake tended to be higher for the normocalciuric group. Animal protein intakes in 2 groups were almost the same. This result, though its implications are unclear, differs from the findings of Iguchi *et al.* [14].

When patients were divided into hyperuricosuric and normouricosuric groups, protein intake was higher for the former group. Then, dietary counseling significantly reduced dietary protein intake, which resulted in a decrease in the urinary excretion of uric acid. This might suggest that an increase in urinary uric acid is of greater significance in this population. The importance of urate in urine has already been reported [4]. It is said to decrease the activity of urinary inhibitors and promote the epitaxial growth of calcium oxalate crystal [7, 15]. Grover *et al.* [12] also re-emphasized the promotive role of hyperuricosuria in urolithiasis.

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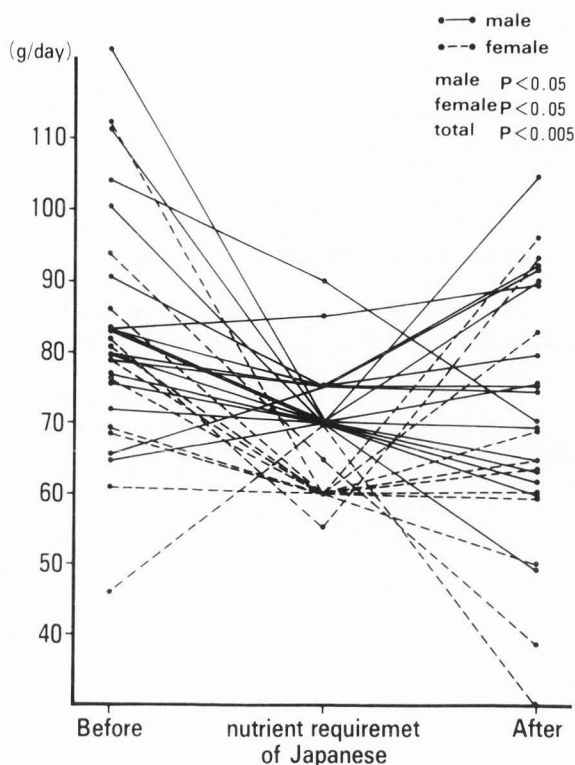


Figure 3. Change of total protein intake resulting from dietary counseling.

Urinary oxalate may be the most important risk factor in the formation of stones [8, 23]. Thus, a slight rise in the excretion of oxalate in urine expressed as "mild hyperoxaluria" may be a powerful promoter of stone formation. Furthermore, the urinary excretion of oxalate is said to increase in patients with calcium stones [13, 17]. There is a report that phenylalanine, tyrosine and tryptophan contained in animal protein are metabolized to increase urinary oxalate [3], but the extent of their influence is unknown. The decrease in urinary oxalate after dietary guidance in our study may not reflect the true situation because of the small number of subjects ($n = 3$) studied.

The ratio of calories provided by carbohydrate to total calories is said to be lower in patients with renal stones than in normal individuals [11]. Our data also show that the intake of carbohydrate was less than the requirement, which seems to reflect the fact that these patients took a lot of animal protein. High intake of refined carbohydrate or sugar has been implicated as a cause of increasing the incidence of upper urinary tract stones [2]. Since we have not divided carbohydrate into refined carbohydrate and unrefined one in the present study, it is unclear whether the patients took a large amount of refined carbohydrate or not.

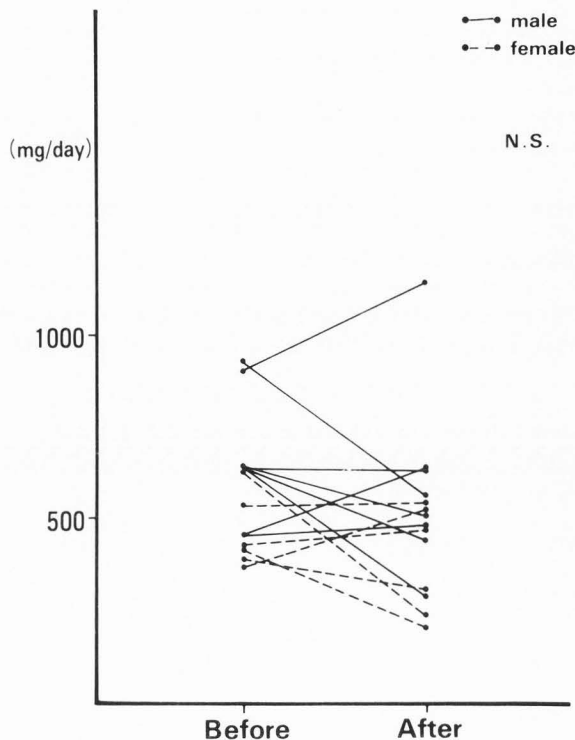


Figure 4. Change of uric acid excretion level resulting from counseling.

High dietary salt intake is said to result in an increase in the urinary excretion of calcium [21]. Our results from the hypercalciuric ($n = 7$) and normocalciuric ($n = 29$) groups showed that the urinary excretion of sodium tended to be higher in the former (6364 ± 1943 mg versus 5017 ± 1863 mg, not significant).

Iguchi *et al.* [14] reported that calcium intake in patients with stones fell short of the calcium requirement for the Japanese. This was confirmed by our study. We previously reported that the combined administration of calcium and citrate preparations reduced urinary oxalate without increasing urinary calcium [18, 19]. Dietary advice based on the same idea should produce the same effect. This involves reducing protein intake and eating more sea-weed and vegetables, while increasing calcium intake. Our study may provide some interesting suggestions in this respect. That is, calcium could be safely administered to patients with stones because the dietary calcium intake is low in these patients.

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Discussion with Reviewers

D.J. Kok: Did the dietary counseling consist only of giving the recommended intake values, or did it also include dietary advice specific for stone-formers, like restriction of oxalate intake (explaining why oxalate excretion went down) and drinking advice? Why was urinary citrate not measured? Urinary citrate is known to be involved in the physicochemistry of stone formation and known to be strongly affected by diet. Since uric acid is said here to play a role in stone formation, it would be helpful to include the urinary volume and the urinary pH in the results in order to assess the supersaturation with uric acid.

Authors: The dietary counseling consists only of giving the recommended intake values. Urinary citrate is now being measured in our laboratory, so we will get the citrate data in the near future. It might be difficult to measure urinary pH of 24-hour urine.

W.G. Robertson: There was a 20% reduction in animal protein consumption by stone formers after dietary advice, yet uric acid hardly fell. What dietary constituents were reduced during the advice period? Was there only a reduction in the consumption of eggs and dairy produce but not in meat, fish and poultry?

J. Costello: The authors refer to a decrease in protein intake decreasing uric acid excretion and conclude from this the significance of uric acid in stone formation. However, urinary uric acid did not decrease significantly (Table 4). How can these conclusions be supported by the authors' data?

Authors: We think that all types of proteins were reduced after dietary advice. Although the decrease of uric acid was not significant, it did decrease and the decrease would become significant if a study with a larger number of patients could be done.

J. Costello: Was protein intake correlated with urinary oxalate excretion before or after dietary counseling?

Authors: Protein intake did not correlate with urinary oxalate excretion before or after dietary counseling.

J. Costello: There was no control group studied that did not receive dietary counseling. This would have been most helpful.

W.G. Robertson: In this paper, you have compared the actual intakes of a number of nutrients in stone formers with recommended daily intakes for these individuals. How do these data compare with the intakes of these nutrients in normal control subjects?

Authors: We would like to do a case-control study as the next step.

P.P. Singh: Urinary ascorbic acid adds extra oxalate during collection of urine in 1.2 N HCl. I have not gone through the method of Fraser and Campbell (text reference 10) for oxalate determination but I suspect that ascorbic acid might be contributing additional oxalate during precipitation. Authors should check if this is the reason for high oxalate values in their patients.

Authors: We checked the pH of 24-hour urine prior to measurement of oxalate and found that the pH was below 2.0. Therefore, it seems that ascorbic acid does not contribute additional oxalate.

P.P. Singh: In the western population calcium intake has also gone up along with animal protein owing to increased intake of non-vegetarian foods and dairy products, while in the Japanese population the consumption of these foods has gone up several fold and has come up almost at par with western subjects, but their calcium intake remains relatively much lower. Neither Iguchi *et al.* (text reference 14) nor the present authors have explained the reasons for that. The authors should, therefore, include the names of foods responsible for low calcium levels.

Authors: Animal protein does not contain large amounts of calcium. Japanese people take much less milk and dairy products than western people. We think that that is one of the reasons why calcium intake in Japanese is less than in western people.