On supplementing the selenium intake of New Zealanders

2. Prolonged metabolic experiments with daily supplements of selenomethionine, selenite and fish

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1. The daily intake of selenium by three subjects was supplemented with 100 μg Se as selenomethionine (Semet-Se) or sodium selenite (selenite-Se)/d for 10–11 weeks, or with 65 μg Se as in mackerel (*Scomber japonicus*) (fish-Se)/d for 4 weeks.

2. Urinary and faecal excretion of Se was measured and also Se concentration in whole blood, plasma and erythrocytes. Measurements on blood were made at intervals after supplementation had ceased.

3. Selenite-Se was not as well absorbed (0·46 of the intake) during the first 4 weeks as Semet-Se (0·75 of the intake) and fish Se (0·66 of the intake).

4. Blood Se increased steadily with Semet-Se, from 0·08 to 0·18 μg Se/ml, but more slowly with selenite-Se, reaching a plateau in 7–8 weeks at 0·11 μg Se/ml. Plasma Se increased more rapidly with Semet-Se than with selenite-Se, so that initially with Semet-Se plasma Se was greater than erythrocyte Se.

5. Daily urinary excretion increased with all forms of supplement, with initially a greater proportion of absorbed selenite-Se being excreted than Semet-Se or fish-Se. A close relationship was found between plasma Se and 24 h urinary excretion. The findings suggested that there was a rapid initial excretion of presumably unbound Se then a slower excretion of residual unbound, loosely bound or bound Se.

6. Total retentions of 3·5 mg selenite-Se and 4·5 mg Semet-Se were large when compared with an estimate of body content of 6 mg Se, derived in another paper (Stewart, Griffiths, Thomson & Robinson, 1978). Retentions of Semet-Se and fish-Se appeared to be reflected in blood Se, whereas for selenite-Se, blood Se reflected retention for only a short period after which Se appeared to be retained without altering the blood Se. This suggested that Semet-Se and selenite-Se were metabolized differently.

7. A double blind-dosing trial with 100 μg Semet-Se was carried out for 12 weeks on twenty-four patients with muscular complaints in Tapanui, a low-Se-soil area. Blood Se increased in the experimental group (from 0·067 to 0·143 μg Se/ml); clinical findings were not conclusive and will be presented elsewhere.

8. Blood Se was measured in New Zealand residents before travelling to Europe or to North America. On return their blood Se was increased, and depending upon the period of time spent outside New Zealand some values reached concentrations found in visitors and new settlers to New Zealand.

9. The results from these studies and the earlier studies of single and multiple dosing have been used to look at the various criteria in use for assessing Se status of subjects. It is suggested that plasma Se be used in preference to 24 h urinary excretion, and in addition to whole blood Se and glutathione peroxidase (*EC* 1.11.1.9) activity.

The dietary intake of selenium by New Zealand residents is low (6–35 μg Se/d), except for days when liver, kidney or fish are eaten when the intake could increase to 102 μg Se/d (Thomson, 1972; Griffiths, 1973; Stewart *et al.* 1978). This is almost 100 μg Se less than intakes of 113–220 μg Se/d for four Canadian diets (Thompson, Erdody & Smith, 1975) and 60–150 μg Se/d calculated for USA diets (Schroeder, Frost & Balassa, 1970).

The present paper describes the daily supplementation of the diet of three subjects with 100 μg Se/d for periods of 1–3 months. Because so little is known about the form of Se present in foods, three forms of Se were chosen for the supplement. Selenomethionine (Semet-Se) is the major form of Se in cereals and possibly other foods (Butler & Peterson, 1961), and canned mackerel (*Scomber japonicus*) is a rich source of Se (fish-Se) which is also readily obtained. Sodium selenite (selenite-Se) was included in this study because of

its successful use in treating animal deficiencies of Se, and also because of its increasing use for self-medication by residents in low-Se-soil areas in New Zealand (Thomson, Burton & Robinson, 1978). A preliminary account of the daily supplementation with seleno-methionine has been published (Robinson, Rea & Stewart, 1976).

METHODS

Expt 1. Supplementation of diet with physiological doses of Se

The subjects were two women (subjects H and C) and one man (subject S) with body-weights of 74, 56 and 76 kg.

Expt 1a. Semet-Se. Subject H ingested daily for 11 weeks 100 μg Semet-Se (Sigma Chemical Co., St Louis, Missouri, USA) prepared in solution. Samples of blood (20 ml) were collected before dosing on day 1, twice weekly for 3 weeks and thereafter at weekly intervals for 8 weeks. The samples were taken at least 6–7 h after the last dose. Whole blood, erythrocytes and plasma were analysed for Se. Urine samples (24 h) and all stools were collected for 1 d before the first dose, and for the next 11 weeks.

No liver or kidney was eaten throughout the study and fish was eaten only after week 2, on one occasion in weeks 3, 4, 5 and 7 and twice in week 6 and three times in weeks 10 and 11.

Expt 1b. Fish-Se. Subject C ingested daily for 4 weeks as part of her midday meal half a can of mackerel, containing on average 130 μg Se/can (range 118–141 μg Se/can). The cans were from the same batch. Blood samples were taken in the morning before dosing, at weekly intervals until dosing ceased and for a further 13 weeks. Twenty-four hour urines and all stools were collected for 7 d before dosing, daily during the dosing period and for a further 7 d.

No kidney or liver was eaten, and fish other than mackerel on only one occasion.

Expt 1c. Selenite-Se. Subject S ingested 100 μg selenite-Se in solution daily for 10 weeks. A blood sample was taken before dosing, at weekly intervals for 10 weeks of dosing and for a further 3 weeks after dosing ceased, and then monthly for the next 3 months. A 24 h urine collection and a single stool collection were made each week, usually on the day before the blood was collected. Fish, liver and kidney were not eaten on the day of collection, nor on the day before collections were made.

Expt 2. Tapanui trial using Semet-Se (1975)

Twenty-four patients (10–60 years old, mean 35 ± 13 years) suffering from muscular complaints were selected from a general medical practice in Tapanui, South Otago, New Zealand. Twelve patients ingested 5 ml of a solution containing 100 μg Semet-Se daily for 12 weeks and the other twelve patients ingested 5 ml of a placebo solution. The experiment was carried out as a double blind trial. All the patients except one from the control group completed the study. A blood sample was taken from each patient before dosing, at two-weekly intervals for 12 weeks and finally 8 weeks after dosing. At each of these sampling times a clinical examination was made and the patients' own assessment noted.

Expt 3. Overseas travellers from New Zealand

Blood samples were taken from seven New Zealand residents before travelling to Europe or to North America, and again as soon as possible after their return to New Zealand, 7 weeks–2 years later. While in UK and USA subject H and her husband subject J sent back blood samples to New Zealand for analysis.
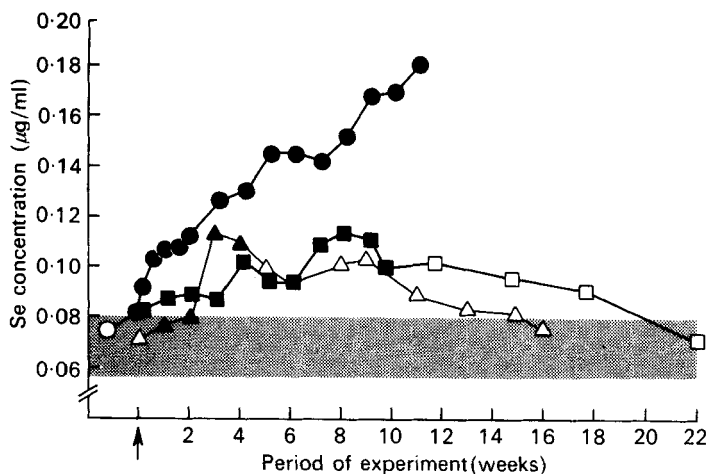
Fig. 1. Whole blood selenium concentration (μg/ml) during daily supplementation with 100 μg Se as selenomethionine (●) for subject H; 100 μg Se as selenite (■) for subject S; and 65 μg Se as in mackerel (▲) for subject C. Bloods for non-supplemented periods are given for subject H (○), subject S (□), subject C (△) and (↑) indicates the start of daily supplementation. (▦) range for mean ±SD (0·068±0·013 μg Se/ml) for New Zealand subjects (Griffiths & Thomson, 1974). For details of experimental procedure, see p. 590.

Techniques

Collection and storage of samples. Urine, faeces and blood were collected and stored as described previously (Thomson, 1974). Faeces were pooled for each week, after allowing 1 d for intestinal transit time for subject H (Thomson, 1974) and 3 d for subject C (Stewart *et al.* 1978).

Analytical method. Se was measured by a modification (Thomson, 1973; Thomson *et al.* 1978) of the diaminonaphthalene fluorimetric method described by Watkinson (1966).

RESULTS

Expt 1. Effect of supplementing diet with Se

Blood Se concentration. Fig. 1 show that blood Se of subject H increased steadily during 11 weeks of dosing with Semet-Se from 0·082 to 0·181 μg Se/ml, a rate of increase of 0·009 μg Se/ml per week. A similar rate was observed for subject C during 4 weeks with the smaller daily supplements of approximately 65 μg fish-Se. However, with selenite-Se blood Se of subject S increased more slowly and appeared to reach a plateau at 7 weeks at 0·11 μg Se/ml, an increase of 0·036 μg Se/ml or 0·004 μg Se/ml per week. Blood Se of subjects C and H decreased steadily after the end of dosing except for a short period at weeks 6–9 when it was found that subject C was eating mackerel for lunch occasionally. No further blood was obtained for 3 months from subject H who had left for a 7 month visit to Europe and North America.

Fig. 2*a* shows that during the first 2 weeks with Semet-Se, plasma Se of subject H had increased rapidly to 0·13 μg Se/ml, which was above erythrocyte Se (0·10 μg/ml). Thereafter plasma Se increased more slowly so that during the last few weeks the erythrocyte Se was again greater (0·18 μg/ml) than plasma Se (0·16 μg/ml). With selenite-Se, plasma Se (Fig. 2*b*) and erythrocyte Se of subject S had increased at similar rates and had reached 0·097 μg Se/ml and 0·12 μg Se/ml respectively at the end of dosing. Unfortunately measurements were made only on whole blood of subject C.
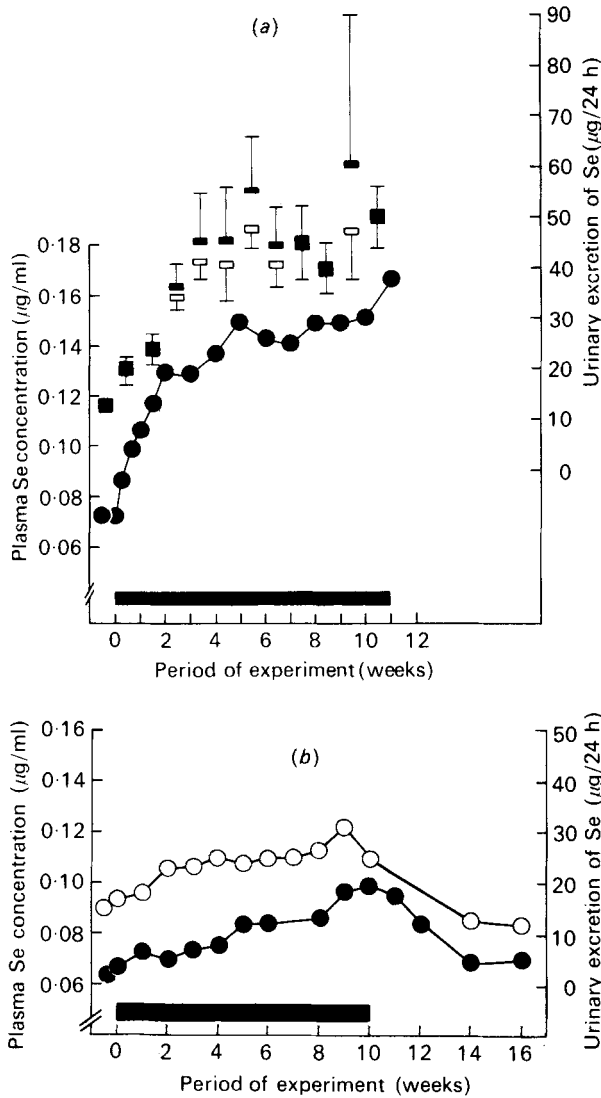
Fig. 2. Plasma concentration (μg/ml) (●) and urinary excretion (μg/24 h) of selenium during supplementation (■■■) with (a) 100 μg Se as selenomethionine (■) for subject H and (b) 100 μ as selenite (○) for subject S. The points for urinary output are mean values for each week and standard deviations represented by vertical bars. Mean urinary outputs are also given for non-fish days (□). For details of experimental procedure, see p. 590.

Urinary excretion. Fig. 2 shows a striking relationship between 24 h urine and plasma concentration (r 0·95, $P < 0·001$ for subject H; r 0·83, $P < 0·001$ for subject S). When fish was eaten the mean ($\pm$ SD) are given as well for the non-fish days in that week: for subject C, excretion (μg Se/d) increased from a predosing weekly mean of $11·2 \pm 1·6$ to $14·2 \pm 1·0$, $18·4 \pm 2·3$, $23·4 \pm 2·5$ and $20·9 \pm 2·9$ for weeks 1–4 respectively, of fish-Se supplements, a net increase of 10 μg Se/d. This was similar to the increase for subject S (from 15 to 25 μg Se/d) during the first 4 weeks with selenite-Se, and both were much smaller than the increase of 32 μg Se/d for subject H (from 13 to 45 μg Se/d). Thereafter the urinary excretion and also plasma Se changed little until the end of dosing.
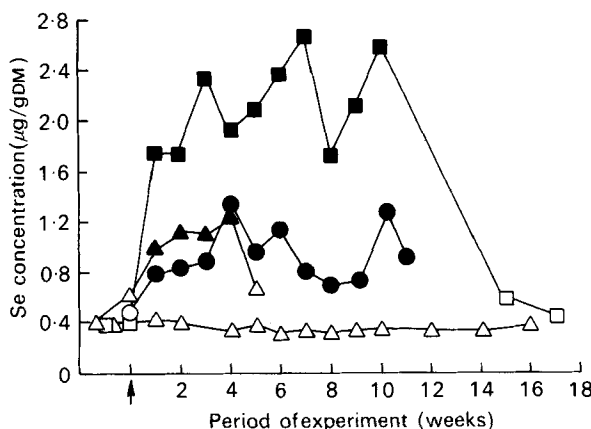
Fig. 3. Faecal concentration of selenium (μg/g dry matter (DM)) during daily supplementation with 100 μg Se as selenomethionine (●) for subject H; 100 μg Se as selenite (■) for subject S; and 65 μg Se as in mackerel (▲) for subject C. Faecal concentration for non-supplemented periods are given for subject H (○), subject S (□), subject C (△) and (↑) indicates the start of daily supplementation. Baseline faecal concentration for subject C (△) from previous study (Griffiths, Stewart & Robinson, 1976). For details of experimental procedure, see p. 590.

Faecal concentration. Fig. 3 shows that faecal concentration (μg Se/g dry matter) increased rapidly during the first 3–4 weeks and then reached a plateau. Faecal Se was considerably greater during ingestion of selenite-Se than it was for the two other forms of Se, and all were greater than the baseline faecal concentration for subject C on a self-chosen diet, during which it remained relatively constant (Stewart *et al.* 1978).

Balance of Se. The difference between the total intake and the combined urinary and faecal outputs was taken as the balance and, since it was always positive, the retention of Se (Table 1). Total intake was derived from the daily Se supplement and the Se intake contributed by the food other than mackerel. Food Se was estimated from the sum of the urinary and faecal excretion of Se in the predosing period (Stewart *et al.* 1978), and was 26, 23 and 30 μg Se for subjects H, C and S respectively. These estimates agreed remarkably well with previous measurements of duplicate diets for subjects H and C (Griffiths, Stewart & Robinson, 1976; Robinson, unpublished results). An additional 50 μg Se was added to the daily intake when a meal of fish had been eaten (Robinson, 1976).

During the first 4 weeks (supplement period 1) daily faecal output from supplements of selenite-Se was twice that from the other two supplements which indicated that selenite-Se was less well absorbed. Daily urinary output for selenite-Se (0·17 of the intake) was less than for Semet-Se and for fish-Se (0·21 of the intake), but when allowance is made for differences in absorption (intake−faecal output), more of the absorbed selenite-Se was excreted than of the other two forms. It should be noted that during the 1st week more of absorbed selenite-Se than Semet-Se was excreted (0·30 and 0·21 of the absorbed intake respectively), whereas in week 4 the converse occurred, with more of absorbed Semet-Se than selenite-Se being excreted (0·46 and 0·42 of the absorbed intake respectively). Thus over all during supplement period 1, a little less selenite-Se was retained (0·63 of the absorbed intake) than for the other two forms of supplement (0·68 of the absorbed intake). In terms of intake, approximately half the intake with Semet-Se and with fish-Se were retained compared with 0·3 of the intake with selenite-Se.

For the remainder of the studies of Semet-Se and selenite-Se (supplement period 2), the urinary output from selenite-Se changed little whereas that from Semet-Se had increased to almost half the absorbed intake. This resulted in a lowered retention of Semet-Se (0·53 of

Table 1. *Intake, absorption and retention of selenium by three subjects with daily supplementation of 100 μg Se as selenomethionine (Semet-Se), or selenite (selenite-Se), or of 65 μg Se as in mackerel (Scomber japonicus) (fish-Se)**

Expt	Subject	Form of supplement	Supplement period	Duration of supplement period	Intake		Faecal excretion (μg Se/d)	Apparent† absorption		Urinary excretion		Retention‡	
					mg Se	(μg Se/d)		μg Se/d	Proportion of intake	μg Se/d	Proportion of absorbed intake	μg Se/d	Proportion of absorbed intake
1a	H	Semet-Se	1	Week 0–4	3·6	130	33	97	0·75	31	0·32	66	0·68
			2	Week 5–11	6·7	136	33	103	0·76	48	0·47	55	0·53
1b	C	Fish-Se	1	Week 0–4	2·5	90	31	59	0·66	19	0·32	40	0·68
1c	S	Selenite-Se	1	Week 0–4	3·6	130	70	60	0·46	22	0·37	38	0·63
			2	Week 5–10	5·5	130	51	79	0·61	26	0·33	53	0·67

* For details of experimental procedure, see p. 590.
† Calculated as the difference between intake and faecal output.
‡ Calculated as the difference between intake and combined urinary and faecal output.

Table 2. *Retention of selenium and increase in Se concentration of blood and plasma in three subjects with daily supplementation of* 100 *μg Se as selenomethionine* (*Semet-Se*) *or selenite* (*selenite-Se*) *or of* 65 *μg Se as in mackerel* (*fish-Se*)*

Expt	Subject	Form of supplement	Sup-plement period	Duration of supplement period	Retention of Se†		Increase in Se concentration (μg Se/ml per week)	
					mg Se	mg Se/week	Blood	Plasma
1a	H	Semet-Se	1	Week 0–4	1·8	0·45	0·012	0·015
			2	Week 5–11	2·7	0·39	0·007	0·004
1b	C	Fish-Se	1	Week 0–4	1·1	0·28	0·009	—
1c	S	Selenite-Se	1	Week 0–4	1·1	0·28	0·007	0·003
			2	Week 5–10	2·3	0·39	0·002	0·003

* For details of experimental procedure, see p. 590.
† Calculated as the difference between intake and combined urinary and faecal output.
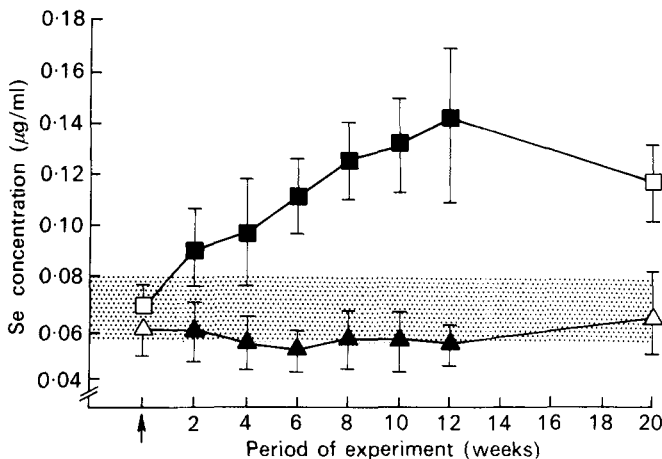

Fig. 4. Whole blood selenium concentration (μg/ml) of patients from Tapanui, South Otago, New Zealand, during and after daily supplementation with oral doses of 100 μg Se as selenomethionine (■) or with placebo (▲); (↑) indicates the start of daily supplementation. The points are mean values and standard deviations represented by vertical bars. (▦), range for mean ±SD (0·068 ± 0·013 μg Se/ml) for New Zealand subjects (Griffiths & Thomson, 1974). For details of experimental procedure, see p. 590.

the absorbed intake). Even so, the same proportion of the intakes (0·40 of the intake) of Semet-Se and selenite-Se were retained.

Table 2 shows that in supplement period 1, weekly retentions of Se were accompanied by comparable increases in blood Se, whereas in supplement period 2 retentions of Semet-Se and selenite-Se were identical, but the changes in blood Se were very different with an increase of 0·007 μg Se/ml per week compared with 0·002 μg Se/ml per week.

Expt 2. *Tapanui trial* (1975). Fig. 4 shows that daily supplements of Semet-Se had increased blood Se of all subjects by a mean of 0·07 μg Se/ml to reach 0·14 μg Se/ml. In the next 2 months it had decreased but was still significantly higher ($P < 0.001$) than the mean concentration for the control group, which had remained more or less constant throughout the study.

Twelve of the patients had relief of their symptoms, and seven of these patients were

Table 3. *Expt 3. Blood selenium concentration (μg Se/ml) of New Zealand residents before travelling overseas and after return to New Zealand**

| Subjects | Blood (μg Se/ml) | | Period absent from New Zealand (months) | Countries visited |
	Before departure	On return		
H	0·18†	0·162	7	Europe, UK, North America
J	0·082	0·138	7	Europe, UK, North America
R	0·080	0·154	21	Europe, North and South America
M	0·045	0·180	17	North America, UK
PK	0·049	0·129	10	UK
MR	0·069	0·110	2	UK
BM	0·069	0·098	2	UK

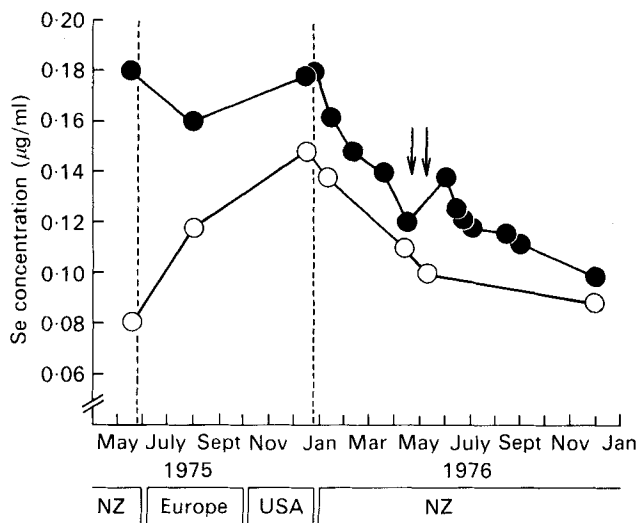* For details, see p. 590.
† Subject H had just completed Expt 1 a.

Fig. 5. Whole blood selenium concentration (μg/ml) of subjects H (●) and J (○) from May 1975 to December 1976, including period outside New Zealand (NZ), June–December 1975. Subject H had participated in Expt 1 a (May 1975; for details, see p. 590); and in Expt 1 (May 1976) of previous study (Thomson, Burton & Robinson, 1978) to monitor the response to single oral dose (↓) of selenomethionine (for details of experimental procedure, see p. 580 and Fig. 2 of Thomson *et al.* 1978).

from the experimental group. The interpretation of the clinical findings will be presented elsewhere.

Expt 3. Overseas travellers from New Zealand. Before departure all subjects had a blood Se typical for New Zealand residents, except subject H who had just completed Expt 1 a (Table 3). The increase in blood Se ranged from 0·03 μg Se/ml after 7 weeks in England (subject BM) to an increase of 0·13 μg Se/ml after 17 months overseas (subject M). Blood Se of subject J (Fig. 5) had increased steadily in the 7 months outside New Zealand and reached 0·15 μg Se/ml at the end of 2 months in USA. Meanwhile the increased blood Se of

subject H had been maintained, and on return blood Se for both subjects decreased, except for a period of dosing with Semet-Se for subject H (Thomson *et al.* 1978).

DISCUSSION

Semet-Se was more effective in increasing the blood Se of Tapanui residents than selenite-Se, since with even larger daily doses of 0·5 mg Se (Thomson *et al.* 1978) a plateau at approximately 0·10 μg Se/ml blood was reached within 1 week. On the other hand with supplements of Semet-Se, blood Se had almost reached blood Se of the overseas travellers. This suggested that selenite-Se and Semet-Se might be handled differently, which had already been indicated from our studies with tracer doses of [75Se]selenite and [75Se]selenomethionine (Thomson & Stewart, 1974; Griffiths *et al.* 1976).

It would have been easier to compare the three forms of supplement if fish-Se had provided the same amount of Se as the others. It would also have been preferable to investigate them all in each subject, but this was not feasible because after each period of dosing it takes up to 9 months for the blood Se to return to the predosing values. Also with each period of dosing the body pool of Se has presumably increased and it is not known whether it would have also returned to the predosing values with the blood Se. Thus each supplement was studied in only one subject, but subjects were chosen who, though familiar with metabolic procedures, had not participated recently in a Se-dosing trial.

No attempt was made to correct the urinary or faecal excretion for baseline excretion as in the previous study (Thomson *et al.* 1978), so that the intake corresponding to each measured output comprised Se in the habitual diet as well as that in the supplement, and was designated according to the supplement.

No correction was made for endogenous faecal output in estimating absorption in this study. For New Zealand subjects whose dietary intake was 24 μg Se and endogenous faecal output was 5–6 μg Se, the apparent absorption of food Se (0·55 of the intake) was an appreciable underestimate of the true intestinal absorption (0·80 of the intake) (Stewart *et al.* 1978). On the other hand for large doses of 1 mg Se there was little difference (10–20 μg Se) between apparent and true intestinal absorption (Thomson, 1974). Thus in the present study, the endogenous faecal output could lie between 6 and 20 μg Se, in which case the true intestinal absorption would become 0·8–0·9 of the intake for Semet-Se, and 0·6–0·7 of the intake for selenite-Se, with fish-Se between them. Such values are not much greater than the corresponding values for apparent absorption used in this study.

Urinary excretion

Increasing the Se intake increased the daily urinary output of Se, but by different amounts depending on the form and intestinal absorption of the supplement. Excretion during the first week possibly reflected the different rates with which the absorbed Se was taken up by the liver and became protein-bound (Thomson *et al.* 1978). Semet-Se was more effective than selenite-Se in increasing plasma Se and with it the excretion of Se. Plasma samples were taken at least 6 h after the supplement when most of the absorbed Se was bound to protein. After administration of [75Se]selenite Burk (1974) showed that 85 % appeared to be protein-bound by 6 h and 97 % by 24 h. Whether this appearance was due to an increase in binding, or to the unbound or loosely-bound Se being excreted, is not clear. A comparable study with selenomethionine has not been reported, but from other studies with [75Se]selenomethionine the tracer seemed to be mainly protein-bound (Awwad, Potchen, Adelstein & Dealy, 1966; Oldendorf & Kitano, 1963; Oldendorf, 1968; Eaton & Kipnis, 1972). Thus the urinary output of Se can be considered in two phases, a rapid initial excretion of presumably unbound Se, then a slower excretion of residual unbound, loosely-bound or bound Se, the excretion

being related to the plasma concentration. This could account in the present study for more of absorbed Semet-Se than selenite-Se being excreted in week 4 when the effect of the increased plasma Se with Semet-Se had overlapped the rapid initial excretion after selenite-Se.

Retention of Se and blood Se

Se was retained with all supplements with more being retained during the first 4 weeks from Semet-Se (1·8 mg Se) than from selenite-Se (1·1 mg Se), but as the study progressed with urinary excretion of Semet-Se increasing, comparable amounts (0·39 mg Se/week) of Semet-Se and selenite-Se were retained. Over all 4·5 mg Semet-Se and 3·5 mg selenite-Se were retained. Such retentions are large when compared to an estimate of whole-body content of 6 mg Se for four New Zealand women, including subject C whose whole-body content was calculated to be 4·8 mg Se (Stewart et al. 1978).

Retentions of Se seemed to be reflected in the blood Se for fish-Se and Semet-Se, apart from the initial increase in plasma Se with Semet-Se. But for selenite-Se, blood Se reflected retention for only a short period, after which Se appeared to be retained without altering the blood Se. The same effects on blood Se were shown by the two Tapanui trials. It is noteworthy that the same level of 0·10–0·12 μg Se/ml blood was reached with selenite-Se regardless of whether the supplement was ingested daily in small doses as by subject S, or in large doses as in the first Tapanui trial (Thomson et al. 1978), or as by some residents near Lincoln College, Christchurch, New Zealand, who over 10 years or more had been dosing themselves regularly or spasmodically with large single doses of 1–2 mg selenite-Se (Thomson et al. 1978).

Our tracer studies have indicated that ^{75}Se from [^{75}Se]selenomethionine was metabolized differently and incorporated more efficiently into body tissues than that from [^{75}Se]selenite (Thomson & Stewart, 1974; Griffiths et al. 1976). Thus it was suggested that Semet-Se might prove more effective than selenite-Se for improving a possible low Se status in New Zealand subjects. Blood Se is often used to assess Se status of animals including rats and sheep (Underwood, 1977) but the findings in the present study with selenite-Se being retained without changing the blood Se accordingly, cast some doubts on the reliability in using blood Se for assessment of Se status of human subjects.

An alternative explanation could be that the respiratory and dermal losses had become significant as the study progressed. Only trace amounts of Se were detected in respiratory excretion after single large doses of selenite-Se (0·01–0·02 of the dose) (Thomson, 1974), but whether they are important with repeated supplements requires investigation. Furthermore, blood Se had not increased above 0·12 Se/ml in any of our studies with selenite-Se.

Assessment of nutritional status with respect to Se

Plasma Se has largely replaced urinary excretion as an indicator of nutritional status, partly because it is easier to collect, but of more importance it is less influenced by the occasional ingestion of Se-rich foods (Griffiths & Thomson, 1974; Burk, 1976). It remains to be shown whether there is any relationship between plasma Se and muscle Se, whole-body Se or some other criterion, and the meaning of any such relationship.

A few new settlers who were studied shortly after arrival in New Zealand excreted more Se in urine than most New Zealanders and sometimes even more than their own Se intake; with increasing period of residence their urinary output and plasma Se had decreased to New Zealand levels (Griffiths & Thomson, 1974, unpublished results). Further plasma Se and urinary outputs of patients on neglible Se intakes during total parenteral nutrition had reached some of our lowest values until Se supplements were given (McKenzie, Rea, van Rij & Robinson, 1976; van Rij, Thomson, McKenzie & Robinson, unpublished results). It seems that the body content of Se is relatively labile and can fluctuate with the level of intake.

Whether the body Se is regulated or not is not known, but Burk (1976) has proposed that homoeostasis is maintained in man as in rats by urinary excretion of Se metabolites. If such urinary metabolites could be identified as well as the specific Se-protein complexes and other Se components in plasma from patients, healthy residents and new settlers to New Zealand, some insight might be obtained into the relationship between plasma Se and urinary Se, and whether either criterion might be an indicator of body Se content.

There is increasing awareness that although the availability of Semet-Se for uptake and retention in the tissues of most animals is greater than selenite-Se, it might not be so for biological availability. Selenite-Se has been found more effective than Semet-Se in preventing exudative diathesis in chicks (Noguchi, Cantor & Scott, 1973), and further that blood levels were significantly higher in chicks fed on tuna meal, although the biological availability of tuna meal was very small compared with selenite-Se. Cantor, Scott & Noguchi (1975) suggested that biological availability was determined by the ability of chicks to utilize various forms of Se for activity of the enzyme glutathione peroxidase (*EC* 1.11.1.9) (GSHPx). However, some species differences in GSHPx activities in different organs and tissues and their response to dietary Se have been reported (Ganther, Hafeman, Lawrence, Serfass & Hoekstra, 1976), so it is not possible to extrapolate from animal species to man. A high correlation was found between Se concentrations and GSHPx activities in blood of New Zealand residents (Thomson, Rea, Doesburg & Robinson, 1977) and in all our present studies measurements of both were carried out. Most of the enzyme activity is present in the erythrocytes, and studies of the relationship between dietary forms of Se and erythrocyte GSHPx activities in man are in progress.

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