Selenium: Dietary Threshold for Urinary Excretion in the Rat (36991)

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(Introduced by H. E. Sauberlich)

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Regulation of the body burden of selenium is important because selenium deficiency and excess both lead to pathologic conditions (1, 2). We showed that after intraperitoneal injection of $^{75}SeO_3^{2-}$ urinary excretion of ^{75}Se increased as dietary selenium was raised within the range of 0 to 1 ppm (3). Fecal and expired ^{75}Se had no such relationship with dietary selenium under those conditions. Since our previous study showed a marked increase in urinary ^{75}Se when only 0.1 ppm selenium was added to the diet, and since the urine seems to be the major route of selenium excretion, we decided to study even lower dietary selenium levels to determine whether there was a dietary selenium threshold above which urinary selenium began to increase.

Methods and Procedures. Five groups of 4 weanling male Holtzman rats each[1] were fed a vitamin E-adequate (250 IU *dl*-α-tocopherol/kg diet) torula yeast diet (3) with 0, 0.030, 0.060, 0.090, and 0.120 ppm selenium added as Na_2SeO_3, respectively. The basal diet without selenium supplementation contained 0.024 ppm selenium.[2] Rats were weighed weekly and no differences in growth rate were observed among groups. After the rats had consumed the diets for 25 days, each animal was injected intraperitoneally with 2 μCi of $^{75}SeO_3^{2-}$ (sp act 119 Ci/g of selenium)[3] and placed in a metabolism cage. Urine and feces were collected for 7 days and percentage of administered ^{75}Se in them was determined as before (3). Whole-body counting was performed daily for 17 days. Then the animals were sacrificed and percentage of whole-body ^{75}Se in various organs was determined as described previously (3).

Results. Figure 1 shows the whole-body retention of ^{75}Se. The 0 and the 0.030 ppm selenium groups retained the same percentage of the ^{75}Se dose whereas differences among all other groups were highly significant. Urinary excretion accounted for the differences in whole-body retention as shown in Fig. 2. Urinary and fecal excretion accounted for all losses of ^{75}Se as calculated from whole-body retention.

In contrast to the identical ^{75}Se total body retention of the 0 and 0.030 ppm groups, tissue distribution in these groups was markedly different as is seen in Fig. 3. Testes ($p < 0.001$), adrenals ($p < 0.005$), spleen ($p < 0.001$), thymus ($p < 0.01$), and brain ($p < 0.001$) all contained significantly more of the whole-body ^{75}Se per gram in the 0 ppm group, while liver ($p < 0.005$), blood ($p < 0.005$), heart ($p < 0.05$) and skeletal muscle ($p < 0.05$) contained more in the 0.030 ppm group.

Discussion. The whole-body and excretion results indicate the existence of a dietary selenium threshold somewhere between 0.054 ppm (0.024 + 0.030 ppm) and 0.084 ppm (0.024 + 0.060 ppm) for the forms of selenium used in this experiment below which a constant percentage of the administered ^{75}Se is excreted in the urine. Above the threshold

[1] In conducting research described in this report, the investigators adhered to the "Guide for Laboratory Animal Facilities and Care," as promulgated by the Committee on the Guide for Laboratory Animal Facilities and Care of the Institute of Laboratory Animal Resources, National Academy of Sciences-National Research Council.

[2] Analysis was kindly performed by Mr. Earle Cary of the U.S. Department of Agriculture's Plant, Soil, and Nutrition Laboratory at Cornell University, Ithaca, NY using the method of Olson, J. Ass. Offic. Anal. Chem. 52, 627 (1969).

[3] Purchased from New England Nuclear, Boston, MA.

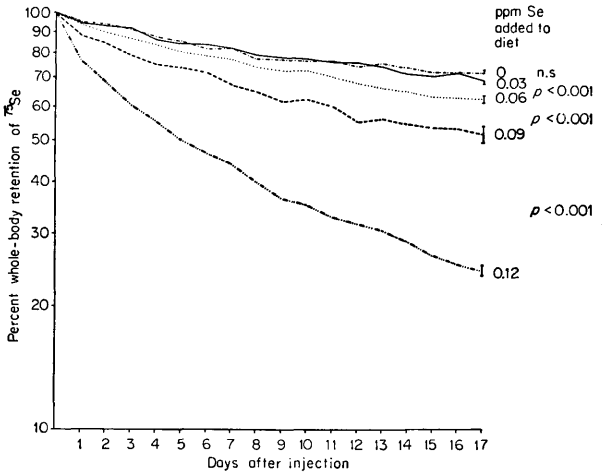

FIG. 1. Whole-body ^{75}Se retention curves of rats fed diets with different amounts of selenium added. Standard deviations and p values (t test) are given for the last day's values. Semilogarithmic graph paper was used.

an increase in dietary selenite leads to an increase in the percentage of the administered ^{75}Se in the urine, at least up to a level of 1 ppm (3).

With regard to the values given for the threshold, it should be stated that they can be expected to vary according to the biological availability of the dietary selenium. Since the availability of selenium found in torula yeast has been reported to be virtually nil (4), it is likely that the threshold value for selenite is lower than 0.054 to 0.084 ppm.

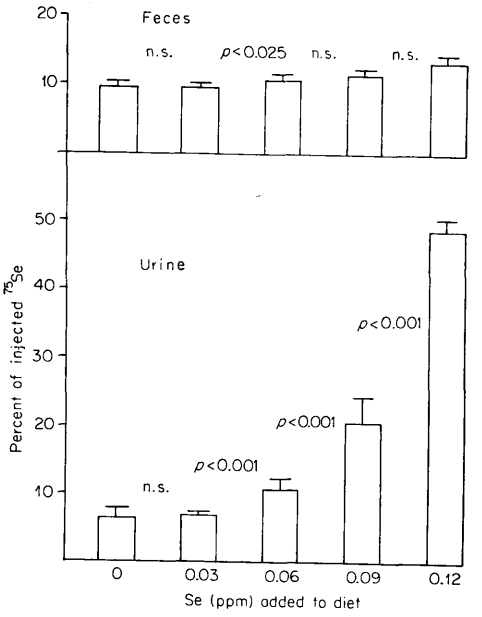

FIG. 2. Cumulative 7-day urinary and fecal ^{75}Se of rats fed diets with different amounts of selenium added. Standard deviation and p values (t test) are indicated.

The initiation of increase in urinary excretion could be related to reaching a critical body burden of selenium corresponding to the dietary threshold. Altering the body burden below this critical value results in changes of tissue distribution but has no effect on excretion of the label.

The ^{75}Se tissue distribution shows trends similar to those previously reported (3). Of interest is the large ^{75}Se content of the adrenal glands of animals fed the 0 selenium diet. It is not known whether selenium deficiency affects adrenal function.

The metabolic process underlying the increase in urinary excretion is probably related to production of urinary metabolites such as trimethylselenonium ion (5), but renal threshold for these metabolites may also be involved.

Ewan, Pope and Baumann (6) reported that the addition of 0.05 ppm selenium to a torula yeast diet actually increased the biological half-life of injected ^{75}Se. However, experimental conditions were different in that all their rats were being fed the basal diet at

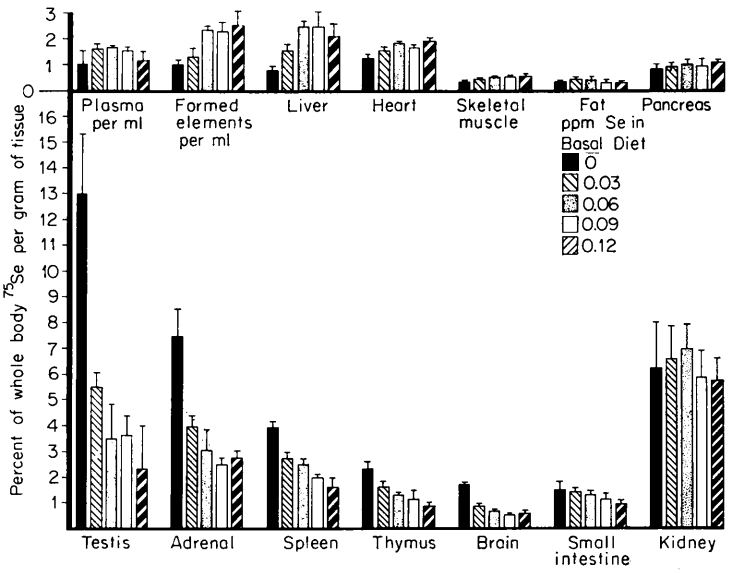

FIG. 3. Effect of dietary selenium on tissue retention and distribution of ^{75}Se 17 days after injection of a tracer dose of $^{75}SeO_3^{2-}$. Values are percentages of total body ^{75}Se at the time of death. Vertical lines indicate 1 SD. Each group had 4 rats.

the time of injection and the 0.05 ppm supplement was added 1 wk later. We did not note such an increased retention either here or in unpublished experiments where 0.05 ppm selenium was added to the diet.

It is possible that the threshold is related to the nutritional requirement for selenium inasmuch as its value is reasonably close to that needed to prevent dietary liver necrosis (7). Whether such a relationship exists or not, the shutting down of the urinary excretory pathway below the threshold is almost certainly an important mechanism for the conservation of selenium by the animal receiving very little in the diet.

Summary. Radioselenium studies in rats utilizing whole-body counting and determination of urinary and fecal ^{75}Se indicate the existence of a threshold dietary level of selenium above which urinary excretion of selenium is directly related to its dietary level and below which it is not. The threshold lies between 0.054 and 0.084 ppm for the forms of selenium used here. Tissue distribution of ^{75}Se was markedly different in all groups and exhibited no threshold under the conditions of this experiment.

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