

Risk assessment of selenium¹

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During the revision of the Guidelines for Drinking-Water Quality, which was recently completed by the World Health Organization (WHO), the risk associated with selenium exposure via drinking water was discussed.

It has been proved scientifically that selenium, as a constituent of the human enzymes cytoplasmic and plasma glutathione peroxidase, is an essential trace element for humans. This element is also a constituent of other enzymes (eg, tetraiodothyronine deiodinase) and has several other less well-defined functions in the human body (1, 2). In the volume on selenium in the WHO *Environmental Health Criteria* series (3) it was estimated that the minimum daily adult requirements were 13.3 and 19.1 $\mu\text{g} \cdot \text{d}^{-1}$ for women and men, respectively. Metabolic balance studies of healthy North Americans have shown that, to stay in balance, about 0.8 $\mu\text{g} \cdot \text{kg} \text{ body weight}^{-1} \cdot \text{d}^{-1}$ is needed. However, lower intakes were needed for this purpose by other groups with lower prior selenium intake. To maintain plasma glutathione peroxidase at the maximum level, Chinese adult men needed about 40 $\mu\text{g} \cdot \text{d}^{-1}$. The recommended daily intake was recently set by the United States National Research Council (1) at 1.7 $\mu\text{g} \cdot \text{kg}^{-1}$ for infants and 0.9 $\mu\text{g} \cdot \text{kg}^{-1}$ for adults to maintain good nutrition in healthy populations.

Acute and chronic selenium toxicity have been demonstrated in a wide variety of animal species, including humans. Soluble selenium salts are of approximately similar toxicity, and there is only minor variation among animal species. Although organic-bound selenium in food is considered to be less toxic than inorganic selenium compounds, little is known about the toxic potency of different selenium compounds in humans (3).

Except for selenium sulfide, experimental data do not indicate that selenium is carcinogenic. Adequate human data do not exist. With regard to selenium sulfide, some uncertainty exists as to whether this compound can cause cancer in humans. It is a man-

ufactured product and is not normally found in water. Genotoxicity has not been demonstrated in humans, whereas such effects have been seen in several in vitro systems. It is possible, however, that the latter effects may be dose dependent in vivo and not occur at nutritionally adequate intakes (4).

There is no evidence for teratogenicity in humans, and macaques (*Macaca fascicularis*) fed selenomethionine, the most teratogenic selenium compound in avian species, showed no sign of teratogenesis (5).

In view of these findings and the fact that selenium is an essential trace element in human nutrition, it is appropriate to define a threshold level in the safety assessment of selenium.

Although some toxicity studies with rats have been reported and both a no-observed adverse-effect level (NOAEL) and a lowest-observed adverse-effect level (LOAEL) have been suggested, it is recommended that human studies should be used as a basis for the evaluation of adverse health effects.

Early critical effects of selenium toxicity on humans are nail changes, skin lesions, liver toxicity, and an increased prothrombin time, probably due to subclinical liver toxicity with depressed protein synthesis.

Despite the many studies on the nutritional role of selenium and the extensive use of selenium supplementation, remarkably few studies on the tolerable selenium exposure of humans have been performed. Except for the early investigations of the population in seleniferous areas in the United States (6, 7), the recent Chinese studies of endemic selenium intoxication in humans (8–10) and an American study from 1991 (11), there are only anecdotal reports. On the basis of the Chinese studies, the minimum dietary intake sufficient to cause symptoms of selenosis is about 1200 μg . Symptoms were also seen in a man with an intake of 900 $\mu\text{g} \cdot \text{d}^{-1}$. An increased prothrombin time was seen at dietary intakes above 750–850 $\mu\text{g} \cdot \text{d}^{-1}$ (9). In the American study (11), no clinical or biochemical signs of toxicity were seen in a population consuming an average of 239 (range 68–724) $\mu\text{g} \cdot \text{d}^{-1}$. However, the liver enzyme alanine aminotransferase in serum, although within the reference range, showed a correlation with selenium intake. In a small study, patients with rheumatoid arthritis receiving 0.25 mg of selenium as organic selenium, in addition to a dietary intake assumed to be about 0.1 mg, showed decreased somatomedine

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C in serum (12). [This protein originates in the liver.] However, this finding was *not confirmed* in the American study. Taken together, an increased prothrombin time, a slight increase in alanine aminotransferase, and a possible decrease in somatomedin C are all signs of subclinical liver affection. However, the clinical relevance is uncertain. The selenium intakes in these studies could be used as LOAEL values for humans.

On the basis of these data, an intake of selenium of up to about $4 \mu\text{g} \cdot \text{kg body weight}^{-1}$ could be considered as safe and tolerable. This value, which is about 2.5 times the recommended daily intake for children and four times that for adults, is also based on the assumption that the soluble selenium salts in drinking water might be more toxic than organic-bound selenium from food, which was the source of the selenium exposure in the Chinese and American studies. Drinking water usually contributes less than 1% to selenium intake and not more than 10% in highly seleniferous areas. However, the drinking water should *not* be regarded as a nutritional source of selenium, and intake from it should therefore be less than 10% of the tolerable exposure.

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