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# SELENIUM IN NUTRITION

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■ Every useful substance—water, salt, air, nutrients, and vitamins as well as therapeutic agents— has a range below which it loses effectiveness and above which it becomes harmful. With selenium the optimum range is fairly narrow, and the penalties for transgression can be dramatic.

## FUNCTIONS OF SELENIUM

There are three major functions of selenium. First, as an antioxidant it (1) enables organisms to survive with less oxygen and (2) reduces the formation of undesirable oxidative by-products of metabolism. Many of these by-products are highly reactive molecules that may function as carcinogens, mutagens, or inactivators by steric blockage.<sup>1</sup>

Second, selenium is a constituent in metabolically important enzymes such as glutathione peroxidase, and several other enzymes of less well-defined function.<sup>2</sup>

Third, selenium reacts with toxic metals, forming biologically inert compounds.<sup>3</sup> This is important because the process by which selenium inactivates mercury, cadmium, or arsenic is not chelation. Selenium thus provides

an alternative to chelation in dealing with certain heavy metal poisonings.

These three main functions may not cover the entire spectrum of selenium's activities. For example, there appears to be a correlation between night vision acuity of an organism and the selenium content of its retina.<sup>4</sup> Vitamin E, the other principal antioxidant, is insoluble in water and is not able to enter the transparent parts of the eye.

In addition, selenium appears to play a part in the synthesis of enzymes other than glutathione peroxidase, particularly some of the transaminases, and in ubiquinone, a key substance in the oxidation chain.<sup>5,6</sup>

## TOXICITY OF SELENIUM

The toxic properties of selenium were known long ago. Indian tribes considered super-selenated areas cursed. Early toxicologists viewed selenium only as a hazard. Even today, researchers hesitate to explore the possible values of this element in human therapy or nutrition.

Symptoms of toxicity are intense and appear early enough to impel withdrawal before any lasting damage has occurred. Early symptoms include a garlic-like odor associated with volatile methyl-selenium compounds, loss of

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hair, and soreness of nails (or claws or hoofs in animals).

The lethal dose for rats is about 3 to 5 mg/kg body weight. It is possible that selenium toxicity is in part caused by its excessive inactivation of useful or necessary metallic ions, notably zinc, copper, chromium, cobalt, and perhaps iron. With the possible exception of zinc, these elements would probably be automatically replaced in a normal balanced diet, largely by skim milk or cottage cheese. It is not precisely known what levels humans can tolerate, although 1 mg/kg seems safe.

Sodium selenite has not been reported to be carcinogenic in any context; on the contrary, epidemiologic evidence shows a lowered incidence of cancer in selenium-rich areas.<sup>7</sup> However, one report indicates that large doses of selenate have caused cancer in rats.

In spite of increasing use of selenium in animal husbandry, there have been no known major accidents involving humans.

A 15-year-old white girl in New Zealand intentionally drank 400 ml of a sheep-dipping concentrate containing sodium selenate 5 mg/ml. This was 22.3 mg Se/kg body weight. She was admitted to the hospital 45 minutes after ingestion, so there had been considerable time for absorption. She was discharged from the hospital 17 days later, apparently fully recovered.<sup>8</sup>

#### EFFECTS OF SELENIUM DEFICIENCY

The variation of concentration of selenium in grains grown in seven different countries is shown in Table 1.

Use of selenium in animal nutrition has expanded dramatically in recent years. Selenium administration has made animal husbandry possible in large areas where it previously was unprofitable.

In animals, survival rate of offspring is sensitive to selenium deprivation. For instance, in areas of Finland with low selenium, an average sow has 4.5 surviving offspring, whereas with 0.1 mg selenite added per 1000 gm feed, this figure increases to an average of 10.<sup>9</sup> Similar observations have been made in cattle.

In humans, there seems to be a correlation between myocardial infarctions and selenium deprivation. This is illustrated in Figure 1.

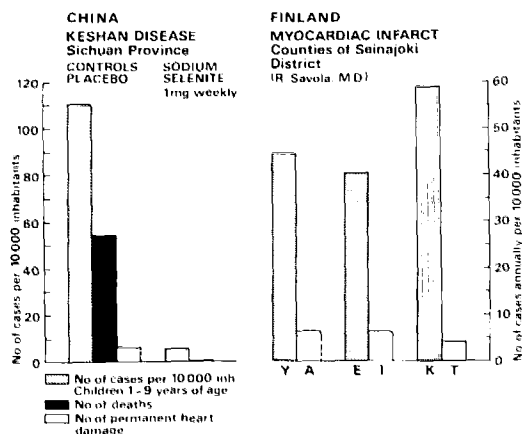
**Table 1** • Average Selenium Content of Typical Cereals (mg/kg)

Rye	United States	0.080
	Argentina	0.071
	Turkey	0.059
	Sweden	0.006
	Finland	0.004
Wheat	Canada	1.300
	United States	0.368 to 0.703
	Argentina	0.520
	Sweden	0.007 to 0.022
	Finland	0.004 to 0.085
	China	0.0053 to 0.0196 (low selenium area)

which includes data from both Finland and China.<sup>10-12</sup>

Deficiency disease of selenium-deprived children in China corresponds to that for Finnish cattle, and to the myocardial infarction rate of Finnish selenium-deprived adults.

Deaths from myocardial infarction are high-



**Figure 1.** Difference in frequency of two heart syndromes, both related to availability of selenium. Chinese Keshan disease has been abolished; Finnish myocardial and muscular syndrome has been controlled in cattle, but continues to account for exceptional frequency of infarcts in people of working age (15 to 64).

Selenium figures are all counted as 100% Se. Letters under the right column designate matched Finnish counties of Ylihärmä, Alahärmä; Evijärvi, Isokyrö; and the extremes: Korttesjärvi, Tövsä.

est in Finland,<sup>9</sup> New Zealand,<sup>13</sup> and perhaps South Africa,<sup>14</sup> countries where selenium deficiency is more widespread than in the United States. In addition to farmers in these countries being at high risk for death from myocardial infarction, child mortality and sudden death syndrome are higher than elsewhere.

Savola compiled figures on the incidence of myocardial infarction in the Seinäjoki district of Finland, listing data for each of 30 counties.<sup>12</sup> No specific cause was apparent for differences between counties with populations similar in nutrition. Savola did not mention selenium, but implied that a factor not yet considered must explain the differences.

Figure 1 shows the extent of these differences between two pairs of matched counties, in which no known factor other than selenium is apparent. A search for poisons, infections, or deleterious trace elements yielded only a slightly positive correlation between copper content and number of infarctions.

Hair samples from persons randomly selected from adjoining counties with different frequencies of infarction have shown averages of 0.7 ppm versus 0.3 ppm selenium, with lower infarction where selenium content was higher. Similar observations were made in China. No consistent differences have yet been found in Finland (generally a low-selenium area) in the selenium content of soil or water between the counties with different infarction frequencies.

While selenium deficiency appears to be a major cause of myocardial morbidity as evidenced by the dramatic effects of selenium supplements given to Chinese children and to Finnish cattle, there are indications in both countries that there may be some undetermined local factor, insignificant where selenium is ample, but critically affecting selenium uptake when general selenium content in an area is borderline.<sup>9,11</sup>

The United States has a selenium level 10 to

20 times higher than the deprived zones in Finland and China, but local differences in selenium concentrations can be significant. It might be worthwhile to look at the selenium content in areas with conspicuously higher infarct rates than similar neighboring areas.

#### APPLICATIONS OF SELENIUM IN NUTRITION

Optimum human intake of selenium has still not been determined; this decision must take into account which of the three independent functions is of main concern to the patient. The patient's general state of health, and other conditions such as those synergists and antagonists listed in Table 2, must also be considered.

The Food and Drug Administration has approved 0.2 mg/kg of feed as 100% selenium for animal nutrition.<sup>15</sup> Selenite, 1 mg/day, appears safe for humans under medical supervision, and an excess of sodium selenite is excreted. (Blood selenium levels remained within tolerable limits even in water with the highest selenium content in Venezuela, where urinary selenium excretion was many times the officially permitted maximum).

Selenium in selenium methionate and in high-selenium wheat or yeast tends to accumulate progressively in the human body. But one physician has used selenite, 4 mg/day, for several months as supporting therapy for terminal cancer patients who did not show symptoms of selenium toxicity.

It appears that selenium could become increasingly important in preventive medicine, as well as in therapy for threatened anoxia, and in cases of intoxication with arsenic, mercury, or cadmium and perhaps lead and silver.

Sodium selenite is the most common form of selenium administration. Preparations of organically bound selenium include selenium methionate as well as tablets of yeast grown in a selenite-rich medium.

**Table 2 • Synergists and Antagonists of Selenium**

Synergists	Antagonists
Vitamin E (lipophilic antioxidant)	Most polyvalent metals; arsenic, cadmium, mercury, perhaps iron, probably copper, a prooxidant
Vitamin C (hydrophilic antioxidant)	
Lecithin (needed for transport)	

## CONCLUSION

Selenium has had dramatic acceptance in animal husbandry. However, in those countries where selenium content is minimal, the farmer who feeds his cattle selenium supplement is often himself the victim of infarctions that would have been prevented by a selenium supplement. Knowledge has gradually accumulated, and the hazards defined. Use of selenium in human nutrition and preventive medicine has become feasible.

While most of the United States has adequate selenium, some natural deficiency occurs in areas where heavy rains are common. Inclusion of selenium in dietary supplements was discussed at the U. S. Quartermaster Conference on Antioxidants in Natick, MA in 1979. A detailed specific geriatric formula in which selenium was one ingredient was published in the proceedings.<sup>15</sup> This formula is not patented and has not been on the market, but has been used regularly by some persons for several years with apparent satisfaction. ▲

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