PRESENT KNOWLEDGE IN NUTRITION

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CHAPTER XXXI

PRESENT KNOWLEDGE OF SELENIUM

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Selenium is an unusual mineral, in that natural foods can contain either so much of the element that a toxicity results or so little that a deficiency occurs. The presence of toxic amounts of selenium in foodstuffs was discovered in the 1930's by workers in the United States who were studying a condition in livestock known as "alkali disease" (I. Rosenfeld and O. A. Beath, Selenium. Academic Press, New York, 1964). This malady was shown to be a chronic form of selenium poisoning caused by ingestion of grains and forages containing moderately high levels of selenium (5 to 40 p.p.m.). An acute seleniumosis, "blind staggers," was observed in animals consuming certain species of plants which are able to accumulate several thousand p.p.m. of selenium. In both of these cases the ultimate source of the selenium was the soil upon which the plants grew and, subsequently, significant quantities of selenium have been found in the soil of several Great Plains and Rocky Mountain regions.

The public health problem of selenium toxicity in agricultural products has been minimized in North America by careful delineation of potentially dangerous selenium areas. Unfortunately, such complete data on the geochemical distribution of selenium does not exist in other sectors of the world where there appears to be a possibility of selenium poisoning. In Venezuela, for example, some plant samples of different rural regions contained 10 p.p.m. of selenium (W. G. Jaffé, J. F. Chávez, and M. C. Mondragón, Arch. Latinamer. Nutr. 17, 59 (1967)).

Since a concentration of 5 p.p.m. in common foods is considered hazardous, the need for thorough surveys to assess the magnitude of the problem is clear.

After the initial finding of K. Schwarz and C. M. Foltz (J. Biol. Chem. 233, 245 (1953)) that trace quantities of selenium protect against liver necrosis in rats fed Torula yeast diets lacking vitamin E, many reports appeared regarding favorable biological effects of minute amounts of selenium. Among the many disorders which have been successfully treated with selenium are infertility, unthriftness, and white muscle disease in sheep, white muscle disease in calves, hepatisis diaetetica in pigs, and exudative diathesis and muscular dystrophy in poultry.

Although the need for selenium seems to be adequately documented for laboratory and farm animals, there is no known corresponding deficiency disease in man. Yet there are some preliminary studies which suggest that selenium deficiency might be a complicating factor in certain types of kwashiorkor. Two Jamaican children suffering from protein malnutrition who did not gain weight after overcoming the initial acute phase responded immediately after receiving daily supplements of 25 µg. selenium as gamma, gamma'-diseleno-di-valeriac acid (Schwarz, Fed. Proc. 20, 666 (1961)). A. S. Majaj and L. L. Hopkins, Jr. described malnourished Jordanian infants who showed a striking reticuloecyte response after administration of 30 to 50 µg. selenium per day as sodium selenite (Lancet 2, 592 (1960)). Majaj and Hopkins also cite work of Viteri, Burke, and W. N. Pearson, who found that selenium levels in the blood of Guatemalan children afflicted with kwashiorkor were about half those of normal children (First Internat. Selenium in Biomedicine Co., Westport, Conn.).

Promising evidence itself. Schwarz has reported that 0.007 p.p.m. of naturally occurring organoselenium the 50 per cent effect of necrosis in rats, whereas 0.05 to 0.10 p.p.m. of selenite was needed to prevent exudative diathesis in turkeys (Fed. Proc. 20, 666 (1961)). E. Oldfield, J. R. Muth were able to induce disease in lambs by foregeminantly an alfalfa-hay diet containing 0.06 p.p.m. of selenium

In regard to human beings, it is pointed out that intake of selenium is by no means constant, as organoselenium could initiate organ damage. It is possible that in organs that are in contact with selenium in the form of selenium sulfide may initiate organ damage. It is possible that in organs that are in contact with selenium in the form of selenium sulfide, atomic selenium is reduced to elemental selenium which is then converted to organoselenium. The loss of selenium from the body is by excretion in the urine and feces.
children (First International Symposium on Selenium in Biomedicine. AVI Publishing Co., Westport, Connecticut, 1967). The promising evidence from these early trials indicates the need for further research regarding the possible role of selenium in human nutrition.

Any attempt to set a selenium requirement must take into account several variables, including the form of dietary selenium itself. Schwarz has repeatedly emphasized that 0.007 p.p.m. of selenium as the naturally occurring organic form ("Factor 3") is the 50 per cent effective dose against liver necrosis in rats, whereas inorganic selenite or selenate is effective only at 0.02 to 0.03 p.p.m. (Nutrition Reviews 15, 123 (1960)). M. C. Nesheim and M. L. Scott found that 0.05 to 0.10 p.p.m. of selenium as sodium selenite was needed in a Torula yeast diet to prevent exudative diathesis in chicks and turkeys (Fed. Proc. 20, 674 (1961)), while J. E. Oldfield, J. R. Schubert, and O. H. Muth were able to eliminate white muscle disease in lambs by feeding their dams prenatally an alfalfa-hay-oats diet containing 0.06 p.p.m. of selenium (J. Agr. Food Chem. 11, 388 (1963)).

In regard to human nutrition, it should be pointed out that many organic selenium compounds are quite unstable and are easily lost by heating, so that over-cooking of foods might drive off volatile selenium and thus render diets inadequate in this element. The loss of selenium from heated grains is well known, but few data exist concerning the effect of various processing methods on the selenium content of foods. It is possible that under certain conditions factors known to modify the metabolism of selenium could influence the need of an organism for the element. Linseed oil meal counteracts chronic selenium toxicity (A. W. Halverson, C. M. Hendrick, and O. E. Olson, J. Nutrition 56, 51 (1955)) and might affect the selenium balance in an animal, and recently arsenic has been shown to increase biliary excretion of selenium under a wide variety of conditions (O. A. Levander and C. A. Baumann, Toxicol. Appl. Pharmacol. 9, 106 (1966)).

Addition of selenium to foodstuffs for animals or humans should be done with caution until the controversial status of the element as a possible carcinogen is completely clarified. The first report of selenium as a potential cancer inducing agent was that of A. A. Nelson, O. G. Fitzhugh, and H. O. Calvery, who fed seleniferous wheat and (KNH3)2Se in life-term rat studies, and saw adenomas or low grade carcinomas in 11 of 53 rats surviving more than 18 months (Cancer Res. 3, 230 (1943)). Similar results were obtained by L. A. Cherkes, S. G. Aptekar, and M. N. Volgarev, who fed sodium selenate and found tumors in ten out of 23 rats living 18 months (Biull. Eksp. Biol. Med. 3, 78 (1962)).

However, this work has been criticized by D. V. Frost (World's Poultry Sci. J. 21, 139 (1965)), and a rather complete study involving almost 1,500 rats fed several levels of sodium selenite or selenate over a period of three and one-half years led to the conclusion that "no neoplasms found could be attributable to selenium" (J. R. Harr et al., First International Symposium on Selenium in Biomedicine). Although this would seem to indicate the non-carcinogenicity of dietary selenite and selenate in rats, the possibility of tumor-producing organic forms of selenium or of selenium producing tumors in other species cannot be excluded.

The function of selenium in cellular metabolism remains a mystery. The many nutritional interrelationships between selenium and vitamin E, and the demonstrated activity of several selenium compounds as effective antioxidants and radioprotective agents in vitro, constitute the basis for the theory that the sole metabolic action of selenium is that of a nonspecific antioxidant (A. L. Tappel, Fed. Proc. 24, 73 (1965)). However, there are a number of typical
vitamin E deficiencies which do not respond to treatment with selenium, such as resorption sterility in rats, muscular dystrophy in rabbits, and encephalomalacia in chicks, and this has convinced other workers that, while selenium may act as an antioxidant in some cases, there is sufficient evidence to suggest a more subtle role for the element. I. D. Desai, C. C. Calvert, and Scott performed a time sequence study of the inter-relationships of peroxidation, lysosomal enzymes, and nutritional muscular dystrophy in the chick, and concluded that increased susceptibility of muscle lipids to peroxidation and increased lysosomal enzyme activity are not the primary abnormalities responsible for the onset of muscular dystrophy (see Nutrition Reviews 23, 80 (1965)).

Schwarz has postulated that vitamin E and selenium have independent effects in alternate pathways of metabolism and that this explains why the absence of both nutrients is necessary to develop certain deficiency states (Fed. Proc. 24, 58 (1965)). He has also presented work which indicates that the ability of selenium, sulfur amino acids, and tocopherol to halt the development of respiratory decline in rat liver slices could be rationalized by considering the effects of these materials on one enzyme system, α-ketoglutarate oxidase. That selenium may have an effect independent of vitamin E is also supported by the data of Nesheim and Scott, who showed a growth stimulating activity of selenium in chicks receiving adequate amounts of vitamin E (Ibid. 20, 674 (1961)). Lastly, there is the intriguing report of J. Pinessent that traces of selenite and molybdate are essential for the production of the enzyme formic dehydrogenase in Escherichia coli (Biochem. J. 57, 10 (1954)). This experiment suggests a role for selenium in protein biosynthesis which might have important consequences in mammalian systems.

About 30 years as a dietary element and as a constituent of zinc containing trace minerals, selenium has been widely studied as a potential anti-oxidant and as a catalyst for a wide range of biological processes. Selenium deficiency has been associated with various health problems in animals and humans, including cardiovascular disease, cancer, and neurodegenerative disorders. The role of selenium in human health is still under investigation, but it is clear that selenium is an essential trace element for optimal health.

Relatively recent advances in the understanding of the biological role of selenium in human health have been made in recent years. Selenium deficiency has been associated with various health problems in animals and humans, including cardiovascular disease, cancer, and neurodegenerative disorders. The role of selenium in human health is still under investigation, but it is clear that selenium is an essential trace element for optimal health.

The first unequivocal evidence for the role of selenium in humans was provided by Follis, Jr., in 1934, who revealed, as described above, that selenium deficiency is associated with reduced growth and development, anemia, and an increase in mortality. More recently, selenium has been shown to have a protective effect against certain forms of cancer, particularly in animals and humans. Selenium is also known to have a role in the immune system, and may be important in the prevention of infections.

In summary, selenium is an essential trace element for optimal health, and its role in human health is still under investigation. Further research is needed to fully understand the biological role of selenium in human health, and to develop strategies to prevent and treat selenium deficiency.