

Selenium Deficiency

What is selenium?

Selenium is a trace element which plays many vital roles in the human body, including:

- Cancer protection
- DNA repair
- Glutathione peroxidase (antioxidant enzyme)
- Immunity
- Thyroid hormone activation
- Prostaglandin production
- Assists vitamin E.

A selenium deficiency can therefore be expected to take the form of increased susceptibility to free radical diseases (cancer, heart disease, etc) Aids, infections and thyroid problems.

How recommended selenium intakes are set

The enzyme glutathione peroxidase is made by the body with selenium and is a vital antioxidant. Low activity of this enzyme can indicate a selenium deficiency.

Glutathione peroxidase activity was measured in selenium-deficient individuals in China, and selenium was then supplemented until the enzyme reached maximum levels. This occurred at 40 micrograms a day for a body weight of 60 kilos. The US RDA was set at 70 mcg per day for men and 55 mcg for women to take into account higher body weights.

Levander OA, Journal of the American Dietetic Association, Dec 1991 v91 n12 p1572(5). A similar basis is used for the UK Dietary Reference Values.

Main dietary sources of selenium

- Cereals (grains), meat, fish and eggs.
- The best sources are brazil nuts (254 mcg per 100 grams of nuts), kidney and crab. 20 brazil nuts a day would ensure adequate selenium intake.

The selenium content of grains depends on selenium levels in the soil. The selenium content of meat and eggs depends on the selenium levels in the diet of the livestock and hens. This may be a

diet of grass and/or grains grown on selenium-poor soil.

Average selenium intake

USA About 100 mcg/day

Japan About 200 mcg/day

France 40-60 mcg/day

UK 30-34 mcg/day

The upper safe intake is thought to be within the range of 200-600 mcg/day.

Selenium adequacy in the UK diet

Selenium content of wheat for bread making in Scotland. (Research by the West of Scotland Agricultural College, Auchincruive.) The proportion of Canadian flour used for bread-making in Scotland has continued to decrease since these researchers last reported on the subject in 1986 (from 26 per cent to 13.8 per cent). As a result there is a continuing decline in dietary selenium content, estimated in 1992 at only 30 micrograms a day for the United Kingdom as a whole. *Selenium content of the wheat for bread making in Scotland and the relationship between glutathione peroxidase (EC.1.11.1.9) levels in whole blood and bread consumption. Barclay MNI, MacPherson A, British Journal of Nutrition 1992, 68:261-270.*

Effects of selenium deficiency in the UK Research

University of Manchester, departments of Medicine and Chemistry. The adequacy of the selenium status of 25 healthy volunteers, 94 general medical patients and 106 allergy clinic patients was investigated in 1987/88 by measuring serum selenium concentration and platelet glutathione peroxidase activity. Significant correlations between serum selenium concentration and peroxidase activity indicate that a substantial proportion of both healthy volunteers and medical patients are of low selenium nutritional status. 25 per cent of healthy volunteers and 50 per cent of medical patients had serum selenium levels below those required for full expression of

selenium-dependent enzyme activity. This may affect the morbidity of a wide range of human disease states.

Pearson DJ, Day JP, Suarez-Mendez VJ, Miller PF, Owen S, Woodcock A: Human selenium status and glutathione peroxidase activity in the North West of England. European Journal of Clinical Nutrition 1990, 44:277-283.

REVIEW PAPER Some implications of selenium for human health

French studies

Show that selenium levels in a variety of locally grown foods are lower than in similar foods from the United States, but similar to those of nearby European countries. Although average French selenium consumption is 40-60 mcg/day, they infer that selenium supplementation of the French diet may be advisable and noted the frequency of selenium-responsive growth abnormalities in French livestock.

Pregnancy

They also recommend supplementation of diets for pregnant women with 25 to 50 micrograms of selenium daily, to prevent deficiency in their infants.

Thyroid

Experiences with selenium deficiency in animals have shown a link with impaired thyroid metabolism. These have been followed up recently by a group at the Rowett Research Institute in Aberdeen, Scotland. When they gave rats a selenium-deficient diet they noted decreased production of pituitary growth hormone and thyroid hormones.

Schizophrenia

Foster at the University of Victoria reports results of a survey of environmental and medical data which show a strong negative correlation between the amount of selenium entering the food chain and incidence of schizophrenia in the United States. Foster has also proposed the possibility of a causal relationship between selenium deficiency and multiple sclerosis. Norwegian workers had

previously shown multiple sclerosis to be more prevalent in inland agricultural areas than in coastal fishing communities and suggested that the incidence might be related to milk consumption.

Immune function

In a more general protective role, research continues to be directed toward the involvement of selenium in the development of immune functions in animals. New York investigators (Kiremidjian, Schermacher et al, 1990) showed that selenium deficiency inhibited the ability of lymphocytes to proliferate. The same group demonstrated with mice enhancement of tumour cytodestruction through dietary supplementation with 1 x [10.sup.-7] M selenium and suggested selenium's role as being in the generation of cytotoxic lymphocytes rather than at some later stage of lytic cytotoxicity.

In a recent review (Spallholz et al, 1990), three major functions were listed for selenium in cells of the immune system:

- 1.Reduction of organic and inorganic peroxides formed by metabolic and environmental initiators of free radical reactions.
- 2.Metabolism of hydroperoxides leading to the synthesis of leukotrienes, thromboxanes, prostaglandins and lipoxins.
- 3.Modulation of the oxidative production of the respiratory burst of phagocytic cells.

Cancer research

The importance of cancer as a leading cause of death in humans has stimulated a great deal of research attempting to link selenium status to incidence or severity of cancer, in both animals and humans. The results have been equivocal but epidemiological studies which have assessed selenium status as a predictor of cancer incidence and mortality have generally shown that a selenium-rich diet significantly reduces deaths from cancer of the breast, digestive tract, liver and respiratory organs.

A Polish study (Pawlowicz et al, 1989) listed breast cancer as the most common form of malignancy in women, accounting for 7 per cent of the total female mortalities. Blood selenium levels were lower in breast cancer patients than in healthy persons, and breast cancer mortalities were lower in areas of adequate (greater than 0.1 ppm) selenium

than they were in areas of selenium deficiency. Schrauzer and others (1985) reported a lower incidence of breast cancer in women from Japan than from the United States (San Diego area). They noted lower blood selenium levels in breast cancer patients than in healthy subjects in both countries and suggested that the lower Japanese incidence might be related to higher dietary selenium levels in that country.

In studies of other types of cancer, an inverse relationship between liver cancer incidence and selenium content of whole blood and grains was found in Jiangsu province, a region in China with a high incidence of liver cancer. Animal experiments there showed reduced liver cancer following selenium supplementation in rats exposed to aflatoxin. Selenium also inhibited the growth of transplanted tumours.

This Review Paper was written by J E Oldfield, and published in Nutrition Today, July-August 1991, 26(4):6.

More Cancer Research

Prediagnostic serum selenium and risk of cancer

Harvard School of Public Health, Brigham Women's Hospital, Harvard Medical School, Johns Hopkins School of Hygiene and Public Health, University of Missouri, University of Texas, Duke University, and Cardiovascular Epidemiology unit, Evans, County, Georgia, USA: Selenium levels in serum samples collected in 1973 from 111 people who developed cancer during the next five years were compared with cancer-free individuals. Those who developed cancer had previously had significantly lower selenium levels than those who did not. Cancer risk was doubled in those with the lowest selenium levels. Simultaneously low vitamin A and vitamin E levels increased the risk still further.

Willett et al, Lancet July 16, 1983.

Selenium in forage crops and cancer mortality in U.S. counties

Forage selenium (FSe) levels in alfalfa, a common crop, were analysed. FSe levels were low in the Northeast, high in the Northwest and Southwest, and variable in the Southeast USA. When potentially confounding variables were included in the data analysis (for instance employment rates in certain industries),

low FSe levels were associated with higher cancer mortality in rural counties, and in all counties (two different statistical analyses were used). This was true for cancer in several sites: lung, oesophagus, colon, rectum, bladder, breast, cervix, although all sites did not significantly correlate with FSe levels in both analyses. *Clark, Larry C et al, Archives of Environmental Health Jap-Feb 1991, 46(1):37.*

Decreased incidence of prostate cancer with selenium supplementation

974 men with a history of cancer were divided into two groups, one of which was given a selenium supplement of 200 mcg per day, and the other a dummy product (placebo). After 6½ years, the rate of prostate cancer was 63% less in the supplemented group than in the placebo group. *Clark LC et al, Br J Urol 1998 May;81(5):730-4.* Also *Yoshizawa K et al, J Natl Cancer Inst 1998 Aug 19;90(16):1219-24.*

These papers on selenium and cancer are representative of dozens more which come to similar conclusions.

Asthma

Selenium, glutathione peroxidase and asthma

This review paper (a paper which compares the conclusions of a wide range of research papers) demonstrates that low activity of the selenium-dependent enzyme glutathione peroxidase is linked with a 6-fold increase in asthma. *Editorial: Clinical and Experimental Allergy 1991, 21:157-159.*

Selenium supplementation in intrinsic asthma

24 asthmatics were given either selenium supplements or a dummy substance (placebo) for 14 weeks. The supplemented group experienced a significant increase in glutathione peroxidase levels (a marker of selenium sufficiency), accompanied by significant improvement in their asthma. *Hasselmark L et al, Allergy 1993, 48(1):30-6.*

Immunity

Selenium and immune responses

Selenium deficiency affects all components of the immune system. A deficiency of selenium has been shown to lower resistance to microbial and viral infections, neutrophil function, antibody

production, proliferation of T and B lymphocytes and effectiveness of T lymphocytes and natural killer cells. Increasing selenium intake has been shown to restore immune function, stimulating the production of white blood cells and antibodies. Research to date suggests that the maintenance of adequate selenium status may be important for the maintenance of general health, the control of immunodeficiency disorders, and the prevention of cancer. *Kiremidjian-Schumacher L, Stotzky G, Environmental Research 1987, 42:277-303.*

Lymphocyte response is enhanced by supplementation of elderly subjects with selenium-enriched yeast

After six months supplementation with selenium a group of elderly people experienced significant stimulation of their immune system. *Peretz A et al: Am J Clin Nutr 1991, 53(5):1323-8.*

Serum selenium predicts outcome in HIV infection

Selenium levels were measured in the serum of 95 HIV positive patients. The lower the selenium, the higher the rates of death and opportunistic infection. The patients' prognosis could be predicted purely on the basis of the amount of selenium in their blood, irrespective of their CD4 cell count. *Constans J et al: J Acquir Immune Defic Syndr Hum Retrovirol 1995, 10(3):392.*

Selenium deficiency in the Acquired Immunodeficiency Syndrome (Aids)

Levels of the selenium-dependent enzyme glutathione peroxidase were compared in the serum of normal people, and those diagnosed as HIV positive. The latter were found to be selenium deficient. *J Parent and Ent Nutr 1986, 10:405-407. Also Dworkin BM et al: Biol Trace Elem Res 1988, 15:167-177.*

Reduced cardiac selenium content in the acquired immunodeficiency syndrome

Eight Aids patients examined at autopsy were all found to have heart muscle abnormalities which are found in association with a severe selenium deficiency. *Dworkin BM et al: J Parent Ent Nutr 1989, 13(6):644-7.*

Host nutritional status and its effect on a viral pathogen

In selenium- and vitamin E-deficient mice, a harmless strain of coxsackievirus B3 mutated, became virulent and caused myocarditis. The mutated virus was able to infect and cause disease in well-nourished mice. *Beck MA, Levander OA, J Infect Dis 2000 Sep;182 Suppl1:S93-6.*

Thyroid

Selenium, zinc and thyroid hormones

Selenium is needed to make an enzyme which converts thyroid hormone to its active T3 form. A study on older people showed that those with low selenium levels had much lower levels of T3 than those with higher selenium levels. *Olivieri O et al, Biol Trace Elem Res 1996 Jan;51(1):31-41.*

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Resources

www.cc.nih.gov/ccc/supplements/selenium.html

US National Institutes of Health, Office of Dietary Supplements site on selenium.