SELENIUM IN AUSTRALIAN HEALTH AND DISEASE

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Summary

Once of interest mainly to agriculturalists because of its toxicity to animals, selenium (Se) is now known to play an essential role in animal and human metabolism. Selenium deficiency disorders, such as Keshan disease, an endemic cardiomyopathy occurring in remote regions of China, and certain other clinical conditions related to Se are recognised. The element forms part of the enzyme glutathione peroxidase (GSH.Px) which protects cells against peroxide damage. It may also have other biological roles. Selenium is unevenly distributed in soils, and consequently in diets, throughout the world. Australia appears to have an adequate supply of the element in foods and there is no evidence that the general population suffers from Se deficiency. However, deficiency can occur in special groups such as those following restricted diets and patients on total parenteral nutrition.

I. INTRODUCTION

Selenium has fascinated scientists ever since it was discovered by Berzelius in 1818. He named it after Selene, the goddess of the moon. Like the moon, selenium has two faces. Berzelius was aware of the dark face, the toxic qualities and obnoxious odour of its compounds. The bright face was not revealed, until, in the 1950s it was discovered that the element was also an essential nutrient. The swing from concern with its toxicity to investigation of its essentiality is well illustrated by the titles of two papers published 16 years apart. In 1972 Douglas Frost asked in his title 'Can selenophobia be cured?' (Frost 1972), while in 1988 Clare Casey entitled her review of current interest in Se, 'Selenophilia' (Casey 1988). This paper is designed to clarify some points about that love-hate relationship between nutritionists and the moon element, in the context of Australian health and disease.

(a) The element

Selenium is a metalloid, neither a true metal nor a non-metal, which shares the physical and chemical properties of both classes of elements. In the Periodic Table, it lies between sulphur and tellurium in group VIA. Its chemical properties are similar to those of sulphur, forming both inorganic and organic compounds, corresponding to the sulphides, sulphates, and sulphur amino acids.

Of significance are the remarkable photoelectrical and photochemical properties which allow Se to be used in many electrical and electronic applications, as well as in chemical, metallurgical and pharmaceutical industries. Though the total quantity of the element used is relatively small, Se turns up in a remarkable number of operations and products. Consequently, this toxic element has become a significant environmental contaminant.

Though widely distributed in rocks and soil, Se is not a common element, with about 0.05mg/kg in most soils. It is normally associated with ores of other metals and is obtained as a by-product in copper and other refineries. SELSUN®: antidandruff shampoo

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(b) Biological properties

Selenium plays important roles in the human body. It is found in all human tissues, at an average concentration of about 0.2 μg/g, with highest concentrations in liver and kidneys. Levels normally reflect dietary intake. In blood, they can range from 0.05 -0.08 μg/ml in people living in low Se areas, to as much as 3 μg/ml in seleniferous regions. The element occurs in tissues in association with protein, both loosely bound and as Se analogues of sulphur amino acids.

Selenium has been found to prevent liver necrosis in vitamin E-deficient rats, and of exudative diathesis in chickens deficient in both vitamin E and selenium. Selenium supplementation can also prevent several other disorders in animals, including white muscle disease, a muscular dystrophy affecting cattle and sheep. Pigs, horses, and dogs have also been shown to suffer from Se-responsive syndromes. In 1973, the element was found to be a component of the enzyme glutathione peroxidase (GSH.Px) which acts as a scavenger of reactive oxygen species and free radical intermediates of lipid peroxidation (Rostruck et al. 1973).

Up to the present, GSH.Px is the only well characterised functional selenoprotein. Other selenoproteins are recognised and will, no doubt, eventually be shown to have important roles. As has been reported by John Arthur and colleagues, there is good evidence for the involvement of Se in thyroid metabolism (Arthur et al. 1987).

II. THE WORLD SCENE

While most studies on Se deficiency have been carried out on animals, there is a growing body of evidence pointing to similar effects in humans. Most dramatically, this has been shown in China where Keshan disease, an endemic myocardial pathology, has been found to respond to Se supplementation (Yang et al. 1988). Another disease associated with Se deficiency, also found in China, is Kaschin-Beck or "big joint" disease, a severe osteoarthropathy. Both diseases occur in isolated regions where levels of Se in the soil are low and overall nutrition is poor. It is ironical that China also has the unenviable distinction of having regions where Se occurs in high concentrations causing endemic intoxication or selenosis (Yang et al. 1983).

Less dramatic cases of diseases related to Se deficiency have been reported in other parts of the world. Low levels in infusion fluids have been shown to result in deficiency of Se in patients on parenteral nutrition, with symptoms similar to those of Keshan disease (Johnson et al. 1981). Connections between Se deficiency and cancer have been postulated (Schrauzer et al. 1977). Though the hypothesis is controversial, evidence points towards an inverse relationship between dietary Se and certain forms of cancer. Selenium has, in fact, been linked, on evidence ranging from significant to, at best, dubious, with a wide range of disorders. Casey (1988) lists 12 of these. We could add several others, as is shown in Table 1.

Table 1. Disorders attributed to selenium deficiency

Ageing	Immunodeficiency
Arthritis	Low birth weight
Cancer	Lymphoblastic anaemia
Cataracts	Muscular dystrophy
Cystic fibrosis	Oxidative damage
Cardiovascular disease	Phenylketonuria
Dental caries	Senile macular degeneration
Goitre	Sudden infant death syndrome

Investigations of levels of Se in food and diets are now being carried out in many countries, though, until recently considerable difficulties were experienced with the analytical procedures. Se is very volatile and it is difficult to prevent losses during sample preparation. This difficulty is compounded by the fact that Se occurs in most foods at very low levels. Though great care and technical skills are still required, the availability of sealed and microwave digestion systems, efficient background correction, through use, for example, of Zeeman-mode atomic absorption spectrophotometry, and of second generation certified reference materials, have meant that reliable results are now becoming available.

Distribution of Se is not uniform worldwide. Some countries have adequate levels, others marginal or even inadequate intakes. While in the US, for instance, intakes up to 216 μg/d were recorded, levels in Finnish diets were found to be as low as 30 μg/d (Levander 1982). Similar findings of low intakes compared to US figures were also obtained in other countries, but not all authorities responded to them as they did in Finland. There the outcome might be described as a panic reaction. To quote from a recent paper," the interest of Finnish agricultural and public health authorities was aroused by the selenium problem and, as a result the Ministry of Agriculture and Forestry appointed an Expert Working Group on Selenium to evaluate the selenium problem" (Pyykko et al.. 1988). Then on the grounds of a possible association between low serum Se and cardiovascular diseases and cancer, the government decreed that Se must be added to fertilisers. The intention was to increase levels in farm produce and thus in diets. The effect has been remarkable. In the four years following introduction of the scheme in 1984, daily intake of Se in Finland reached the US level, with corresponding increases in blood levels.

The general public in Finland was not slow in deciding that their intake of Se needed a boost. "Do it yourself and prescribed selenium supplementation has become popular and the....pill business has boomed", to quote from a Finnish report, via Casey (1988).

Quite a different reaction to the problem was seen in New Zealand where low intake and low blood Se have also been found. Daily intakes were found to be 28-32 μg, with blood levels between 0.05-0.1 μg/ml, almost identical with the pre-1984 Finnish figures. However, no Se-responsive conditions were observed in those who consumed a normal well-balanced diet. It was concluded that "as yet there is no justification for Se supplementation for the general population" (Thomson and Robinson 1980). Unfortunately, while health authorities acted on this cautious advice, not everyone in the community did so. There have been reports of New Zealanders dosing themselves with Se-containing veterinary preparations, including sheep drench, with serious consequences (Civil and McDonald 1978).

III. THE AUSTRALIAN SCENE

Australian scientists have long had an interest in Se in the field of agriculture. Relatively recently, this has extended to human nutrition and health.

Seventy years ago, a plant from Cape York Peninsula which caused selenosis-like symptoms such as "hoof drop"in horses, was identified as *Morinda reticulata* by the Queensland herbarium. This species was later found to contain high concentrations of Se, with nearly one g/kg in some specimens. McCray and his colleagues, of the then Queensland Department of Agriculture and Stock, later reported on several outbreaks of selenosis in farm animals in northern parts of the State associated with *M. reticulata* and other plants with similar Se-accumulating abilities (Knott and McCray 1959).

Selenosis in farm animals is not, in fact, an important problem in Australia. Toxic regions are found in remote areas which are not of great agricultural importance. Of far greater

consequence are regions of Se deficiency which occur right across Australia and are associated with outbreaks of white muscle disease and ill thrift in sheep and lambs and various other symptoms in a variety of animals, including poultry.

Australian Food Standards set a maximum permitted level for Se in foods sold to the public of 0.2 mg/kg for beverages, 2.0 for offal and 1.0 for all other food. These levels do not appear to be generally exceeded, except for certain nuts, such as Brazil and cashews, which are natural accumulators of the element (Reilly 1991). Fish and other marine organisms can also accumulate significant amounts of Se and are for many the most important source of the element in the diet (Morris and Levander 1970). However, none of nine widely used fish species from New South Wales' waters were found to contain more than 0.8 mg/kg of Se. It is unlikely that, even with a large intake, consumers of these fish would be at any risk.

Cereals are also a major source of Se in diets as has been shown in several countries, including Australia (Reilly et al. 1990). We found concentrations of 0.1-0.15 mg/kg, in wheat, which is higher than levels reported for New Zealand, but comparable to US figures (Andrews et al. 1968).

Until quite recently, no studies on actual dietary intakes of Se by the general public had been carried out in Australia and nutritionists were left to manage as best they could with estimates, based on food composition data from overseas. In spite of that gap in our knowledge, the National Health and Medical Research Council took the brave step of establishing a Recommended Daily Intake, the first Se RDI in the world (Dreosti 1986). The RDI is somewhat higher than the US RDA which was introduced in 1989 but considerably lower than the top of the US Estimated Safe and Adequate Daily Intake (ESADI), as is seen in Table 2 (Levander 1991).

Table 2. Comparison of Australian RDI and US ESADI

Age group	Australian RDI(μg)	US ESADI (μg)]
Infants:		
0-6 months (Breastfed & bottlefed)	10	10-40
7-12 months	15	20-60
Children:		
1-3 years	25	20-80
4-7 years	30	-
4-6 years	-	30-120
Adolescents:		
7-10 years	-	50-200
8-11 years (males)	50	50-200
12-18 years (males)	85	50-200
8-11 years (females)	50	50-200
12-18 years (females)	85	50-200
Adults:		
19-64 years &+(males)	85	50-200
(females)	70	50-200
Pregnancy	+10	-
Lactation	+10	-

Source of Se dairy 32% egg 4.5%
cereal 25%
meat/fish 31%
poultry

Do Australians meet this RDI? Our studies and those few others so far reported, show that the majority do. An estimate of intakes by Adelaide residents (Baghurst et al. 1987), based on UK food composition data, found that women were consuming on average 108 and men 129 μg of Se daily. Estimates of intake based on actual analyses of Australian foods (Fardy et al. 1989) found intakes lower than Baghurst's, with means of 57 μg for women and 87 μg for men and, for a two year old and an infant 43 and 23 μg respectively. These are close to the Australian RDI and are similar to our own measurements in Brisbane, as shown in Table 3. Though our figures indicate that some individuals fail to meet their RDI, the majority do. In the case of a group of young children, for instance, we found that 90% had intakes above the RDI and none had less than 70% of that figure (Reilly et al. 1991).

Studies by Cumming and colleagues on breast milk consumption by infants in Brisbane found an intake of 10.7 (%S.D.4.1) μg/d, just above the RDI (Cumming et al. 1991).

There are, however, Australians whose diets fail to meet the RDI for Se. Children suffering from phenylketonuria, an inherited metabolic disease which requires strict dietary control aimed at limiting their intake of the amino acid phenylalanine, have been found to have a low intake of the element, as is also shown in Table 3. The deficiency has been traced to the children's restricted intake of protein-rich foods, which are the principal source of Se in normal diets (Reilly et al. 1990).

Studies by McHarg and her colleagues in Brisbane (McHarg and Murphy 1990) show that patients maintained on long-term tube feeds are also at risk of Se deficiency.

Table 3. Selenium intakes of Queensland residents

Group	Se (μg/d)	
	Mean	Range
Adult males	89	35-204
Adult females	59	23-141
Children	56	21-114
PKU children	8	4-18

Apart from these special cases, there is no evidence that Se deficiency is a widespread problem in Australia. While we have evidence that there can be considerable variations in levels of Se in certain foodstuffs such as milk and cereals, depending on soil levels in areas of production, the possibility of a mixed diet being deficient in the element is unlikely. What, then, of the view that Se supplementation is desirable for the general population? This view is not supported by hard evidence. It also overlooks the undoubted problem of Se toxicity. Over-dosing is easy, and has occurred.

However, we are still far from knowing the final answer and, with increasing recognition of the important protective role played by Se in the body, perhaps there are grounds for its use pharmaceutically as a protective agent. This might begin, with good effect, by encouraging people to consume foods which are naturally rich in Se.

Selenium in Australian foods and diets remains a fascinating area of study, with many unanswered questions. It is a great pleasure for me to been invited to speak on this most

Eskimos who consume fish contain high level of Hg.
have high level of Se (biologically protective may be via selenoprotein P)

interesting trace element in Perth, where that pioneer of trace element studies, the late Professor Eric Underwood worked. Like many others I have been inspired in my research by his classic text on trace elements in man and animals. I hope that the investigations of my colleagues and myself are worthy contributions to the field of knowledge to which Eric Underwood contributed so much.

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