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Selenium Geochemistry and Health

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Introduction

Selenium (Se) is a naturally occurring metalloid element, which is essential to human and other animal health in trace amounts but is harmful in excess. Of all the elements, Se has one of the narrowest ranges between dietary deficiency (< 40 μg day^{-1}) and toxic levels (> 400 μg day^{-1}) (1) making it necessary to carefully control intakes by humans and other animals hence the importance of understanding the relationships between environmental exposure and health. Geology exerts a fundamental control on the concentrations of Se in the soils on which we grow the crops and animals that form the human food chain. The Se status of populations, animals and crops vary

markedly around the world as a result of different geological conditions. Since diet is the most important source of Se in humans, understanding the biogeochemical controls on the distribution and mobility of environmental Se is key to the assessment of Se-related health risks.

Selenium in the Environment

The element was first identified in 1817 by the Swedish chemist Jons Jakob Berzelius, its chemical behaviour resembles that of sulphur and it exists in the 2^-, 0, 4^+ and 6^+ oxidation states. As a result of this complex chemistry, Se is found in all natural materials on Earth including rocks, soils, waters, air and plant and animal tissues. Se is widely used in a number of industries, as a pigment in glass and ceramic manufacture; as the light-sensitive photoconductor layer in photocopiers, as a catalyst in organic synthesis; as an antioxidant in inks and oils and as an anti-fungal agent in pharmaceuticals (2, 3, 4).

Although the element is derived from both natural and man-made sources, an understanding of the links between environmental geochemistry and health is particularly important for Se as rocks are the primary source of the element in the terrestrial system (5, 6).

Selenium in Rocks

In general, Se concentrations in rocks are low. Sedimentary rocks contain more of the element than igneous rocks, but even so, levels in most limestones and sandstones rarely exceed 0.1 mg kg^{-1}. Se is often associated with the clay fraction in sediments and is found in greater concentrations in shales (0.06 mg kg^{-1}) than limestones or sandstones. Very high concentrations (≤ 300 mg kg^{-1}) have also been reported in some phosphatic rocks. Coals and other organic-rich deposits can be enriched in Se relative to other rock types, typically ranging from 1 to 20 mg kg^{-1}, although values of over 600 mg kg^{-1} have been reported in some black shales. Se is often found as a minor component of sulphide mineral deposits whereas elemental Se^0 is only occasionally reported (5, 6, 7, 8, 9, 10). Therefore, the distribution of Se in the geological environment is highly variable reflecting the variability of different rock types.

Selenium in Soils

In most circumstances there is a very strong correlation between the concentration of Se in geological parent materials and the soils derived from them. The Se content of most soils is very low 0.01 - 2 mg kg^{-1} (world mean 0.4 mg kg^{-1}) but high concentrations of up to 1200 mg kg^{-1} have been reported in some seleniferous areas (5, 6, 8, 11).

Although the underlying geology is the primary control on Se in soils, the mobility and uptake into plants and animals, known as the bioavailability, is determined by a number of bio-physio-chemical parameters. These include the pH and redox conditions; the chemical form or speciation of Se; soil texture and mineralogy; organic matter content and the presence of competitive ions. An understanding of

these controls is essential to the prediction and remediation of health risks from Se as, even soils that contain adequate total Se concentrations can result in Se deficiency if the element is not in readily bioavailable form. Under most natural redox conditions, selenite (Se^{4+}) and selenate (Se^{6+}) are the predominant inorganic phases. Selenite is adsorbed onto soil particle surfaces with greater affinity than selenate, especially at low pH in the presence of iron oxide and organic matter. Hence selenite is less bioavailable than selenate. In contrast, selenate is generally soluble, mobile and readily available for plant uptake in neutral and alkaline soils. Elemental Se (Se^{0}) and selenides (Se^{2-}) tend to exist in reducing, acid and organic-rich environments only and are largely unavailable to plants and animals (5, 8, 11).

Therefore, in any study of the Se status of soil, consideration of the likely bioavailability is important. Several different techniques are available to assess bioavailability but one of the most widely accepted indicators is the water-extractable Se content, which is generally < 0.1 mg kg^{-1} in most soils (7, 8).

Selenium in Plants

Although there is little evidence that Se is essential for vegetation growth, it is incorporated into the plant structure. Se concentrations in plants generally reflect the levels of Se in the environment. However, an important factor that may determine whether or not Se-related health problems manifest in animals and humans is the very wide-ranging ability of different plant species to accumulate Se. Rosenfield and Beath (12) were the first to classify plants on the basis of Se uptake when grown on seleniferous soils. Se-accumulator plants can absorb > 1000 mg kg^{-1} of the element,

whereas non-accumulators such as grain crops and grasses, usually contain < 50 mg kg^{-1}. Some species of the plant genera *Astragalus*, *Haplopappus* and *Stanleya* are characteristic of seleniferous semi-arid environments, however, other species in these genera are non-accumulators (4, 5, 8).

Selenium in Water

Se forms a very minor component of most natural waters and rarely exceeds 10 μg L^{-1}. Typically ranges are < 0.1 – 100 μg L^{-1} with most concentrations below 3 μg L^{-1} (4, 8). In general, groundwaters contain higher Se concentrations than surface waters due to greater contact times for rock-water interactions (10). Groundwaters containing 1000 μg L^{-1} Se have been noted in Montana, USA and up to 275 μg L^{-1} in China (8, 13). The World Health Organization (WHO) currently set a maximum admissible concentration (MAC) of 10 μg L^{-1} for Se in drinking water. However, the most important exposure route to Se for animals and humans is the food we eat, as concentrations are orders of magnitude greater than in water and air in most circumstances (1).

Selenium Toxicity and Health

Se toxicity problems related to natural exposure occur rarely in animals and humans but have been reported in Australia, Brazil, China, Ireland, Israel, Russia, South Africa and the United States.

Selenium Toxicity in Animals

Se toxicity problems have been recorded for hundreds of years although the cause was unknown. A hoof disease in livestock was reported in Colombia in 1560 and in South Dakota, USA in the mid-19th century where the symptoms were termed alkali disease. In 1931, this disease was identified as Se toxicosis (selenosis).

The relationships between geology, soil Se, uptake into plants and health outcomes in animals were first examined in detail during the 1930s by Moxon (14). Soils capable of producing Se-rich vegetation toxic to livestock were reported over black shales of the Great Plains of the USA. Subsequent studies into Se-deficiency diseases in animals lead to one of the first maps of the Se status of soils, vegetation and animals and the establishment of the classic Great Plain seleniferous soil types (15).

In natural conditions, acute Se intoxication, which results in death, is uncommon as animals are not normally exposed to high-Se forage. Chronic Se intoxication after ingestion of plants containing 5 – 40 mg kg^{-1} over weeks or months is more common and leads to two conditions known as alkali disease and blind staggers in grazing animals. Alkali disease is characterized by dullness, lack of vitality, emaciation, rough coat, sloughing of the hooves, erosion of the joints and bones, anaemia, lameness, liver cirrhosis and reduced reproductive performance. Blind staggers results in impaired vision and blindness, anorexia, weakened legs, paralyzed tongue, laboured respiration, abdominal pain, emaciation and death (1, 4, 16).

Although much of the work into Se toxicity has focused on agricultural species, selenosis has also been reported in wild aquatic species and birds. One of the best-known examples affected birds at the Kesterson Reservoir, California, USA. Se concentrations in agricultural drainage water entering the Kesterson Reservoir area between 1983 and 1985 were 300 mg L^{-1} as a result of contact with seleniferous soils developed over marine black shales in the catchment area. In this arid alkaline environment, 98% of the Se was in the most readily bioavailable selenate form. Studies revealed that 22% of bird eggs contained dead or deformed embryos as a result of Se toxicity. It is estimated that at least 1000 birds died at Kesterson in the period 1983 – 1985 as a result of consuming plants and fish with 12 – 120 times the normal amount of Se (8).

Selenium Toxicity in Humans

Overt Se toxicity in humans is far less widespread than Se deficiency. Nine cases of acute Se intoxication due to the intake of nuts of the *Lecythis ollaria* tree in a seleniferous area of Venezuela have been reported resulting in vomiting and diarrhoea followed by hair and nail loss and the death of one two-year old boy (4).

In China, an outbreak of endemic human selenosis was reported in Enshi District, Hubei Province during the 1960s. The condition was associated with consumption of high-Se crops grown on soils derived from coal containing up to 6000 mg kg^{-1} Se. Enshi is interesting because elsewhere in the District, Se-deficiency diseases (Keshan Disease (KD)) occur within 20 km of the seleniferous region entirely as a result of geology. Jurassic sandstones, which contain low concentrations of Se, underlie the

northwest of the District and KD is present in this area. Studies revealed Se concentrations in soil, food and human samples from areas underlain by coal up to 1000 times higher than in samples from the selenium-deficient areas. In the seleniferous region, between 1923 and 1988, 477 cases of human selenosis were reported. Hair and nail loss were the prime symptoms of the disease (Figure 1) but disorders of the nervous system, skin, and paralysis also occurred (7, 17, 18). Further investigations carried out by Fordyce et al. (13) showed that in the seleniferous villages, concentrations of Se in soils and foodstuffs could vary markedly from low to toxic within the same village, these variations being dependent on the outcrop of the coal strata and use of coal ash to condition the soil. Villagers were advised to avoid cultivating fields underlain by the coal and were counselled against using ash as a soil conditioner. No incidences of Se toxicity have been reported in recent years and it is no longer considered a public health problem in China.

Selenium Deficiency and Health

Se was identified as an essential trace element during pioneering work into Se-responsive diseases in animals in the late 1950s and early 1960s. In terms of biological function, approximately 25 essential selenoproteins have now been identified in microbes, animals and humans, many of which are involved in redox reactions acting as components of the catalytic cycle (1, 19). In complex interactions with vitamin E and fatty acids, Se plays an essential biological role as part of the enzyme glutathione peroxidase (GSH-Px), which protects tissues against oxidative

damage. As such, Se has been linked to enzyme activation, immune system function, pancreatic function, DNA repair and detoxification (1, 4, 16, 20). Se has been identified as a component of the cytochrome P_{450} system in humans and animals; however, the exact biological role of this seleno-protein has yet to be established (1, 4, 21). Important developments in recent years have shown that Se is beneficial to thyroid hormone metabolism. There are three selenoenzymes, which exert a major influence on cellular differentiation, growth and development (22). Se is also important in reproduction, it aids the biosynthesis of testosterone. Morphological deformities, immotility and reduced fertility have been reported in sperm in Se-deficient experimental animals (1, 4, 19).

Selenium Deficiency in Animals

Due to the complementary role of Se and Vitamin E, practically all Se deficiency diseases in animals are concordant with vitamin E deficiency. Se is necessary for growth and fertility and clinical signs of deficiency include reduced appetite, growth, production and reproductive fertility, unthriftyness and muscle weakness (1, 4, 16, 23). These disorders are generally described as white muscle disease (WMD).

Indeed, Se deficiency in animals is very common around the globe affecting much of South America, North America, Africa, Europe, Asia, Australia and New Zealand. Many western countries now adopt Se supplementation programs in agriculture but these are often not available in South America, Africa and Asia and livestock productivity is significantly impaired by Se deficiency in these regions (1, 4, 16, 23).

Selenium Deficiency In Humans

In humans, no clear-cut pathological condition resulting from Se deficiency alone has been identified, however, the element has been implicated in a number of diseases (1).

Keshan Disease

Kehsan Disease (KD) is an endemic cardiomyopathy (heart disease) that occurs in China. Outbreaks have been reported in a broad belt stretching from Heilongjiang in the northeast to Yunnan in the southwest that transcends, topography, soil types, climatic zones and population types. The worst affected years on record were 1959, 1964 and 1970 when the annual prevalence exceeded 40 per 100 000 with more than 8000 cases and 1400 – 3000 deaths each year (17).

Although the disease occurred in a broad belt across China, investigators noticed that WMD in animals occurred in the same areas and further studies demonstrated that soils and crops were low in Se and affected populations were characterized by poor Se status indicated by hair contents of < 0.12 mg kg^{-1} (17, 24). On the basis of these findings, large-scale mineral supplementation was carried out. During the four years of investigation, 21 cases of the disease and 3 deaths occurred in the Se-supplemented group whereas 107 cases and 53 deaths occurred in the control group.

Although the disease proved to be Se-responsive, the exact biological function of the element in the pathogenesis was less clear and seasonal variations in disease prevalence suggested a viral connection. Recent work by Beck (25), has shown that a

normally-benign strain of coxsackie B3 (CVB3/0) alters and becomes virulent in either Se-deficient or vitamin E-deficient mice. This work demonstrates not only the importance of Se deficiency in immuno-suppression of the host but in the toxicity of the viral pathogen as well. As with many environmental conditions, KD is likely to be multi-factorial but even if Se deficiency is not the main cause of the disease, it is clearly an important factor.

As a result of widespread Se supplementation programmes and economic and communication improvements in China, the incidence of the disease has dropped to such a low level in recent years that it is no longer considered a public health problem.

As an example of the need to understand the bioavailability of environmental Se, Johnson et al. (26) examined soil, staple crop (wheat and oats), water and human hair Se levels in the KD affected Zhangjiakou region of China. Hair, grain and water Se concentrations showed an inverse relationship with disease prevalence as expected, the highest Se contents were reported in villages with lowest prevalence of the disease. However, soil total Se contents showed the opposite relationship and were highest in the villages with greatest disease prevalence. Further examinations into the soil geochemistry demonstrated that KD-village soils were black or dark brown with a high organic matter content and low pH hence Se was not readily bioavailable as it was held in organic matter in the soil. Although these soils contained adequate total Se contents, levels of water-soluble Se were deficient. On this basis, conditioning treatments to raise the soil pH thus increasing the bioavailability of Se or foliar application of Se fertilizer to crops to avoid Se adsorption in the soils were

recommended as remediation strategies to increase the levels of Se in local food stuffs.

Kashin-Beck Disease

Kashin-Beck Disease, an endemic osteoarthropathy causing deformity of the affected joints, occurs in Siberia, China, North Korea and possibly parts of Africa (1, 16, 17). In China, the pattern of disease incidence is concordant with KD in the north of the country but the links with Se-deficient environments are less clear (17). However, children and nursing mothers were supplemented with 0.5 – 2.0 mg sodium selenite per week for a period of 6 years and the disease prevalence dropped from 42% to 4% in children aged 3 – 10 years as a result (17). Other factors have been implicated in the pathogenesis of KBD including mycotoxins and humic substances in drinking water, and it's likely that KBD is multi factorial and occurs as a consequence of oxidative damage to cartilage and bone cells when associated with decreased antioxidant defence.

Iodine Deficiency Disorders (IDD)

The recent establishment of the role of selenoenzymes in thyroid function means that Se deficiency is now being examined in relation to the IDD goitre and cretinism. Many areas around the world where IDD are prevalent are deficient in Se including China, Sri Lanka, India, Africa and South America (1, 4). Concordant Se and iodine deficiency are thought to account for the high incidence of cretinism in Central Africa, in Zaire and Burundi in particular (27) and Se deficiency has been

demonstrated in populations suffering IDD in Sri Lanka (28). However, these links require further investigation to determine the role of Se in these diseases.

Cancer

Following studies that revealed an inverse relationship between Se in crops and human blood versus cancer incidence in USA and Canada (29), the potential anti-carcinogenic effect of Se has generated a great deal of interest in medical science. Many studies to examine the links between Se and cancer have been carried out, however, to date, the results are equivocal. There is some evidence to suggest that Se is protective against cancer due to its anti-oxidant properties, however, other studies have shown that Se may promote cancer. Studies have demonstrated low levels of Se in the blood of patients suffering gastrointestinal cancer, prostrate cancer or non-Hodgkinson's lymphoma but there is some evidence to suggest that Se increases the risks of pancreatic and skin cancer (1, 4, 7, 21, 30, 31). A recent study by Appleton et al. (32) found no relationship between Se deficiency and oesophageal cancer in Cixian, China.

Finland provides an interesting case because the government was so concerned about the low level of Se intake in the Finnish diet that in 1984 a national program was initiated to increase the Se content of foodstuffs by adding sodium selenate fertilizers to crops. Mean daily intakes rose from 45 μg day^{-1} in 1980 to 110 – 120 μg day^{-1} between 1987-1990 and 90 μg day^{-1} in 1992. Studies of cancer incidence over this time carried out in Finland, Sweden and Norway showed no reduction in colon cancer, non-Hodgkinson's lymphoma or melanoma in Finland but researchers

question whether it is valid to make such inter-societal assessments without a control group for comparison (33).

Future Issues

In recent years, concern is growing in Europe over declining Se intakes. Europe traditionally imported large quantities of wheat from North America, which contained high Se contents as it was grown over the black shales of the Prairies, but since the advent of the European Union, most cereals are now more locally derived and as a consequence, daily intakes of Se have been falling. In the UK, for example, marked declines are evident even over a four-year period from intakes of 43-μg day^{-1} in 1991 to 29 – 39 μg day^{-1} in 1995, which are well below the recommended daily intakes of 55 - 75 μg day^{-1} (19). It is also recently that work has shown better health outcomes in HIV-AIDS patients given Se supplements (34). Indeed, the evidence of viral mutageny under Se-deficiency established by Beck (25) in the case of the coxsackie B virus has major implications in terms of the toxicity and immuno-response to many viral infections, particularly AIDS in light of the widespread Se-deficient environments of Central and Southern Africa where the disease has reached epidemic proportions. Similarly scientists are currently investigating the role of Se-deficiency in the mutageny of the influenza virus and avian flu (35), the implication being that the more recent virulent strains have emerged in Se-deficient environments and that Se supplementation can protect birds against the virus (36). Looking to the future, understanding the biogeochemical controls on the distribution and mobility of environmental Se is key to the assessment of Se-related health risks. Although overt

clinical symptoms of Se toxicity and deficiency are rarely reported, the possible sub-clinical effects are at present poorly understood and should not be under estimated as medical science continues to uncover new essential functions for this biologically important element.

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Figure 1. Hair loss as a result of Se toxicity, Enshi District, China