Chapter 16

Selenium Deficiency and Toxicity in the Environment

Fiona Fordyce
British Geological Survey

Contents

I. Background

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, selenium has one of the narrowest ranges between dietary deficiency (<40 $\mu g day^{-1}$) and toxic levels (>400$\mu g day^{-1}$) (WHO, 1996), which makes 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 selenium in the soils on which we grow the crops and animals that form the human food chain. The selenium status of populations, animals, and crops varies markedly around the world as a result of different geological conditions. Because diet is the most important source of selenium in humans, understanding the biogeochemical controls on the distribution and mobility of environmental selenium is key to the assessment of selenium-related health risks. High selenium concentrations are associated with some phosphatic rocks, organic-rich black shales, coals, and sulfide mineralization, whereas most other rock types contain very low concentrations and selenium-deficient environments are far more widespread than seleniferous ones. However, health outcomes are not only dependent on the total selenium content of rocks and soils but also on the amount of selenium taken up into plants and animals—the bioavailable selenium. This chapter demonstrates that even soils containing adequate total amounts of selenium can still produce selenium-deficient crops if the selenium is not in a form ready for plant uptake.

The links between the environmental biogeochemistry of selenium and health outcomes have been documented for many years. Selenium was first identified in 1817 by the Swedish chemist Jons Jakob Berzelius; however, selenium toxicity problems in livestock had been recorded for hundreds of years previously although the cause was unknown. Hoof disorders were noted in livestock in Colombia in 1560 and in South Dakota (U. S.) in the mid-19th century where the symptoms were called “alkali disease” (Reilly, 2006). In the early 1930s this disease, which is characterized by hair and hoof loss and poor productivity, was identified as selenium toxicosis (selenosis) (Franke, 1934; Moxon, 1937, Rosenfield & Beath, 1964). Since

then, seleniferous areas have been reported in Ireland, Israel, Australia, Russia, Venezuela, China, the United States, India and South Africa (Levander, 1986; Oldfield, 1999; Hira et al., 2004).

Conversely, selenium was identified as an essential trace element during pioneering work into selenium-responsive diseases in animals in the late 1950s and early 1960s (Swartz and Foltz, 1957). Selenium forms a vital constituent of the biologically important enzyme glutathione peroxidase (GPx), which acts as an antioxidant preventing oxidative cell degeneration (Rotruck et al., 1969). In animals, selenium deficiency has been linked to muscular weakness and muscular dystrophy, but it also causes reduced appetite, poor growth and reproductive capacity, and embryonic deformities. These disorders are generally described as white muscle disease (WMD). Following these discoveries, selenium deficiencies in crops and livestock have been reported in all regions of the world including the United States, the UK, Finland, Denmark, Sri Lanka, New Zealand, Australia, India, Canada, Thailand, Africa, and China and selenium supplementation has become common practice in agriculture (Levander, 1986; WHO, 1987; Oldfield, 1999).

Selenium deficiency has also been implicated in the incidence of a heart disorder (Keshan disease) and bone and joint condition (Kashin-Beck disease) in humans in various parts of China (Chen et al., 1980; Yang et al., 1983). More recent research has shown that selenium deficiency also adversely affects thyroid hormone metabolism, which is detrimental to growth and development (Arthur & Beckett, 1994). Indeed, 25 essential selenoproteins have now been identified in humans, many of which are involved in catalytic functions in the body (Papp, et al., 2007; Rayman, 2012). Selenium deficiency has also been implicated in a host of conditions including cancer, heart disease, immune system function, and reproduction. This chapter outlines some of the health problems in humans and animals that can arise as a result of selenium deficiency and toxicity in the natural environment. These links are more obvious in regions of the world where the population is dependent on local foodstuffs in the diet, but studies show that even in countries such as the United States where food is derived from a range of exotic sources, the local environment still determines the selenium status of the population. This fact should not be ignored because medical science continues to discover new essential functions for this biologically important element.

II. Selenium in the Environment

The naturally occurring element selenium belongs to group VIA of the periodic table and has chemical and physical properties that are intermediate between metals and non-metals (Table I). Selenium occurs in nature as six stable isotopes; however, it should be noted that although ^{82}Se is generally regarded as a stable isotope, it is actually a β^- emitter with a very long half-life of 1.4×10^{20} yr. The chemical behavior of selenium resembles that of sulfur and like sulfur, selenium can exist in the 2^-, 0, 4^+, and 6^+ oxidation states (Table II). As a result of this complex chemistry, selenium is found in all natural materials on Earth including rocks, soils, waters, air, and plant and animal tissues (Table III) (see also Chapter 2, this volume).

At the global scale, selenium is constantly recycled in the environment via the atmospheric, marine, and terrestrial systems. Estimates of selenium flux indicate that anthropogenic activity is a major source of selenium release in the cycle, whereas the marine system constitutes the main natural pathway (Table IV) (Haygarth, 1994). Selenium cycling through the atmosphere is significant because of the rapidity of transport, but the terrestrial system is most important in terms of animal and human health because of the direct links with agricultural activities and the food chain.

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 selenium as rocks are the primary source of the element in the terrestrial system (Table V) (Fleming, 1980; Neal, 1995). Selenium is dispersed from the rocks through the food chain via complex biogeochemical cycling processes including weathering to form soils, rock-water interactions, and biological activity (Figure 1). As a result, selenium is not distributed evenly across the planet, rather concentrations differ markedly depending on local conditions and an understanding of these variations is essential to aid the amelioration of health problems associated with selenium deficiency and toxicity. The following sections of this chapter provide a brief summary of anthropogenic sources of the element before going on to discuss the important aspects of selenium in the natural biogeochemical cycle and impacts on health.

A. Man-Made Sources of Selenium

Following its discovery in 1817, little industrial application was made of selenium until the early 20th century when it began to be used as a red pigment and improver in glass and ceramic manufacture; however, it was not until the invention of the photocopier in the 1930s that demand for the element significantly increased due to its photoelectric and semi-conductor properties. Today the use of selenium in photocopiers is declining as it has been replaced by organic photoreceptor compounds, which give better performance at lower cost (USGS, 2007). However, selenium is widely used in a number of industries (Table VI); most commonly selenium dioxide is employed as a catalyst in metallurgy and organic synthesis and as an antioxidant in inks, mineral, vegetable, and lubricating oils. Selenium mono- and disulfide are also used in anti-dandruff and antifungal pharmaceuticals (WHO, 1987; Haygarth, 1994; ATSDR, 2003).

The world industrial output of selenium was estimated at 3,000 - 3,500 tonnes in 2010, and the largest producers are Japan, Germany, and the United States. It is used mainly in the metallurgy and glass industries (Table VI). It is not economical to mine mineral deposits specifically for selenium; rather the element is recovered from the electrolytic refining of copper and lead and from the sludge accumulated in sulfuric acid plants (ATSDR, 2003).

Selenium compounds are released to the environment during the combustion of coal and petroleum fuels; during the extraction and processing of copper, lead, zinc, uranium, and phosphate; and during the manufacture of selenium-based products. According to monitoring data in the United States, in 2002 over 2700 tonnes of selenium compounds were released to the environment, primarily from power and sanitation industries (Table VII) (U.S.-EPA, 2002).

It is estimated that 76,000–88,000 tonnes yr^{-1} of selenium are released globally from anthropogenic activity, compared to natural releases of 4500 tonnes yr^{-1}, which gives a biospheric enrichment factor value of 17. This value is significantly higher than 1 indicating the important influence of man in the cycling of selenium (Nriagu, 1991). For example, long-term monitoring data from the Rothamstead Agricultural Experimental Station in the UK demonstrate the impact of anthropogenic activity on selenium concentrations in herbage. Samples collected between 1861 and 1990 bulked at 5-year intervals reveal that the highest concentrations occurred between 1940 and 1970 which coincided with a period of intensive coal use. Due to the move to fuel sources such as nuclear, oil, and gas in more recent decades, selenium concentrations in herbage are declining (Haygarth, 1994).

Selenium is also released inadvertently into the environment from the agricultural use of phosphate fertilizers, from the application of sewage sludge and manure to land, and from the use of selenium-containing pesticides and fungicides (Table V). For example, in the European Union (EU) it is no longer permissible to dump sewage sludge at sea; consequently the application to land has increased in recent years. To help avoid potential environmental problems, a maximum permissible concentration (MAC) of selenium in sewage sludge in the UK is set at $25 mg kg^{-1}$ and in France at $200 mg kg^{-1}$, whereas the MAC in soil after application is $3 mg kg^{-1}$ in the UK and $10 mg kg^{-1}$ in France (Haygarth, 1994; DOE, 1996). Clearly, the application of sewage sludge to land increases the selenium content of the soil; however, there are relatively few studies of uptake into plants. Those that have been conducted suggest soil-to-plant concentration factors of $1.16 – 9.36 \times 10^{-3}$ $mg kg^{-1}$ for sludge amended soils (EA, 2009). The application of selenium-bearing fertilizers to land has been used to remediate selenium deficiency in a number of countries and is discussed in Section V of this chapter. Environmental problems related to selenium emissions may also arise in areas surrounding selenium processing or fossil-fuel burning industries. Selenium concentrations in the air within 0.5–10km of copper-sulfide ore processing plants have been reported to reach $0.15–6.5 \mu g m^{-3}$ (WHO, 1987).

It is clear that man-made sources of selenium have a major impact upon the selenium cycle; despite this, the natural environment is still a very important source and pathway of selenium in animal and human exposure and requires careful consideration in selenium-related health studies (see also Chapter 4, this volume).

B. Selenium in Rocks

The most important natural source of selenium in the environment is the rock that makes up the surface of the planet. Selenium is classed as a trace element as average crustal abundances are generally very low ($0.05–0.09 mg kg^{-1}$; Taylor & McLennan, 1985). Average concentrations in magmatic rocks such as granites rarely exceed these values (Table III). Relationships with volcanic rocks are more complicated. Volcanoes are a major source of selenium in the environment and it is estimated that over the history of the Earth, volcanic eruptions account for 0.1g of selenium for every cm^2 of the Earth's surface. Ash and gas associated with volcanic activity can contain significant quantities of selenium and, for example, values of $6–15 mg kg^{-1}$ have been reported in volcanic soils on Hawaii and high concentrations are associated with volcanic tuffs in the Prairies of North America. Conversely, because selenium escapes as high-temperature gases during volcanic activity, selenium concentrations left behind in volcanic rocks such as basalts and rhyolites are usually very low (Fleming, 1980;

Jacobs, 1989; Nriagu, 1989; Neal, 1995). In general terms, sedimentary rocks contain greater concentrations of selenium than igneous rocks, but even so, levels in most limestones and sandstones rarely exceed 0.1mgkg^{-1} (Neal, 1995). Since these major rock types account for most of the Earth's surface, a picture should begin to emerge that selenium-deficient environments are far more widespread than selenium-adequate or selenium-toxic ones. Exceptions to the generally low concentrations occur in particular types of sedimentary rocks and deposits. Selenium is often associated with the clay fraction in sediments and is found in greater concentrations in rocks such as shales (0.06mgkg^{-1}) than limestones or sandstones. Very high concentrations (≤300mgkg^{-1}) of selenium have also been reported in some phosphatic rocks, probably reflecting similarities between organically derived PO_4^{3-} and SeO_4^{2-} anions (Fleming, 1980; Jacobs, 1989; Nriagu, 1989; Neal, 1995). Selenium concentrations in coal and other organic-rich deposits can be high relative to other rock types and typically range from 1 to 20mgkg^{-1} (although values of over 600mg kg^{-1} have been reported in some black shales) with selenium present as organo-selenium compounds, chelated species, or adsorbed element (Jacobs, 1989). Selenium is often found in sulfide mineral deposits and has been used as a pathfinder for gold and other precious metals in mineral exploration (Boyle, 1979). In most situations, selenium substitutes for sulfur in sulfide minerals due to similarities in crystallography, however, elemental Se^0 is occasionally reported (Fleming, 1980; Neal, 1995; Tokunaga et al., 1996). The main mineral forms and common mineral associations of selenium are outlined in Table VIII.

Therefore, the distribution of selenium in the geological environment is highly variable depending on different rock types. An illustration of the relationships between geology and selenium distribution is shown in the map of Wales (Figure 2). The highest selenium concentrations in stream sediment are associated with the mineralized areas of Parys Mountain, the Harlech Dome, and Snowdon in north Wales. In South Wales they are seen in the Forest of Dean and South Wales Coalfields and in the Permian Mercia Mudstone Group of the Welsh borderlands. In contrast concentrations over Devonian age sandstones in mid-Wales are extremely low (< 0.4mgkg^{-1}) (see also Chapter 2, this volume).

C. Selenium in Soil

In many circumstances there is a strong correlation between the concentration of selenium in geological parent materials and the soils derived from them. The selenium content of most soils is very low at 0.01–2mgkg^{-1} (world mean is 0.4mgkg^{-1}), but high concentrations of up to 1200mgkg^{-1} have been reported in some seleniferous areas (Table IX) (Fleming, 1980; Jacobs, 1989; Mayland, 1994; Neal, 1995). The relationships between geology, soil selenium concentrations, uptake into plants, and health outcomes in animals were first examined in detail in pioneering work carried out during the 1930s by Moxon (1937). Soils capable of producing selenium-rich vegetation toxic to livestock were reported over black shale, volcanic tuff and sandstone deposits of the Great Plains in the United States. Subsequent studies into selenium-deficiency-related diseases in animals lead to one of the first maps of the selenium status of soils, vegetation, and animals and the establishment of the classic Great Plain seleniferous soil types (Figure 3) (Muth & Allaway, 1963). The organic matter content of soils also determines soil selenium concentrations due to the propensity for selenium to adsorb to organic materials. Several studies have demonstrated that in low selenium environments organic matter is the dominant control on soil Se composition (e.g. Johnson et al., 2000; Ander et al., 2010; Fordyce et al., 2010).

Although the underlying geology and organic matter content are the primary controls on selenium concentrations in soils, the mobility and uptake of selenium into plants and animals, known as the bioavailability, is determined by a number of bio-physiochemical parameters. These include the prevailing pH and redox conditions, the chemical form or speciation of selenium, soil texture and mineralogy, and the presence of competitive ions. An understanding of these controls is essential to the prediction and remediation of health risks from selenium as even soils that contain adequate total selenium concentrations can result in selenium deficiency if the element is not in readily bioavailable form.

The principal controls on the chemical form of selenium in soils are the pH and redox conditions (Figure 4). Under most natural redox conditions, selenite (Se^{4+}) and selenate (Se^{6+}) are the predominant inorganic phases with selenite the more stable form. Selenite is adsorbed by ligand exchange onto soil particle surfaces with greater affinity than selenate. This process is pH dependent and adsorption increases with decreasing pH. In acid and neutral soils, selenite forms very insoluble iron oxide and oxyhydroxide complexes such as $Fe_2(OH)_4\ SeO_3$. The low solubility coupled with stronger adsorption makes selenite less bioavailable than selenate. In contrast, selenate, the most common oxidation state in neutral and alkaline soils, is generally soluble, mobile, and readily available for plant uptake. For example, experiments have shown that addition of selenate to soils results in ten times more plant uptake than addition of the same amount of selenium as selenite (Jacobs, 1989; Neal, 1995).

Elemental selenium (Se^0), selenides (Se^{2-}), and selenium sulfide salts tend to exist in reducing, acid and organic-rich environments only. The low solubility and oxidation potential of these element species make them largely unavailable to plants and animals. However, the oxidation and reduction of selenium is closely linked to microbial activity, for example, the bacterium *Bacillus megaterium* is known to oxidize elemental selenium to selenite. It is estimated that perhaps 50% of the selenium in some soils may be held in organic compounds; however, few have been isolated and identified. To date, selenomethionine has been extracted from soils and is two to four times more bioavailable to plants than inorganic selenite whereas selenocysteine is less bioavailable than selenomethionine (Jacobs, 1989; Mayland, 1994; Neal, 1995).

The bioavailability of the different selenium species in soils is summarized in Figure 5. In summary, selenate is more mobile, soluble, and less well adsorbed than selenite, thus, selenium is much more bioavailable under oxidizing alkaline conditions and much less bioavailable in reducing acid conditions (Figure 4) (Fleming, 1980; Jacobs, 1989; Neal, 1995) (see also Chapter 14, this volume).

In addition to the speciation of selenium in soils, other soil properties affect mobility. The bioavailability of selenium in soil generally correlates negatively with clay content due to increased adsorption on fine particles; indeed, the selenium uptake in plants grown on clay-loamy soils can be half that of plants grown on sandy soils. Iron also exerts a major control on selenium mobility as both elements are affiliated under oxidizing and reducing conditions and adsorption of selenium by iron oxides exceeds that of clay minerals. As mentioned above, the capacity of clays and iron oxides to adsorb selenium is strongly influenced by pH, reaching a maximum between pH 3–5 and decreasing with increasing pH (Jacobs, 1989; Neal, 1995). Soil organic matter also has a large capacity to remove selenium from soil solution possibly as a result of fixation by organometallic complexes. For example, plant uptake of selenate added to organic-rich soils can be ten times less than from mineral soils (Jacobs, 1989; Neal, 1995).

The presence of ions such as SO_4^{2-} and PO_4^{3-} can influence selenium uptake in plants by competing for fixation sites in the soil and plants. SO_4^{2-} inhibits the uptake of selenium by plants and has a greater effect on selenate than selenite. The addition of PO_4^{3-} to soils has been shown to increase selenium uptake by plants as the PO_4^{3-} ion is readily adsorbed in soils and displaces selenite from fixation sites making it more bioavailable. Conversely, increasing the levels of PO_4^{3-} in soils can dilute the selenium content of vegetation by inducing increased plant growth (Jacobs, 1989; Mayland, 1994; Neal, 1995).

Therefore, in any study of the selenium status of soil, consideration of the likely bioavailability is important. Several different chemical techniques are available to assess bioavailability but one of the most widely accepted indicators is the water-soluble selenium content (Jacobs, 1989; Tan, 1989; Fordyce et al., 2000b). In most soils, only a small proportion of the total selenium is dissolved in solution (0.3–7%) and water-soluble selenium contents are generally $< 0.1 mgkg^{-1}$ (Table III) (Jacobs, 1989).

The importance of soil selenium bioavailability and health outcomes is exemplified by seleniferous soils in the United States. Toxicity problems in plants and livestock have been reported in soils developed over the Cretaceous shales of the northern mid-West which contain $1–10 mgkg^{-1}$ total selenium because up to 60% of the element is in water-soluble readily bioavailable form in the semi-arid alkaline environment. In contrast, soils in Hawaii with up to $20 mgkg^{-1}$ total selenium do not cause problems in vegetation and livestock, because the element is held in iron and aluminum complexes in the humid lateritic soils of that region (Oldfield, 1999).

D. Selenium in Plants

Although there is little evidence that selenium is essential for vegetation growth, it is incorporated into the plant structure. Selenium concentrations in plants generally reflect the levels of selenium in the environment such that the same plant species grown over high and low selenium-available soils will contain concentrations reflecting the soil composition. However, an important factor that may determine whether or not selenium-related health problems manifest in animals and humans is the very wide-ranging ability of different plant species to accumulate selenium (WHO, 1987; Jacobs, 1989; Neal, 1995).

Rosenfield and Beath (1964) were the first to classify plants into three groups on the basis of selenium uptake when grown on seleniferous soils. Some examples of this scheme are outlined in Table X. Selenium accumulator plants grow well on high-selenium soils and can absorb $>1000 mgkg^{-1}$ of the element, whereas secondary selenium absorbers rarely concentrate more than $50–100 mgkg^{-1}$. The third group, which includes grains and grasses, usually accumulates less than $50 mgkg^{-1}$ of selenium. Selenium concentration in plants can range from $0.005 mgkg^{-1}$ in deficient crops to $5500 mgkg^{-1}$ in selenium accumulators, but most plants contain $<10 mg\ kg^{-1}$ selenium. Some species of the plant genera *Astragalus*, *Haplopappus*, and *Stanleya* are characteristic of seleniferous semi-arid environments in the western United States and other parts of the

world and are often used as indicators of high-selenium environments. It should be noted, however, that other species in these genera are non-accumulators (WHO, 1987; Jacobs, 1989; Neal, 1995).

The reason why some plants are better at accumulating selenium than others depends upon selenium metabolism. Plants contain many different selenium compounds and the main form in non-accumulator species is protein-bound selenomethionine; however, selenocysteine and selenonium have also been reported (Jacobs, 1989; Neal, 1995). In contrast, the selenium metabolism in accumulator plants is primarily based on water-soluble, non-protein forms such as Se-methylselenomethionine. The exclusion of selenium from the proteins of accumulator plants is thought to be the basis of selenium tolerance (Jacobs, 1989; Neal, 1995). Plants also reduce selenate to elemental Se^0 and selenide Se^{2-} forming the volatile organic compounds dimethylselenide and dimethyldiselenide, which are released to the air during respiration giving rise to a "garlic" odor characteristic of selenium-accumulating plants (Mayland, 1994).

Despite these coping mechanisms, plants can suffer selenium toxicity via the following processes (Jacobs, 1989; Fergusson, 1990; Mayland, 1994; Wu, 1994):

- Selenium competes with essential metabolites for sites in the plant biochemical structure.
- Selenium may replace essential ions, mainly the major cations (for example, iron, manganese, copper, and zinc).
- Selenate can occupy the sites for essential groups such as phosphate and nitrate.
- Selenium can be incorporated into analogues of essential sulfur compounds in plant tissues.

No phytotoxicity symptoms have been reported in nature in the United States, but experimental evidence has shown a negative correlation between increased selenium contents in soil and growth (plant dry weight, root length, and shoot height all decrease). For example, alfalfa yields have been shown to decline when extractable selenium exceeds $500 mg kg^{-1}$ in soil. Other symptoms include yellowing, black spots, and chlorosis of plant leaves and pink root tissue (Jacobs, 1989; Wu, 1994). However, phytotoxicity has been reported in nature in China, where high concentrations in soil caused pink discoloration of maize corn-head embryos; the pink color was attributed to the presence of elemental selenium. Levels of $>2 mg kg^{-1}$ and $>1.25 mg\ kg^{-1}$ selenium were detrimental to the growth and yield of wheat and pea crops, respectively (Yang et al., 1983). In addition to disturbances to the plant metabolism, a more recent study has shown that at low concentrations, selenium acts as an antioxidant in plants inhibiting lipid peroxidation but at high concentrations (additions of $>10 mg kg^{-1}$), it acts as a pro-oxidant encouraging the accumulation of lipid peroxidation products, which results in marked yield losses (Hartikainen et al., 2000).

Food crops tend to have relatively low tolerance to selenium toxicity, and most crops have the potential to accumulate the element in quantities that are toxic to animals and humans. In general, root crops contain higher selenium concentrations than other plants (Table XI) and plant leaves often contain higher concentrations than the tuber. For example, Yang et al. (1983) noted that selenium concentrations in vegetables ($0.3–81.4 mg kg^{-1}$) were higher than in cereal crops ($0.3–28.5 mg\ kg^{-1}$ in rice and maize) in seleniferous regions of China. Turnip greens were particularly high in selenium, with an average of 457 and ranged up to $24{,}891 mg kg^{-1}$ compared to an average of $12 mg kg^{-1}$ in the tuber. In moderate to low selenium environments, alfalfa (Sp. *Medicago*) has been shown to take up more selenium than other forage crops, which may be due to deeper rooting accessing more alkaline conditions, hence more bioavailable selenium at depth. However, in general, crop species grown in very low-selenium soils show little difference in take up and changing the type of plants makes little impact on the selenium content of crops (Jacobs, 1989). An exception is reported in New Zealand (Section V of this chapter).

E. Selenium in Water

It is estimated that the annual global flux of selenium from land to the oceans is 14,000 tonnes yr^{-1} via surface and groundwaters, which represent a major pathway of selenium loss from land in the selenium cycle (Nriagu, 1989). Approximately 85% of the selenium in most rivers is thought to be in particulate rather than aqueous form, however, the cycling of selenium from the land to the aqueous environment is poorly understood and requires further investigation (Haygarth, 1994).

The average concentration of selenium in seawater is estimated at $0.09 \mu g L^{-1}$ (Cutter & Bruland, 1984), but the mean residence time for selenium is thought to be 70 years in the mixed layer and 1100 years in the deep ocean, hence, the oceans constitute an important environmental sink for selenium (Haygarth, 1994). Biogenic volatilization from seawater to the atmosphere is estimated at 5000–8000 tonnes annually (Nriagu, 1989) and Amouroux et al. (2001) have demonstrated that the biotransformation of dissolved selenium in seawater during spring blooms of phytoplankton is a major pathway for the

production of gaseous selenium emission into the atmosphere. This makes the oceans an important component of the selenium cycle.

Although the oceans via seafood do play a role in human selenium exposure, water used for drinking is more important. Selenium forms a very minor component of most natural waters and rarely exceeds 10μg L^{-1}. Typically ranges are <0.1–100μgL^{-1} with most concentrations below 3μgL^{-1} (Plant et al., 2004). A garlic odor has been noted in waters containing 10–25μgL^{-1}, whereas waters containing 100–200μgL^{-1} selenium have an acerbic taste (WHO, 1987; Jacobs, 1989). In general, groundwaters contain higher selenium concentrations than surface waters due to greater contact times for rock-water interactions (Hem, 1992). Groundwaters containing 1000μgL^{-1} selenium have been noted in seleniferous aquifers of Montana in the United States and up to 275μgL^{-1} in China (Jacobs, 1989; Fordyce et al., 2000b) (Table III). Although rare in nature, concentrations of up to 2000μgL^{-1} selenium have also been reported in saline lake waters in the United States, Venezuela, and Pakistan (Afzal et al., 2000). Anthropogenic sources of selenium can impact surface water quality as a result of atmospheric deposition from fossil fuel combustion, industrial processes, and sewage disposal. For example, concentrations of 400μgL^{-1} in surface waters have been reported around the nickel-copper smelter at the Sudbury ore deposit in Ontario, Canada (Nriagu, 1989) and sewage effluents are known to contain 45–50μgL^{-1} selenium (Jacobs, 1989). Irrigation practices can also affect the amount of selenium in water such as at Kesterson Reservoir in the San Joaquin Valley, California (Jacobs, 1989). (See Section VI of this chapter).

F. Atmospheric Selenium

The volatilization of selenium from volcanoes, soil, sediments, the oceans, microorganisms, plants, animals, and industrial activity all contribute to the selenium content of the atmosphere. It is estimated that natural background levels of selenium in non-volcanic areas are very low, around 0.01–1ngm^{-3}; however, the residency time of selenium can be a matter of weeks, which makes the atmosphere a rapid transport route for selenium in the environment. Volatilization of selenium from the surface of the planet to the atmosphere results from microbial methylation of selenium from soil, plant, and water surfaces and is affected by the availability of selenium, carbon source, oxygen availability, and temperature (Haygarth, 1994).

The majority of gaseous selenium is thought to be in dimethylselenide form and it is estimated that terrestrial biogenic sources contribute 1200 tonnes of selenium per year to the atmosphere. Atmospheric dusts derived from volcanoes and wind erosion of the Earth's surface (180 tonnes per year) and suspended sea salts (550 tonnes per year) from the oceans also constitute significant sources of atmospheric selenium (Nriagu, 1989). It is suggested that particle-bound selenium can be transported several thousand kilometers before deposition back to the Earth's surface in both wet and dry forms. Wet deposition is thought to contribute 5610 tonnes per year to land (Haygarth, 1994). For example, in the UK it has been demonstrated that wet deposition (rain, snow, etc.) accounts for 76–93% of total deposition with >70% of selenium in soluble form. In the proximity of selenium sources (such as industrial emissions), atmospheric deposition can account for 33–82% of uptake in the leaves of plants (Haygarth, 1994).

G. Selenium Is All Around Us

From the descriptions above, it is clear that selenium is present in varying quantities in the environment all around us as a result of natural and man-made processes. Animals and humans are exposed to environmental selenium via dermal contact, the inhalation of air, and via ingestion of water and of plants and animals in the diet produced on soils containing selenium.

III. Selenium in Animals and Humans

A. Selenium Exposure

In most non-occupational circumstances atmospheric exposure is insignificant as concentrations of selenium are so low ($<10 ngm^{-3}$). However, occupational inhalation exposure may occur in the metal, selenium-recovery, and paint industries. In these circumstances, acute (short-term) exposure of humans to hydrogen selenide, the most toxic selenium compound, which exists as a gas at room temperature, results in irritation of the mucous membranes, pulmonary edema, severe bronchitis, and bronchial ammonia whereas inhalation of selenium dust can cause irritation of the membranes in the nose and throat, bronchial spasms, and chemical pneumonia. Selenium dioxide gas is the main source of problems in industrial situations as selenious acid is formed on contact with water or sweat causing irritation. Indigestion and nausea, cardiovascular effects, headaches, dizziness, malaise, and irritation of the eyes have also been reported in occupational selenium exposure (WHO, 1987, 1996) (see also Chapter 23 this volume).

As a result of these effects, hydrogen selenide gas is classed as a highly toxic substance and the common selenium-bearing compounds sodium selenite and sodium selenate are considered pollutants of concern (ATSDR, 2003). Some regulatory values for selenium compounds in air are presented in Table XII. Little information on the long-term (chronic) effects of selenium inhalation is available. In seleniferous areas of China, there is some evidence to suggest that the selenium-loading of the population is enhanced by inhalation of coal smoke from open fires used for cooking as concentrations have been known to rise to $160{,}000 ngm^{-3}$ in air during combustion (Yang et al., 1983). However, it is difficult to assess the amount of exposure via this route compared to other sources (Fordyce et al., 1998). Smoking is an inadvertent inhalation exposure route to selenium as tobacco commonly contains $0.03–0.13 mgkg^{-1}$ (WHO, 1987). Assuming a cigarette contains 1g of tobacco and that all the selenium is inhaled, a person smoking 20 cigarettes could intake $1.6 \mu g$ Se day^{-1}. The inhalation of locally grown selenium-rich tobacco in seleniferous regions of China may contribute to the loading of the local population (selenium concentration is $9.05 mgkg^{-1}$, Fordyce et al., 1998). In general, however, inhalation is a less important exposure route than ingestion. For example, studies carried out on dogs found that only 52 and 73% of selenium in the form of metal and selenious acid aerosols were adsorbed in the lungs compared to 73 and 96% absorption in the gut (Levander, 1986; WHO, 1987).

Very few studies have examined the effects of dermal exposure to selenium although sodium selenite and selenium oxychloride solutions have been proved to absorb into the skin of experimental animals. The insoluble compound selenium sulfide is used in anti-dandruff shampoos and is not normally absorbed through the skin, but elevated selenium concentrations in urine have been noted in people with open skin lesions who use these products. In an occupational setting, selenium dioxide gas can result in burns and dermatitis and an allergic body rash. In most normal circumstances, however, dermal contact is not an important exposure route (Levander, 1986; WHO, 1987, 1996) (see also Chapter 23, this volume).

In the majority of cases, water selenium concentrations are extremely low ($<10 \mu gL^{-1}$) and do not constitute a major exposure pathway; however, aquatic life-forms are sensitive to selenium intoxication as soluble forms of selenate and selenite are highly bioavailable and cause reduced reproduction and growth in fish (Jacobs, 1989). For this reason, the U.S.-EPA has set acute ecotoxicity thresholds of $258 \mu gL^{-1}$ selenite and $417 \mu gL^{-1}$ selenate in surface fresh-water (US-EPA, 2004). Selenium is a bioaccumulator, which means that plants and animals retain the element in greater concentrations than are present in the environment (Table XIII) and the element can be bioconcentrated by 200–6000 times. For example, concentrations in most waters are approximately $1 \mu gL^{-1}$ whereas freshwater invertebrates generally contain up to $4 mgkg^{-1}$ of selenium (Jacobs, 1989). Phytoplanktons are efficient accumulators of dissolved selenomethionine and incorporate inorganic selenium into amino acids and proteins (estimated bioconcentration factors range from 100 to 2600) (Jacobs, 1989). However, the reported lethal doses of selenium in water for invertebrates ($0.34–42 mgL^{-1}$) and fish ($0.62–28.5 mgL^{-1}$) indicate that in most circumstances water alone is not a major environmental problem. It should be noted, however, that inorganic and organic selenium enter the food chain almost entirely via plants and algae and bioconcentration from high-selenium waters could cause problems, because selenium passes up the food chain from algae and larval fish to large fish, birds, and humans (WHO, 1987; Jacobs, 1989). A chronic aquatic life criterion of $7.9 mgkg^{-1}$ (dry weight) selenium in fish tissue has been proposed in the United States to prevent toxicity and the uptake of too much selenium into the food chain (U.S.-EPA, 2004)). At concentrations $>50 \mu gL^{-1}$ in water, selenium intake can contribute significantly to overall dietary intake in animals and humans and the U.S.-EPA (2012) currently recommends this as the MAC for selenium in drinking water. The World Health Organization currently sets a MAC of $40 \mu gL^{-1}$ selenium for drinking water (WHO, 2011).

However, the most important exposure route to selenium for animals and humans is the food we eat, as concentrations are orders of magnitude greater than in water and air in most circumstances (WHO, 1996). An excellent review of the selenium content in foodstuffs is provided by Reilly (2006). In summary, in terms of the human diet, organ meats such as liver and kidney are good sources of selenium and some seafoods contain almost as much. Muscle meats are also a significant source and garlic and mushrooms contain more than most other vegetables. Cereals are another important source, however, white bread and flour contain less selenium than whole meal by about 10–30% (Table XIV) (WHO, 1987; Reilly, 2006; Rayman, 2008). Brazil nuts sold in the UK are high in selenium, indeed, cases of selenium poisoning in Amazon peoples following

consumption of nuts of the Lecythidaceae family have been reported in Brazil. These incidents resulted in nausea, vomiting, chills, diarrhea, hair and nail loss, painful joints, and death in some cases (see Section III.F of this chapter). Cooking reduces the selenium contents of most foods, and studies have shown that vegetables that are normally high in selenium such as asparagus and mushrooms lose 40% during boiling. Other studies estimate 50% of the selenium content is lost from vegetables and dairy products during cooking especially if salt and low pH foods such as vinegar are added, whereas frying foods results in much smaller losses (Levander, 1986; WHO, 1987, 1996) (see also Chapter 7, this volume).

Levels of dietary selenium intake show huge geographic variation and are dependent upon the geochemical conditions of the food source environments as well as differences in dietary composition. For example in 1995, cereals accounted for 75% of the total 149μg day^{-1} selenium intake in Canada but only 10% of the 30μg day^{-1} intake in Finland (WHO, 1996). In general terms, cereals grown in North America contain more selenium than European crops and concern is growing in Europe over declining selenium intakes. The UK traditionally imported large quantities of wheat from North America but since the advent of the EU, most cereals are now more locally derived and as a consequence, daily intakes of selenium in the UK have been falling (Broadley et al., 2006). Marked declines are evident particularly over a 4-year period from intakes of 60μg day^{-1} in 1991 to 43μg day^{-1} in 1995 (Figure 6) (FSA, 2009). This downward trend is also attributed to a reduction in cereal consumption in the UK, which fell from 1080g $person^{-1}$ $week^{-1}$ in 1970 to 756g $person^{-1}$ $week^{-1}$ in 1995 (MAFF, 1997) and changes in the bread making process (Johnson et al., 2010). The selenium content of Irish bread is also significantly lower than in the United States and only marginally higher than the UK (Table XIV) (Murphy & Cashman, 2001). Other cereal crops such as rice generally contain low selenium contents (Table XIV) and can have a significant influence on overall dietary intake when consumed as the staple food as in most of Asia. Conversely Japanese diets can be very high in selenium (up to 500μg day^{-1}) in areas where a large amount of seafood is consumed (WHO, 1987).

Some examples of daily dietary selenium intakes from around the world are listed in Table XV. On a global scale it is estimated that dietary intakes in adults range from 3 to 7000μg day^{-1} and for infants in the first month of life from 5 to 55μg day^{-1}. The wide ranges are attributed to selenium contents in the environment (WHO, 1996; Rayman, 2008). The greatest variations in dietary intake are reported from selenium-deficient and seleniferous regions of China (Tan, 1989), but contrasts also occur in South America between high daily intakes (100–1200μg) associated with foodstuffs grown on selenium-rich shales in the Andes and Orinoco River of Venezuela and widespread selenium deficiency in Argentina (WHO, 1987; Oldfield, 1999; Rayman, 2008). Dietary intakes in countries such as New Zealand, Finland, and Turkey are also poor as a consequence of low-selenium soils, whereas intakes in Greece, Canada, and the United States are generally adequate (WHO, 1987). On the basis of selenium requirement studies, a range of 50–200μg day^{-1} has been recommended by the U.S. National Research Council (NRC) for adults depending on various factors such as physiological status. Balance studies to more precisely determine the ratio of selenium inputs and outputs in human beings were attempted, however, these were not successful as humans have the ability to modify fecal and urinary excretion of selenium depending on levels of intake (WHO, 1996). Current recommended daily allowances (RDAs) of dietary selenium range from approximately 55μg in women to 75μg day^{-1} in men and 8.7–10μg day^{-1} in infants (Table XV) (WHO, 1996; ATSDR, 2003; MAFF, 1997).

Just as bioavailability is an important factor in terms of plant uptake of selenium, it is also an important factor in the diets of animals and humans. Dietary studies have shown that selenomethionine is more readily absorbed in the guts of animals and humans than selenate, selenite, or selenocysteine. More than 90% of ingested selenomethionine and selenate is absorbed, whereas the rate for sodium selenite is slightly lower (>80%). Selenides and elemental selenium are poorly absorbed and in general organic forms of selenium are more readily bioavailable than inorganic forms (Lyons et al., 2007; Rayman et al., 2008). As an indication of the diet in general, studies carried out in New Zealand have shown that 79% of selenium present in natural foods is bioavailable. In addition to foodstuffs, mineral supplements are a source of dietary selenium to humans and animals. Chemical supplement tests show 97% adsorption of selenomethionine, 94% of selenate, and 60% of sodium selenite in this dietary form (Levander, 1986; WHO, 1987).

In animals, 85–100% of dietary plant selenium is absorbed whereas only 20–50% of the selenium present in meat and fish is taken up by birds and mammals. In general terms, selenium in plant forms is more readily bioavailable than selenium in animal forms (Levander, 1986; WHO, 1987, 1996) (see also Chapter 20, this volume).

Until recently, very few studies had examined the chemical form of selenium in foodstuffs , but advances in analytical techniques have revealed more information. Previous evidence suggested that 7.6-44% of selenium in tuna was in the form of selenate -with the remainder present as selenite and selenide (WHO, 1987). However, it has now been demonstrated that selenoneine is the main organo-selenium compound in fish such as tuna and mackerel (Yamashita & Yamashita, 2010). In contrast, 50% of the selenium in wheat and 15% in cabbage had been shown to be in the form of selenomethionine (WHO, 1987). More recent studies confirm that selenomethionine is the main compound in plant food sources particularly cereal crops and yeast and it is the main selenium constituent in Brazil nuts and some selenium supplements. Se-methylselenocysteine and γ-glutamyl-Se-methylselenocysteine are found in yeast, garlic, onions and broccoli; whereas

selenocysteine is the main form in animal foodstuffs. Some selenate is found in fish and plant sources such as cabbage (Lyons et al., 2007; Rayman, 2012). These differences in the chemical forms of selenium are reflected in the rate of absorption and bioavailability of the element in foodstuffs. For example, it is estimated that over 90% of the selenium in Brazil nuts and beef kid-ney is bioavailable, compared to only 20–60% in tuna. However, other seafood, such as shrimp, crab, and Baltic herring, have higher bioavailability (Levander, 1986; WHO, 1987).

The bioavailability of selenium to humans and animals is not only dependent on the amount of absorption but also on the conversion of the ingested selenium to metabolically active forms. In humans, studies based on the activity of the selenium-dependent enzyme GPx have shown that the bioavailability of sele-nium in wheat is >80% whereas the bioavailability of selenium in mushrooms is very low (WHO, 1987). Conversely, other studies report good bioavailability in selenium-enhanced mushrooms (Rayman et al., 2008). In a comparison between wheat and mineral selenate supplements, while the latter were shown to enhance GPx activity, patients fed wheat demonstrated greater increases and better long-term retention of selenium (WHO, 1987).

Fairweather-Tait et al. (2010) conclude that the bioavailability of selenium is difficult to quantify due to the complexity of selenium compounds in foodstuffs. Therefore, much has still to be learned about the uptake of selenium in humans and animals; however, it is clear that in most normal circumstances food forms the major exposure route as selenium accumulates from the environment via plants and algae through the food chain to animals and man. Selenium in the form of selenomethionine and other organic compounds is highly bioavailable to animals and humans and foodstuffs that contain high proportions of these forms, such as organ and muscle meats, Brazil nuts, and wheat, are good sources of the element in the diet (WHO, 1987; Reilly, 2006; Rayman, 2012).

B. Selenium in the Body of Animals and Humans

Once ingested into the body, most selenium is absorbed in the small intestine of animals and humans, but the rates and mechanisms of selenium metabolism vary between different animal species. In general, single-stomached animals absorb more selenium than ruminants due to the reduction of selenite to insoluble forms by rumen microorganisms. Experiments on rats indi-cate very little difference in the process of absorption of different selenium forms; 92% of selenite, 91% of selenomethionine, and 81% of selenocysteine were absorbed primarily in the small intestine and none in the stomach. Approximately 95% of the total selenium intake was absorbed regardless of whether the rats were fed a low- or high-selenium diet indicating that selenium intake is not under homeostatic control. This is true in general for intake in animals and humans. However, other studies have shown that oral doses of selenomethionine are retained more readily and turned over more slowly than selenite in humans, therefore unlike rats there is a difference in the metabolism of different forms of selenium. In fact, selenomethionine, the main form of uptake from plants to animals, becomes associated with protein tissues in the body whereas inorganic selenium is absorbed into other tissues (Levander, 1986; WHO, 1987, 1996; Rayman et al., 2008). Selenite is taken up by red blood cells, bound to albumin and transferred to the liver. Selenate is taken up directly by the liver or excreted into the urine (Lyons et al., 2007).

Indeed, most of the ingested selenium is quickly excreted in the urine, breath, perspiration, and bile and the remainder becomes bound or incorporated into blood and proteins. Urine is the primary route of excretion (70–80%) in single-stomached animals, however, in ruminants selenium is mostly excreted in the feces and studies have shown that the majority of this selenium is in unavailable elemental form. Chemical selenium tracer experiments in humans suggest that the main extraction pathway is via urine, however, in studies using natural foods, excretion in feces was equal to that of urine; whereas minimal amounts of selenium were exuded in sweat and respiration and expulsion of volatile forms of selenium only occurred at very high exposures. Unlike selenium absorption, which is not homeostatically regulated, selenium excretion in animals and humans is directly influenced by nutritional status: excretion rises as intake increases and decreases when selenium intakes are low (Levander, 1986; WHO, 1987, 1996) (see also Chapters 7, 8, and 20, this volume).

The remaining selenium is transported rapidly around the body and concentrates in the internal organs, which are rich in protein. This pattern is present in a number of animal species (Figure 7). Hence, in normal conditions in humans, selenium levels are highest in the liver and kidneys and lower in muscle tissues. However, the largest total amount of selenium in the human body is in the muscles as these form the main body mass. It is estimated that muscles account for 46.9% whereas kidneys contain only 4% of the total selenium in the human body (Lyons et al., 2007). Total human body selenium contents are estimated at 3–14.6mg (WHO, 1987).

In rats fed selenium-deficient diets, however, the pattern of selenium distribution is different with selenium reserved in the testes, brain, thymus, and spleen. Also in humans the supply to the testes has priority over the other tissues during selenium

deficiency, because the element is found in the mitochondrial capsule protein (MCP) and is involved in biosynthesis of testosterone. Consequently, the selenium content of the testes increases considerably during puberty (Levander, 1986; WHO, 1987).

Both inorganic and organic selenium are converted by animals and humans to mono-, di-, or trimethylated forms by the main metabolic pathway, rarely reduction. Trimethylselenonium, was thought to be the main urinary excretion form, but recent research suggests the selenosugar 1 metabolite may predominate following increased selenium intake (Lyons et al., 2007). However, in cases of selenium toxicity, the urinary pathway becomes overloaded and the volatile selenium metabolite dimethylselenide is produced and exhaled via the lungs, which results in the characteristic "garlic breath" symptom in animals and humans suffering selenosis. There is much debate over the form of selenium held in protein tissues. Non-ruminant animals and humans cannot synthesize selenite into selenomethionine, but there is evidence to suggest that selenomethionine from food sources can be incorporated into protein tissues directly in place of methionine (Lyons et al., 2007; Rayman et al., 2008). However, in the case of rats it is then converted to selenite or selenate. Rabbits and rats can also convert selenite into selenocysteine tissue proteins. Selenium may also be present in proteins in the selenotrisul-fide and acid-labile form. Early work suggested that selenium intake in all naturally occurring organic forms was retained in tissues to a greater extent than inor-ganic forms, however, experiments with mice using selenite, Se-methylselenocysteine, and selenomethionine showed that mice fed selenomethionine had greater quantities and better long-term retention of selenium than those fed selenite or Se-methylselenocysteine. There is evidence for metabolic pools of selenium in animals and humans. For example, studies with ewes fed selenium-adequate and then selenium-deficient diets showed that they were able to pass on adequate levels of selenium to their lambs even though the lambs were born 10 months into the selenium-deficient diet. Two likely metabolic pools have been proposed. The main exchangeable pool includes all forms of Se derived from inorganic selenite and selenate and is an active pool for selenoprotein synthesis. The second pool comprises the se-questration of selenomethionine or other selenoamino acids incorporated into protein structures that are then released during protein turnover (Levander, 1986; WHO, 1987; Lyons et al., 2007; Rayman et al., 2008).

In most circumstances there is a close correlation between the levels of selenium in the diet of humans and animals and blood selenium content. On average, plasma levels vary from 0.079 to 0.252mgL^{-1} depending on selenium intake, whereas the mean concentration of selenium in human whole blood is 0.2mgL^{-1} (WHO, 1987, 1996). Human whole blood selenium levels show marked geographic variation depending on dietary intake. Ranges of 0.021–3.2mgL^{-1} have been reported worldwide with highest concentrations in seleniferous areas of China and Venezuela and lowest concentrations in the selenium-deficient regions of Scandinavia, New Zealand, and China (Table XVI) (WHO, 1996; Oldfield, 1999). Similarly, concentrations in hair, nails, and urine vary according to differences in dietary intake, and some examples of the selenium composition of these tissues are given in Table XVI. Selenium levels in human milk are affected by maternal intake and infants and young children have a high requirement for the element during the rapid growth periods of early life. However, the age of mother and the concentration of selenium during pregnancy do not affect the weight of baby or the length of pregnancy. Wide ranges of 2.6–283mgL^{-1} in human milk have been reported from selenium-deficient and seleniferous regions in China, compared to ranges of 7–33mgL^{-1} in the United States (Levander, 1986.)

In terms of biological function, 25 essential selenoproteins containing selenocysteine have now been identified in humans, many of which are involved in redox reactions acting as components of the catalytic cycle (WHO, 1996; Papp et al., 2007; Rayman, 2012). A selection of selenoproteins with known health functions is listed in Table XVII (Papp et al., 2007; Rayman, 2012). Enzyme activity is attributed to the glutathione peroxidase, thioredoxin reductase, iodothyronine deiodinase, and selenophosphate synthetase groups. In complex interactions with vitamin E and polyunsaturated fatty acids, selenium plays an essential biological role as part of the enzyme GPx, which protects tissues against peroxidative damage by catalyzing the reduction of lipid hydrogen peroxide or organic hydroperoxides. Together, GPx, vitamin E and superoxide dismuthases form one of the main antioxidant defense systems in humans and animals. Selenium also appears to enhance T-cell production and natural killer cell activity (Rayman, 2012). As such, selenium has been linked to enzyme activation, immune system function, pancreatic function, DNA repair, and the detoxification of xenobiotic agents such as paraquat, however, the exact mechanisms of detoxification are still being established (Combs & Combs, 1986; Levander, 1986; WHO, 1987, 1996; Papp et al., 2007). Selenium is found in the prosthetic groups of several metalloenzymes and appears to protect animals against the toxic effects of arsenic, cadmium, copper, mercury, tellurium, and thallium in most circumstances, but this is not always the case and the biological response depends on the ratio of selenium/metal involved (WHO, 1987; Fergusson, 1990). Selenium behaves antagonistically with copper and sulfur in humans and animals inhibiting the uptake and function of these elements. Selenium also appears to affect the P-450 cytochrome enzyme system in humans and animals. However, the exact biochemical function of selenium is still being established. Several studies have shown no reduction in P-450 activity under selenium-deficient conditions whereas recent work suggests that selenium inhibits P-450 enzymes. Since these enzymes activate carcinogenic substances such as polynuclear aromatic hydrocarbons (PAHs) and phenobarbital, this

may explain why selenium has been shown to prevent cancers induced by these substances in laboratory animals ((Shimada, et al., 2011). Other important developments in more recent years have shown that selenium is beneficial to the thyroid hormone metabolism. There are three iodothyronine deiodinase (Dio) selenoenzymes. Types 1 and 2 are involved in the synthesis of active 3, 3′ and 5-triiodothyronine (T3) hormones, whereas type 3 Dio catalyzes the conversion of thyroxine (T4) to inactive T3(rT3). These hormones exert a major influence on cellular differentiation, growth, and development, especially in the fetus and child (Arthur & Beckett, 1994). Selenium also appears to be important in reproduction. In addition to aiding the biosynthesis of testosterone (see above), the selenium contents of avian eggs are high whereas morphological deformities, immotility, and reduced fertility have been reported in sperm in selenium-deficient experimental animals (WHO, 1987, 1996; Rayman, 2012). Although many of the *in vivo* functions of selenium are still poorly understood, deficient and excessive dietary intakes of selenium have a marked effect on animal and human health, some of which are discussed below.

C. Selenium Deficiency—Effects in Animals

Due to the complementary role of selenium and Vitamin E, all selenium deficiency diseases in animals are concordant with vitamin E deficiency with the exception of neutrophil microbicidal activity reduction and the 5-deiodinase enzymes responsible for the production of triiodothyronine from thyroxine. Selenium is necessary for growth and fertility in animals and clinical signs of deficiency include dietary hepatic apoptosis in rats and pigs; exudative diathesis, embryonic mortality, and pancreatic fibrosis in birds; nutritional muscular dystrophy, known as white muscle disease, and retained placenta in ruminants and other species; and mulberry heart disease in pigs. Clinical signs of selenium deficiency in animals include reduced appetite, growth, production and reproductive fertility, unthriftyness, and muscle weakness (Levander, 1986; WHO, 1987, 1996; Oldfield, 1999).

White muscle disease is a complex condition that is multifactorial in origin and causes degeneration and apoptosis of the muscles in a host of animal species. This disease rarely affects adult animals but can affect young animals from birth. In lambs born with the disease, death can result after a few days. If the disease manifests slightly later in life, animals have a stiff and stilted gait, arched back, are not inclined to move about, lose condition, become prostrate and die. The disease responds to a combination of vitamin E and selenium supplementation (Levander, 1986; WHO, 1987, 1996; Oldfield, 1999).

Exudative diathesis in birds leads to massive hemorrhages beneath the skin as a result of abnormal permeability of the capillary walls and accumulation of fluid throughout the body. Chicks are most commonly affected between 3–6 weeks of age and become dejected, lose condition, show leg weakness, and may become prostrate and die. The disease responds to either vitamin E or selenium supplementation, but it will not respond to vitamin E alone if selenium is deficient (WHO, 1987).

Hepatic apoptosis in pigs generally occurs at 3–15 weeks of age and is characterized by necrotic liver lesions. Supplements of alpha-tocopherol and selenium can protect against death (Levander, 1986).

Low-selenium pastures containing 0.008–0.030mgkg^{-1} are associated with a condition called “ill thrift” in lambs and cattle from New Zealand. The disease is characterized by subclinical growth deficits, clinical unthriftyness, rapid weight loss, and sometimes death but can be prevented by selenium supplementation with marked increases in growth and wool yields (Levander, 1986; WHO, 1987).

The level of dietary selenium needed to prevent deficiency depends on the vitamin E status and species of the host. For example, chicks receiving 100mg of vitamin E require 0.01mgkg^{-1} of selenium to protect against deficiency, whereas chicks deficient in vitamin E require 0.05mgkg^{-1} of selenium. Under normal vitamin E status, concentrations of 0.04–0.1mgkg^{-1} (dry weight) in feedstuffs are generally adequate for most animals with a range of 0.15–0.20mgkg^{-1} for poul-try and 0.03–0.05mgkg^{-1} for ruminants and pigs (Levander, 1986; WHO, 1987).

Selenium deficiency and WMD are known to occur in sheep when blood selenium levels fall below 50μgL^{-1} and kidney concentrations below 0.21mgkg^{-1} (dry weight). Blood levels of 100μgL^{-1} selenium are needed in sheep and cattle and 180–230μgL^{-1} in pigs to maintain the immunoresponse systems. Studies have shown that most farmland grazing in the UK is not able to provide enough selenium to support 0.075mgL^{-1} in blood in cattle. Indeed, selenium deficiency in animals is very common and widespread around the globe affecting much of South America, North America, Africa, Europe, Asia, Australia, and New Zealand. Many western countries now adopt selenium supplementation programs in agriculture, but these are often not available in South America, Africa, and Asia and livestock productivity is significantly impaired by selenium deficiency in these regions (Levander, 1986; WHO, 1987, 1996; Oldfield, 1999) (see also Chapter 20, this volume).

D. Selenium Deficiency—Effects in Humans

No clear-cut pathological condition resulting from selenium deficiency alone has been identified in humans, however, the element has been implicated in a number of diseases (WHO, 1996; Rayman, 2012) (see also Chapters 8 and 23, this volume).

1. Keshan Disease

Keshan disease (KD) is an endemic cardiomyopathy (heart disease) that mainly affects children and women of childbearing age in China. The disease has been documented for over 100 years, but the name is derived from a serious outbreak in Keshan County, northeast China in 1935. Outbreaks have been reported in a broad belt stretching from Heilongjiang Province in the northeast of China to Yunnan province in the southwest that transcends topography, soil types, climatic zones, and population types (Figure 8). This disease manifests as an acute insufficiency of the heart function or as a chronic moderate-to-severe heart enlargement and can result in death. Seasonal variations in outbreak were noted with peaks in the winter in the south and in the summer in the north. 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 (Tan, 1989).

Although the disease occurred in a broad belt across China, all of the affected areas were characterized by remoteness and a high proportion of subsistence farmers who were very dependent on their local environment for their food supply. Investigators noticed that WMD in animals occurred in the same areas and further studies demonstrated that the soils and crops were very low in selenium. KD occurred in areas where grain crops contained $<0.04 mg kg^{-1}$ of selenium and dietary selenium intakes were extremely low, between 10 and 15μg day^{-1}. Affected populations were characterized by very low selenium status indicated by hair contents of $<0.12 mg kg^{-1}$ (Xu & Jiang, 1986; Tan, 1989; Yang & Xia, 1995). On the basis of these findings, large-scale mineral supplementation was carried out on 1- to 9-year-old children who were at high risk of the disease. In a trial carried out in Mianning County, Sichuan Province, from 1974 to 1977, 36,603 children were given 0.5- to 1.0-mg sodium selenite tablets per week whereas 9642 children were given placebo tablets. During the 4 years of investigation, 21 cases of the disease and 3 deaths occurred in the selenium-supplemented group whereas 107 cases and 53 deaths occurred in the control group. By 1977 all the children were supplemented with selenium and the disease was no longer prevalent in either group. The results showed that supplements of 50-μg day^{-1} selenite could prevent the disease but if the disease was already manifest, selenium was of no therapeutic value (Anonymous, 2001).

Although the disease proved to be selenium-responsive, the exact biological function of the element in the pathogenesis was less clear and the seasonal variation in disease prevalence suggested a viral connection. Subsequent studies have demonstrated a high prevalence of the Coxsackie B virus in KD patients (see, for example, Li et al., 2000) and studies have proved increased cardiotoxicity of this virus in mice suffering from selenium and vitamin E deficiency. For a number of years it was thought that selenium deficiency impaired the immune function lowering viral resistance, however, more recent work by Beck (1999) has shown that a normally benign strain of Coxsackie B3 (CVB3/0) alters and becomes virulent in either selenium-deficient or vitamin E-deficient mice. Once the mutations are completed, even mice with normal nutritional status become susceptible to KD. These changes in the virus are thought to occur as a result of oxidative stress due to low vitamin E and low selenium status. This work demonstrates not only the importance of selenium deficiency in immunosuppression of the host but in the toxicity of the viral pathogen as well. Other studies have implicated moniliformin mycotoxins produced by the fungi *Fusarium proliferatum* and *F. subglutinans* in corn as a possible cause of KD (Pineda-Valdes & Bullerman, 2000). As with many environmental conditions, KD is likely to be multifactorial but even if selenium deficiency is not the main cause of the disease, it is clearly an important factor.

During the 1980s the prevalence of KD dropped to less than 5 per 100,000 with less than 1000 cases reported annually. The reason for this is twofold: first, widespread selenium supplementation programs have been carried out on the affected populations and secondly, economic and communication improvements in China as with the rest of the world mean that the population is increasingly less dependent on locally grown foodstuffs in the diet. In recent years the incidence of the disease has dropped still further so that it is no longer considered a public health problem in China (Burk, 1994).

2. Kashin-Beck Disease

Kashin-Beck disease (KBD), an endemic osteoarthropathy (stunting of feet and hands) causing deformity of the affected joints, occurs in Siberia, China, North Korea, and possibly parts of Africa. The disease is named after the Russian scientists who first described it between 1861 and 1899. It is characterized by chronic disabling degenerative osteoarthrosis affecting the peripheral joints and the spine with apoptosis of the hyaline cartilage tissues. Impairment of movement in the extremities

is commonly followed by bone development disturbances such as shortened fingers and toes and in more extreme cases, dwarfism (Figure 9) (Levander, 1986; Tan, 1989; WHO, 1996). Indeed the main feature of KBD is short stature caused by multiple focal apoptosis in the growth plate of the tubular bones. In China, the pattern of disease incidence is concordant with KD in the north of the country, but the links with selenium-deficient environments are less clear (Tan, 1989).

Initial studies revealed that rats fed grain and drinking water from the affected areas in China suffered acute massive liver apoptosis and foodstuffs from the affected areas were found to be low in selenium. Children and nursing mothers were supplemented with 0.5–2.0mg 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 (Tan, 1989). More recent studies carried out since the early 1990s demonstrated KBD-like cartilage changes and bone mineral density reduction in selenium-deficient rats (Sasaki et al., 1994; Moreno-Reyes et al., 2001). However, other factors have been implicated in the pathogenesis of KBD. The main theory proposed by Russian investigators was that the disease was a result of mycotoxins in the diet, and other work carried out in China has suggested ingestion of contaminated drinking water as a possible cause. In China, higher fungal contamination of grain in KBD areas has been known for a number of years. Other work suggests that the presence of humic substances in drinking water is a factor, and the mechanism of action is free radical generation from the oxy and hydroxyl groups of fulvic acid. Nonetheless, selenium was confirmed as a preventative factor in KBD in these studies (Peng et al., 1999).

There are similarities between KBD and the iodine-deficiency disorder cretinism. Several studies have considered the relationships between KBD and selenium and iodine deficiency. Work in the Yulin District of China (Zhang et al., 2001) carried out on 353 rural school children aged 5–14 years compared data between three endemic KBD villages (prevalence rates 30–45%) and a non-endemic village. Higher fungal contamination was recorded in cereal grain stores in KBD areas than in the non-endemic village, and hair selenium and urinary iodine concentrations were lower in families suffering from the disease than in control groups. However, iodine deficiency did not correlate significantly with increased KBD risk. More recent work into the disease has focused on Tibet and it does implicate iodine in the pathogenesis. Among 575 5- to 15-year-old children examined in 12 villages, 49% had KBD, 46% had the iodine deficiency disorder goiter, and 1% had cretinism. Of the examined population, 66% had urinary iodine contents of $<0.02\mu gL^{-1}$ and the content was lower in KBD patients ($0.12\mu gL^{-1}$) than in control subjects ($0.18\mu gL^{-1}$). Hypothyroidism was more frequent in the KBD group (23%) compared to 4% in the controls. Severe selenium deficiency was present in all groups with 38% of subjects with serum concentrations of $<5mgL^{-1}$ (normal range 60–$105mgL^{-1}$). Statistical analyses revealed an increased risk of KBD in groups with low urinary iodine in the severe selenium-deficient areas. Here also, mesophilic fungal contamination in barley (*Alternaria* sp.) was higher in KBD areas than non-endemic areas and disease prevalence correlated positively with the humic content of drinking water. The results suggest that KBD is multifactorial and occurs as a consequence of oxidative damage to cartilage and bone cells when associated with decreased antioxidant defense. Another mechanism that may coexist is bone remodeling stimulated by thyroid hormones whose actions are blocked by certain mycotoxins (Suetens et al., 2001).

3. Iodine Deficiency Disorders and Thyroid Function

In addition to the links between selenium and iodine deficiency in KBD, the establishment of the role of the selenoenzyme, iodothyronine deiodinase (Dio), in thyroid function means that selenium deficiency is now being examined in relation to the iodine deficiency disorder (IDD) goiter and cretinism. Many areas around the world where IDD is prevalent are deficient in selenium including China, Sri Lanka, India, Africa, and South America (WHO, 1987, 1996). Concordant selenium and iodine deficiency are thought to account for the high incidence of cretinism in Central Africa, in Zaire and Burundi in particular (Kohrle, 1999), and selenium deficiency has been demonstrated in populations suffering IDD in Sri Lanka (Fordyce et al., 2000a). Relationships between low selenium status and thyroid tissue damage and goiter in France and with thyroid cancer in Norway have been reported. Selenium supplementation has also been shown to protect against Hashimoto's thyroiditis and Graves' disease (Rayman, 2012).

4. Cancer

Following studies that revealed an inverse relationship between selenium in crops and human blood versus cancer incidence in the United States and Canada (Shamberger & Frost, 1969), the potential anti-carcinogenic effect of selenium has generated a great deal of interest in medical science. Many studies to examine the links between selenium and cancer in animal experiments and humans have been carried out; however, to date, the results are equivocal. There is some evidence to suggest that selenium is protective against bladder, colorectal, lung and prostate cancer due to its antioxidant properties, the ability to counteract heavy metal toxicity, the ability to induce cell death, the ability to inhibit cell growth, and the ability to inhibit nucleic acids and protein synthesis, but trial results are mixed (WHO, 1987, 1996; Clark et al., 1996; Varo et al., 1998;

Rayman, 2012). However, other studies have shown that selenium may promote cancer based on the pro-oxidant mutagenic and immunosuppressive actions of some selenium compounds. For example, the supplementation of sodium selenate, sodium selenite, and organic selenium have been shown to reduce the incidence of several tumor types in laboratory animals, but selenium sulfide has been shown to be carcinogenic in animals and has been classified as a Group B2 compound—a possible human carcinogen (WHO, 1987, 1996; ATSDR, 2003). Human studies have demonstrated low levels of selenium in the blood of patients suffering gastrointestinal cancer, prostate cancer, or non-Hodgkin's lymphoma, but there is some evidence to suggest that selenium increases the risks of pancreatic and skin cancer (WHO, 1987, 1996; Birt, et al., 1989).

Excellent reviews of the work into selenium and cancer are presented by Vinceti et al. (2000) and Rayman (2012) and are summarized as follows. In a Nutritional Prevention of Cancer study in 1996 of patients with a history of basal or squamous cell skin cancer, selenium intakes of 200μg day^{-1} appeared to reduce mortality from all cancers and the incidence of lung, colorectal, and prostate cancers. However, it did not prevent the appearance of skin cancer. Indeed, some studies have shown an inverse relationship with melanoma risk but other studies have shown no relationship with non-melanoma skin cancer. However, Vinceti et al. (1998) carried out assessments of populations inadvertently exposed to high selenium in drinking water and reported higher mortality from lung cancer, melanoma, and urinary cancer among men and lymphoid neoplasm in women in the exposed group compared to controls. Other studies have shown an increased risk of colon and prostate cancer in populations taking selenium supplements in Iowa in the United States and Finland than in control populations. However, a study in Montreal carried out between 1989 and 1993 found no association between selenium status (measured by toenail selenium) and breast or prostate cancer but showed an inverse relationship with colon cancer (Vinceti et al., 2000). The Selenium and Vitamin E Cancer Trial (SELECT) showed that supplementation with 200 μg selenium per day did not reduce the risk of localized prostate cancer in 35,533 American men but the men were not of low selenium status to begin with (Lippman et al., 2009). More recent studies have shown no significant association between selenium status and lung cancer and a complex relationship with prostate cancer whereby selenium appears to protect against risk of advanced rather than localized or low grade disease particularly in smokers (Rayman, 2012).

In a study of stomach cancer in Finland and The Netherlands, an inverse relationship between selenium status and disease prevalence was found in Finnish men but not in Finnish women or in men or women from The Netherlands. No relationship between selenium status and stomach cancer was evident in studies carried out in Japan. A link between low-selenium status and pancreatic cancer was observed in Maryland in the United States and in Finland, but a similar relationship with bladder and oropharyngeal cancer was evident in Maryland only (Vinceti et al., 2000). Indeed Finland provides an interesting case because the government was so concerned about the low level of selenium intake in the Finnish diet that in 1984 a national program was initiated to increase the selenium content of Finnish foodstuffs by adding sodium selenate fertilizers to crops. Mean daily intakes rose from 45μg day^{-1} in 1980 to 110–120μg day^{-1} between 1987 and 1990 and 90μg day^{-1} in 1992 (Varo et al., 1998). Studies of cancer incidence over this time carried out in Finland, Sweden, and Norway showed no reduction in colon cancer, non-Hodgkin's lymphoma, or melanoma in Finland whereas breast and prostate cancer rates increased compared to the other two countries. Populations in Finland and New Zealand are known to have much lower selenium status than many other countries and yet no excess incidence of breast and colon cancer is evident. Similarly no relationship between cancer prevalence and selenium intakes as low as 14μg day^{-1} was identified among rural farmers in China. Conversely, work by Finley et al. (2001) has demonstrated a link between consumption of high-selenium broccoli and reduced colon and mammary cancer prevalence. Based on the evidence presented above, it is fair to say that "the jury is still out" in terms of the beneficial effects or otherwise of selenium and cancer.

5. Cardiovascular Disease

Selenium deficiency has also been implicated in cardiovascular health and it is suggested that serum concentrations of less than 45μgL^{-1} increase the risk of ischemic heart disease. Animal studies have demonstrated that selenium could play a protective role by influencing platelet aggregation and increasing production of thromboxane A2 while reducing prostacyclin activity as well as several cardiometabolic effects that have been linked to selenium dependant enzymes such as GPx and selenoprotein S. However, the epidemiological evidence and studies into selenium status and disease risk provide contradictory results (Levander, 1986; WHO, 1987, 1996). Randomized trials based on selenium supplementation have shown no protective effect on cardiovascular disease but there is some evidence of an inverse association between coronary heart disease and low selenium status (Rayman, 2012).

6. Reproduction

The full role of selenium in reproduction has yet to be established; however, selenium deficiency has been shown to cause immotile and deformed sperm in rats (Wu et al., 1979; Hawkes & Turek, 2001). In men the testis takes up selenoprotein P1 required for adequate GPx4 activity, which is essential for sperm motility. Trials have shown reduced GPx4 in infertile men and selenium supplementation has been shown to increase sperm motility. There is some evidence of lower selenium status in women suffering miscarriages and low selenium intake has also been linked to pre-eclampsia (Rayman, 2012).

7. Other Diseases

Selenium deficiency has been linked to a number of other conditions in man as the concentration of the element is decreased in the serum/plasma or erythrocytes of patients with AIDS, trisomy-21, Crohn's and Down syndrome, and phenylketonuria. The evidence of viral mutogeny under selenium deficiency established by Beck (1999) in the case of the Coxsackie B virus has major implications in terms of the toxicity and immunoresponse to many viral infections, particularly AIDS, in light of the widespread selenium-deficient environments of central and southern Africa where the disease has reached epidemic proportions (Longombe et al., 1994). Two randomized trials in the U.S. have shown benefits from selenium supplementation in HIV infection whereas one in Tanzania did not (Rayman, 2012). Selenium supplementation is now being used alongside other treatments to help the fight against HIV in Africa.

Selenium deficiency has also been linked to mus-cular dystrophy (a similar human disease to WMD in animals) and muscular sclerosis, but again the medical evidence for the role of the element is equivocal. Selenium supplementation has proved beneficial to patients suffering renal disease and finally an inverse relationship between selenium status and asthma incidence has also been postulated (WHO, 1987).

Dietary intakes of 0.1–0.2mgkg^{-1} selenium are considered nutritionally generous converting to 50–100μg day^{-1} for a typical person and 0.7–2.8μgkg body weight^{-1}. Even in New Zealand and Finland, where selenium intake is 30–50μg day^{-1}, compared with 100–250μg day^{-1} in the United States and Canada, overt clinical signs of selenium deficiency are rare among humans (WHO, 1987, 1996). Nonetheless, research increasingly shows the essential nature of selenium to human health and the potential for subclinical effects should not be underestimated. Concern is growing in many regions of the world over low levels of dietary selenium intake in human populations.

E. Selenium Toxicity—Effects in Animals

Experiments on laboratory animals have demonstrated that hydrogen selenide is the most toxic selenium compound by inhalation, sodium selenite the most toxic via ingestion, and elemental selenium in the diet has low toxicity as it is largely insoluble (ATSDR, 2003; WHO, 1987). Sodium selenite or seleniferous wheat containing 6.4mgkg^{-1} selenium causes growth inhibition and hair loss in animals and at concentrations of 8mgkg^{-1}, pancreatic enlargement, anemia, elevated serum bilirubin levels, and death follow (Levander, 1986; WHO, 1987). In addition to food intake, the application of sodium selenate in drinking water has been shown to cause fetal deaths and reduced fertility in mice. Selenium sulfide is the only compound proven to be carcinogenic in animal studies which results in increased liver tumors in rats. Although it is used in anti-dandruff shampoos it is not normally found in food and water. The oral lethal dose for sodium selenite in laboratory animals has been shown to range from 2.3 to 13mgkg^{-1} body weight. Methylation of selenium is used as a detoxification mechanism by animals, and inorganic and organic forms of selenium are metabolized to form mono-, di-, or trimethylated selenium, of which monomethylated forms are most toxic. For example, dimethylselenide is 500–1000 times less toxic than selenide (Se^{2-}) (WHO, 1987) (see also Chapter 20, this volume).

In natural conditions, acute selenium intoxication is uncommon as animals are not normally exposed to high selenium forage and tend to avoid eating selenium accumulator plants. Abnormal posture and movement, diarrhea, labored respiration, abdominal pains, prostration, and death, often as a result of respiratory failure, characterize toxicity. The characteristic symptoms of selenium poisoning are the garlic odor due to exhalation of dimethylselenide, vomiting, shortness of breath, and tetanic spasms. Pathological changes include congestion of the liver and kidneys, and swelling and hemorrhages of the heart (Levander, 1986; WHO, 1987, 1996).

Chronic selenium intoxication is more common and leads to two conditions known as alkali disease and blind staggers in grazing animals. Alkali disease occurs after ingestion of plants containing 5–40mgkg^{-1} over weeks or months and is characterized by dullness, lack of vitality, emaciation, rough coat, sloughing of the hooves, erosion of the joints and bones, anemia, lameness, liver cirrhosis, and reduced reproductive performance. Although much of the work on alkali disease has

focused on cattle, consumption of feeds containing 2mgkg^{-1} of selenium has also been shown to cause hoof deformation, hair loss, hypochromic anemia, and increased alkali and acid phosphatase activities in sheep (Levander, 1986; WHO, 1987).

Blind staggers occurs in cattle and sheep but not in horses and dogs and occurs in three stages:

- Stage 1: The animal wanders in circles, has impaired vision, and is anorexic.
- Stage 2: The stage 1 effects get worse and front legs weaken.
- Stage 3: The tongue becomes partially paralyzed and the animal cannot swallow and suffers blindness, labored respiration, abdominal pain, emaciation, and death.

Pathological changes include liver apoptosis, cirrhosis, kidney inflammation, and impaction of the digestive tract. Treatment of the condition involves drenching with large amounts of water and ingestion of strychnine sulfate. However, selenium may not be the main cause of blind staggers, which has similarities to thiamine deficiency. High sulfate intake has been implicated in the disease and may enhance the destruction of thiamine (WHO, 1987).

In addition to alkali disease and blind staggers, high selenium intakes in pigs, sheep, and cattle have been shown to interfere with normal fetal development. Selenosis has been known to cause congenital malformation in sheep and horses and reproductive problems in rats, mice, dogs, pigs, and cattle whereby females with high selenium intakes had fewer smaller young that were often infertile. Blood selenium levels of >2mgL^{-1} in cattle and >0.6–0.7mgL^{-1} in sheep are associated with selenosis with borderline toxicity at 1–2mgL^{-1} in cattle (Levander, 1986; WHO, 1987).

Although much of the work into selenium toxicity has focused on agricultural species, selenosis has also been reported in wild aquatic species and birds. Selenium concentrations of 47–53μgL^{-1} in surface waters results in anemia and reduced hatchability of trout whereas concentrations of 70–760μgL^{-1} in water are toxic to most aquatic invertebrates. Cranial and vertebral deformities occur in frogs exposed to 2000μgL^{-1} in surface waters. Selenium toxicity is also associated with embryonic deformities in birds; indeed, the hatchability of fertile eggs is a sensitive indicator of selenium intoxication. At concentrations of 6–9mgkg^{-1} in the diet, embryos suffer brain tissue, spinal cord, and limb bud deformities whereas >7mgkg^{-1} causes reduced egg production and growth (WHO, 1987; Jacobs, 1989).

F. Selenium Toxicity—Effects in Humans

The toxicity of selenium compounds to humans depends on the chemical form, concentration, and on a number of compounding factors. The ingestion of selenious acid is fatal to humans, preceded by stupor, hypertension, and respiratory depression whereas the toxicity of methylated selenium compounds depends not only on the dose administered but also on the previous level of selenium intake. Higher selenium intake prior to dosing with methylated compounds has been shown to be protective against toxicity in animal experiments. Poor vitamin E status increases the toxicity of selenium and the nutritional need for the element, whereas sulfate counteracts the toxicity of selenate but not of selenite or organic selenium and increases selenium urinary excretion. Methylmercury enhances selenium deficiency but inorganic mercury increases methylated selenium toxicity. At intakes of 4–8mgkg^{-1}, selenium increases the copper contents of the heart, liver, and kidneys but has a detoxifying or protective effect against cadmium and mercury (WHO, 1987; Bedwal et al., 1993). High selenium intake has also been shown to decrease sperm motility in healthy men (Hawkes & Turek, 2001) and has been related to increased incidence of some forms of cancer including pancreatic and skin cancer (see Section III.D in this chapter). Possible increased risk of Type-2 diabetes as a result of selenium supplementation has also been reported in recent cancer trials. This increased risk may relate to the effect of high selenium on insulin signaling (Rayman, 2012).

Overt selenium toxicity in humans is far less widespread than selenium deficiency. Following the discovery of seleniferous environments and the incidence of alkali disease in animals in the Great Plains in the United States during the 1950s, concern about potential adverse affects on the human population were raised. The health status of rural populations in seleniferous areas was examined. Results showed elevated urinary selenium levels in the population but no definite links to clinical symptoms of selenosis. However, a higher incidence of gastrointestinal problems, poor dental health, diseased nails, and skin discoloration were reported (Smith & Westfall, 1937). In similar studies in a seleniferous region of Venezuela, the prevalence of dermatitis, hair loss, and deformed nails among children was higher than in non-seleniferous areas. The hemoglobin and hematocrit values in children from the seleniferous areas were lower than in controls but did not correlate with blood or urine selenium levels and evidence of selenium toxicity effects was rather inconclusive. Nine cases of acute selenium intoxication due to the intake of nuts of the *Lecythis ollaria* tree in a seleniferous area of Venezuela have been reported to result in

vomiting and diarrhea followed by hair and nail loss and the death of a two-year-old boy (WHO, 1987) (see also Chapter 23, this volume).

In China, an outbreak of endemic human selenosis was reported in Enshi District, Hubei Province, and in Ziyang County, Shanxi Province, during the 1960s. This condition was associated with consumption of high-selenium crops grown on soils derived from coal containing >300mgkg^{-1} selenium. In the peak prevalence years (1961 to 1964) morbidity rates reached 50% in the worst affected villages, which were all located in remote areas among populations of subsistence farmers. Hair and nail loss were the prime symptoms of the disease but disorders of the nervous system, skin, poor dental heath, garlic breath, and paralysis were also reported. Although no health investigations were carried out at the time, subsequent studies in these areas carried out in the 1970s revealed very high dietary intakes of 3.2–6.8mg with a range of selenium in the blood of 1.3–7.5mgL^{-1} and hair selenium levels of 4.1–100mgkg^{-1} (Yang et al., 1983; Tan, 1989).

Selenium toxicity related to mineral supplement intake has also been reported in the United States. In 1984, 12 cases of selenosis due to intakes over 77 days of tablets labeled to contain 0.15–0.17mg selenium, but which actually were found to contain 27–31mg selenium were reported. Patients suffered nausea, vomiting, nail damage, hair loss, fatigue, irritability, abdominal cramps, watery diarrhea, skin irritation, and garlic breath and had blood serum levels of 0.528mgL^{-1} (WHO, 1987). The U.S.-EPA recommends an upper limit of mineral supplementation of selenium of 0.1mgkg^{-1}.

Indeed, a whole list of symptoms has been implicated in elevated selenium exposure including severe irritations of the respiratory system, metallic taste in the mouth, tingling and inflammation of the nose, fluid in the lungs, pneumonia, the typical garlic odor of breath and sweat due to dimethylselenide excretion, discoloration of the skin, dermatitis, pathological deformation, and loss of nails (Figure 10), loss of hair (Figure 11), excessive tooth decay and discoloration, lack of mental alertness and listlessness, peripheral neuropathy, and gastric disorders. The links with dental health are somewhat equivocal and many of the studies indicating a possible link with selenium failed to take into account other factors such as the fluoride status of the areas of study (WHO, 1987).

Part of the problem in assessing high selenium exposure is that there is some evidence to suggest populations can adapt to or tolerate high selenium intakes without showing major clinical symptoms. Investigations are also hampered by the lack of a sensitive biochemical marker of selenium overexposure (WHO, 1996). Hair loss and nail damage are the most common and consistent clinical indications of the condition. Chinese studies carried out in the seleniferous areas of Hubei and Ziyang have demonstrated that these effects are evident above dietary intakes of 900μg day^{-1}, blood plasma levels of 1mgL^{-1}, and whole blood concentrations of 0.813mgL^{-1} (Yang et al., 1983). Interestingly, further work in China has shown a marked reduction in the ratio of selenium in plasma compared to that in erythrocytes at dietary intakes of 750mgkg^{-1}. This is the first indication of a biochemical response to high selenium intakes prior to the development of clinical symptoms (Yang et al., 1989). There is still a great deal of uncertainty about harmful doses of selenium, but a maximum recommended dietary intake of 400μg day^{-1} has been proposed based on half the level of intake found in the Chinese studies (WHO, 1996).

In summary, there is a U-shaped association between selenium intake and health and this may explain the contradictory results from the clinical trials into selenium impacts on disease. Populations of low-selenium status may benefit from selenium supplementation in terms of disease/health outcomes; whereas populations with pre-existing adequate or high status may not benefit and may in fact suffer detrimental health outcomes (Rayman, 2012).

IV. Measuring Selenium Status

Thus far in this chapter selenium deficiency and toxicity in the environment, plants, animals, and human beings has been discussed, but in order to assess selenium status, it is important to consider how it is measured. Information about the chemical composition of the terrestrial environment is generally collated by national survey organizations concerned with geology, soil, water, agriculture, and vegetation. In terms of geology, for example, over 100 countries around the world carry out national geochemical mapping programs. These programs are based on systematic collection of materials such as soil, sediment, water, rock, and vegetation, which are then analyzed for a range of element compositions and used to produce maps of element distributions in the environment. This type of approach was pioneered in the 1950s by Russian geochemists and the wide application of these methods has been made possible by improvements in rapid multi-element analysis techniques over the last 60 years.

However, selenium is not an easy element to analyze, partly because concentrations in natural materials are so low. Therefore, in many multi-element geochemical surveys, selenium was not included in the analysis. It was not until the last 30

years that analytical advances have allowed the detection of selenium at low enough concentrations to be of real interest to environmental studies but because these techniques are more expensive than routine analytical programs, selenium is still often missing from the group of determinants despite its environmental importance (Darnley et al., 1995). A summary of some of the selenium data available around the world is provided by Oldfield (1999).

Analytical methods that give good limits of detection (<1mgkg^{-1}) include colorimetry, neuron activation analysis (NAA), x-ray fluorescence spectrometry (XRF), atomic fluorescence spectrometry (AFS), gas chromatography (GC), inductively coupled mass spectrometry (ICP-MS), and inductively coupled atomic emission spectrometry (ICP-AES). Of these, AFS is the most widely used for natural materials such as foods, plants, and soils. NAA is often used to determine different selenium isotopes, especially in tracer studies using ^{75}Se, etc., and gives good detection limits, but it is a more specialized form of analysis. For studying stable isotopes of selenium (for example, ^{78}Se and ^{82}Se) ICP-MS may be used, but it requires enriched and expensive isotope materials. In more recent years, hydride-generation techniques have improved the detection limits of spectrometric methods such as ICP-AES. Ion exchange chromatography has been extensively used to determine selenium compounds in plants whereas gas chromatography is employed to determine volatile selenium compounds. Ion exchange or solvent extraction methods are used to distinguish selenate and selenite species in solution. Recently developed anion exchange high-performance liquid chromatography (HPLC) and ICP-dynamic-reaction–cell MS methods can be used to measure selenium isotopes and selenoamino acids including selenocysteine and selenomethionine. Using these techniques it is now possible to measure relatively low selenium concentrations and selenium element species in a wide variety of environmental and biological materials (WHO, 1987).

In animals and humans a variety of bio-indicators of selenium status have been employed. Due to the close association between the level of dietary selenium intake and GPx activity, the fact that the enzyme activity represents functional selenium and that assessments of this enzyme are easier to perform than selenium tests, GPx activity has been used extensively to measure selenium status, especially in animals. However, this method requires caution because GPx activity is influenced by other physiological factors and a non-selenium-dependent GPx enzyme is also present in animals and humans. Furthermore, the enzyme activity may provide an indication of selenium status at lower levels of intake, but at higher concentrations of selenium the GPx activity becomes saturated and the enzyme cannot be used to indicate toxic selenium status (WHO, 1996) (see also Chapters 23 and 30, this volume).

Other indicators of selenium status include whole blood, plasma, or serum; hair; toenail; and urine content. Of these, hair has been used extensively as it is easy to collect. However, caution is required to ensure that samples are not contaminated with residues from selenium-containing shampoos. It should also be noted that urinary selenium cannot be used to measure inhalation exposure to hydrogen selenide gas, selenium oxychloride, or organic-selenium compounds as severe damage to the lungs occurs before elevated selenium contents are evident in the urine (WHO, 1987). Dietary surveys are also commonly used as an indication of selenium intake. Single-day dietary surveys can give errors of up to 90% when used to estimate the real long-term exposure to selenium, because wide ranges in daily intake are commonplace (0.6–221μg day^{-1}). Comparisons of different methods have shown that three-week dietary observations give estimates of overall intake to within 20% and are a much more reliable indication of likely selenium status (WHO, 1987).

Regardless of the material sampled, whether it is soil, food, blood, water, hair, etc., selenium status is determined by comparison to a set of thresholds and normative values that have been determined by examining the levels at which physiological effects occur in plants, animals, and humans. Some of these thresholds are listed in Table XVIII. In general, total soil selenium contents of 0.1–0.6mgkg^{-1} are considered deficient as these are the concentrations of selenium found in regions where selenium-deficient livestock are commonplace such as New Zealand, Denmark, and the Atlantic Region of Canada. Work regarding Keshan disease in China suggests levels of 0.125mgkg^{-1} total selenium in soil cause selenium deficiency in the food chain (Yang et al., 1983; Yang & Xia, 1995). However, it should be kept in mind that the amount of total selenium in the soil is not necessarily the critical factor determining selenium status. Several studies have demonstrated that the total selenium content of the soil can be considered "adequate" but if the selenium is not in bioavailable form, it is not taken up into plants and animals and selenium deficiency can result (see, for example, Fordyce et al., 2000a). Total selenium concentrations in soil can give an indication of likely selenium status but do not necessarily tell the whole story, and a selenium deficient environment is not necessarily one in which total concentrations of selenium in soil are the lowest. In more recent years soil with water-soluble selenium has been used as an indicator of the bioavail-able fraction and Chinese scientists have recommended soil deficiency and toxicity thresholds on this basis, 0.003 and 0.020mgkg^{-1}, respectively (Tan, 1989).

Due to the many different factors that can influence the uptake of selenium from soil into plants, vegetation often provides a better estimate than soil of likely environmental status with regard to health problems in animals and humans. Feed crops containing more than 0.1mgkg^{-1} of selenium will protect livestock from selenium deficiency disorders, whereas levels of >3–5mgkg^{-1} in plants have been shown to induce selenium toxicity in animals (Levander 1986; Jacobs, 1989). The current

MAC for selenium additives in animal feedstuffs in the United States is $0.3 mg kg^{-1}$. In terms of cereal crops for human consumption, Chinese workers suggest deficiency and toxicity thresholds of 0.02 and $0.10 mg kg^{-1}$, respectively, based on epidemiological studies in Keshan disease and areas affected with selenosis (Tan, 1989). Determination of the selenium status of water is usually made using comparisons to the WHO maximum admissible concentration of $40 \mu g L^{-1}$.

In veterinary science, concentrations of $<0.04 mg L^{-1}$ selenium in animal whole-blood are considered deficient and are related to WMD in ruminant species whereas $0.07–0.10 mg L^{-1}$ is considered adequate, which highlights the extremely narrow range in selenium status between clinical and non-clinical outcomes (Levander 1986; WHO, 1987). Human selenium status is rather more difficult to categorize because of the lack of overt clinical symptoms in many populations exposed to supposedly deficient or toxic intakes, but based on work in China, deficiency and toxicity thresholds in human hair of 0.2 and $>3 mg kg^{-1}$ (Yang et al., 1983; Tan, 1989; Yang & Xia, 1995), respectively, have been suggested whereas dietary limits of 40 and $400 \mu g\ day^{-1}$ are proposed by the WHO as an indication of human selenium status (WHO, 1996).

V. Remediation

A variety of methods have been used to try and counteract the impacts of selenium deficiency and toxicity in environments and within animals and humans as follows.

A. Remediating Selenium Deficiency

Methods to enhance selenium in the environment and uptake into agricultural crops and animals have been developed over a number of years. One approach is to alter the species of crops grown on deficient soil to plant types that take up more selenium. Switching from white clover production to certain grasses to increase the selenium content of fodder crops has been used successfully in New Zealand (Davis & Watkinson, 1966). Another approach is to apply selenium-rich fertilizers to the soil to increase the amount of selenium taken up by plants, animals, and humans. Some rock phosphate fertilizers are rich in selenium and can be used to enhance uptake; however, there is some risk associated with application of selenates to alkali and neutral soils because of high bioavailability. Use of selenate fertilizer results in much higher selenium contents of first cuts of crops or forage, which decrease sharply with subsequent cropping. Addition of selenite to acid-neutral soils can result in some loss of selenium to soil adsorption, which decreases the effectiveness of the application, but in some cases this mechanism can ensure that levels of uptake are not toxic (Fleming, 1980; Jacobs, 1989). The selenium concentration of foods can also be increased by supplementing ordinary fertilizers with soluble selenium compounds. Finland, New Zealand, and parts of Canada and China allow selenium-enhanced fertilizers to be used for the cultivation of food crops and trials have recently been conducted in the UK (Broadley et al., 2010). These countries mainly use fertilizers based on sodium selenate (Oldfield, 1999). For example, in New Zealand 1% granular selenium is mixed with granulated fertilizer and is applied at a rate of $10 g Se ha^{-1}$ over about a quarter of the agricultural land in the country (in 1998 1.2 million of 4.5 million ha underwent selenium fertilization) (Jacobs, 1989; Oldfield, 1999).

Problems of uptake associated with retention of selenium in the soil can be circumvented by direct application of the fertilizer to the plants themselves. Foliar application of selenite to plants has been successfully used to increase the selenium content of crops and animals. Spraying selenium at $3–5 g ha^{-1}$ has been shown to increase the content in grain whereas sodium selenite applied at $50–200 g Se ha^{-1}$ maintained $>0.1 mg kg^{-1}$ contents in crops through three harvests. Studies have shown that the selenium content of crops is enhanced by mid-tillering spraying with selenium fertilizer but it cannot be applied successfully to seeds (Jacobs, 1989).

For example, Chinese workers have reported much better uptake of selenium in maize crops grown on aerated oxygenated soils than in rice grown in the same soils under waterlogged conditions due to reduction of selenium to insoluble forms. To avoid poor uptake of selenium from soils as a consequence of the water-logged conditions, foliar spraying of sodium selenite at an early shooting stage of the rice plant growth was found to improve the selenium content of the grain and hull (Cao et al., 2000). In another study, the average wheat selenium contents in Kashin-Beck endemic areas were $0.009 mg kg^{-1}$ dry weight resulting in daily intakes of $12 \mu g$ in the local population. Following foliar selenium fertilizer application, wheat contents increased to $0.081 mg kg^{-1}$ dry weight and human daily dietary intakes rose to $47 \mu g$ (Tan et al., 1999).

In Finland, the bioavailability of soil selenium for plants is generally poor due to the relatively low selenium concentration, low pH, and high iron content of the soil as much of the country comprises very ancient hard crystalline granite and gneiss rocks. This is very similar to eastern Canada where selenium supplementation is also practiced (Jacobs, 1989). In 1984, the Finnish government approved a program of selenium supplementation in fodder and food crops. The program initially involved spraying a 1% selenium solution onto fertilizer granules giving an application rate of 6gSeha^{-1} for silage and 16gha^{-1} for cereal crops. Within two years a threefold increase of mean selenium intake in the human population was observed and human serum contents increased by 70%. The supplementation affected the selenium content of all major food groups with the exception of fish. In 1990 the amount of selenium that was supplemented was reduced to 6gSeha^{-1} for all crops and the mean human selenium intake fell by 30% and the serum selenium concentration decreased by 25% from the highest levels observed in 1989. According to data obtained, supplementation of fertilizers with selenium is a safe and effective means of increasing the selenium intake of both animals and humans and is feasible in countries like Finland with relatively uniform geochemical conditions (Aro et al., 1995). In other countries where the low level of selenium intake is currently of concern, such as in the UK, this kind of intervention would require careful planning and monitoring of the effects on both animal and human nutrition and the environment, because geochemical conditions vary markedly across the country as a result of a diverse geological environment.

In addition to attempts to enhance selenium in fodder crops and animal feeds supplemented with sodium selenite or selenate, selenium deficiency in animals is also prevented by veterinary interventions such as selenium injections to females during late gestation and/or to the young stock shortly after birth, dietary supplements, salt licks, and drenches (Levander, 1986).

In humans also, direct dietary supplementation methods have been used successfully to counteract selenium deficiency. Pills containing selenium alone or in combination with vitamins and/or minerals are available in several countries. Selenium supplements contain selenium in different chemical forms. In the majority of supplements, the selenium is present as 35 selenomethionine; however, in multivitamin preparations, infant formulas, protein mixes, and weight-loss products sodium selenite and sodium selenate are predominantly used. In other products, selenium is present in protein-chelated or amino acid chelated forms. Current animal studies and epidemiological evidence favors selenomethionine as the most bioavailable and readily taken up form of selenium in mineral supplements. A dosage of 200μg day^{-1} is generally considered safe and adequate for adults of average weight consuming a North American diet (WHO, 1987). Studies carried out in KD areas of China have shown that both selenite and selenium-yeast supplements were effective in raising GPx activity of selenium-deficient populations, but selenium-yeast provided a longer lasting body pool of selenium (Alfthan et al., 2000). Altering the diets of humans to include selenium-rich foods has also proved successful in preventing selenium deficiency. In China, selenium-rich tea, mineral water, and cereal crops are now marketed in selenium-deficient areas.

B. Remediating Selenium Toxicity

One of the most common methods to reduce the effects of selenium in soil is phytoremediation. This practice is carried out by growing plant species, which accumulate selenium from the soil and volatilize it to the air to reduce levels in soil. For example, the hybrid poplar trees *Populus tremula x alba* can transfer significant quantities of selenium by volatilization from soil to air; the rate for selenomethionine is 230 times that of selenite and 1.5 times higher for selenite than selenate. These trees have been used successfully to reduce selenium contents in soil in the western areas of the United States (Oldfield, 1999) and have been tested in seleniferous regions of India (Dhillon et al., 2008).

There is some evidence to suggest that the presence of phosphate and sulfate in soils can inhibit the uptake of selenium in plants and application of these minerals as soil treatments could be beneficial against selenium toxicity in agricultural crops. Studies have shown a tenfold increase in sulfate content reduced uptake from selenate by >90% in ryegrass and clover, whereas a similar increase in phosphate content caused 30–50% decreases in selenium accumulation from selenite in ryegrass, but in clover such decreases only occurred in the roots. Therefore, sulfate-selenate antagonisms were much stronger than phosphate-selenite antagonisms. The addition of sulfur or calcium sulfate (gypsum) to seleniferous soils in North America was not successful in reducing uptake into plants probably because these soils already contain high quantities of gypsum. However, additions of calcium sulfate and barium chloride have been shown to markedly reduce the uptake of selenium in alfalfa in the United States (90–100%) probably due to the formation of $BaSeO_4$, which is barely soluble. The practicalities of this type of selenium remediation method are rather limited (Jacobs, 1989).

It is more common to counteract selenium toxicity with veterinary and medical interventions. Sodium sulfate and high protein intakes have been shown to reduce the toxicity of selenate to rats but not of selenite or selenomethionine in wheat.

Arsenic, silver, mercury, copper, and cadmium have all been shown to decrease the toxicity of selenium to laboratory animals and they have been used to alleviate selenium poisoning in dogs, pigs, chicks, and cattle (Moxon, 1938; Levander, 1986; WHO, 1987). The protective effect of arsenic is thought to be a consequence of increased biliary selenium excretion. Laboratory evidence suggests that mercury, copper, and cadmium exert a beneficial effect due to reactions with selenium in the intestinal tract to form insoluble selenium compounds. However, consideration must be given to the toxic effects of these elements before they are applied as selenium prophylaxis. Linseed meal has also been found to counter selenium toxicity in animals by the formation of selenocyanates, which are excreted (WHO, 1987).

In terms of human diets, dietary diversification can also help reduce selenium toxicity. In China, high-selenium cereal crops are banned from local consumption and exported out of the seleniferous regions where they are mixed with grains from elsewhere before they are sold in selenium-deficient parts of the country.

VI. Case Histories

A. Selenium Toxicity in Animals—Kesterson Reservoir, United States

One of the best known and most studied incidences of selenium toxicity in animals has been recorded at Kesterson Reservoir, California, in the United States. The information summarized here is taken from Jacobs (1989), Wu et al. (2000), Wu (1994), and Tokunaga et al. (1996). These publications should be referred to for further details.

Due to a scarcity of wetlands in California, wildlife resource managers tried using irrigation runoff from subsurface agricultural drains to create and maintain wetland habitats at the Kesterson Reservoir. The reservoir comprises 12 shallow ponds acting as evaporation and storage basins for agricultural drain waters from the San Joaquin Valley. During part of the year, the water from the reservoir was to be discharged via the San Luis drain back into the Sacramento-San Joaquin River delta when river flows were high enough to dilute the contaminants present in the agricultural water. However, construction of the San Luis drain was halted in 1975 due to increased environmental concerns about the impact of the drain water on the river delta. During the 1970s surface water flow into the reservoir predominated, but into the 1980s almost all the flow was shallow subsurface agricultural drainage water. Selenium 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 in the catchment area. In this arid alkaline environment, 98% of the selenium was in the most readily bioavailable selenate form with only 2% present as selenite. The effects of this water on plants and animals were relatively unknown prior to studies carried out between 1983 and 1985 by the U. S. Wildlife Service comparing Kesterson to the adjacent Volta Wildlife area, which was supplied with clean irrigation water with normal concentrations of selenium. The mortality of embryos, young and adult birds, survival of chicks, and embryonic deformities were compared between the two sites. The selenium content of the livers of snakes and frogs from the two areas were also examined in addition to tissues from 332 mammals of 10 species, primarily moles. Results of some of the comparisons between biota from the two sites are shown in Table XIX. In all cases, the levels of selenium in biological materials at Kesterson Reservoir exceeded those of the Volta Wildlife area several-fold. Concentrations of selenium in water were compared to those in biota collected from the same site and bioaccumulation factors of more than 1000 for animals were found at Kesterson. Although no overt adverse health effects were noted in reptile or mammal species such as voles and raccoons in the area, the levels of selenium present were of concern in terms of bioaccumulation in the food chain. In contrast, the overt health effects on birds were very marked with 22% of eggs containing dead or deformed embryos as a result of selenium toxicity. The developmental deformities included missing or abnormal eyes, beaks, wings, legs and feet, and hydrocephaly, and were fatal. It is estimated that at least 1000 adult and juvenile birds died at Kesterson from 1983 to 1985 as a result of consuming plants and fish with 12–120 times the normal amount of selenium (Jacobs, 1989).

Following these revelations, Kesterson Reservoir was closed and a series of remedial measures were tested by a team of scientists who were able to provide a more thorough understanding of processes leading to selenium transport and biologic exposure in this environment. Some of the schemes proposed included the development of an *in situ* chemical treatment to immobilize soluble selenium in drained evaporation pond sediments by amendment with ferrous iron, which occludes selenate and selenite in ferric oxyhydroxide (FeOOH). Phytoremediation techniques were also tested. These included the growing of barley (*Hordeum vulgare* L.) and addition of straw to the soil, which contained $0.68 mg kg^{-1}$ soluble selenium and $6.15 mg kg^{-1}$ total selenium. Four treatments were evaluated: soil only, soil + straw, soil + barley, and soil + straw + barley. At the end of the experiments, selenium in barley represented 0.1–0.7% of the total selenium in the system, and volatilized

selenium accounted for 0.2–0.5% of total selenium. In contrast, straw amendments were found to greatly reduce the amount of selenium in soil solution by 92–97% of the initial soluble selenium and represented a possible remediation strategy for the reservoir. The planting of canola (*Brassica napus*) was also evaluated but accumulated 50mgkg^{-1} (dry weight), which accounted for less than 10% of total selenium lost in the soil solution during the post-harvest period.

Bioremediation through the microbial reduction of toxic oxyanions selenite and selenate into insoluble Se^0 or methylation of these species to dimethylselenide was proposed as a potential bioremediation cleanup strategy. Field trials demonstrated that microorganisms, particularly *Enterobacter cloacae*, were very active in the reduction of selenium oxyanions in irrigation drainage water, into insoluble Se^0 and, by monitoring various environmental conditions and the addition of organic amendments, the process could be stimulated many times. Based upon the promising results of these studies, a biotechnology prototype was developed for the cleanup of polluted sediments and water at Kesterson.

A soil excavation plan had been proposed to remove selenium-contaminated material from the site; however, extensive monitoring of porewater in the vadose zone demonstrated that this plan would be ineffective in reducing the elevated selenium concentration in ephemeral pools present during the winter at Kesterson. Furthermore, extensive biological monitoring demonstrated that selenium concentrations in the dominant species of upland vegetation at Kesterson were near or equal to "safe" levels.

On the basis of these studies, a cost-effective remediation strategy was devised. First, the groundwater under Kesterson was protected from selenium contamination by naturally occurring biogeochemical immobilization. Secondly the contaminated soil and sediment was left in place but low-lying areas were infilled to prevent the formation of the ephemeral pools that attracted wildlife. The area was then planted over with upland grassland species. Monitoring studies carried out on soil and vegetation between 1989 and 1999 showed that selenium losses from soil via volatilization were approximately 1.1% per year. Soil selenium concentrations in the fresh soil fill sites increased in the top 15cm, which indicated that the plants were able to effectively take up soluble soil selenium from the lower soil profile and deposit it at the land surface thus reducing the rate of leaching of soil selenium. In general plant tissue concentrations reflected the amount of soil water-soluble selenium present, which was low. In 1999 plant tissue concentrations averaged 10mgkg^{-1} (dry weight) and soil water-soluble selenium contents 110mgkg^{-1} giving an estimated bioaccumulation value for the upland grassland of less than 10% of the previous wetland habitat. It was concluded that the new Kesterson grassland did not pose a risk to the environment (Wu et al., 2000).

B. Selenium Toxicity and Drinking Water—Reggio, Italy

Examples of high selenium exposure related to intakes in water are very scarce. An exception is reported by Vinceti et al. (1998) and occurred in the town of Reggio, Italy, between 1972 and 1988 where the population in the Rivalta neighborhood was inadvertently exposed to wells containing 3–13μgL^{-1} selenium as selenate and resultant tap water containing 7–9μgL^{-1} compared to selenium contents in the drinking water of adjacent neighborhoods of <1μgL^{-1}. The wells were closed off in 1989 and the population was no longer exposed to water from this source. Apart from the selenium content, water quality between Rivalta and the other neighborhoods was the same. Using residency and water supply records, 2065 people (1021 men and 1044 women) were identified as having been exposed for at least 11 years to the elevated selenium content in the water between 1975 and 1988. This cohort was compared to a control population of non-exposed individuals from the same town. To examine the effects of this exposure on cancer incidence in the local population, all cases of pathologically confirmed primary invasive melanoma occurring during 1996 were collated for the entire town of Reggio as well as records on age, sex, educational level, and occupation. The exposed and non-exposed populations had similar educational and occupational profiles and once the data were corrected for age and sex, a higher prevalence of skin cancer was noted in the exposed population. On the basis of melanoma rates in the unexposed population, 2.06 cases would be expected in the exposed population whereas 8 cases were reported. Although other confounding factors could not be taken into account in this study, there is some evidence to suggest that the skin is a target organism in chronic selenium toxicity and that inorganic selenium can act as a pro-oxidant and mutagen and cell apoptosis suppressant, which may account for the higher prevalence of cancer in the exposed group. It should be noted that selenium is ineffective against melanoma although beneficial for other forms of cancer (Clark et al., 1996).

C. Selenium Deficiency in Humans—Zhangjiakou District, Hebei Province, China

Zhangjiakou District, Hebei Province, in China lies between Inner Mongolia to the north and Beijing to the south and is one of the remotest regions of China lying within the northeast-southwest KD belt (Figure 8). The area is underlain by Archaen metamorphic and Jurassic volcanic rocks, which are overlain by Quaternary loess and alluvial deposits, all of which contain low amounts of selenium. Within Zhangjiakou District, the KD belt follows the mountainous watershed between the two rock types, which reflects the fact that villages in the remotest locations where populations are most dependent on locally grown foodstuffs are most at risk from the disease. However, within the KD belt, prevalence rates show marked variability between villages ranging from 0 to 10.8% between 1992 and 1996. In a study to examine why this variation may occur and to pinpoint the relationships between environmental selenium and disease, Johnson et al. (2000) examined soil, staple crop (wheat and oats), water, and human hair selenium levels in 15 villages in the region classified according to disease prevalence into three groups: (1) no KD 0% prevalence; (2) moderate KD, 0–3% prevalence; and high KD, >3% prevalence. Results showed that hair, grain, and water selenium concentrations showed an inverse relationship with disease prevalence as expected; the highest selenium contents were reported in villages with lowest prevalence of the disease. However, contrary to expectations, soil total selenium contents showed the opposite relationship and were highest in the villages with greatest disease prevalence (Figure 12). Indeed comparisons between the data collected from high prevalence villages for the study and selenium deficiency thresholds proposed by Tan (1989) indicated that the selenium contents of all sample types were very low, whereas hair (geometric mean 177ngg^{-1}, threshold 200ngg^{-1}) and grain (geometric mean 7.8ngg^{-1}, threshold 25ngg^{-1}) contents would be classed as deficient, soil total selenium contents would not (geometric mean 171ngg^{-1}, threshold 125ngg^{-1}). There was a strong correlation between the selenium content of grain and the selenium status of the local population determined by hair sampling, but relationships with local soils were less clear. Further examinations into the soil geochemistry demonstrated that soils in the high KD prevalence villages were black or dark brown with a high organic matter content and lower pH than other soils in the region. Although these soils contained high total selenium contents, it was not in a readily bioavailable form as it was held in the organic matter in the soil. Despite the higher total selenium contents, water-soluble selenium in the high prevalence villages was in fact lower than deficiency threshold values (geometric mean 0.06ngg^{-1}, threshold 3ngg^{-1}). This study concluded that when environmental concentrations of selenium are low, any factor that is responsible for reducing the mobility of selenium may have a critical effect and emphasizes the importance of determining the bioavailability of selenium rather than the total selenium content when assessing impacts on human health. On the basis of this study, conditioning treatments to raise the soil pH thus increasing the bioavailability of selenium in the organic-rich soils or foliar application of selenium fertilizer to crops to avoid selenium adsorption in the soils were recommended as remediation strategies to increase the levels of selenium in local diets. The study also demonstrates the importance of understanding the biogeochemical environment in the determination of selenium-deficient regions and appropriate remediation techniques. However, here as with elsewhere in China, no incidences of KD have been reported in the area since 1996 as economic and communication improvements diversify the diet and enhance the health of the population.

D. The Geological Impact of Selenium on Human Health—Deficiency and Toxicity, Enshi District, Hubei Province, China

If there is one place on Earth that demonstrates the importance of geological controls on selenium and human health it is Enshi District, Hubei Province, in China, which lies approximately 100km south of the Yangtze River Gorges and 450km west-southwest of the provincial capital Wuhan (Figure 8). In Enshi District, selenium-deficiency related diseases (Keshan disease) and selenium toxicity (selenosis) occur within 20km of each other; their incidence is controlled by geology. The area is very mountainous with little connectivity between villages; some of which can only be reached on foot, hence, populations are very dependent on the local environment for their food supply.

Jurassic sandstones, which contain low concentrations of trace elements including selenium, underlie the northwest part of Enshi District and KD is present in this area. Selenium toxicity, on the other hand, is associated with high environmental selenium derived from Permian age coal-bearing strata in the center and east of the Enshi District. Soils developed over Jurassic sandstones comprise red-purple sands whereas light-brown silts and clays containing many carbonaceous fragments are typical in areas underlain by the Permian strata.

Studies into the selenium balance of local populations were carried out during the 1960s and 1970s by the Enshi Public Health Department in response to outbreaks of selenium-related diseases in the area. Between 1923 and 1988, 477 cases of

human selenosis were reported. Of these cases, 338 resulted in hair and nail loss and disorders of the nervous system. They occurred between 1959 and 1963 in Shadi, Xin Tang and Shuang He communities. In Yu Tang Ba village, Shuang He community, the population was evacuated after 82% (19 out of 23 people) suffered nail and hair loss and all livestock died from selenium poisoning. During the same period, 281 selenosis cases were reported in five villages in the Shadi area. Cases of selenosis in pigs reached peak prevalence between 1979 and 1987 when 280 out of 2238 animals were affected in Shatou, which resulted in 122 deaths. No human cases of selenium toxicity have been reported in recent years but animals commonly suffer hoof and hair loss as a result of the high environmental selenium.

During the late 1960s and 1970s, an area of selenium deficiency in Lichuan County to the northwest of Enshi District was also identified and lies within the KD belt across China. In total, 312 people have suffered KD in the county, an average incidence rate of 103 per 100,000. Among the 312 cases, 136 recovered, 163 died, and 13 persons still suffer from the disease. The village of Chang Ping was the worst affected with a total of 259 cases out of a population of 20,368 and 117 of those affected died. Children between the ages of 3 and 8 accounted for 83.4% of the total cases and 80% of the children affected by the disease died. Following peak prevalence in 1969 (106 cases), the number of cases has fallen dramatically and current prevalence rates are unknown as no medical investigations have been carried out in recent years.

Yang et al. (1983) were the first to compare levels of selenium in soil, crops, drinking water, human urine, blood, nail, and hair samples from the Enshi area with other regions of China and demonstrate that the endemic selenium intoxication of humans in Enshi was related to the occurrence of Permian selenium-enriched shaley coal, which contains up to 6471mgkg^{-1} selenium. There is some evidence to suggest that selenium in these rocks is in the form of micro particles of elemental selenium in association with organic carbon and that the carbon content of the rock controls the selenium content. However, some selenium is also found in the lattice of pyrite minerals. Selenium concentrations in soil, food, and human samples from areas underlain by carbonaceous strata were up to 1000 times higher than in samples from selenium-deficient areas where KD
was prevalent and dietary intakes of selenium greatly exceed the U. S. NRC and Chinese recommended standards (Table XX). It was estimated that locally grown crops constituted 90% of the diet in the Enshi area and cereal crops (rice and maize) accounted for 65–85% of the selenium intake, which indicated the importance of the local environment to selenium in the food chain. In addition to exposure via soils and foodstuffs, villagers in the selenosis region also mine the carbonaceous shale for fuel and use burnt coal residues as a soil conditioner. Although the epidemiological investigations revealed that selenosis occurred in areas of high environmental selenium associated with the carbonaceous strata, not all villages underlain by this strata were affected.

Further studies carried out by Fordyce et al. (2000b) into three groups of villages: one suffering KD, one with high environmental selenium but no selenosis, and one with high environmental selenium and selenosis. In villages with high selenium, concentrations in soils and foodstuffs could markedly vary from low to toxic within the same village, with these variations dependent on the outcrop of the coal-bearing strata. The wide range in geochemical conditions could in part explain why some villages suffered selenosis and others did not as did practices such as using coal ash as a soil conditioner (Li et al., 2012).

Therefore, villagers were advised to avoid cultivating fields underlain by the coal and were counseled against using coal-derived products, such as ash, to condition the soil. In the KD affected villages of Lichuan County, selenium concentrations in staple food crops (rice and maize), drinking water, and the human populations (measured in hair samples) were very low and soils in this area had lower pH contents than soils in the high-selenium villages, which would further inhibit the uptake of selenium into plants. Conditioning the soil with lime to increase the pH making selenium more mobile was suggested as a remediation strategy.

Although all the villages in the low-selenium area had a marginally deficient selenium status and the majority of villages in the high-selenium area had excessive amounts of selenium in the environment and human population using the thresholds defined by Tan (1989) (Table XXI), no new incidents of either KD or overt selenium poisoning have occurred in recent years. This suggests that the local population may have adapted to the high and low selenium intakes present in the different environments and that the historical occurrences of clinical effects related to selenium imbalances were caused by other factors. The outbreaks of human selenosis in Enshi during the late 1950s and early 1960s coincided with a drought and the failure of the rice crop. The crop failure had serious implications for the dietary intake and health of the local population with less food available, reduced protein intake, and higher dependence on vegetables and maize and natural plants. These factors may have lead to the severe outbreaks of selenosis in the Enshi area and demonstrate that in geologically controlled high- or low-selenium environments additional stresses can lead to serious health outcomes in the local population.

E. The Geological Impact of Selenium on Animal Health—Deficiency and Toxicity, Queensland, Australia

Another example of the effects of geology on selenium and health has been reported in Queensland, Australia. Here seleniferous limestones and shales of the Tambo Formation cause selenium toxicity symptoms in livestock grazing plants in this area, whereas less than 100km to the south selenium deficiency and WMD in grazing animals is a problem over Tertiary volcanic soils. Grain grown over the seleniferous limestone rocks contains >0.2mgkg^{-1} selenium whereas over the southern selenium-deficient region concentrations rarely exceed 0–0.05mgkg^{-1} in grain (Oldfield, 1999). This is another example of how geologically controlled geochemical variation can influence selenium status and health over relatively short distances.

F. Selenium Status in Western Countries—Is Environment Still Important?

With the exception of Italy, the human case studies presented in this chapter refer to developing countries where populations are very dependent on the local environment to provide the correct mineral balance. Under these circumstances it is easy to see why considerations of selenium status may be important. But what of the western world where people generally move around more during their lifetimes, products are derived from all around the world, and people buy food in large supermarkets rather than growing it in their own back yard? Under these conditions, the links between environment and health are less direct. Nonetheless, the impact of the selenium status of the environment on animals and humans is still evident. It has already been pointed out in this chapter that New Zealand is a generally selenium-deficient country compared to other areas of the world; indeed cereal grains grown in New Zealand contain 10 times less selenium than grain from Canada and the United States. In years when the crops in New Zealand are poor, wheat is imported from Australia and a corresponding notable increase in blood selenium levels is seen in the population. Indeed, the selenium status of the New Zealand population has been improved by greater importation of high-selenium Australian wheat (Thomson, 2004). Studies have also shown that the average total body contents of selenium are only 3–6.1mgkg^{-1} in New Zealand compared to 14.6mgkg^{-1} in the United States, and studies into individual tissues of the body show that in New Zealand, concentrations are half that of the United States. A marked lowering of blood selenium levels has been noted in populations moving from selenium-adequate areas of the United States to New Zealand; however, the actual resultant values also depend on factors such as physiological status (WHO, 1987). There is clear evidence therefore of the influence of the geochemical environment on food and human selenium status when either food or people move from one area to another. But what about variation within a country? Perhaps the most compelling evidence that environmental differences are important even within western countries comes from the United States where, despite one of the most diverse and mobile food supply chains in the world, selenium concentrations in animals and humans reflect the surrounding environment. Studies have shown that despite the widespread use of agricultural management practices including selenium supplementation, the selenium content of skeletal muscle in cattle shows marked geographic variation concordant with selenium contents in soils and grasses and perhaps even more surprisingly, human blood selenium levels are higher in the seleniferous western United States than in selenium-poor areas. For example, serum selenium contents average 0.161μgL^{-1} in Ohio compared to 0.265μgL^{-1} in South Dakota (WHO, 1987). Hence, even in populations who now live one step removed from their natural environment, the cycling of selenium from nature into humans is still of fundamental importance to health.

VII. Future Considerations

This chapter has demonstrated that human exposure to the biologically important element selenium is largely dependent on dietary intakes in food and water, which are significantly controlled by variations in the geology of the Earth's surface. Although much work has been done over the past 40 years to enhance our understanding of environmental selenium, over large areas of the globe information is still missing because until recently selenium was a difficult element to analyze. More work is required to understand not just the total amounts of selenium present but also the bioavailability of the element and cycling through the environment. For example, it is only relatively recently that the importance of the oceans in the cycling of selenium has been recognized. The selenium status of the human and animal populations around the globe closely reflect environmental levels and although overt clinical symptoms of selenium toxicity and deficiency are rarely reported, the possible subclinical effects and implications of selenium status are only beginning to be understood and should not be

underestimated as medical science continues to uncover new essential functions for the element. In the future, closer collaboration between medical and environmental scientists will be required to evaluate the real environmental health impact of this remarkable element in diseases such as cancer, AIDS, and heart disease.

See Also the Following Chapters

Chapter 2 (Natural Distribution and Abundance of Elements) · Chapter 7 (Biological Functions of the Elements) · Chapter 15 (Bioavailability of Elements in Soil) · Chapter 17 (Soils and Iodine Deficiency) · Chapter 21 (Animals and Medical Geology) · Chapter 25 (Environmental Pathology) · Chapter 33 (Modeling Groundwater Flow and Quality)

Further Reading

Afzal, S., Younas, M. and Ali, K. (2000). Selenium Speciation Studies from Soan-Sakesar Valley, Salt Range, Pakistan, *Water Int.*, 25, 425–436.

Akesson, B. and Steen, B. (1987). Plasma Selenium and Glutathione Peroxidase in Relation to Cancer, Angina Pectoris and Short-Term Mortality in 68-year-old Men, *Comprehens. Gerontol.*, A(1), 61–64.

Alfthan, G., Xu, G. L., Tan, W. H., Aro, A., Wu, J., Yang, Y. X., Liang, W. S., Xue, W. L. and Kong, L. H. (2000). Selenium Supplementation of Children in a Selenium-Deficient Area in China—Blood Selenium Levels and Glutathione Peroxidase Activities, *Biolog. Trace Element Res.*, 73(2), 113–125.

Amouroux, D., Liss, P. S., Tessier, E., Hamren-Larsson, M. and Donard, O. F. X. (2001). Role of the Oceans as Biogenic Sources of Selenium, *Earth Planet. Sci. Lett.*, 189(3–4), 277–283.

Ander, E. L., Fordyce, F. M., Johnson, C. C. and Schofield, D. I. (2010). Controls on the Distribution of Selenium in the Soils of East Anglia, UK. *Geol. Soc. Am. Abs. Section Meeting, 13-16 March, Baltimore, Maryland*, 143.

Anonymous (2001). Observations on the Effect of Sodium Selenite in the Prevention of Keshan Disease (reprinted from the *Chinese Medical Journal*, Vol. 92, pp. 471–476, 1979), *J. Trace Elements Exp. Med.*, 14(2), 213–219.

Aras, N. K., Nazli, A., Zhang, W. and Chatt, A. (2001). Dietary Intake of Zinc and Selenium in Turkey, *J. Radioanal. Nucl. Chem.*, 249(1), 33–37.

Aro, A., Alfthan, G. and Varo, P. (1995). Effects of Supplementation of Fertilizers on Human Selenium Status in Finland, *Analyst*, 120(3), 841–843.

Arthur, J. R. and Beckett, G. T. (1994). New Metabolic Roles for Selenium, *Proc. Nutr. Soc.*, 53, 615–624.

ATSDR. (2003). *Toxicology Profile for Selenium*. Agency for Toxic Substances and Disease Registry, Atlanta, Georgia.

Beck, M. A. (1999). Selenium and Host Defense Towards Viruses, *Proc. Nutr. Soc.*, 58(3), 707–711.

Bedwal, R. S., Nair, N., Sharma, M. P. and Mathur, R. S. (1993). Selenium—Its Biological Perspectives, *Med. Hypotheses* 41(2), 150–159.

Birt, D. F., Pour, P. M. and Pelling, J. C. (1989). The Influence of Dietary Selenium on Colon, Pancreas and Skin Tumorigenesis. In *Selenium in Biology and Medicine* (A. Wendel, Ed.), Springer-Verlag, Berlin, pp. 297–304.

Boyle, R. W. (1979). *The Geochemistry of Gold and its Deposits: Together with a Chapter on Geochemical Prospecting for the Element*, Bulletin 280, Geological Survey of Canada, Ottawa.

British Geological Survey. (2000). *Regional Geochemistry of Wales and Part of West-Central England: Stream Sediment and Soil*, British Geological Survey, Keyworth, Nottingham.

British Geological Survey. (2011). *London Earth.* British Geological Survey, Keyworth. http://www.bgs.ac.uk/gbase/londonearth.html. Access Date March 2012.

Broadley, M. R., White. P. J., Bryson. R. J., Meacham. M. C., Bowen. H. C., Johnson. S. E., Hawkesford, M. J., McGrath, S. P., Zhao, F. J., Breward, N., Harriman, M. and Tucker, M. (2006). Biofortification of UK Food Crops with Selenium. *Proc Nutr Soc.,* 65, 1-14.

Broadley, M. R., Alcock. J., Alford. J., Cartwright. P., Fairweather-Tait. S. J., Foot. I, Fairweather-Tait, S. J., Hart, D. J., Hurst, R., Knott, P., McGrath, S.P., Meacham, M. C., Norman, K., Mowat, H., Norman, K., Stroud, J. L., Tovey, M., Tucker, M., White, P. J., Young, S. D. and Zhao, F. J. (2010). Selenium Biofortification of High-Yielding Winter Wheat (Triticum aestivum L.) by Liquid or Granular Se Fertilisation. *Plant Soil*, 32(1–2), 5-18.

Burk, R. F. (Ed.) (1994). *Selenium in Biology and Human Health*, Springer-Verlag, New York.

Cao, Z. H., Wang, X. C., Yao, D. H., Zhang, X. L. and Wong, M. H. (2000). Selenium Geochemistry of Paddy Soils in the Yangtze River Delta, *Environ. Int.*, 26(5–6), 335–339.

Chen, X., Yang, G., Chen, J., Chen, X., Wen, Z. and Ge, K. (1980). Studies on the Relations of Selenium and Keshan Disease. *Biol Trace Elem. Res.*, 2, 91–107.

Chilimba, A. D. C., Young, S. D., Black, C. R., Rogerson, K. B., Ander, E. L., Watts, M. J., Lammel, J. and Broadley, M. R. (2011). Maize Grain and Soil Surveys Reveal Suboptimal Dietary Selenium Intake is Widespread in Malawi. *Sci. Rep.* 1, 72, 1-9.

Clark, L. C., Combs, G. F., Turnbill, B. W., Slate, E. H., Chalker, D. K., Chow, J., Davies, L. S., Glover, R. A., Graham, G. F., Gross, E. G., Krongrad, A., Lesher, J. L., Park, H. K., Sander, B. G., Smith, C. L. and Taylor, J. R. (1996). Effects of Selenium Supplementation for Cancer Prevention in Patients with Carcinoma of the Skin, *J. Am. Med. Assoc.*, 276, 1957–1963.

Combs, G. F. and Combs, S. B. (1986). *The Role of Selenium in Nutrition*, Academic Press, Orlando, FL.

Cutter, G. A. and Bruland, K. W. (1984). The Marine Biogeochemistry of Selenium: A Re-Evaluation, *Liminol. Oceanogr.*, 29, 1179–1192.

Darnley, A. G., Björklund, A., Bølviken, B., Gustavsson, N., Koval, P. V., Plant, J. A., Steenfelt, A., Tauchid, M. and Xuejing Xie, X. (1995). *A Global Geochemical Database for Environmental and Resource Management. Recommendations for International Geochemical Mapping*, Earth Science Report 19, UNESCO Publishing, Paris.

Davies, E. B. and Watkinson, J. H. (1966). Uptake of Native and Applied Selenium by Pasture Species, *N. Z. J. Agric. Res.*, 9, 317–324.

Dhillon, K. S., Dhillon, S. K. and Thind, H. S. (2008). Evaluation of Different Agroforestry Tree Species for Their Suitability in the Phytoremediation of Seleniferous Soils. *Soil Use Manage.*, 24, 208-216.

DOE. 1996. *Code of Practice for Agricultural Use of Sewage Sludge*. Department of the Environment, HMSO, London.

EA. (2009). *Soil Guideline Values for Selenium in Soil*. Science Report SC050021. UK Environment Agency, Bristol.

Fairweather-Tait, S. J., Collings. R. and Hurst, R. (2010). Selenium Bioavailability: Current Knowledge and Future Research Requirements. *Am J Clin Nutr*.,91, 1484S–91S.

Fergusson, J. E. (1990). *The Heavy Elements: Chemistry, Environmental Impact and Health Effects*, Pergamon, London.

Finley, J. W., Ip, C., Lisk, D. J., Davis, C. D., Hintze, K. J. and Whanger, P. D. (2001). Cancer-Protective Properties of High-Selenium Broccoli, *J. Agric. Food Chem.*, 49(5), 2679–2683.

Fleming, G. A. (1980). Essential Micronutrients II: Iodine and Selenium. In *Applied Soil Trace Elements* (B. E. Davis, Ed.), John Wiley & Sons, New York, pp. 199–234.

Fordyce, F. M., Brereton, N., Hughes, J., Luo, W. and Lewis, J. (2010). An Initial Study to Assess the Use of Geological Parent Materials to Predict the Se Concentration in Overlying Soils and in Five Staple Foodstuffs Produced on Them in Scotland. *Sci. Tot. Env.*, 408(22), 5295-5305.

Fordyce, F. M., Johnson, C. C., Navaratne, U. R. B., Appleton, J. D. and Dissanayake, C. B. (2000a). Sele-nium and Iodine in Soil, Rice and Drinking Water in Relation to Endemic Goiter in Sri Lanka, *Science Total Environ.*, 263(1–3), 127–142.

Fordyce, F. M., Nice. S. E., Lister. T. R., Ó Dochartaigh. B. É., Cooper. R., Allen. M., Ingham. M., Gowing. C., Vickers. B. P. and Scheib, A. (2012). *Urban Soil Geochemistry of Glasgow*. Open Report, OR/08/002 British Geological Survey, Edinburgh.

Fordyce, F. M., Zhang, G., Green, K. and Liu, X. (1998). *Soil, Grain and Water Chemistry and Human Selenium Imbalances in Enshi District, Hubei Province, China*, Overseas Geology Series Technical Report WC/96/54, British Geological Survey, Keyworth, Nottingham.

Fordyce, F. M., Zhang, G., Green, K. and Liu, X. (2000b). Soil, Grain and Water Chemistry and Human Selenium Imbalances in Enshi District, Hubei Province, China, *Appl. Geochem.*, 15(1), 117–132.

Franke, K. W. (1934). A New Toxicant Occurring Naturally in Certain Samples of Plant Foodstuffs. 1. Results Obtained in Preliminary Feeding Trials. *J. Nutr*., 8, 597-608.

FSA. (2009). *Survey on Measurement of the Concentrations of Metals and Other Elements from the 2006 UK Total Diet Study*. Food Survey Information Sheet 01/09. Food Standards Agency, London.

Gawalko, E., Garrett, R. G., Warkentin, T., Wang, N. and Richter, A. (2009) Trace Elements in Canadian Field Peas: A Grain Safety Assurance Perspective. *Food Add and Contamin*., 26(7), 1002-1012.

GSNI (2012). *The Tellus Project.* Geological Survey of Northern Ireland, Belfast. http://www.bgs.ac.uk/gsni/tellus/geochemical_survey/index.html. Access Date March 2012.

Hartikainen, H., Xue, T. L. and Piironen, V. (2000). Selenium as an Anti-Oxidant and Pro-Oxidant in Ryegrass, *Plant Soil*, 225(1–2), 193–200.

Hawkes, W. C. and Turek, P. J. (2001). Effects of Dietary Selenium on Sperm Motility in Healthy Men, *J. Androl.*, 22(5), 764–772.

Haygarth, P. M. (1994). Global Importance and Cycling of Selenium. In *Selenium in the Environment* (W. T. Frankenberger and S. Benson, Eds.), Marcel-Dekker, New York, pp. 1–28.

Hem, J. (1992). *Study and Interpretation of the Chemical Characteristics of Natural Water*, Water Supply Paper 2254, U. S. Geological Survey, Reston, VA.

Hira, C. K., Partal, K. and Dhillon, K. S. (2004). Dietary Selenium Intake by Men and Women in High and Low Selenium Areas of Punjab. *Pub Health Nutr*., 7(1), 39-43.

Jacobs, L. W. (Ed.) (1989). *Selenium in Agriculture and the Environment*, Soil Science Society of America Special Publication 23, SSSA, Madison, WI.

Johnson, C. C., Fordyce, F. M. and Rayman, M. P. (2010). Factors Controlling the Distribution of Selenium in the Environment and Their Impact on Health and Nutrition. *Proc Nutr Soc*., 69 (1), 119-132.

Johnson, C. C., Ge, X., Green, K. A. and Liu, X. (2000). Selenium Distribution in the Local Environment of Selected Villages of the Keshan Disease Belt, Zhangjiakou District, Hebei Province, People's Republic of China, *Appl. Geochem.*, 15(3), 385–401.

Kohrle, J. (1999). The Trace Element Selenium and the Thyroid Gland, *Biochimie*, 81(5), 527–533.

Levander, O. A. (1986). Selenium. In *Trace Elements in Human and Animal Nutrition* (W. Mertz, Ed.), Academic Press, London, pp. 139–197.

Li, Y., Peng, T., Yang, Y., Niu, C., Archard, L. C. and Zhang, H. (2000). High Prevalence of Enteroviral Genomic Sequences in Myocardium From Cases of Endemic Cardiomyopathy (Keshan Disease) in China, *Heart*, 83(6), 696–701.

Li, S., Xiao, T. and Zheng, B. (2012). Medical Geology of Arsenic, Selenium and Thallium in China. *Sci. Tot. Env*. 421-422, 31–40.

Lippman S. M., Klein, E. A., Goodman, P. J., Lucia, M. S., Thompson, I. M., Ford, L. G., et al. (33 authors). (2009). Effect of Selenium and Vitamin E on Risk of Prostate Cancer and Other Cancers: The Selenium and Vitamin E Cancer Prevention Trial (SELECT). *J Amer Med Assoc*., 301(1). 39–51.

Longombe, A. O., Arnaud, J., Mpio, T. and Favier, A. E. (1994). Serum Selenium in HIV-Infected Zairian Patients, *Trace Elements Electrolytes*, 11(2), 99–100.

Lyons, M. P., Papazyan, T. T. and Surai, P. F. (2007). Selenium in Food Chain and Animal Nutrition: Lessons from Nature. *Asian-Aust. J. Anim. Sci*., 20(7), 1135-1155.

MAFF (1997). Food Surveillance Information Sheet of the Joint Food Safety and Standards Group, 126, Ministry of Agriculture Fisheries and Food, London.

Mahapatra, S., Tripathi, R. M., Raghunath, R. and Sadasivan, S. (2001). Daily Intake of Selenium by the Adult Population of Mumbai, India, *Sci. Tot. Env.*, 277(1–3), 217–223.

Mayland, H. F. (1994). Selenium in Plant and Animal Nutrition. In *Selenium in the Environment* (W. T. Frankenberger and S. Benson, Eds.), Marcel-Dekker, New York, pp. 29–47.

Moreno-Reyes, R., Egrise, D., Neve, J., Pasteels, J. L. and Schoutens, A. (2001). Selenium Deficiency-Induced Growth Retardation is Associated with an Impaired Bone Metabolism and Osteopenia, *J. Bone Miner. Res.*, 16(8), 1556–1563.

Moxon, A. L. (1937). *Alkali Disease or Selenium Poisoning*, Bulletin 311, South Dakota Agricultural Experimental Station, Vermillion.

Moxon, A. L. (1938). The Effect of Arsenic on the Toxicity of Seleniferous Grains, *Science*, 88, 81.

Murphy, J. and Cashman, K. D. (2001). Selenium Content of a Range of Irish Foods, *Food Chem.*, 74(4), 493–498.

Muth, O. H. and Allaway, W. H. (1963). The Relationship of White Muscle Disease to the Distribution of Naturally Occurring Selenium, *J. Am. Vet. Med. Assoc.*, 142, 1380.

Neal, R. H. (1995). Selenium. In *Heavy Metals in Soils* (B. J. Alloway, Ed.), Blackie Academic & Professional, London, pp. 260–283.

Nriagu, J. O. (1989). *Occurrence and Distribution of Selenium*, CRC Press, Boca Raton, FL.

Nriagu, J. O. (1991). *Heavy Metals in the Environment*, 1 CEP Consultants, Edinburgh.

Oldfield, J. E. (1999). *Selenium World Atlas*, Selenium-Tellurium Development Association, Grimbergen, Belgium.

Papp, L. A., Lu, J., Holmgren, A. and Khanna, K. K. (2007). From Selenium to Selenoproteins: Synthesis, Identity, and Their Role in Human Health. *Antioxid Redox Signal,* 9, 775–806.

Peng, A., Wang, W. H., Wang, C. X., Wang, Z. J., Rui, H. F., Wang, W. Z. and Yang, Z. W. (1999). The Role of Humic Substances in Drinking Water in Kashin-Beck Disease in China, *Environ. Health Perspect.*, 107(4), 293–296.

Pineda-Valdes, G. and Bullerman, L. B. (2000). Thermal Stability of Moniliformin at Varying Temperature, pH and Time in an Aqueous Environment, *J. Food Prot.*, 63(11), 1589–1601.

Plant, J. A., Kinniburgh, D., Smedley, P., Fordyce, F. M. and Klinck, B. (2004). Chapter 9.02: Arsenic and Selenium. In: *Environmental Geochemistry*. (B Sherwood Lollar Ed). Treatise on Geochemistry Series (Holland H D and Turekain K K. Exec Eds). Volume 9. Elsevier, Amsterdam. 17 – 66.

Rapant, S., Vrana, K. and Bodis, D. (1996). *Geochemical Atlas of Slovakia: Part 1 Groundwater*, Geological Survey of the Slovak Republic, Bratislava.

Rawlins, B. G., McGrath, S. P., Scheib, A. J., Breward, N., Cave, M., Lister, T. R., Ingham, M., Gowing, C. and Carter, S. (2012). *The Advanced Soil Geochemical Atlas of England and Wales*. British Geological Survey, Keyworth.

Rayman, M. (2008). Food-chain Selenium and Human Health: Emphasis on Intake. *Br. J. Nutr.* 100, 254-268.

Rayman, M., Goenaga Infante, H. and Sargent, M. (2008). Food-chain Selenium and Human Health: Spotlight on Speciation. *Br. J. Nutr.* 100, 238-253.

Rayman, M. (2012). Selenium and Human Health. *The Lancet*. 379, 1256-1268.

Reilly, C. (2006). *Selenium in Food and Health*. Springer. New York.

Reimann, C. and Caritat, P. (1998). *Chemical Elements in the Environment*, Springer-Verlag, Heidelberg.Romero, C. D., Blanco, F. L., Sanchez, P. H., Rodriguez, E. and Majem, L. S. (2001). Serum Selenium Concentration in a Representative Sample of the Canarian Population, *Sci. Total Environ.*, 269(1–3), 65–73.

Rosenfield, I. and Beath, O. A. (1964). *Selenium, Geobotany, Biochemistry, Toxicity and Nutrition*, Academic Press, New York.

Rotruck, J. T., Pope, A. L. Ganther, H. E., Swanson, A. B., Hafeman, D. G. and Hoekstra, W. G. (1969). Selenium: Biochemical Role as a Component of Glutathione Peroxidase. *Science,* 179, 588–590.

Ruston, D., Henderson, L., Gregory, J., Bates, C. J., Prentice, A., Birch, M., et al. (2004). Nutritional Status (Anthropometry and Blood Analytes), Blood Pressure and Physical Activity. *The National Diet and Nutrition Survey: Adults Aged 19-64 Years*, 4. The Stationary Office, London.

Sasaki, S., Iwata, H., Ishiguron, N., Habuchi, O. and Miura, T. (1994). Low-Selenium Diet, Bone and Articular-Cartilage in Rats, *Nutrition*, 10(6), 538–543.

Schwarz, K. and Foltz, C. M. (1957). Selenium as an integral part of factor 3 against dietary necrotic liver degeneration. *J. Am. Chem. Soc.*, 79, 3292–3293.

Shamberger, R. J. and Frost, D. V. (1969). Possible Protective Effect of Selenium Against Human Cancer, *Can. Med. Assoc. J.*, 100, 682.

Shimada, T., Murayama. N., Tanaka, K., Takenaka. S., Guengerich. F. P., Yamazaki, H. and Komori M. (2011). Spectral Modification and Catalytic Inhibition of Human Cytochromes P450 1A1, 1A2, 1B1, 2A6, and 2A13 by Four Chemopreventive Organoselenium Compounds. *Chem Res Toxicol*., 24(8), 1327-37.

Smith, M. I. and Westfall, B. B. (1937). *Public Health Report 52*, U. S. Public Health Department, Washington DC.

Suetens, C., Moreno-Reyes, R., Chasseur, C., Mathieu, F., Begaux, F., Haubruge, E., Durand, M. C., Neve, J. and Vanderpas, J. (2001). Epidemiological Support for a Multifactorial Etiology of Kashin-Beck Disease in Tibet, *Int. Orthop.*, 25(3), 180–187.

Tan, J. (Ed.) (1989). *The Atlas of Endemic Diseases and Their Environments in the People's Republic of China*, Science Press, Beijing.

Tan, J., Wang, W., Yang, L., Zhu, W., Li, R. and Hou, S. (1999). The Approaches to Amelioration of Selenium Eco-Cycle in Selenium-Deficient Biogeochemical Area and Its Effects on Selenium Dietary Intake and Health in China, In *Proceedings of the 5th International Conference on the Biogeochemistry of Trace Elements 2* (W. W. Wenzel, D. C. Adriano, B. E. Alloway, H. E. Doner, C. Keller, M. Lepp, R. Mench, R. Naidu and G. M. Pierzynski, Eds.), Vienna, Austria, 620–621.

Taylor, S. R. and McLennan, S. M. (1985). *The Continental Crust: Its Composition and Evolution*, Blackwell, Oxford, England.

Thomson, C. D. (2004). Selenium and iodine intakes and status in New Zealand and Australia. *Br J Nutr* 91, 661–672.

Thornton, I., Kinniburgh, D. G., Pullen, G. and Smith, C. A. (1983). Geochemical Aspects of Selenium in British Soils and Implications to Animal Health. In *Trace Substances in Environmental Health XVII* (D. D. Hemphill, Ed.), University of Missouri, pp. 391–398.

Tokunaga, T., Pickering, I. and Brown, G. (1996). Selenium Transformations in Ponded Sediments, *Soil Sci. Soc. Am. J.*, 60, 781–790.

U.S.-EPA. (2002). *Toxic Release Inventory 2002*. United States Environmental Protection Agency, Washington. Accessed via Scorecard.org. http://scorecard.goodguide.com/. Access Date April, 2012.

US-EPA. (2004). *Draft Aquatic Life Water Quality Criteria for Selenium - 2004.* United States Environmental Protection Agency, Washington.

U.S.-EPA. (2012). *Basic Information About Selenium in Drinking Water Fact Sheet*. United States Environmental Protection Agency, Washington.

USGS. (2007). *2006 Minerals Yearbook – Selenium and Tellurium*. United States Geological Survey, Reston, Washington.

USGS. (2011). *2010 Minerals Yearbook – Selenium and Tellurium*. United States Geological Survey, Reston, Washington.

Varo, P., Alfthan, G., Ekholm, P. and Aro, A. (1998). Effects of Selenium Supplementation Fertilizer on Human Nutrition and Selenium Status. In *Environmental Chemistry of Selenium* (W. T. Frankenberger and R. A. Engberg, Eds.), Marcel-Dekker, New York.

Vinceti, M., Rothman, K. J., Bergomi, M., Borciani, N., Serra, L. and Vivoli, G. (1998). Excess Melanoma Incidence in a Cohort Exposed to High Levels of Environmental Selenium, *Cancer Epidemiol. Biomarkers Prev.*, 7, 853–856.

Vinceti, M., Rovesti, S., Bergomi, M. and Vivoli, G. (2000). The Epidemiology of Selenium and Human Cancer, *Tumori*, 86, 105–118.

World Health Organization. (1987*). Environmental Health Criterion 58—Selenium*, World Health Organization, Geneva.

World Health Organization. (1996). *Trace Elements in Human Nutrition and Health*, World Health Organization, Geneva.

World Health Organization. (2011). *Guidelines for Drinking Water Quality.* Fourth Edition. World Health Organization, Geneva.

Wu, A. S., Oldfield, J. E., Shull, L. R. and Cheeke, P. R. (1979). Specific Effect of Selenium Deficiency on Rat Sperm, *Biol. Reprod.*, 20, 793–798.

Wu, L. (1994). Selenium Accumulation and Colonization of Plants in Soils with Elevated Selenium and Salinity. In *Selenium in the Environment* (W. T. Frankenberger and S. Benson, Eds.), Marcel-Dekker, New York, pp. 279–326.

Wu, L., Banuelos, G. and Guo, X. (2000). Changes of Soil and Plant Tissue Selenium Status in an Upland Grassland Contaminated by Selenium-Rich Agricultural Drainage Sediment After Ten Years Transformed From a Wetland Habitat, *Exotoxicol. Environ. Safety*, 47(2), 201–209.

Xu, G. and Jiang, Y. (1986). Selenium and the Prevalence of Keshan and Kashin-Beck Diseases in China. In *Proceedings of the First International Symposium on Geochemistry and Health* (I. Thornton, Ed.), Science Reviews Ltd., Northwood, England, pp. 192–205.

Yamashita, Y. and Yamashita, M. (2010). Identification of a Novel Selenium-containing Compound, Selenoneine, as the Predominant Chemical Form of Organic Selenium in the Blood of Bluefin Tuna, *J. Biol. Chem.*, 285(24), 18134-18138.

Yang, G. and Xia, M. (1995). Studies on Human Dietary Requirements and Safe Range of Dietary Intakes of Selenium in China and Their Application to the Prevention of Related Endemic Diseases, *Biomed. Environ. Sci.*, 8, 187–201.

Yang, G., Wang, S., Zhou, R. and Sun, S. (1983). Endemic Selenium Intoxication of Humans in China, *Am. J. Clin. Nutr.*, 37, 872–881.

Yang, G., Yin, S., Zhou, R., Gu, L., Yan, B., Lui, Y. and Liu, Y. (1989). Studies of Safe and Maximal Daily Dietary Selenium Intake in a Seleniferous Area in China. Part 2, *J. Trace Element Electrolytes Health Dis.*, 3, 123–129.

Zhang, W. H., Neve, J., Xu, J. P., Vanderpas, J. and Wang, Z. L. (2001). Selenium, Iodine and Fungal Contamination in Yulin District (People's Republic of China) Endemic for Kashin-Beck Disease, *Int. Orthop.*, 25(3), 188–190.

FIGURE 1 Simplified schematic diagram of the cycling of selenium from the environment to man. The main geochemistry and health pathways are shown in red/thicker arrows.

FIGURE 2 Distribution of selenium in stream sediments of Wales, showing high concentrations over the coalfields of south Wales, the mineralized areas (Parys Mountain, Snowdon, Harlech Dome) of north Wales, and the Mercia Mudstone in the Welsh Borderlands. Contrasting low values occur over the sandstones and siltstones of mid-Wales demonstrating a very strong relationship between selenium in the environment and geology. (Adapted with permission from British Geological Survey, 2000.)

FIGURE 3 The geographic distribution of selenium-rich soils (shading), localities where plant selenium concentrations are known to exceed $50 mg kg^{-1}$, and reported incidences of the selenium-deficiency-related disorder WMD in animals in the United States. (Adapted with permission from Muth and Allaway, 1963.)

FIGURE 4 Schematic diagram showing the main controls on the chemical speciation and bioavailability of selenium in soils.

FIGURE 5 Decreasing order of bioavailability of the different forms of selenium found in soils.

FIGURE 6 Bar chart showing the decline in the average daily dietary intake of selenium in UK adults 1974–2006.

FIGURE 7 Relative concentrations of selenium in the tissues of different animals, decreasing in concentration from left to right.

FIGURE 8 Distribution of the incidence of KD in China. (Adapted with permission from Tan, 1989.)

FIGURE 9 Kashin-Beck disease patient (left) and woman of the same age. (Reproduced with permission from Tan, 1989.)

FIGURE 10 Nail deformities as a result of selenium poisoning in Enshi District, China. (Photo: Professor Mao Dajun. Reproduced with permission from the British Geological Survey, Keyworth, Nottingham.)

FIGURE 11 Hair loss as a result of selenium toxicity in Enshi District, China. (Photo: Professor Mao Dajun. Reproduced with permission from the British Geological Survey, Keyworth, Nottingham.)

FIGURE 12 Box and whisker plots of selenium concentrations in soil, grain, drinking water and human hair samples from Zhangjiakou District, Hebei Province, China where the selenium-deficiency related condition KD is prevalent in the local population. Samples were collected from three village groups classified into no KD (0% prevalence), moderate KD (0–3% prevalence), and high KD (>3% prevalence). Medians are represented by horizontal bars within the box and upper and lower quartiles ±1.5 times the quartile range are represented by the whiskers. Deficiency thresholds from Tan (1989) are shown as dashed lines on the plots for soil total selenium, grain selenium, and human hair selenium contents. (Reproduced with permission from the British Geological Survey, Keyworth, Nottingham.)

TABLE I. Physical Properties of Selenium

Element name	*Selenium*
Chemical symbol:	Se
Atomic number:	34
Periodic table group:	VIA
Atomic mass:	78.96
Density:	4808kgm^{-3}
Melting point:	220¡C
Boiling point:	685¡C
Vapor pressure:	1mmHg @ 356¡C
Natural isotopes:	Abundance:
^{74}Se	0.87%
^{76}Se	9.02%
^{77}Se	7.58%
^{78}Se	23.52%
^{80}Se	49.82%
^{82}Se	9.19%

From Jacobs (1989) and -ATSDR (2003).

TABLE II. Chemical Forms of Selenium in the Environment

Oxidative state	*Chemical forms*
Se^{2-}	Selenide (Se^{2-}, HSe^{-}, H_2Se_{aq})
Se^{0}	Elemental selenium (Se^{0})
Se^{4+}	Selenite (SeO_3^{2-}, $HSeO_3^{-}$, H_2SeO_{3aq})
Se^{6+}	Selenate (SeO_4^{2-}, $HSeO_4^{2-}$, H_2SeO_{4aq})
Organic Se	Selenomethionine, Selenocysteine

From Jacobs (1989) and Neal (1995).

TABLE III. Selenium Concentrations in Selected Natural Materials

Material	*Total Se ($mgkg^{-1}$)*	*Water-soluble Se (ngg^{-1})*	*Material*	*Total Se($mgkg^{-1}$)*
Earth's crust:	0.05		Water (μgL^{-1}):	
			World freshwater	0.02
Igneous rocks (general):	0.35		Brazil River Amazon	0.21
Ultramafic (general)	0.05		U. S. (general)	<1
Mafic (general)	0.05		U. S. seleniferous	50–300
Granite (general)	0.01–0.05		U. S. Kesterson	<4200
			U. S. River Mississippi	0.14
Volcanic rocks (general):	0.35		U. S. River Colorado	10–400
United States	<0.1		U. S. River Gunnison	10
Hawaii	<2.0		U. S. Lake Michigan	0.8–10
Tuffs (general)	9.15		U. S. seleniferous gw	2–1400
			U. S. drinking water	0.0–0.01
Sedimentary rocks:			Spain freshwater	0.001–0.202
Limestone (general)	0.03–0.08		China Se-deficient sw	0.005–0.44
Sandstone (general)	<0.05		China Se-adequate sw	1.72
Shale (general)	0.05–0.06		China seleniferous sw	0.46–275
W. USA shales	1–675		Finland stream water	0.035–0.153
Wyoming shales	2.3–52		Canada stream water	1–5
South Korea shales	0.1–41		Norway groundwater	0.01–4.82
China Carbon-shale	206–280		Slovakia groundwater	0.5–45
Mudstones (general)	0.1–1500		Bulgaria drinking water	<2
Carbonates (general)	0.08		Sweden drinking water	0.06
Marine carbonates	0.17		Germany drinking water	1.6–5.3
Phosphates (general)	1–300		Ukraine surface water	0.09–3
U. S. Coal	0.46–10.65		Ukraine groundwater	0.07–4
Australia Coal	0.21–2.5		Argentina surface water	2–19
China stone-coal	<6471		Reggio, Italy dw	7–9
Oil (general)	0.01–1.4		Sri Lanka drinking water	0.056–0.235
			Greece drinking water	0.05–0.700
Soil:			Polar ice (general)	0.02
World (general)	0.4		Seawater (general)	0.09
World seleniferous	1–5000			
U. S. (general)	<0.1–4.3		Plants:	
U. S. seleniferous	1–10		U. S. grasses	0.01–0.04
England/Wales (general)	<0.01–16	50–390	U. S. clover and alfalfa	0.03–0.88
Scotland (general)	0.115-0.877	6.69-26.78		
Northern Ireland (general)	< 0.02-7.8			
Ireland seleniferous	1–1200		Norway moss	0.8–1.23
China (general)	0.02–3.81		Canada tree bark	2–16
China Se-deficient	0.004–0.48	0.03–5	Norway grain	0.006–0.042
China Se-adequate	0.73–5.66		Norway forage	0.05–0.042
China seleniferous	1.49–59.4	1–254	Finland hay	0–0.04
Finland (general)	0.005–1.241		Finland grain	0.007
India Se-deficient	0.025–0.71	19–66		
India seleniferous	1–19.5	50–620	Algae:	
Sri Lanka Se-deficient	0.112–5.24	4.9–43.3	Marine (general)	0.04–0.24
Norway (general)	3–6		Freshwater (general)	<2
Greece Se-deficient	0.05–0.10			
Greece Se-adequate	>0.2		Fish:	
New Zealand (general)	0.1–4		Marine (general)	0.3–2
Malawi (general)	0.05-0.62		Freshwater (general)	0.42–0.64
Urban Soils:				
London	<0.2-20		Animal tissue (general):	0.4–4

Glasgow	1-15		
Air (ng m^{-3}) (general):	0.00006–30	Stream sediments: Wales	0.4–83
Atmospheric dust (general):	0.05–10		

Note: gw = groundwater, sw = surface water, dw = drinking water.

From Fleming (1980); Thornton et al. (1983); Levander (1986); WHO (1987); Jacobs (1989); Nriagu (1989); Tan (1989); Fergusson (1990); Hem (1992); Haygarth (1994); Neal (1995); Rapant et al. (1996); Fordyce et al. (1998); Reimann and Caritat (1998); Vinceti et al. (1998); Oldfield (1999); British Geological Survey (2000); Fordyce et al. (2000a); Fordyce et al. (2010); British Geological Survey (2011); Chilimba et al. (2011); Fordyce et al. (2012); GSNI (2012); Rawlins et al. (2012) .

TABLE IV. Global Selenium Fluxes

Cycle	*Selenium flux (tonnes per year)*
Anthropogenic	76,000–88,000
Marine	38,250
Terrestrial	15,380
Atmospheric	15,300

Modified from Haygarth (1994).

TABLE V. Main Sources of Selenium in the Environment

Natural sources	*Comments*
Volcanic activity	Important source
Weathering of rocks	Important source
Sea spray	Concentrations in ocean water are only an order of magnitude lower than those in rocks
Atmospheric flux	From the ocean surface to the atmosphere
Volatilization and recycling from biota	
Aerial deposition	For example, in the UK annual selenium deposition = 2.2–6.5gha^{-1}
Man-made sources	*Comments*
Selenium-based industries	
Metal processing industries	Important source
Burning of fossil fuels	Important source
Disposal of sewage sludge to land	Typical selenium contents 1–17mgkg^{-1}
Agricultural use of pesticides	Potassium ammonium sulfide ($[K(NH_4)S]_5Se$)
Agricultural use of lime	Typical selenium contents 0.08mgkg^{-1}
Agricultural use of manure	Typical selenium contents 2.4mgkg^{-1}
Agricultural use of phosphate fertilizers	Typical selenium contents 0.08–25mgkg^{-1}

From Fleming (1980); Haygarth (1994); and Neal (1995).

TABLE VI. Industrial Uses of Selenium

Industry	*Percentage of total world production used by various industries in 2010*
Metal alloys/metallurgy	30%
Glass manufacture	30%
Agriculture Fertilizer Nutritional additive to livestock feed Medical use, e.g., dietary supplements	10%
Electrical components—semi-conductors, cables, and contacts Photocopier components	10%
Pharmaceutical catalyst Fungicide Pesticide Anti-dandruff shampoo Pigments in plastics, paints, enamels, inks, rubber, textiles Additive to petroleum fuel and lubricant products Accelerator and vulcanizing agent in rubber manufacture Photographic emulsions, printing, and graphics	10%
Other	10%

From USGS (2011).

TABLE VII. Industrial Dispersion of Selenium Compounds in the U. S. in 2002

Selenium compounds released to land and water in 2002		
Source (tonnes)	*Water*	*Land*
Top 5 States:		
Alabama	308	301
Nevada	196	195
Utah	166	164
Oregon	82	82
Texas	157	81
Main industries:		
Electric, Gas, Sanitary Services	13	767
Metal/Coal Mining	0.1	217
Primary Metal Industries	0.8	63
Chemicals and Allied Products	0.002	0.1
Petroleum and Coal Products	1.2	0.1
Totals	925	1869

U.S.-EPA (2002).

TABLE VIII. Most Common Mineral Forms of Selenium in Natural Rocks

Selenium–mineral	*Chemical formula*
Crookesite	$(Cu,Tl,Ag)_2Se$
Clausthalite	PbSe
Berzelianite	Cu_2Se
Tiemannite	HgSe
Elemental selenium	Se
Selenium is also commonly found in the sulfide host minerals	
Pyrite	FeS_2
Chalcopyrite	$CuFeS_2$
Pyrrhotite	FeS
Sphalerite	ZnS
Typical mineral associations with selenium:	
Polymetallic sulfide ores	Se-Hg-As-Sb-Ag-Cu-Zn-Cd-Pb
Copper-pyrite ores	Cu-Ni-Se-Ag-Co
Sandstone-uranium deposits	U-V-Se-Cu-Mo
Gold-silver selenide deposits	Au-Ag-Se

From Fleming (1980); Neal (1995); and Reimann and Caritat (1998).

TABLE IX. Some Examples of Seleniferous Soils and Geological Parent Materials

Country	*Parent material*
U. S.	Cretaceous shale, tuff, Jurassic shales and sandstones, Triassic sandstones
Canada	Cretaceous shales
Colombia	Black slates
Puerto Rico	Volcanic soils
Ireland	Carboniferous shales and limestones
UK	Carboniferous and Ordovician shales and slates
Israel	Cretaceous limestone
South Africa	Cretaceous shales and sandstones
Australia	Cretaceous shales and limestones
Russia	Jurassic sandstones
China	Permian coal and shales

Modified from Fleming (1980).

TABLE X. Examples of the Three Types of Selenium Accumulating Vegetation

Type	*Examples (genus, family, or species)*
Primary accumulator	G. *Astragalus* (e.g., milk vetch)
	G. *Machaeranthera* (woody aster, U. S.)
	G. *Haplopappus* (North and South American goldenweed)
	G. *Stanleya* (Prince's Plume)
	G. *Morinda* (rubiaceous trees and shrubs, Asia/Australia)
	F. Lecythidaceae (South American trees)
	Sp. *Neptunia* (Legume Asia/Australia)
Secondary accumulator	G. *Aster*
	G. *Astragalus*
	G. *Atriplex* (Saltbush)
	G. *Castilleja* (North and South American perennials)
	G. *Grindelia* (gummy herbs of western North and Central America)
	G. *Gutierrezia* (perennial herbs of western North and South America)
	G. *Machaeranthera*
	G. *Mentzelia* (bristly herbs of western America)
	Sp. *Brassica* (mustard, cabbage, broccoli, cauliflower)
Non-accumulator	Sp. *Pascopyrum* (wheat grass)
	Sp. *Poasecunda* (blue grass)
	Sp. *Xylorhiza* (Woody Aster)
	Sp. *Trifolium* (clover)
	Sp. *Buchloe* (buffalo grass)
	Sp. *Bouteloua* (North and South American tuft grass)
	Sp. *Beta* (sugar beet)
	Sp. *Horedeum* (barley)
	Sp. *Triticum* (wheat)
	Sp. *Avena* (oats)

From Rosenfield and Beath (1964); Jacobs (1989); and Neal (1995).

TABLE XI. Relative Uptake of Selenium in Agricultural Crops

Selenium accumulation	*Plant species*
Better accumulators	Cruciferae (broccoli, radish, cress, cabbage, turnip, rape, and mustard)
	Liliaceae (onion)
	Leguminosae (red and white clover, peas)
	Helianthus (sunflower)
	Beta (Swiss chard)
Poorer Accumulators	Compositae (lettuce, daisy, artichoke)
	Gramineae (cocksfoot, ryegrass, wheat, oats, barely)
	Umbelliferae (parsnip, carrot)

Average selenium $mgkg^{-1}$ *dry weight*	*U. S. crop type*
0.407	Roots and bulbs
0.297	Grains
0.110	Leafy vegetables
0.066	Seed vegetables
0.054	Vegetable fruits
0.015	Tree fruits

Jacobs (1989).

TABLE XII. U.S. Inhalation Permissible Exposure Limit for Selenium-Bearing Compounds

Compound	*Value*
Hydrogen selenide	$200\mu gm^{-3}$
Se-hexafluoride	$400\mu gm^{-3}$
Se-compounds	$200\mu gm^{-3}$

From (ATDSR, 2003)

TABLE XIII. Average Concentrations of Selenium in Selected Animals

Animal	*Selenium mgkg^{-1}*
Fish, U. S.	0.5 wet weight
Terrestrial arthropods	1 fresh weight
Earthworms	2.2 (normal soil)–22 (sewage sludge amended soil) fresh weight
Bird livers	4–10 dry weight
Bird eggs	0.4–0.8 wet weight
Bird kidneys	1–3 dry weight
Mammal livers	<2 dry weight

From Jacobs (1989).

TABLE XIV. Concentrations of Selenium in Selected Foodstuffs From Around the World

Food type	*Source*	*Selenium mgkg^{-1}*
Whole meal flour	Ireland	0.077–0.099
White flour	Ireland	0.060–0.069
Wheat flour	Russia	0.044–0.557
Whole meal bread	Ireland	0.086–0.129
White bread	Ireland	0.066
Wheat	World	0.1–1.9
Wheat	Greece	0.019–0.528
Wheat	Colombia	180
Wheat	China	Deficient 0.001–0.105
Wheat	Scotland	0.003--0.006 fresh weight
Wheat	India	Seleniferous 0.742
Wheat	India	Non-seleniferous 0.010
Barley	U. S.	0.2–1.8
Oats	U. S.	0.15–1
Corn	China	Deficient 0.005–0.089
Corn	China	Seleniferous 0.5–28.5
Corn	Venezuela	14
Maize	China	Deficient 0.001–0.105
Maize	China	Seleniferous 0.017–9.175
Maize	China	Adequate 0.021–2.324
Maize	U. S.	0.136
Maize	Malawi	0.005–0.533 fresh weight
Rice	Venezuela	18
Rice	China	Deficient 0.007–0.022
Rice	China	Seleniferous 0.3–20.2
Rice	Sri Lanka	0.0001–0.777
Cereals	World	0.1–0.8 wet weight
Cereals	Finland/New Zealand	0.01–0.07
Cereals	UK	0.070 fresh weight
Bread	UK	0.060 fresh weight
Liver, kidney, seafood	World	0.4–1.5 wet weight
Liver, kidney, seafood	Finland/New Zealand	0.09–0.92 wet weight
Fish	UK	0.420 fresh weight
Muscle meat	World	0.1–0.4 wet weight
Muscle meat	Finland/New Zealand	0.01–0.06 wet weight
Beef steak	Scotland	0.081-1.51 fresh weight
Offal	UK	0.770 fresh weight
Meat	UK	0.140 fresh weight
Dairy products	World	0.1–0.3 wet weight
Dairy products	Finland/New Zealand	0.01 wet weight
Dairy products	UK	0.030 fresh weight
Cow's milk	Turkey	11.28–36.05mgL^{-1}
Cow's milk	Scotland	0.001-0.022 fresh weight
Cow's milk	UK	0.014 fresh weight
Cow's milk	India	Seleniferous 0.050 mgL^{-1}
Cow's milk	India	Non-seleniferous 0.006 mgL^{-1}
Human milk	World	0.013–0.018mgL^{-1}
Human milk	New Zealand	0.005mgL^{-1}

Dried milk	Russia	0.038–0.115
Egg whites	Chile	0.55–1.10
Eggs	UK	0.019 fresh weight
Fruit and vegetables	World	0.1 wet weight
Fruit and vegetables	Finland/New Zealand	0.01–0.07 wet weight
Fruit	UK	< 0.005 fresh weight
Broccoli	Scotland	0.001-0.007 fresh weight
Vegetables	China	Seleniferous 2.0–475
Vegetables	UK	< 0.010-0.018 fresh weight
Brazil nuts	UK	22.3–53
Nuts	UK	0.300 fresh weight
Soyabeans	China	Deficient 0.010
Soyabeans	China	Seleniferous 0.34–22.2
Field peas	Canada	<0.05-79.6

From Yang et al. (1983); Levander (1986); WHO (1987, 1996); Jacobs (1989); Tan (1989); Fordyce et al. (1998); Oldfield (1999); Fordyce et al. (2000a); Murphy and Cashman (2001); Hira et al. (2004); FSA (2009); Gawalko et al. (2009); Fordyce et al. (2010); Chilimba et al. (2011).

TABLE XV. Some Daily Dietary Intakes of Selenium From Around the World (μg day^{-1})

Country	*Year*	*Vegetables and fruit*	*Cereals*	*Dairy*	*Meat and fish*	*Men*	*Women*	*Total*
New Zealand (general)	1981–1982	1–2	3–4	11	12–16			28–32
New Zealand infants	1987							0.5–2.1
Finland	1975–1979	1	3–25	7–13	19			30–60
UK	1978	3	30	5	22			60
UK	1991							43
UK	1995							29–39
UK	2000							32-34
UK	2006							48-58
Japan (general)	1975	6	24	2	56			88
Japan high seafood	1987							500
Canada	1975	1–9	62–133	5–28	25–90			98–224
Canada	1987							149
U.S. (general)	1974–1976	5	45	13	69			132
U.S. (general)	2002							71–152
U.S. South Dakota	1976	10	57	48	101			216
U.S. Maryland	1987							81
China (general)	1987			2–212				
China seleniferous	1983							240–6690
China Se-adequate	1983					19.1	13.3	42–232
China Se-deficient	1983					7.7	6.6	3–22
India, Mumbai	2001							61.9
India seleniferous	1998							475-632
India non-seleniferous	1998							52-65
Turkey	2001							20–53
Venezuela	1999			58				100–1200
Swedish Pensioners	1987							8.7–96.3
Greece	1999							110

Country	*RDA range*	*RDA W*	*RDA M*	*RDA I*
U.S.	50–200	55	55	15-20
UK	60–200	60	75	10
China	40–600			

Note: RDA = Recommended Daily Allowance; W = Women; M = Men; I = Infants.

From Yang et al. (1983); WHO (1987, 1996); Tan (1989); MAFF (1997); Oldfield (1999); Aras et al. (2001); Mahapatra et al. (2001); ATSDR (2003); Hira et al. (2004); FSA (2009).

TABLE XVI. Examples of Selenium Concentrations in Human Tissues From Around the World

Country	Selenium (mgL^{-1}) Whole blood	Year	Selenium (mgL^{-1}) Serum	Year
Average (humans)	0.2			
Normal (humans)			0.06–0.105	
Canada, Ontario	0.182	1967		
China, high Se	1.3–7.5	1983		
China, high Se, no disease	0.44	1983		
China, mod Se	0.095	1983		
China, low Se, no disease	0.027	1983		
China, low Se, disease	0.021	1983		
Tibet, low Se			<0.005	1998
Egypt	0.068	1972		
Finland	0.056–0.081	1977		
Guatemala	0.23	1967		
New Zealand	0.083–0.059	1979		
Sweden		1987	0.86	
UK	0.32	1963		
UK		2001	0.087-0.088	2004 (Plasma)
U.S.	0.256–0.157	1968		
Russia	0.11–0.442	1976		
Venezuela seleniferous	0.355–0.813	1972		
Bulgaria			0.0548	1998
Hungary			0.0558	1998
Slovenia			0.0570	1998
Croatia			0.0642	1998
Russia			0.0718	1999
Italy, Lombardy	0.04–0.19	1986	0.033–0.121	1986
Spain, Barcelona			0.060–0.106	1995
Canary Islands			0.008–0.182	2001

	Selenium ($mgkg^{-1}$) Hair	Year	Selenium (μgL^{-1}) Urine
China, Se deficient	0.074	1983	0.007
China, Se deficient	0.170–0.853	1998	
China, Se deficient	0.094–0.359	1996	
China, low Se	0.16	1983	
China, Se adequate	0.343	1983	0.026
China, high Se	1.9–100	1983	0.04–6.63
China, high Se	0.566–141	1998	
Italy, Lombardy		1986	0.0002–0.068
Sri Lanka	0.104–2.551	1998	
India seleniferous	2.31-2.55	1998	0.170-0.267
India non seleniferous	0.048-0.050	1998	0.009-0.012

Yang et al. (1983); Levander (1986); Akesson and Steen (1987); WHO (1987, 1996); Oldfield (1999); Fordyce et al. (2000a); Vinceti et al. (2000); Romero et al. (2001); Fordyce et al. (2000b); Hira et al. (2004); Ruston et al. (2004)

TABLE XVII. List of Main Known Human Selenoproteins

Name	*Function*
Glutathionine peroxidase GPx	Antioxidant enzymes
Sperm nuclei selenoprotein GPx4	Essential for male fertility and sperm maturation
Mitochondrial capsule selenoprotein PHGPx	Protects sperm cells from oxidative damage
Spermatid selenoprotein 34kDa	May protect developing sperm
Iodothyronine deiodinases (Dio)	Regulation and production of active thyroid hormones
Thioredoxin reductases (TrxR)	Reduction of nucleotides and binding of transcription factors in DNA
Selenophosphate synthetase SPS2	Required for selenoprotein synthesis
Selenoprotein P	Protects endothelial cells against perioxynitrite; transport of selenium; possible heavy metal chelator
Selenoprotein W	Skeletal and heart muscle metabolism
Selenoprotein 15	May affect glycoprotein folding and regulate cell apoptosis
Selenoprotein 18-kDa	Found in the kidney
Selenoprotein R: Methionine sulfoxide reductase	May regulate lifespan
Selenoprotein N	May regulate calcium in early muscle development; if deficient may be linked to muscular dystrophy and multiminicore disease
Selenoprotein M	May have a role in Alzheimer's disease
Selenoprotein S (SEPS1)	Anti-inflammatory; linked to glucose metabolism
Selenoprotein K	May be an antioxidant in the heart

From Papp et al (2007); Rayman (2012).

TABLE XVIII. Deficiency and Toxicity Thresholds and Recommended Upper Limits for Selenium in Various Media

	Deficient $mgkg^{-1}$	*Marginal* $mgkg^{-1}$	*Moderate* $mgkg^{-1}$	*Adequate* $mgkg^{-1}$	*Toxic* $mgkg^{-1}$	*Reference*
Soils						
World Total Se	0.1–0.6					Various
China Total Se	0.125	0.175	0.400		>3	Tan (1989)
China Water-Soluble Se	0.003	0.006	0.008		0.020	Tan (1989)
Plants						
World Plants	0.1			0.1–1.0	3–5	Jacobs (1989)
China Cereal Crops	0.025	0.040	0.070		>1	Tan (1989)
Animals						
Fodder, Animals chronic	<0.04			0.1–3	3–15	Jacobs (1989)
Cattle and sheep liver	0.21					WHO (1987)
Cattle/sheep blood mgL^{-1}	<0.04	0.05–0.06		0.07–0.1		Mayland (1994)
Humans						
China Hair	0.200	0.250	0.500		>3	Tan (1989)
Urine Excretion $\mu g\ day^{-1}$				10–200		Oldfield (1999)
Ref. Dose $mgkg^{-1}day^{-1}$					0.005	ATSDR (2003)
Food	<0.05				2–5	WHO (1996)
Diet $\mu g\ day^{-1}$	<40			55–75	>400	WHO (1996)

	Maximum Admissible Concentration $mgkg^{-1}$	*Reference*
UK Soil	120–13000	EA (2009)
France Soil	10	Haygarth (1994)
USA Sewage Sludge	100	ATSDR (2003)
UK Sewage Sludge	25	Haygarth (1994)
USA Air $mg\,m^{-3}$	0.2	ATSDR (2003)
World Water μgL^{-1}	40	WHO (2011)
USA Water μgL^{-1}	50	US-EPA (2012)
World Human Urine mgL^{-1}	0.1	WHO (1987)

TABLE XIX. Comparison of Selenium Toxicity Effects in Biota from the Seleniferous Kesterson Reservoir and the Selenium-Normal Volta Wildlife Area, California, United States

Sample type	*Kesterson mgkg^{-1}*	*Volta mgkg^{-1}*
Algae and rooted aquatic plants	18–390	0.17–0.87
Emergent aquatic plants leaves	17–160	<2.0
Terrestrial plants leaves	0.5–27	<4.7
Plankton (geomean)	85.4	2.03
Aquatic insects	58.9–102	1.1–2.1
Mosquito fish	149–380	1.1–1.4
Reptiles (frogs, snakes) liver	11.1–45	2.05–6.22
Birds (coot, duck, stilt, grebe) liver	19.9–43.1	4.41–8.82
Voles liver (geomean)	119	0.228
No. of dead or deformed chick/embryo	22%	1%

From Jacobs (1989).

TABLE XX. Estimated Daily Dietary Intake of Selenium in Three Areas of Enshi District, China. Compared to Recommended Intakes Elsewhere

Source	*Daily dietary intake of selenium (μg)*
Enshi low Se and KD	62–70
Enshi high Se and no selenosis	194–198
Enshi high Se and selenosis	1238–1438
U.S. National Research Council	50–200 RDA
UK Dept of Health	60–200 RDA
China	40–600 RDA

RDA = Recommended Daily Allowance.
From Yang et al. (1983); Tan (1989); WHO (1996); and MAFF (1997).

TABLE XXI. Selenium in Soil, Grain, and Hair from Enshi District, China. Compared to Selenium Deficiency and Toxicity Threshold Values

Threshold	*Soil total Se ($mgkg^{-1}$)*	*Soil water soluble Se (ngg^{-1})*	*Grain Se ($mgkg^{-1}$)*	*Hair Se ($mgkg^{-1}$)*
Deficient	0.125	3	0.025	0.2
Toxic	3	20	1	3
Enshi area village	*Geometric mean Se*		*Concentration ranges (n = 15)*	
Low Se	0.069–0.199	0.21–0.44	0.001–0.003	0.252–0.345
High Se	2.07–19.54	2–61	0.041–2.902	0.692–29.21

From Tan (1989) and Fordyce et al. (2000b)