Too much or too little? A review of the conundrum of selenium

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ABSTRACT

Chemical elements such as selenium, fluoride, iron, calcium and magnesium are essential to the human being, although some are toxic when absorbed in high doses. In this paper, the risks associated with insufficient and excessive intake of selenium in the diet are reviewed, focusing on drinking water. Two different approaches are used to derive recommended nutrient intakes (RNI) for adequate nutritional status and guideline values to prevent excessive exposure. The former is based on the daily intake which meets the nutrient requirements of 97.5% of the population. The latter is a value derivation based on an assumed daily *per capita* consumption at the individual level, a conservative approach used where there is any uncertainty and is related to a negligible risk to health at population level across life stages. There is an increasing need to develop a conceptual framework bringing together aspects of toxicity and essentiality especially for elements apparently exhibiting narrow or overlapping ranges between essentiality and toxicity and to provide guidance on the nature and severity of risks in order to better protect human. While there are a number of frameworks available, these generally only consider food. There is a need to include water, which can be a significant source in some circumstances.

Key words | deficiency, drinking water, environment, health, selenium, toxicity

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INTRODUCTION

As the world population continues to increase, there is progressively more pressure on water resources, including groundwater. Deeper aquifers are increasingly exploited, increasing the potential of accessing mineral-rich groundwater. The pressure on water resources is also leading to the widespread use of desalination or demineralization processes in order to obtain freshwater, which depletes the source water of any essential or beneficial nutrients, which might be present (WHO 2005). These factors will lead to the risk of more populations being exposed to either high levels, of potentially toxic elements or to much lower levels of essential elements where water is an important contributor.

There is increasing public concern about the adverse health effects from chemical elements ingested through drinking-water. However, drinking-water is also used in the preparation of foods that can absorb minerals or in which it

constitutes a major part, with a resulting increase in intake through the diet. For example, it has been reported that between 28 and 35 million people in Bangladesh are exposed to dangerously high levels of arsenic in drinking-water (Barry & Hughes 2008) many of whom suffer the health consequences of this exposure. It is important that such concerns do not result in authorities losing sight of considerations of practical achievability and the fact that some elements do provide benefits.

Selenium is a naturally occurring element and can be found at varying concentrations at the Earth's surface, whether in rocks, soil, plants or water. In water, its concentration ranges from $<1\,\mu g/L$ to about $400\,\mu g/L$, although depending on geological factors, concentrations as high as $6,000\,\mu g/L$ have been recorded, leading to a wide spectrum of human exposure. Human exposure to selenium

is primarily through food, followed by water consumption and least through air. The contribution of selenium from drinking-water to the total diet can vary extensively, although in many regions it is very low. However, this contribution has not yet been adequately quantified and is not taken into account with respect to total dietary intake. Its role and metabolism in the human body is complex. Unlike arsenic or other toxic elements, there needs to be a balance between a safe and sufficient intake and toxicity. Cases of selenium deficiency (Keshan disease) and selenium toxicity have occurred within 20 km of one another in Hubei Province, China (Fordyce *et al.* 2000). These cases were linked to selenium levels in the environment and specifically to geological substrata. This particular study emphasizes the localized variation in geological distribution that may occur in any one region, and that availability of selenium may be controlled not only by geology but also by other factors, including total soil selenium content and pH, which will influence uptake by plants (Fordyce *et al.* 2000).

Studies have shown beneficial effects of selenium for health and it is implicated in the protection of body tissues against oxidative stress, maintenance of defenses against infection, and modulation of growth and development. Excessive intake of selenium, on the other hand, is reported to be linked to a number of adverse health outcomes, including loss of hair and nails, skin lesions and gastro-intestinal disturbances among others.

The present World Health Organization (WHO) guideline value for selenium in drinking-water was set at 10 μg/L by the WHO in the second edition of the *Guidelines for Drinking-Water Quality* (WHO 1996) and this was maintained at the publication of the third edition in 2004. However, the process of "rolling revision" of the guidelines has identified the need to reconsider the value in part in response to the tension between nutritional and toxic effects.

SELENIUM AND THE ENVIRONMENT

Selenium in the environment is distributed unevenly between the terrestrial, aquatic and atmospheric compart-ments. The natural processes that distribute selenium throughout the compartments are: volcanic activity; rock and soil weathering; leaching of soils; transportation by groundwater; uptake and release by plants, animals and micro-organisms; adsorption–desorption reactions; chemically and biologically mediated oxidation–reduction reactions; and mineral formation (McNeal & Balistrieri 1989). Selenium concentration in rocks usually ranges from 0.05 to 0.09 mg/kg, and is commonly associated with sulphide ore deposits (Adriano 2001).

Elevated concentrations of selenium are found in the environment in localized areas of Australia (Combs 2001; Tinggi 2003), Argentina (Oldfield 2002), Bangladesh (Oldfield 2002), Brazil (Lemire *et al.* 2006), Canada (Combs 2001), China (Yang *et al.* 1989a,b; Fordyce *et al.* 2000; Zhu & Zheng 2001), India (southern parts of Haryana, Punjab, Rajasthan, West Bengal) (Dhillon & Dhillon 2003; Yadav *et al.* 2005), Italy (Vinceti *et al.* 1994, 2000a,b, 2001), New Zealand (Oldfield 2002), Poland (Oldfield 2002), South Africa (Oldfield 2002), United States of America (USA) (Olson & Palmer 1984; Combs 2001; Hamilton 2004) and Venezuela (Bratter *et al.* 1991, 1993). For example, an assessment of what accessory elements were concentrated with uranium and vanadium in the ore deposits in Utah, USA, reported selenium levels up to 6,000 μg/L in ground-water (Cannon 1964). Levels between 26 and 1,800 μg Se/L in spring water were also reported in New Mexico (USA) by Valentine *et al.* (1978). Three springs were tested and all three contained high levels of both uranium and selenium in the proximity of mines. Selenium in well waters used by an Ute Indian family in Colorado (USA) was found in a concentration of 9,000 μg Se/L (Beath 1962). Other studies have reported varying concentrations of selenium in ground and surface water, ranging from low concentrations of 0.06 μg Se/L to what is considered to be elevated levels, in excess of 50 μg Se/L (Lindberg 1968; Barceloux 1999) (Table 1).

Chemical speciation is of particular interest in environmental and toxicological analyses as the toxicity of an element, its biological availability and transport mechanisms often depend on the chemical form in which it is present. This may have implications for the use of a water as a source for drinking-water (De *et al.* 2002). The mobility, bioavailability and toxicity of selenium in water are controlled by various biological, chemical and physical conditions, such as pH, redox reactions, absorption,

Table 1 | Selenium in water

Country	Se concentrations	Source	Reference
Zhoukoudian area, Beijing (China)	0.017 µg/L	Drinking-water	Li *et al.* (2007)
Sweden	0.11–0.15 µg Se/ L	Groundwater	Robberecht & van Grieken (1982)
Pacific Ocean	0.13 µg Se/L	Seawater	Adriano (2001)
U.S. rivers	0.2 µg Se/L	River water	Adriano (2001)
San Francisco Bay (USA)	0.07–0.4 µg Se/L	Seawater	Adriano (2001)
U.S. drinking water	3.5 µg Se/L (average)	Drinking-water	Shamberger (1980)
Italy	7 µg Se/L	Drinking-water	Vinceti *et al.* (2000a)
China	12.27 µg Se/L	Domestic water supplies	Yang *et al.* (1989b)
China	50–160 µg Se/L	Drinking-water	Fawell (1993)
New Mexico (USA)	26–1,800 µg Se/L	Spring water	Valentine *et al.* (1978)
South Dakota (USA)	1,600 µg Se/L	Well waters	Byers (1936)
Utah (USA)	6,000 µg Se/L	Groundwater	Cannon (1964) and Glover *et al.* (1979)
Colorado (USA)	9,000 µg Se/L	Well waters	Beath (1962)

complexation, precipitation and organic uptake (Plant *et al.* 2005), which have significant implications for uptake by humans. Selenium commonly exists in the environment in one or more of four oxidation states: selenide [Se(II)]; elemental selenium [Se(0)]; selenite [Se(IV)] and selenate [Se(VI)]. Inorganic selenate and selenite are the more mobile forms of selenium and tend to predominate in water (ATSDR 2003), while selenide and elemental selenium tend to be present more in seleniferous soils and sediments (Zhang & Moore 1996). Selenate has been reported to be more mobile than selenite in water and in soils (McLean & Bledsoe 1992; Strawn *et al.* 2002).

The major source of selenium intake for humans is usually food, with seafood and meat, as well as grains and cereals, being the most important sources. Organic selenium compounds (selenomethionine, selenocysteine) are the major selenium species in foods. Cereals and vegetables contain less than 0.01 mg Se/kg, while root vegetables and sulfur-rich plants (broccoli, mustard) can contain higher concentrations (Barceloux 1999). Meats and seafood usually contain concentrations between 0.4 and 1.5 mg Se/kg (WHO/FAO/IAEA 1996). The selenium contents of foods from plants and most livestock will depend, ultimately, on the levels and species of selenium in soils. Cereals grown in low selenium soils will give rise to low selenium levels in the grain and vice versa. Similarly, grasses grown on low selenium soils lead to the need to provide supplements for cattle feeding on the grass.

SELENIUM & HEALTH

Selenium is an essential element for humans and animals for adequate bodily function. Studies have shown beneficial effects for health, and it is implicated in the protection of body tissues against oxidative stress, maintenance of defences against infection, and modulation of growth and development as well as its possible anti-carcinogenic properties (Fishbein 1986; Hocman 1988; Schrauzer 1992, 2000; Ganther 1999; Combs *et al.* 2001; Spallholz *et al.* 2004; Rayman 2005; Zeng *et al.* 2005). Among the literature on selenium's beneficial effects, a review by Spallholz *et al.* (2004) suggests that low selenium dietary intakes may be a contributory factor for arsenicosis and cancer in Bangladesh as well as in West Bengal in India. A relationship between low-level selenium status and the prevalence of cancer and heart disease has also been suggested by a number of different studies (Brawley *et al.* 2001; Wojtczak 2003; Klein & Thompson 2004), although this remains controversial (Moyad 2002; Allen *et al.* 2004).

Vinceti *et al.* (1994) studied cardiovascular mortality in a town in northern Italy, in which the selenium concentration of drinking water had been reduced from 7 µg/L to less than 1 µg/L. They reported an apparent increase in cardiovascular mortality. One death in males and two in females occurred from coronary heart disease prior to the change (between 1986 and 1988); following the

decrease of selenium in drinking water, 21 males and 10 female deaths from coronary heart disease were reported in the subsequent 4-year period (between 1988 and 1992) in a cohort of 4419 individuals, previously exposed for at least five years to the drinking water with higher selenium content.

Another study by Vinceti *et al.* (2001) suggested that selenium species exhibit a bivalent effect in cancer, either increasing or decreasing risk. However, the studies carried out by Vinceti *et al.* (1994; 2000a,b; 2001) are difficult to interpret due to small size, difficulties in assessing total exposure or difficulties in accounting for confounding factors with what are essentially multifactorial diseases. The debate remains unresolved over the protective effect of selenium for various cancers or cardiovascular disease.

Selenium, in combination with other minerals, has been reported to play an active role in the prevention of myopathies and vascular lesions in which the element functions in concert with vitamin E. Although some evidence for the beneficial use of supplements exists, it has been suggested by Moyad (2002) that "embellished" past study findings may lead to an inappropriate use of dietary supplement such as selenium and that the use of selenium and vitamin E supplements for the reduction of prostate cancer risk should be reconsidered. Furthermore, two recent studies suggest that the evidence is insufficient to prove the presence or absence of benefits from use of multivitamin and mineral supplements to prevent cancer and chronic disease (Huang *et al.* 2006a,b), particularly where diets are considered adequate.

Conditions related to low concentrations of selenium in the environment include white muscle disease in cattle (Ellison 2002), Keshan disease in humans that has been linked to an endemic degenerative heart disease and an endemic osteoarthropathy (Kaschin-Beck Disease) (Fordyce *et al.* 2000) which causes deformity of affected joints (Tan 1989). Early manifestations of selenium deficiency include fatigue, cardiac arrhythmia and palpitations, loss of appetite, cardiac insufficiency and cardiomegaly; and pathological changes include multifocal myocardial necrosis and fibrosis (WHO/FAO 2004). Selenium deficiency has also been linked to a number of health outcomes which include cardiovascular diseases (Gissel-Nielsen *et al.* 1984; Rayman 2000;

Brawley *et al.* 2001; Wojtczak 2003; Klein & Thompson 2004), cancers (Gissel-Nielsen *et al.* 1984; Cao *et al.* 2001; Klein & Thompson 2004; Spallholz *et al.* 2004), and reproductive disorders (WHO 1987).

Available reports indicate that some people can tolerate severe selenium depletion without apparent adverse clinical manifestations. This is notably the case for populations living in New Zealand who seem to be extremely tolerant to low levels of selenium that are insufficient to support the maximal expression of seleno-enzymes (Duffield & Thomson 1999; De Jong *et al.* 2001; Thomson 2004). There is, however, no evidence that an individual or group can adapt to a low selenium intake, and the fact that New Zealanders are healthy is most likely due to the fact that they are otherwise well nourished, and that selenium deficiency alone does not cause metabolic impairment (G. F.Combs, personal communication). Most of the selenium enzymes are participants in redundant systems, and even low selenium intakes will support their expression at appreciable, if sub-maximal, levels.

Estimates derived from Chinese and North American studies have reported selenium daily requirement for adults between 7.4 and 80 μg/day, emphasizing the importance of basing requirement estimates on functional criteria derived from evidence describing the minimum levels of intake (WHO/FAO 2004). The determination of selenium nutrient requirements uses the risk assessment approach with results based on epidemiological evidence from study areas in China (Yang *et al.* 1983, WHO 1996). The WHO/FAO report (2004) further suggests that the most appropriate approach, until new opportunities for the development of biochemical indices of selenium adequacy are exploited, is monitoring changes in the relationship between serum selenium and dietary selenium supply. The approach to deriving selenium lower limits outlined in (WHO/FAO/IAE 1996) was adapted by WHO/FAO (2004) to "estimate population minimum intakes with adequate allowance for the variability associated with estimates of the average selenium intakes from the typical diets of many communities". The average normative requirement for selenium is used as the basis for calculating recommended nutrient intake values after interpolating estimates of average requirements by allowing for differences in weight and basal metabolic rate of age groups up to 65 years

and adding a 25% increase, i.e. 2 × assumed standard deviation, to allow for individual variability in the estimates (WHO/FAO 2004). This report also suggests that predicting selenium intake from diets rather than measuring levels could potentially result in the risk of underestimating levels in the diet greatly.

Difficulties arise when estimating selenium intake requirements. Assessing selenium requirements from simple input–output balance data is impractical due to the different mechanisms interacting at individual level between absorption, retention and excretion, resulting in experiments producing data of limited value (Levander 1987). Furthermore, intake from drinking-water is not usually included in dietary surveys and only water used to prepare food items is analysed (Donohue *et al.* 2005), although this may only be by analysis of the prepared food item with little consideration of the contribution from water. The contribution of selenium in drinking-water may in some cases represent an important proportion in the total diet, however, as this contribution is excluded from nutrient intake recommendations (Donohue *et al.* 2005), this may have significant health implications at sub-population level.

Selenium poisoning, on the other hand, may be acute or chronic and is collectively referred to as selenosis. A comprehensive assessment of the clinically significant biochemical manifestations of chronic and acute intoxication from selenium arising from high concentrations in food, drinking water, and the environment was published jointly by WHO, UNEP and ILO over 20 year ago (WHO 1987).

Several epidemiological studies and case studies have reported the link between chronic exposure to selenium compounds in the diet and adverse health effects in humans. The adverse effect of chronic high selenium exposure has been widely reported from various regions in China, where populations exhibited typical symptoms of chronic exposure to selenium, fatigue, lesions of the skin, loss of nails and hair, loss of appetite, gastrointestinal disturbances, cardiac insufficiency and congestive heart failure (Yang *et al.* 1983, 1988, 1989*a*,*b*; Yang & Xia 1995; Bratter *et al.* 1991; Ge & Yang 1993; Yang & Zhou 1994; Combs 2001). Other studies reporting signs of selenium toxicity as a result of excessive exposure through drinking-water have been conducted in rural families living in seleniferous areas in Nebraska and South Dakota (USA). Values as high as 92 μg Se/L in drinking water were reported; however, intake from other sources was not clear (Smith *et al.* 1936, Johnson & Roth 1978). Symptoms included gastrointestinal disturbances, discoloration of the skin and decayed teeth (Smith & Westfall 1937). The average dietary intake of selenium associated with selenosis has been reported to be >900 μg/day (Yang *et al.* 1989*b*; ATSDR 2003). One case of selenium poisoning directly attributable to a water source has been reported in a family that was exposed for about three months to well water containing 9,000 μg/L of selenium. They suffered hair loss, weakened nails, and neurological symptoms, but recovered once they ceased consuming water from the contaminated well (Smith & Westfall 1937; Rosenfeld & Beath 1964).

Data from studies in China indicate that in areas in which selenium intake was high but in which no symptoms of selenosis were apparent, the average daily intake was 0.75 mg/day, and in areas of chronic selenosis, selenium intake was 3.2–6.99 mg/day (Yang *et al.* 1983). However, other studies (Longnecker *et al.* 1991) have failed to identify adverse effects in populations in North Dakota consuming similar quantities of selenium to those identified in China (Levander 1994), possibly demonstrating the impact of differences in overall nutritional status. In a study of adults taking selenium supplements, Reid *et al.* (2004) found that there were no adverse effects in individuals taking 1,600 μg selenium/day and although a group taking 3,200 μg/day reported adverse effects, these did not coincide with peaks of blood selenium, and no clinical effects were observed. It may be that differences in exposure levels, at which population-level effects are detectable, relate to other aspects of diet, overall nutritional and health status. There is also the possibility of subtle (sub-clinical) effects that are not clinically apparent. For example, studies by Valentine *et al.* (1980, 1987, 1988) reported that, while no noticeable effects were experienced in populations (exposed to high or low levels of selenium) a reduction in glutathione peroxidase activities in the highly exposed individuals was observed. This was in contrast to circumstances in which selenium supplements were given to individuals who were selenium deficient and showed an increase in glutathione peroxidase activity (Valentine *et al.* 1988). Such differences could impact on the way in which the body handles other stressors and toxicants.

SELENIUM LEVELS IN THE DIET

Recommended nutrient intake derivations use both experimental and epidemiological studies, by deriving estimates of the safe range of population mean intakes and of the lower limits of both basal and normative group mean intakes. In addition, the approach for estimating RNIs can further be divided into several approaches: the clinical approach, nutrient balance, functional indicators of nutritional sufficiency (biochemical, physiological, molecular) and optimal nutrient intake (WHO/FAO 2004). A range of values can, hence, result from these different approaches, leading to public health planning and management difficulties at country and local level.

WHO and FAO (2004) have published RNIs for women at 26 µg/day and 34 µg/day for men. A study in China reports a minimal daily requirement of 55 µg/day for women and 62 µg/day for men (Yang *et al.* 1989a), while the minimum dietary requirement for the prevention of Keshan disease, an endemic cardiomyopathy prevalent amongst children and young women in selenium-deficient areas of China has been reported to be 17 µg/day (Yang & Xia 1995).

In the USA, the current RNI for selenium, established by the Food and Nutrition Board of the National Research Council (National Academy of Sciences), is 55 µg/day for male and female adults (approximately 0.8 µg/kg/day). This represents a decrease from the previous RNI of 70 µg/day for males; 55 µg/day was already the RNI for females (ATSDR 2003). The RNIs for young children are 15 µg/day between 0 and 6 months, 20 µg/day between 6 and 12 months, 30 µg/day between 1 and 3 years, 30 µg/day between 4 and 8 years and 40 µg/day between 9 and 18 years (ATSDR 2003). A higher requirement was set for pregnant and lactating women of 60 and 70 µg/day respectively (ATSDR 2003). The wide range of recommended values in different populations, highlights the complexity of setting levels for such a complex element.

SELENIUM & WATER

The control of the chemical quality of drinking-water requires the development of management plans in order to provide the basis for system protection and process control to ensure that the concentrations of chemicals present a negligible risk to public health (WHO 2004). Water quality targets are established for constituents and are expressed as guideline values for the substances of concern (WHO 2004).

A guideline value represents the level of a substance that will not pose a significant risk to health from a lifetime of exposure including accounting for differences in sensitivity across life stages. Guideline values are derived through a process that takes account of all relevant available information and normally undertakes numeric derivation through the most relevant study or studies.

In the first edition of the *WHO Guidelines for Drinking-Water Quality*, the guideline value for selenium (10 µg/L) was based on an allocation of 10% of a maximum recommended intake of 400 µg/day (WHO 1984). The associated summary statement noted that there were significant uncertainties surrounding the guideline value. The guideline value for selenium maintained in the second edition of the *WHO Guidelines for Drinking-Water Quality* (1996) was 10 µg/L based on a 1974 study in children in Venezuela, Chinese studies from Keshan region and studies in patients given selenium supplements for rheumatoid arthritis (WHO/FAO/IAEA 1996). From these studies, the no observed adverse effect level (NOAEL) in humans was estimated to be about 4 µg/kg of body weight per day, based on data in which a group of 142 persons with a mean daily intake of 4 µg/kg of body weight per day showing no clinical or biochemical signs of selenium toxicity (WHO 2004). An allocation of 10% of this calculated NOAEL to drinking water, assuming a 60 kg adult drinking 2 L of water per day resulted in a drinking water guideline value of 10 µg/L.

In most settings, the most achievable means to reduce excessive exposure to selenium through drinking-water involves changing sources or blending water from multiple sources. Where needed, reduction of selenium in water can be achieved through processes such as coagulation (50% or more removal), ion exchange (80% or more removal), activated alumina (80% or more removal) or membrane filtration (80% or more removal) (WHO 2004). Advanced oxidation processes and membrane treatment are technically complex and the cost of this type of treatment is considerable when compared to alternatives. The requirement to remove a specific substance results in

additional costs and complexities in delivering safe water that can result in other problems. It is, therefore, important that guideline values are developed that are not excessively conservative.

DISCUSSION

Selenium exhibits two interesting and challenging conundrums to public health policy and practice.

The first is shared with many nutrient minerals and relates to the fact that both toxicity and essentiality of selenium vary greatly *between individuals*. It has become more and more apparent that disease associated with inadequate or excessive intake of selenium is multifactorial in origin. Different exposures and sensitivities across life stages result in varying nutritional status among populations and individuals along with their own specific physiological and genetic characteristics. Certain populations as well as individuals are able to endure severe selenium depletion without apparent adverse clinical manifestations (e.g. New Zealand), while in other populations (e.g. USA) there are no apparent adverse effects noted at significantly higher intakes. The varying degree of exposure and sensitivities across regions as suggested by the data from New Zealand, China, Venezuela and USA illustrate the challenge in the current established recommended nutrient intakes and guidelines values, and in the importance of developing appropriate guideline values for selenium in drinking-water.

The second conundrum relates to the use of fundamentally different approaches to derivation of RNI level on the one hand and guideline values for drinking-water quality on the other, making direct comparison between the two misleading. Determination of RNI relies on 95% of the population being covered by their dietary needs. A guideline value normally represents the concentration of a constituent that does not result in any significant risk to health over a lifetime of consumption (WHO 2004).

In the case of selenium, applying these two approaches – both which seem at first glance to be in a comparable unit (i.e. ug/kg or ug/L) leads to a range between essentiality and toxicity that is apparently narrow, but is actually not directly comparable. The process of applying uncertainty factors may result in an intake below the recommended nutrient

intake (Renwick 2006). This may therefore result in making the accepted range excessively narrow with potential serious implications. Overcoming this conundrum between approaches will require aspects of toxicity and essentiality for elements exhibiting narrow and often overlapping ranges to be considered together in a harmonized manner. A level of acceptability for each needs to be reached in order to better protect human health from adverse effects resulting from exposure to either high or low quantities of chemicals such as selenium from the environment through their total dietary intake.

Overall, the data on what constitutes an essential intake of selenium are of high quality. However, the margin between what is considered an essential intake (i.e. safe and sufficient) (26 µg/day for women and 34 µg/day for men) and a level that is toxic (maximum 400 µg/day) (WHO/FAO 2004) makes the development of a guideline for drinking water that is applicable in all circumstances difficult. Differences in diet and water consumption within a specified area or within a population, might lead to intakes apparently adequate for some and excessive for others. Although how this will relate to detectable health benefits or adverse effects is also uncertain.

Most of the work relating to the safety and sufficiency of intakes of elements such as selenium takes place in developed countries. When providing guidance on selenium, it is also important to take into account several considerations that are likely to be of greater importance in developing countries. Firstly, availability and access of food imports from various regions of the world may be more widely available in the wealthier nations than in developing countries. Secondly, water sources are often community-based and limited in availability as well as suffering from limited technical resources. Small community supplies face particular challenges simply because they are small and often remote. Thirdly, health implications with respect to non-compliance may be more critical in developing countries than for developed countries, where there is an inequitable distribution of health risks, and health systems may be insufficient to deal with such problems. Some countries, for example countries in Sub-Saharan Africa, may be at higher risk with limited means to buy imported food and where people are more reliant on subsistence and rain-fed agriculture.

Significant changes in exposure (e.g. drinking water treatment) should be assessed taking into account the total diet and other known factors and monitoring for potential effects may be appropriate at local level. For example, it would be inappropriate to suggest that water should be treated to remove selenium or a supply abandoned when the overall exposure to selenium would suggest that the water could be a beneficial source of the element as part of the overall diet or if overall exposure was such that this would not be expected to result in adverse health outcomes. The *WHO Guidelines for Drinking-Water Quality* emphasize the need to adapt the guidelines to local conditions and the case of selenium is a good illustration of why this is necessary. It is also important that national standards should be sufficiently flexible to reflect specific conditions and to allow some local decisions where this will avoid unnecessary cost with little or no benefit to consumers.

CONCLUSIONS

With an increasing world population and a changing global environment, pressure on water resources will be exacerbated. Such changes are likely to result in more populations consuming waster from sources that are more extreme in their mineral constitution. This may also impact on food supplies from crops grown irrigated with such waters. Such circumstances require a holistic approach to the quality of both water and food in order to achieve the best overall solution for public health. This is particularly true of elements which are essential or beneficial but which are also capable of inducing significant adverse health outcomes, where controlling other sources than water may be more cost effective and practical. While there are a number of frameworks available, these generally only consider food, without taking water aspects into account. What is now needed is the development of a conceptual framework bringing together both aspects of toxicity and essentiality especially for elements apparently exhibiting narrow or overlapping ranges between essentiality and toxicity which includes drinking-water. Furthermore, there is a need to provide adequate guidance on both the nature and severity of risks from excessive

exposure and the nature and severity of the risks associated with deficiency.

There is a necessary difference in approach when deriving guideline values for essential minerals. Because there are benefits associated with low levels the margins that are acceptable and practical between the concentrations found in drinking water and those intakes that cause toxicity are relatively small compared to acceptable margins for substances which have no health benefits but which can be toxic at high concentrations. Because there is a much larger human database, human data are used in deriving safe and sufficient intakes, and so guideline values, there is much less uncertainty in the process. This is in contrast with most other substances for which the database is primarily toxicity in animals, and there are significant uncertainties in extrapolation.

In developing and implementing drinking water standards, values should be adjusted to take into account local circumstances, either in national standards or at a local level. In assessing exposure from drinking-water, fluid intake needs to be carefully considered in relation to the contribution of water constituents to the total diet, with some consideration of local staples and the uptake of minerals in cooking, such as is recommended for fluoride in the WHO Guidelines. However, local circumstances may include economic considerations and the availability of expertise, particularly when there are many small community supplies and limited alternatives.

Although detection of chemical elements in drinking water can be very slow, and often complex and costly, in turn limiting early warning capability, this should not so much be a consideration in the case of selenium. Firstly, detection of selenium in a water source does not require multiple analyses and remains relatively straightforward when compared to other elements. Secondly, effects of selenium in drinking water arise from prolonged exposure levels rather than short-term exposure. Such exposure may or may not pose a health risk to a population. Therefore, any subsequent action, if elevated levels were to be found in water would be to investigate potential clinical symptoms within the population.

There is a need to support the adoption a holistic approach between toxicity and essentiality, and that this approach be taken collaboratively with different sectors and

at different levels within these. Overall, reliance on determination of chemical element detection in drinking water alone is insufficient to protect public health.

This paper has discussed a number of the issues for developing guidance for chemical contaminants in drinking-water, particularly for those elements that are either essential or beneficial at relatively low concentrations and for which there are other significant sources of exposure. Selenium is a good example of the dilemmas and difficulties that are encountered and demonstrates the need to consider guidelines and standards for such constituents of drinking-water in a much more holistic way and not just from the point of view of toxicity. However, some of the issues also apply to those constituents that are not considered to provide benefits since it is important to achieve an appropriate balance between taking a precautionary approach to avoiding toxicity and the costs and practical difficulties that may be encountered by communities on the ground.

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