The Role of Selenium in Chronic Disease

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Selenium functions as a part of proteins known as selenoproteins. Through these selenoproteins, selenium functions as a defensive mechanism for oxidative stress, for the regulation of thyroid hormone activity, and for the redox status of vitamin C and other molecules. In several of its roles, selenium functions as a dietary antioxidant and thus has been studied for its possible role in chronic diseases. This article reviews recent studies regarding selenium status or supplementation in hypertension, cardiovascular disease, cancer, and diabetes mellitus. A few studies regarding aging and mortality are also included. What can be ascertained from this current review is that the maintenance of adequate selenium nutriture and, at minimum, the prevention of a deficiency in selenium would be advisable for all individuals. In addition, the indiscriminant use of selenium supplements should be approached with caution until further randomized, controlled trials monitor the effects of such supplementation, especially on a long-term basis. (Nutr Clin Pract. 2008;23:152-160)

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Selenium Basics

Functions

As reviewed previously by Boosalis and more recently by the Institutes of Medicine, selenium functions through its associations with proteins, known as selenoproteins. Through these selenoproteins, selenium functions as a defensive mechanism for oxidative stress, for the regulation of thyroid hormone activity, and for the redox status of vitamin C and other molecules. Specifically, the 4 known selenium-dependent glutathione peroxidases designated as glutathione peroxidase (GSHPx) 1 through 4 defend against oxidative stress, as do the selenoproteins P and W. Thyroid hormone metabolism is regulated by 3 selenium-dependent iodothyronine deiodinases, while 3 identified thioredoxin reductases function in the regeneration of ascorbic acid from its oxidized metabolites and for the reduction of intramolecular disulfide bonds. Other selenoproteins, such as the isoform of selenophosphate synthetase, participate in selenium metabolism. Functions of the remaining selenoproteins have not, as yet, been characterized to the same extent.

Forms

There are 2 forms of selenium in tissues: selenomethionine and selenocysteine. Selenomethionine is initially synthesized in plants and incorporated randomly in place of methionine in a variety of proteins. It cannot be synthesized by humans, nor does it have any known physiological function apart from that of methionine. Selenocysteine, on the other hand, accounts for the biological activity of selenium in the aforementioned selenoproteins and does not substitute for cysteine in humans. The major form of dietary selenium is selenomethionine. It is estimated to account for at least 50% of selenium in the diet. It, along with selenocysteine, is well absorbed and highly bioavailable. Even the 2 inorganic forms of selenium, selenate and selenite, used frequently in the fortification of foods and/or as dietary supplements, have a bioavailability that exceeds 50%.

Body Pools

There are 2 pools of selenium body stores. Selenomethionine, as it is catabolized by the transsulfuration pathway, provides selenium, yet this turnover of the methionine pool does not respond to the body’s need for selenium. The second body pool is the selenium present in the liver as GSHPx-1. This latter source of selenium
will respond to the body’s need for selenium when required for the synthesis of other selenoproteins.

**Determination of Status**

As reviewed in the dietary reference intake (DRI), the concentration of selenium in the plasma is useful for assessing all forms of selenium when the concentration of the element is low (<0.8 μmol/L [7 μg/dL]). At this level, the synthesis of the various selenoproteins has as not yet plateaued. Three selenoproteins—GSHPx-3, selenoprotein P, and GSHPx-1—have also been used to assess selenium status. Of these 3, the plasma concentration of GSHPx-3 has recently been preferred since its determination is more accurate than that of the erythrocyte enzyme GSHPx-1. Selenoprotein P, a major form of selenium in plasma, is also a good indicator of selenium status, likely equivalent to plasma GSHPx-3, but since its assay is not routinely or broadly available at present, it is not routinely used to estimate a dietary requirement. Toenail concentrations of selenium have been used in epidemiologic studies to assess long-term status selenium status. Most studies reviewed in this article use the concentration of selenium in the blood or plasma to assess selenium status.

**Deficiencies**

The only disease firmly linked to selenium deficiency in humans is Keshan disease, a cardiomyopathy that occurs primarily in children. This disease occurs in areas of selenium deficiency in China with varying frequency. In addition to a dietary deficiency of selenium, decreased levels of selenium in the blood and hair are observed. Keshan disease generally does not occur in populations when the per capita adult selenium intake is 17 μg (0.22 μmol/day) or greater. Another disease, Kashin-Beck disease, has been observed in a few of the selenium-compromised areas of Asia. Kashin-Beck is a widespread disease of cartilage that occurs in preadolescence or adolescence that may occur only in selenium-deficient individuals. On the other hand, since improvement of selenium status has not been demonstrated to prevent Kashin-Beck disease, the role of selenium in its pathogenesis remains uncertain. Other reports of either selenium deficiency or possible compromise in selenium status include individuals receiving parenteral nutrition without added selenium (as reviewed by Boosalis) and thermal injury. Circulating levels of selenium also appear to be decreased during an acute-phase response (currently referred to as a systemic inflammatory response) and following surgery. The DRI, established as a recommended dietary allowance (RDA), is set at the level of selenium that is based on the quantity required to maximize the synthesis of the selenoprotein GSHPx, as determined by the plateau in the activity of the plasma isoform of this enzyme. Generally, this plateau is achieved at a serum or plasma selenium concentration >0.8 to 1.1 μmol/L (7.9 μg/dL). Specifically, the RDA is 55 μg/d for adults and varies according to life stage group, beginning at 15 to 20 μg/d for infants and reaching adult levels by 14 years of age.

**Excesses**

Along with the RDA for selenium, a tolerable upper intake level (UL) has also been established using a risk assessment model. This model establishes the highest daily intake level of a particular nutrient that is likely to pose no risk of adverse health effects to almost all individuals in the general population and, in particular, the most sensitive or vulnerable. The UL for selenium in individuals 14 years of age and older is 400 μg/d based on the adverse effect of selenosis, in particular, the findings of hair and nail brittleness and loss. As reviewed by Boosalis and the DRI report, other signs of selenosis (besides the hair and nail brittleness and loss) include nausea, vomiting and other gastrointestinal disturbances, skin rash, garlic breath odor, fatigue, irritability, and abnormalities of the nervous system including peripheral neuropathy. The UL for selenium decreases for younger individuals and varies between 45 and 280 μg/d. All healthy individuals should be advised against routinely exceeding the UL. It should be noted that the UL for selenium includes intake from both diet and supplements.

**Sources**

The content of selenium in the particular foodstuff reflects the content of selenium in the soil and can vary 10-fold depending on where the plant was grown or the animal raised. Plants do not seem to have a requirement for selenium, whereas animals do. As a result, meat and seafood are the most dependable sources of selenium, although their content of selenium still varies depending on the content of selenium in their respective food supplies. As a result, published food tables that indicate average selenium contents are not reliable. In addition, drinking water in most countries studied does not provide a nutritionally significant source of selenium.

**Content in Diet**

Given the unreliability of food tables to assess dietary intake of selenium, a direct analysis of selenium in the foodstuffs has been necessary. Several studies, details of which are beyond the scope of this article, have been carried out in both the United States and Canada. All findings indicate that residents of the United States and Canada have access to adequate amounts of selenium in their diets to meet their particular DRI. For instance, the...
median calculated intake of selenium in the diet from one report was 87 \( \mu g \) (1.1 \( \mu mol/d \)), with a range of 79 to 104 \( \mu g \) (1.0-1.3 \( \mu mol/d \)). In Canada, the intake of selenium may be somewhat higher, ranging from 113 to 220 \( \mu g \) (from 1.4 to 2.8 \( \mu mol/d \)). In other words, most individuals in the United States and Canada can meet their DRI of selenium with their usual diet.

**Geographic Influences**

Given that the dietary intake of selenium varies across populations and is dependent on both dietary intake (eg, vegetarian vs meat eating) and geographic origin of foodstuffs, the across-population comparisons of selenium's role in chronic disease is more challenging. Many of the studies included in this review originated in geographic regions where the selenium content of the soil may be low. This in turn may influence the outcome of these studies as well as the transferability of their results. The reader is asked to keep these considerations in mind when comparing studies. The extensive transport of food through most of the United States and Canada also lessens any effect that geographic areas of low selenium content may have. This may not be the case in other countries where primarily regional or locally grown foods are eaten. In addition, the current trend and emphasis in the United States for eating locally grown and raised foods may in the future create selenium concerns if the content of the soil in these local areas is marginal or low in this element.

**Role in Chronic Disease**

With this background and overview in mind, a review of the purported role of selenium in chronic diseases begins. The purported role for selenium in chronic disease most likely stems from its certain selenoproteins that function in oxidant defense and, as such, function as dietary antioxidants.

A dietary antioxidant, as defined by the Food and Nutrition Board of the Institute of Medicine, is “a substance in foods that significantly decreases the adverse effects of reactive species, such as reactive oxygen and nitrogen species, on normal physiological function in humans.” Further criteria for this definition are that the dietary antioxidant in question is normally found and quantified in foods routinely consumed in human diets and that this substance decreases the adverse effects of reactive species, in vivo, in humans. Besides selenium (in the form of selenocysteine or selenomethionine), vitamin C and vitamin E are the other food components that meet this definition of a dietary antioxidant. Of interest, other dietary components such as \( \beta \)-carotene and the other carotenoids do not meet this definition of a dietary antioxidant, but they can influence biochemical reactions that involve the oxidative process. Only the potential role of selenium in oxidative stress and chronic disease will be included in this review. When considering the role of oxidative stress in the etiology of chronic diseases, it must be remembered that an entire population is exposed to these types of stresses through oxidative metabolism, but only some individuals in the population develop a chronic disease. Therefore, more research into the exact contribution, if any, of oxidative stress in the etiology of chronic disease is still needed.

For this current review, the possible role of selenium in the etiology or development of hypertension, cardiovascular disease, cancer, and diabetes is included. Only included are studies in the literature since publication of the DRI report, as that report had already reviewed and included all prior relevant studies to date and concluded that although vitamin C, vitamin E, and selenium have been shown to decrease the concentrations of some of the biomarkers associated with oxidative stress, the relationship between such observations and chronic disease remains to be elucidated. As a consequence, it has not been possible to establish that dietary antioxidants or other nutrients that can alter the levels of these biomarkers are themselves causally related to the development or prevention of chronic diseases.

**Selenium and Hypertension**

Nawrot et al\(^{10}\) reported an association between low blood selenium levels and blood pressure readings in a group of Flemish men. Interestingly, this association was not observed in the women in this study group of 710 randomly selected individuals living in 6 rural districts of Belgium in 1991 to 1995. Specifically, using a multivariate-adjusted cross-sectional analysis, these researchers observed that a 20-\( \mu g/L \) (~1 SD) higher value for average selenium concentration in the blood (BS\( e \)) was associated with a lower blood pressure, with effect sizes of 2.2 mm Hg (~1 SD) systolic (95% confidence interval [CI], –0.57 to –5.05; \( P = .009 \)) and 1.5 mm Hg diastolic (95% CI, –0.56 to –2.44; \( P = .017 \)). While these findings were significant, they are not likely clinically relevant. On the other hand, a prospective follow-up on these male participants for an average of 5.2 years (range, 3.4-8.4 years) found that a 20-\( \mu g/L \) higher baseline value for mean BS\( e \) concentration was associated with a 37% (95% CI, –52 to –17; \( P = .001 \)) lower risk of developing a blood pressure of 135/85 mm Hg (high-normal) or greater (hypertension), which may be of public health importance. Again, there was no association between blood selenium levels and blood pressure in women.

Babalola et al\(^{11}\) studied a group of 103 hypertensive patients (44 men and 59 women) and 88 apparently healthy subjects (40 men and 48 women) recruited from
Abeokuta and Ibadan (southwestern Nigeria). The individuals with hypertension (HTN) were classified into 3 groups as follows: group 1, mild HTN with a diastolic blood pressure (DBP) of 90 to 99 mm Hg or systolic blood pressure (SBP) of 140 to 159 mm Hg; group 2, moderate HTN with a DBP of 100 to 109 mm Hg or SBP of 160 to 179 mm Hg; and group 3, severe HTN with a DBP ≥110 mm Hg or SBP ≥180 mm Hg. The mean age of the hypertensive patients was 41.9 ± 10.3 (range, 21-68) years, while the mean age of the healthy subjects was 37.8 ± 8.6 (range, 18-52) years, which was significantly different at \( P < .01 \). The mean BSe concentration was significantly lower in the hypertensive patients (0.136 ± 0.028 mg/L) compared with the healthy controls (0.188 ± 0.026 mg/L; \( P < .001 \)). However, with respect to plasma GSH-Px activity, there was no statistically significant difference between the hypertensive patients (0.126 ± 0.019 U/mL) and the healthy controls (0.127 ± 0.022 U/mL). While the BSe concentrations in groups 1 and group 2 were not significantly different, there were significant differences in the BSe levels of patients between group 2 and group 3 (\( P < .05 \)) and between group 1 and group 3 (\( P < .05 \)), suggesting that BSe concentrations may decrease as the severity of HTN increases. Whether this association is causative or is a secondary phenomenon remains to be determined.

Nonetheless, these 2 studies suggest that there may be a relationship or association between low levels of circulating selenium and blood pressure or HTN. These findings require further confirmation because previous studies \(^ {32-34} \) have been equivocal or negative. In summary, it would appear that adequate selenium status should be maintained at a minimum. Whether additional supplementation is warranted in individuals with HTN or to prevent HTN from occurring still requires further study and independent confirmation by prospective, double-blind, randomized, controlled trials.

**Selenium and Cardiovascular Disease**

Flores-Mateo et al \(^ {35} \) performed a meta-analysis of the relationship between selenium and coronary heart disease. This meta-analysis included 25 observational studies (14 cohort and 11 case-control studies) and 6 randomized trials of selenium supplementation. A moderate but statistically significant inverse association between selenium concentrations and coronary heart disease was observed. In the observational studies, a 50% increase in selenium concentrations was associated with a 24% reduced risk of coronary events. In the few randomized trials that were reviewed, a small, nonsignificant reduction of \(-11\%\) in coronary events was observed. It should be noted that most of those studies supplemented more nutrients than just selenium. Despite these findings, the authors question the validity of any association because of the nature of observational studies and state that “the evidence is still inadequate to establish a protective role of selenium in coronary heart disease” \(^ {35} \) and therefore should not be recommended.

Given the known role of selenium deficiency in the etiology of Keshan disease, an endemic cardiomyopathy in China, the role of selenium in chronic heart failure has also been considered. Several research groups have suggested or speculated that selenium levels may either be low or possibly compromised in individuals with chronic heart failure, \(^ {36-39} \) yet any reported findings have been far from conclusive. Kosar et al \(^ {39} \) found serum concentrations of selenium to be significantly lower (\( P = .000 \)) than in healthy controls, yet these decreased levels were still well within normal limits. Further double-blind, randomized, controlled trials are needed to address this possible association.

**Selenium and Cancer**

Trumbo \(^ {40} \) published a summary of the evidence reviewed to determine if a health claim for selenium’s role in cancer would be allowed. Beginning in 2003, the US Food and Drug Administration (FDA) released a Consumer Health Information for Better Nutrition Task Force report that outlined an evidence-based ranking system to evaluate petitioned health claims for foods based on scientific evidence. Since the release of this report, numerous health claims for food components and food labels have been submitted for approval by the FDA. The review process regarding health claims regarding selenium and cancer actually began in 2002. At that time, 5 intervention trials were reviewed. \(^ {41-45} \)

In 2 of those studies, \(^ {41,42} \) selenium was given along with other micronutrients; thus, any potential independent effect of selenium on cancer risk reduction was impossible to ascertain despite reports of significance. Two of the remaining 3 trials \(^ {43,44} \) were conducted in China, a country known for its areas of selenium deficiency. Included in these aforementioned trials were also individuals with documented malnutrition. With this in mind, Yu et al \(^ {43} \) found a lowered incidence of liver cancer and Blot et al \(^ {44} \) a lower incidence of mortality from stomach cancer. The remaining intervention trial reviewed by the FDA was the Nutritional Prevention of Cancer Trial. \(^ {45} \) This study evaluated whether selenium supplementation of 200 μg/d of high-selenium brewer’s yeast in 1312 subjects could reduce the risk of basal and squamous (nonmelanoma) skin cancers. While supplementation with selenium showed no protective effect against these skin cancers, a post hoc analysis of the data found a statistically significant decrease in several secondary end points including total, lung, colorectal, and prostate cancers in a separate but related study. \(^ {36} \) After a careful review of these aforementioned studies, despite
their flaws and limited numbers, a qualified health claim regarding a relationship between selenium and cancer was allowed by the FDA. Specifically, this means that any health claim regarding selenium and cancer must be qualified by stating that the “FDA has determined that this evidence is limited and not conclusive.”

Several studies have been published since these aforementioned studies that were reviewed to document the qualified health claim regarding selenium and cancer. Specifically, Wei et al. 47 examined the relationship between baseline serum selenium levels and the subsequent risk of death from esophageal squamous cell carcinoma, gastric cancer, and gastric noncardia cancer over 15 years of follow-up (1986-2001) in a nested study from the Nutrition Intervention Trial in Linxian, China. Cox proportional hazards regression models were used to estimate relative risks (RRs) and 95% CIs; the reported RRs estimated the change in risk conferred by a 25% increase in serum selenium relative to the population distribution. In addition, all estimates were adjusted for age, gender, smoking, drinking, and serum cholesterol level. Significant inverse associations between baseline serum selenium and death from esophageal squamous cell carcinoma (RR, 0.83; 95% CI, 0.71-0.98) and gastric cancer (RR, 0.75; 95% CI, 0.59-0.95) were observed in the 1103 subjects randomly selected from the initial cohort. Yet 69% of these subjects (766/1103) were selenium deficient, which may partially explain why the observed associations were significant. In other words, if selenium status had been adequate in this cohort to begin with, perhaps this association would not have been significant. Indeed, the 96th percentile (1.19 μmol/L) in the study cohort was lower than the 1st percentile (1.20 μmol/L) in the third National Health and Nutrition Examination Survey (NHANES III).2

A subsequent review by Haung et al. 48 of studies through February 2006 looked at the efficacy and safety of multivitamin and mineral supplements for the prevention of cancer and other chronic diseases in adults, some of which included selenium. Five randomized, controlled trials that included a total of 47,289 persons in 12 published articles 14,49-59 (the Linxian General Population Trial in China, the SU.VI.MAX trial, 53-55 all participants took a single daily capsule containing 120 mg of ascorbic acid, 30 mg of vitamin E, 6 mg of β-carotene, 100 μg of selenium, and 20 mg of zinc, or a placebo. This study was a randomized, double-blind, placebo-controlled primary prevention trial in which a total of 13,017 French adults (7876 women aged 35-60 years and 5141 men aged 45-60 years) were included and followed for a median follow-up time of 7.5 years. Interestingly, the combined supplementation with vitamin C, vitamin E, β-carotene, selenium, and zinc reduced the rate of cancer by 31% in men but not in women. The study authors speculated that the women were in better physical and nutritional health at the onset of the study compared with the men. While this study might support that a combination of antioxidant nutrients should be taken to reduce cancer, at least in men, any independent effect of selenium on reducing the rate of cancer in this study is impossible to ascertain. Despite these and similar findings, the authors of this review concluded that very little data on safety or efficacy of multivitamin and mineral supplements for use by the general population in the primary prevention of chronic disease currently exist, even though the existing data do suggest a potential benefit of this type of supplementation in persons who either have a suboptimal intake of antioxidants or are overall in poor nutritional status. Yet the applicability of these latter findings to the general US population is limited because of differences in the study sample and in the type and doses of the supplements used. 48

Since studies to date have been suggestive but not necessarily conclusive regarding the role of selenium in various cancers, the National Cancer Institute funded the randomized, controlled Selenium and Vitamin E Cancer Prevention Trial (SELECT). 60 This trial in more than 35,000 men was designed to determine if supplementation of 1 or both vitamin E and/or selenium prevents prostate cancer. This trial began in 2001 and enrolled its last man in 2004; follow-up is to continue for 7 years from the day of the last enrollment. More than 400 sites across the United States, Canada, and Puerto Rico are involved. Men who participate in this study are randomly assigned to take 2 capsules per day, either selenium and vitamin E, selenium and a placebo, vitamin E and a placebo, or 2 placebos; samples of toenails and blood are being collected, an annual questionnaire is administered, and individuals pick up their capsules every 6 months. Results of this extensive, well-controlled study are not expected before 2011 to 2012; however, the results should assist in determining the role of selenium, if any, in prostate cancer and possibly other measured cancer and/or chronic disease end points. As an example, 1 subset of the SELECT study is the Prevention of Alzheimer’s Disease by Vitamin E and Selenium prevention trial, 61 which will look for the presence of memory loss and dementia in a subset of the SELECT study participants.
Selenium in Diabetes Mellitus

Since the publication of the DRI report, there have been several studies suggesting that selenium levels were or may be compromised in individuals with diabetes or chronic pancreatitis and diabetes and possibly in women with gestational diabetes. In addition, Faure et al. observed a significant decrease in elevated nuclear factor-κ B (NFκB) binding activity in individuals with diabetes who were supplemented with selenium. These decreased levels of NFκB activity were similar to those observed in the nondiabetic controls. These findings suggest that oxidative stress in these individuals with diabetes may in fact be reduced by selenium. The reader is referred to an article by Beckett and Arthur for a general review of the postulated role of selenium in the endocrine system.

In contrast to these earlier findings, 2 recent studies have provided either contradictory evidence or evidence questioning selenium’s relationship or role in diabetes. Bleys et al. observed a nonlinear relationship between selenium and the prevalence of diabetes. This group conducted a cross-sectional analysis of 8876 adults (20 years of age and older) who participated in the NHANES III. In this cross-sectional analysis, the study subjects in the highest quintile of serum selenium had a statistically significant increase in their prevalence of diabetes compared with those in the lowest quintile. Interestingly, no clear dose-response pattern in the 3 middle quintiles was observed. In the same year, Stranges et al. reported findings from the Nutritional Prevention of Cancer trial, which observed an increased risk for diabetes among those study participants who were randomly assigned to receive the 200 μg of selenium as selenized yeast for 7.7 years compared with placebo. This unexpected finding was primarily limited to those participants who had selenium levels in the highest tertile (>121.6 ng/mL) at baseline. In fact, the hazard ratio for incident diabetes in persons using the selenium supplements versus placebo was 2.70 (95% CI, 1.30-5.61). Granted, the individuals in this trial were older, had nonmelanoma skin cancer, and were not originally followed for incidence of type 2 diabetes. Nonetheless, the authors urged that supplementation with selenium in individuals with diabetes be avoided until further randomized control trials could be conducted to address this possible adverse relationship. Specifically, since the dietary intake of selenium in most individuals in the United States is adequate, Bleys et al. in an accompanying editorial, wrote that “by taking selenium supplements on top of an adequate dietary intake, people may increase their risk for diabetes.”

Additional Effects of Selenium

Aging, while itself not a chronic disease, is often associated with the presence of a chronic disease. While aging was not considered in this review, some of the studies included in this review were in older individuals, many of whom showed compromised selenium status. The question often asked is, “Do antioxidants have a role in slowing or preventing aging and/or prolonging life?” Studies suggest that selenium and carotenoids can assist in the redox regulation that is involved with inflammation. Inflammation, in turn, can be indicated by the presence of an acute phase or systemic inflammatory response, which has been associated with decreased levels of the carotenoids and an increased mortality among men, not women. Similar findings, as previously mentioned, have been observed for selenium. Recently, Ray et al. found that women who had serum concentrations of either selenium or carotenoids in the lowest quartile had a lower survival rate when compared with women in the upper 3 quartiles (P = .0009 for selenium, P = .01 for carotenoids, by log-rank test for both). The reader is referred to that article for a further discussion of this concept. Interestingly, another study followed serum selenium levels longitudinally in a group of elderly men and women as part of the Etude du Vieillissement Arteriel study. Several contributing factors increased the longitudinal decline in plasma selenium that was observed during this 9-year follow-up. One of these factors was obesity (P = .02). While it is beyond the scope of this article to explore this association further, if validated by further trials, the association between selenium and obesity will need to be monitored and addressed given the current epidemic of obesity.

To address the effect of antioxidant supplementation and mortality, Bjelakovic et al. looked at studies regarding all-cause mortality and antioxidant supplementation that had been published to date. Randomized trials involving adults comparing β-carotene, vitamin A, vitamin C (ascorbic acid), vitamin E, and selenium either singly or combined versus placebo or versus no intervention were included in this analysis. Briefly, after careful review with and without the inclusion of high-/low-bias trials, the authors concluded that “treatment with beta carotene, vitamin A, and vitamin E may increase mortality. The potential roles of vitamin C and selenium on mortality need further study.” It is obvious that no clear-cut answers regarding selenium and/or antioxidant supplementation and mortality exist at the present. Further randomized, controlled trials may address some of these questions in the future.

Conclusions

The studies published since the DRI herein reviewed suggest that while there may be a possible beneficial effect of selenium supplementation in individuals who have hypertension, cardiovascular disease, and/or certain cancers, further randomized controlled trials are necessary for a definite and conclusive answer.
More important, the safety of selenium supplementation in individuals with diabetes, who had adequate selenium, has been strongly questioned.\textsuperscript{67,68,70}

What can be ascertained from this current review is that the maintenance of adequate selenium nutriture and, at minimum, the prevention of a deficiency in selenium would be advisable for all individuals. In addition, the indiscriminant use of selenium supplements should be approached with caution until further randomized controlled trials monitor the effects of such supplementation, especially on a long-term basis. As previously mentioned, results from the SELECT study,\textsuperscript{60} with accompanying analyses, should shed more light on the risks and/or benefits of selenium supplementation in cancer and perhaps other chronic diseases.

References


