Beyond Copper, Iodine, Selenium and Zinc: Other Elements That Will be Found Important in Human Nutrition by the Year 2000

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Over 30 years ago, excitement abounded about the trace elements which were considered the new breakthrough for better health. One trace element after another was identified as essential, or at least suggested to be essential. As these elements were identified, hopes were raised that trace element nutriture was the answer to the puzzle of the cause of some diseases, especially chronic diseases associated with aging. Unfortunately, those hopes have not been realized. Except for iodine, iron, and possibly selenium, trace elements, especially the newer, or ultratrace elements, are not generally thought of as having any widespread clinical importance.

There are probably several reasons that the vision of the past for the trace elements has not materialized; among them would be the following: 1) There is a paucity of clinically useful methods for assessing human trace element status. 2) There is a lack of appreciation for the paradigm that trace and ultratrace elements are most important, or will produce marked pathology only when a nutritional, metabolic, hormonal, or physiological stressor is present that enhances the need, or interferes with the utilization of an element. 3) There is a lack of recognition that the response to a low dietary intake of a mineral element will vary in extent and nature among individuals. Of course, the reason for the unfulfillment of the vision could be that the trace elements really are of minor clinical importance; however, I believe this is not true and that research through the year 2000 will overcome the shortcomings listed above and bring about the realization that trace elements are important for health and well-being; this includes showing that copper and zinc are more important than currently acknowledged.

Perhaps the major reason that the newer, or ultratrace elements, are thought to be nutritionally unimportant is that a specific biochemical function has not been defined for any of the at least 15 elements suggested to be essential since 1959. That is, the lack of a defined function has inhibited the acceptance of any of the ultratrace elements as being nutritionally essential and thus results in the opinion that they do not prevent deficiency diseases; therefore none are important. This viewpoint is often expressed although several of the ultratrace elements have been shown to have effects suggestive of an essential function, and if not this, to have beneficial actions in humans or animal models. In other words, this viewpoint ignores past history which has taught us that a defined essential function is not necessary for a substance to be nutritionally important (e.g., fiber has health benefits). Additionally, it ignores an emerging paradigm in which a nutrient does not have to prevent a deficiency disease to be clinically important. This paradigm is exemplified by a number of recent nutritional recommendations that are based on total health effects, not on the basis of deficiency or essentiality paradigms, including the high intake of antioxidants to protect against the deleterious effects of reactive oxygen radicals, and high intakes of nutrients to help prevent pathological conditions (e.g., calcium for osteoporosis).

Those who research the possible nutritional importance of elements other than copper, iodine, iron, zinc and selenium should be encouraged by, and those who criticize or scorn the use of resources to study

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the ultratrace elements should contemplate the selenium story. Selenium was first suggested to be essential in 1957 based on findings with vitamin E-deficient animals. Even today it is difficult to produce signs of pathology caused by a simple dietary selenium deficiency in animals or humans; a stressor such as vitamin E deficiency or a viral infection is needed to obtain marked pathology. Between 1957 and 1972 selenium was viewed mainly as being of toxicological, especially carcinogenic, concern. Fifteen years after it was suggested to be essential a biochemical function was finally identified for selenium. Since then, many resources and numerous researchers have been devoted to the study of selenium. Yet, only recently, or about 40 years after being suggested as being essential, has selenium become recognized as possibly having widespread clinical or nutritional importance, based upon its effect on viral virulence (Beck et al. 1994) and its protective effect against certain cancers (Clark et al. 1996).

Based on the findings coming forth about the ultratrace elements, I believe in the year 2000 we will become cognizant of other elements with a chronicle similar to that of selenium. These elements probably are among a disparate group of 17 for which there are reports suggesting that they are nutritionally important. The 17 are manganese and molybdenum which have known essential functions but no unequivocally identified practical nutritional importance; boron and chromium which have apparent beneficial, if not essential, actions in humans, but no specifically identified biochemical roles; nickel and vanadium which have identified biochemical roles in lower forms of life and an impressive number of reports describing deprivation signs in animals; arsenic and silicon for which there are reported deprivation signs for animals, and an arsenic-methylating enzyme has been identified in higher animals including humans while silicon has been found to be essential for some lower forms of life; fluorine and lithium which have beneficial pharmacologic actions, but rather limited evidence for essentiality; and finally, aluminum, bromine, cadmium, germanium, lead, rubidium, and tin which have some bits of credible evidence from animal models to suggest that they have at least positive effects under some situations.

Based on the findings reported to date, two elements of the 17 listed above that research in the year 2000 will most likely find to be of practical nutritional or clinical importance are boron and chromium; they will be discussed briefly here. Other good candidates that will not be discussed include arsenic, manganese, silicon and vanadium.

Chromium. At present, chromium is a very controversial element in regards to its nutritional significance. On one side are the zealots who claim that ingesting chromium, most often as a chromium supplement such as chromium picolinate, has numerous beneficial effects; these include building muscle, losing weight without dieting and exercising, and preventing diabetes, osteoporosis, heart disease and aging. On the other side are the disbelievers who feel there is no credible evidence to support most of these claims, and that chromium nutrient, if chromium is an essential nutrient, is an inconsequential concern for almost everyone. However, evidence accumulating since 1959 indicates that the true situation for chromium is somewhere between these two positions.

A recent review (Nielsen 1994a) discloses that there is a large amount of circumstantial evidence which supports the view that chromium is an essential nutrient. The evidence includes the finding that humans on long-term total parenteral nutrition containing a low amount of chromium developed impaired glucose tolerance, or hyperglycemia with glucose spilling into the urine, and a resistance to insulin action; these abnormalities were reversed by chromium supplementation. Additionally, there have been a number of reports from numerous research groups that describe beneficial effects of chromium supplementation of subjects with varying degrees of glucose intolerance ranging from hypoglycemia to insulin-dependent diabetes (Anderson 1993, Ravina et al. 1995). Beneficial effects of chromium supplementation on blood lipid profiles also have been reported. Thus, even the skeptics usually accept the fact that chromium can at least be a beneficial element in some situations.

Although a dietary recommendation of 50 μg/d has been established for chromium in the U.S. (National Research Council 1989), balance studies have demonstrated that people maintain metabolic chromium balance despite consuming diets supplying much less than this (Offenbacher 1992). Additionally, the average daily intake of chromium in the U.S. apparently is well below 50 μg and may be closer to 25 μg, yet widespread apparent cases of chromium deficiency have not been documented. That is, supplemental chromium fed to many individuals apparently consuming chromium at these low amounts did not result in any beneficial effect. Thus, a daily intake of 25 to 35 μg of chromium may be adequate.
On the other hand, some data suggest that an intake of less than 20 μg/d is inadequate. Based on dietary surveys, there are a significant number of people consuming less than 20 μg Cr/d. As a result, it is not surprising that a large number of studies have found individuals that respond to chromium supplementation. Hopefully, research by the year 2000 will identify the mechanism through which chromium affects glucose and lipid metabolism because this knowledge is likely to help confirm the apparent need for concern about inadequate chromium nutriture affecting health and well being of a significant number of people.

**Boron.** Since 1981 circumstantial evidence has been accumulating which suggests that boron is an element of nutritional concern. In humans and animal models a dietary deprivation of boron has consistently resulted in changed biological functions that could be construed as detrimental, and were preventable or reversible by an intake of physiological amounts of boron. Findings involving boron deprivation of humans have come mainly from two studies (Nielsen 1994b) in which men over the age of 45, postmenopausal women and postmenopausal women on estrogen therapy were fed a diet containing about 0.25 mg B/2000 kcal for 63 d, and then fed the same diet supplemented with 3 mg B/d for 49 d. The effects of boron supplementation after depletion included an effect on calcium metabolism evidenced by increased serum 25-hydroxycholecalciferol; an effect on energy metabolism evidenced by increased serum triglycerides; an effect on nitrogen metabolism indicated by decreased blood urea nitrogen and serum creatinine; and an effect on oxidative metabolism indicated by increased erythrocyte superoxide dismutase and serum ceruloplasmin. Boron repletion after depletion also enhanced the elevation in serum 17β-estradiol and plasma copper caused by estrogen ingestion (Nielsen 1994b), altered encephalograms such that they suggested improved behavioral activation (e.g., less drowsiness) and mental alertness, and improved psychomotor skills and the cognitive processes of attention and memory (Penland 1994). Changes similar to those found in humans also have been found in animal models (Hunt 1994).

The findings described above indicate that people consuming about 0.25 mg B/d respond positively to boron supplementation, which suggests that boron intakes should be higher than this. Extrapolations from animal data have resulted in the suggestion that humans may benefit or have a boron requirement between 0.5 and 1.0 mg/d (Nielsen 1992). Because many people consistently consume less than this amount, by the year 2000 boron most likely will be recognized as an element of clinical and nutritional importance.

**References**


