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Linking Agricultural Production Practices to Improving Human Nutrition and Health

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Background/Biographies of Authors:

Ross M. Welch received his BS degree in soil science from Calif. Polytechnic Univ., San Luis Obispo and his MS and PhD degrees in soil science/plant nutrition from the Univ. of Calif., Davis. He was a Lead Scientist at the USDA-ARS, Robert W. Holley Center for Agriculture and Health at Cornell Univ. until his retirement in 2009. He is a Professor (Courtesy) of Plant Nutrition, Department of Crop and Soil Sciences, Cornell Univ., a Guest Professor, Department of Food Sci., Cornell Univ. and a Guest Professor, Zhejiang Univ., Hangzhou, P.R. China. He is co-founder of the HarvestPlus Challenge Program, a Gates Foundation-funded consortium working to improve the diets of resource-poor subsistence farmers in developing countries by plant breeding and fertilizer strategies. He is a member of the Advisory Board of HarvestPlus China (since 2004). He is a Fellow of the Am. Soc. Agronomy and the Soil Sci. Soc. Am. He received the Research Award, N.E. Regional Sec., Am. Soc. Agron. (1992), the USDA-ARS North Atlantic Area Senior Scientist of the Year Award (2003), National USDA-ARS Outstanding Senior Scientist of the Year Award (2003). He was promoted to Super Grade in by the USA Federal Government in 2006. He has 46 years of experience in research and teaching. His research has focused on how to improve the nutritional quality of major food crops especially with micronutrient (e.g., iron, zinc, selenium, etc.). He is a world authority on the micronutrient nutrition of plants and on how to improve the bioavailability of micronutrients in food crops to humans. He has also strived to demonstrate the importance of agriculture in human nutrition and health and in using food system approaches to improving the health and felicity of the resource-poor in the developing world.

Robin D. Graham is an agronomist who took degrees in chemistry, soil science, and plant nutrition before joining the University of Adelaide in 1970 as Lecturer in Agronomy. He held the position of Professor in Plant Science there from 1995-2001, and is currently Honorary Professor, School of Biological Sciences, Flinders University of South Australia. He was Deputy Head, Dept. of Agronomy 1986-7 and Head, Dept. of Plant Science 1992-93. He was Adjunct Professor in Soil and Crop Sciences at Cornell University (1993-2006) and Scientific Coordinator of The CGIAR Micronutrients Program involving five CGIAR international and agricultural research centers and national programs in 14 countries, 1994-2003 and consultant to the International Rice Research Institute 2001-06. He won a Royal Society bursary, 1975-76, and was a Fulbright Senior Professional Fellow in 1990 and 1998 and the 2008 C.M. Donald Medalist of the Australian Society of Agronomy. He is co-founder of the HarvestPlus Challenge Program, a Gates Foundation-funded consortium working to improve the diets of resource-poor subsistence farmers in developing countries by plant breeding and fertilizer strategies. He is a member of the Advisory Board of HarvestPlus China (since 2005), Professorial Fellow of Flinders University and Research Associate of the International Food Policy Research Institute, Washington D.C. His research interests include micronutrients in the food chain; cultivar differences among staple-food crops in ability to extract micronutrients from soils, especially soils of low general fertility, and the genetics and molecular biology of such traits; cultivar differences in ability to load micronutrients into food grains, and the genetics and molecular biology of such traits; the role of adequate micronutrient nutrition in resistance to disease, product quality in general and in the sustainability of cropping systems. Nutrients of particular interest include iron, zinc, copper, manganese, selenium, iodine and boron, as well as the yellow pigments in cereal grains.

Ismail Cakmak received his Ph.D. (1988) at the University Hohenheim in Stuttgart, Germany. He is Professor at the Sabanci University, Biological Sciences and Bioengineering, in Istanbul, Turkey. Before joining the Sabanci University in 2000, he was working at Cukurova University in Adana, Turkey. He is an editorial board member of the journal "Plant and Soil" (Springer) and Review Editor of "Frontiers in Plant Nutrition" (Frontiers Journals). He was also “Honorary Theme Editor” of the “Encyclopedia of Life Support Systems” and edited the section entitled “Impacts of Agriculture on Human Health and Nutrition “published by UNESCO. He is recipient of the IFA (Intl' Fertilizer Assoc.) 2005 "International Crop Nutrition Award", Australian Academy of Technological Sciences and Engineering "Derek Tribe Award Medal” in 2007 and the TUBITAK (The Scientific and Technical Research Council of Turkey)-Science Prize in 1999. He was elected (September, 2012) a member of "Academia Europea". He has published over 135 peer-reviewed journal articles, receiving more than 5750 citations (H-Index: 42) and 7 book chapters. A key achievement was identification and correction of zinc (Zn) deficiency problem in cereals by Zn fertilization trials in Turkey during the mid-1990s under a project supported by NATO-Science for Stability Program. This project yielded significant scientific results as well as spectacular economic outcomes. The Turkish Ministry of Agriculture estimated economic benefits from the Zn fertilization effort at more than US$ 100 million annually. Use of Zn fertilizers contributed also to improved health of the Turkish people. Currently, he is coordinating a global zinc fertilizer project in 12 countries under the HarvestPlus program. For more information: http://myweb.sabanciuniv.edu/cakmak/.

Abstract

Dysfunctional food systems, never designed to improve human nutrition and health, are the basis of malnutrition in many poverty stricken human populations. Notably, all food systems are dependent on agricultural systems as the primary source of nutrients entering food systems. Thus, agricultural systems must play a major role in the development of malnutrition globally. If the products produced from farming systems cannot provide all the nutrients (excluding water) required for human life, malnutrition results causing increases in morbidity and mortality rates, losses in worker productivity and stagnation of development efforts in those populations dependent on these systems.

Food security has been the major focus of many strategies to address malnutrition worldwide. Historically, meeting the caloric needs of populations was sufficient to meet global food security goals. However, just focusing on caloric needs alone is not sufficient. Food security programs should include the necessity that all nutrients be met by agricultural systems to redress the increases in malnutrition in mostly resource-poor families dependent on staple food crops for nourishment. "Nutrient security" should be one of the primary goals of food security programs and producing enough nutrients in agricultural systems to meet nutritional needs of all people during all seasons should be the focus.

In general, well-nourished food crops grown on fertile soils contain more vitamins and micronutrients than nutrient-stressed crops grown on infertile soils. Soil micronutrient status, cropping systems, variety selection (i.e., plant breeding) for micronutrient-dense crops (e.g., biofortification), fertilization practices, some soil amendments and livestock and aquiculture production are important factors that impact the nutrient output of these systems.

A healthy agricultural industry is crucial for providing nutrients to humans. Soil quality and soil fertility have a direct influence on the nutrient levels in food crops. Soil improvements can increase productivity and allow for greater diversity of crops without increasing the area cultivated. Agricultural tools, such as micronutrient-enriched fertilizers, and farming systems designed to meet nutritional needs should be used as sustainable strategies to reduce malnutrition. Plant breeders should include nutritional quality traits as well as yield traits as targets for enhancement when breeding for improved crop varieties. Biofortification is a new strategy that has great potential to help reduce the burden of micronutrient malnutrition globally especially in resource-poor families in rural areas. Clearly, agriculture must be closely linked to human nutrition and health if we are to find sustainable solution to malnutrition.

Background

Dysfunctional food systems, never designed to improve human nutrition and health, are the basis of malnutrition in many poverty stricken human populations. Notably, all food systems are dependent on agricultural systems as the primary source of nutrients entering the food system. Thus, agricultural systems must play a major role in the development of malnutrition globally. If the products produced from farming systems cannot provide all the nutrients required for human life, malnutrition ensues causing increases in morbidity and mortality rates, losses in worker productivity and stagnation in development efforts in those populations dependent on these systems (Bouis et al., 2012; Graham et al., 2007). Because agricultural products are the primary source of all nutrients, agricultural practices and policies have the potential to exacerbate or thwart malnutrition on a global scale. A healthy agricultural industry is crucial for providing nutrients through food systems to human populations.

Food security has been the major focus of many strategies to address malnutrition worldwide. Historically, meeting the caloric and protein needs of populations was sufficient to meet global food security goals. This was accomplished during the 'green revolution' by increasing mainly cereal crop production (i.e., primarily rice, wheat and maize) to provide the energy and protein needs of rapidly growing populations in the Global South thereby staving off massive famines especially in South Asia. However, there were unforeseen consequences of the 'green revolution'. Changes from more diverse traditional cropping systems to mainly cereal production systems resulted in less bioavailable micronutrient output of many farming systems and a rapid increase in micronutrient malnutrition (e.g., deficiencies of iron, zinc and vitamin A) in resource-poor-families dependent on these agricultural systems for sustenance (Welch and Graham, 1999; ACC/SCN, 1992). Many traditional food cropping systems along with their traditional crops were lost; many of these traditional crops as eaten were much more micronutrient-dense compared to the high yielding rice, wheat and maize crops that displaced them (National Research Council, 1996).

Figure 1 illustrates how edible pulse production in South Asia and other developing nations did not keep pace with population growth. Wheat and rice production increase dramatically during the 'green revolution' keeping pace with population growth (Combs, Jr. et al., 1996; Graham et al., 2007). Pulses as generally eaten are much denser in micronutrients (vitamins and essential trace elements) than rice or wheat (for example, see Table 1) and, after milling or polishing, cereal grains contain very low levels of micronutrients (see rice example in Table 2) compared to whole legume seeds. The rise in micronutrient deficiencies in human populations could have been the result of this replacement of a traditional pulse-rice-based or pulse-wheat-based diet with rice or wheat alone (Welch and Graham, 1999; Welch et al., 1997). Current varieties of pulses are more susceptible to disease and environmental stresses, such as flooding, drought and heat, compared to cereal crops and therefore, are more risky to grow. Because of these factors, increases in micronutrient (i.e., essential trace elements and vitamins) deficiencies in human populations at widespread proportions could have been the direct result of the first ‘green revolution’. The unique, global nature of this event puts the above assertion beyond any prospect of rigorous scientific proof (‘one treatment in one replication’), but as a highly rational working hypothesis a second ’green revolution‘ must be focused on increasing micronutrient output of farming systems to meet human needs if we are to avoid the colossal human cost of a further rise in the global burden of micronutrient deficiencies and their impact on overall health and productivity of resource-poor people.

Plant breeding with a major focus on improving yields has also resulted in lower output of micronutrients from cereal-based farming systems (Davis, 2009; Garvin et al., 2006). For example, analysis of historical cereal grain samples have shown that the concentrations of certain micronutrients, such as zinc and iron, remained stable between 1845 and the mid-1960s in the USA, but thereafter, following the release of semi-dwarf cereal cultivars, significantly decreased during ‘green revolution’ (Figure 2). Some of this decline in micronutrient density in cereal crops can be attributed to “biomass dilution” of micronutrients resulting from larger grain size and more seeds per plant in higher yielding varieties with the same total micronutrient content as plants with smaller grain size and fewer seeds. This also is contributing to lower supplies of micronutrients entering food systems from cereal farming systems that feed the world’s disadvantaged .

Food security programs should now broaden their scope to include the necessity that all essential nutrient requirements should be met by agricultural systems to redress the increases in malnutrition in mostly resource-poor families dependent on staple food crops for nourishment. “Nutrient security” should be one of the primary goals of food security programs and producing enough nutrients in agricultural systems to meet nutritional needs of all people should be the objective of such programs (Miller and Welch, 2013). Farmers are nutrient providers and their farming enterprises provide the bulk of all nutrients (except for water) entering food systems.

Very little attention has been given by ecologists to the role that ecosystems play in delivering nutrients to human populations but nutrient delivery to human populations is the most important health aspect of food systems. Without adequate supplies of all essential nutrients to an ecosystem, the system will ultimately fail to support life. Therefore, ecologists should include nutrient inputs to ecosystems and stress the importance of nutrient balance of farming systems to the sustainability of human life (Meis et al., 2003; Ferrucci et al., 2010).

Agricultural Tools for Improving Human Nutrition and Health

Within farming systems what components are most important at shaping their bioavailable micronutrient output? Generally, well-nourished food crops grown on fertile soils contain more vitamins and nutrients than nutrient-stressed crops grown on infertile soils (Welch, 1998; Welch, 2001). Soil nutrient status, cropping systems, variety selection (i.e., plant breeding) for nutrient-dense crops (e.g., biofortification), some soil amendments and livestock and aquiculture production are important factors that impact the nutrient output of farming systems (Tontisirin et al., 2002; Frison et al., 2006; Combs, Jr. and Welch, 1998; Welch, 2008; Allaway, 1986). Generally, the more diverse the farming systems, the more micronutrients are harvested and enter food systems (Kennedy et al., 2003; Tontisirin et al., 2002).

Soil fertility and nutrient status

Soil quality and soil fertility have a direct influence on the nutrient content of food crops and the nutrient output of farming systems (Bruulsema et al., 2012). Soil fertility improvements can increase productivity and allow for greater diversity of crops without increasing the area cultivated. Thus, attention should be given to the role that soil fertility can play in increasing the nutrient output of cropping systems (Graham et al., 2007).

The available levels of micronutrient trace elements in soils that produce the staple food crops that low income families rely on for essential nutrients are a primary factor in determining micronutrient content of crops and therefore, may be one of the primary dysfunctions of the food system leading to widespread deficiencies of these nutrients (Allaway, 1986; Zheng, 2010). This is especially true for trace elements that are essential nutrients for humans but are not known to be essential for plant growth, such as selenium and iodine (Green and Limesand, 2010). For plant essential trace elements, such as zinc, informed farmers with sufficient resources will normally use micronutrient fertilizers to correct a deficiency of these nutrients to maximize crop yields. However, they will not do so for essential trace elements that are not required by the crop, such as selenium and iodine, without incentives or government regulations that would make doing so profitable or mandatory.

There appears to be an association between zinc-deficient soils and zinc deficiency in humans in the Global South (see Figures 3 and 4) (Hotz and Brown, 2004; Huang et al., 2010; Macbeth et al., 2005; Welch, 2008). Possibly, a primary cause of zinc deficiency in humans in some regions of the Global South may be linked to low available levels of zinc in soils that results in diminished levels of zinc in the staple food crops harvested and therefore, could contribute to low levels of zinc entering the food systems in those regions. Interestingly, about 50% of all agricultural soils on earth have been reported to contain inadequate levels of available zinc for optimal crop yields (Sillanpaa, 1982; Sillanpaa, 1990). Thus, some of the zinc deficiency in humans may have its origin in zinc-deficient soils (Macbeth et al., 2005).

Similar soil associated micronutrient deficiencies in humans and livestock have been reported for other micronutrient elements such as iodine and selenium (see Figures 5 and 6) (Allaway, 1975; Allaway, 1986). Historically, in the USA, iodine deficiency disorders in people and livestock were linked to low iodine levels in the water and soils on which food and forage crops were grown (i.e., the "Goiter Belt" region) before the widespread use of iodized salt was introduced (see Figure 5). Low levels of iodine in typical soils are the result of iodine being easily leached from soils by water from rain or irrigation without replenishment from atmospheric sources (i.e., biogeochemical cycling from ocean spray inland). In those areas far from oceans that do not receive such rain supplies of iodine, the soils usually contain very low levels of iodine and produce crops containing inadequate levels of iodine to meet human needs (Johnson et al., 2003). People dependent on crops grown in these regions have high incidences of iodine deficiency disorders. Currently, there are still significant numbers of iodine deficiency disorders mostly in South Asia and Africa (Andersson et al., 2012). Thus, additional strategies that address the root cause of iodine deficiency are needed to find sustainable solutions. The use of iodine fertilizer may be the best option available (discussed below) because it focuses on the root cause of iodine deficiencies – not enough available iodine in the soil (Ren et al., 2008).

The selenium content of food crops is also directly related to the available levels of selenium in the soil on which they are grown (Banuelos and Ajwa, 1999). Local crops cultivated on low selenium soils can lead to selenium deficiency in human populations dependent on these crops for their selenium needs. In China, an endemic selenium deficiency disease (i.e., Keshan disease) causing sudden deaths in humans has been reported in the Keshan region (Ge and Yang, 1993). In the USA, a selenium map (Figure 6) of the 48 conterminous states was prepared and used by epidemiologists to show a negative association between selenium in forage crops (and by inference selenium in soils) and cancer risk in humans (Combs, Jr., 2005). Clearly, the available soil essential trace element levels play an important role in supplying these nutrients to food systems and ultimately to meeting the nutritional requirements of people dependent on the crops grown in these soils.

Other soil related factors can influence the micronutrient output of farming systems. Soil macronutrient fertilizers (e.g., fertilizers that contain nitrogen, potassium, phosphorus, sulfur, calcium and magnesium), soil amendments, such as lime, gypsum and organic matter, can affect the available forms of micronutrients in soils and in the nutritional quality of the crops produced on them. Some of these factors are discussed below (Welch, 2001). Macronutrient fertilizers can also have significant effects on the micronutrient content (both essential trace elements and vitamins) in food crops (Allaway, 1986; Grunes and Allaway, 1985). Detailed reviews of the effects of fertilization practices on micronutrient accumulation in plant foods are discussed in several publications (Allaway, 1975; Cakmak, 2008; Karmas and Harris, 1988; Nagy and Wardowski, 1988; Salunkhe and Deshpande, 1991; Welch, 1997).

Macronutrient fertilization can also affect vitamin levels in edible portions of food crops (Welch, 2001). For example, vitamin C levels in various vegetable crops such as lettuce (*Lactuca sativa* L.), beets (*Beta vulgaris* cicla L.), kale (*Brassica oleracea acephala* DC.), endive (*Cychorium endivia* L.), and brussels-sprouts (*Brassica oleracea gemmifera* DC.) have been reported to be reduced by as much as 26% from excessive applications of nitrogen fertilizers [cited in (Salunkhe and Deshpande, 1991)]. Conversely, increasing potassium fertilizer rates supplied to these crops significantly increased their vitamin C content by about 8–20% depending on the species. The levels of β-carotene in carrot root [*Ducus carota* subsp. *carota sativus* (Hoffm.) Arcang.] increased at first harvest by about 12% in response to increases in the nitrogen supplied [Habben, 1972 cited in (Salunkhe and Desai, 1988)]. In 1979, Vereecke (cited in Salunkhe and Desai, 1991) reported results of studies concerning the effects of combined nitrogen, phosphorus, potassium and magnesium fertilizers on β-carotene and other micronutrient elements in carrot root. Nitrogen, phosphorus and magnesium treatments increased the accumulation of β-carotene by 42% compared to roots from unfertilized control plants. Application of potassium combined with nitrogen and phosphorus fertilizer increased the β-carotene by 27% over fertilized plants without potassium. Removal of magnesium from the fertilizer treatments reduced the increase in β-carotene from 42 to 30%. Magnesium was apparently needed for maximum β-carotene production in carrot roots furnished with adequate nitrogen, phosphorus, and potassium. Vereecke also reported the effects of these treatments on iron, manganese, zinc and copper in carrot leaves at two harvest dates. There were large effects on the manganese and iron levels in the leaves, but the other micronutrients measured were not significantly affected by the fertilizer treatments.

The vitamin C levels in fruits can also be affected by macronutrient fertilizers. As found in vegetable crops, excessive nitrogen fertilization was reported to lower vitamin C concentration in the fruits of several species including oranges, lemons, mandarins, cantaloupe, and apple. Further, higher potassium fertilization rates were associated with greater concentration of vitamin C in fruits (Nagy and Wardowski, 1988). The effects of zinc, magnesium, manganese and copper fertilization on increasing vitamin C concentration in citrus fruits was limited to soils deficient in these nutrients. Increasing the supplying of these nutrients, in excess of that required for optimum yield, did not further increase vitamin C fruit concentrations.

Farmers frequently apply soil amendments and organic matter to improve soil health and productivity. Liming soils with calcium carbonate is done to reduce soil acidity, allowing acid-intolerant plant species to grow. Lime additions to soils also increase the calcium available to plants. However, amending soils with lime may reduce the uptake of certain micronutrient elements including zinc, copper, iron, and cobalt, and increase the uptake of selenium and molybdenum by plants. An alkaline soil pH favors the oxidation of reduced forms of selenium (Se^{2-} and SeO_3^{2-}) to the more soluble and plant-available SeO_4^{2-} anion. Gypsum ($CaSO_4$) and elemental sulfur additions are used to decrease the pH of alkaline soils as well as to provide sulfur for plants and to ameliorate alkali soils high in sodium. Using gypsum and elemental sulfur on alkaline soils can increase available iron, manganese, zinc, copper, and cobalt by reducing the soil pH thereby increasing the soil-solubility of these elements (Graham et al., 2001; Welch, 2001).

Organic matter additions to soils can affect plant-available micronutrient elements by changing both the chemical, physical and biological characteristics of the soil. Moreover, these changes can influence the vitamin and antioxidant content of food crops (Blair, 2012). Many times these changes improve soil physical structure and water holding capacity, resulting in more extensive root development and enhanced soil microbiota and fauna activity, all of which improve micronutrient element levels available to plant roots and plant health (Stevenson, 1991; Stevenson, 1994). However, much more research needs to be done to understand all the implications that soil amendments and organic matter have on the nutritional quality of food crops (Magkos et al., 2003; Benbrook, 2009).

Livestock and fish production

Animal products contribute greatly to the amount of nutrients entering food systems and also to their dietary bioavailability to humans (Randolph et al., 2007). Some animal products are rich sources of some micronutrients (Table 3). Importantly, animal products are the only source of cobalamine (vitamin B_{12}) in human diets because cobalamine is only produced by certain bacteria and not by plants or animals. Ruminant animals accumulate the vitamin in their tissues and milk by absorbing it from their rumens where it is produced by bacteria (Combs, Jr., 2008). Consumption of the flesh of other animals (pigs, poultry and fish), milk, and eggs also contributes to vitamin B_{12} intake in humans (Watanabe, 2007). Thus, animal food sources play a crucial role in meeting the vitamin B_{12} requirements. Vegans may develop B_{12} deficiency unless they consume foods fortified with vitamin B_{12} or take a B_{12} supplement.

Livestock and fish production by farmers, especially in low-income families, is very important to the nutritional health and income of the household and has positive effects on reducing poverty. Livestock production from farming systems is a major source of revenue for the farmer. This affects the ability of farm families to diversify their diets and therefore, meet their nutrient requirements. Animals also play important roles in soil fertility and soil health by providing manures for use on the farm (Randolph et al., 2007).

Eating animal meats provides factors (i.e., "meat factors") that promote the absorption of iron and zinc from staple plant food seeds and grains that contain high levels of antinutrients, such as phytic acid and polyphenols (Fairweather-Tait and Hurrell, 1996; Welch, 2001). Meat in small quantities is required to enhance the bioavailability of these micronutrients in diets high in legume seeds and whole cereal grains that contain significant amounts of these antinutrients (Leroy and Frongillo, 2007). Thus, providing some animal-source foods in the diets of the poor who are dependent on staple food crops is an important strategy for decreasing iron and zinc deficiencies in these populations. These presumed "meat factors" have not yet been isolated or identified and efforts to do so remain a very active research area (Huh et al., 2004; Bonsmann et al., 2007).

Micronutrient-enriched fertilizer impact on nutritional quality of food crops

Fertilization of food crops with micronutrients represents an effective agricultural approach to achieving micronutrient dense food crops (Cakmak, 2008; Cakmak et al. 2010a), a strategy termed "agronomic biofortification". As indicated above, most of the cereal cultivated soils globally are associated with various adverse chemical and physical factors such as low amounts of organic matter and moisture and high levels of pH and CaCO3. Such adverse soil conditions are known to severely reduce chemical solubility and root acquisition of micronutrients, especially zinc and iron. For example, increases in soil pH to the alkaline range (pH 6.5 or greater) depresses (several folds) solubility and transportation of zinc to the root surface and thus its uptake by roots (Marschner, 1993). In a study with peanut, increasing soil pH from 5.2 to 6.8 by liming reduced leaf Zn concentrations from 200 mg zinc kg^{-1} to 20 mg zinc kg^{-1} (Parker and Walker, 1986). Published evidence indicate existence of a strong positive relationship between soil organic matter and soluble zinc concentrations in the soil rhizosphere (Catlett et al., 2002) which highlights the importance of soil organic matter in root absorption of zinc. Consequently, genetic capacity of food crops or newly developed biofortified cultivars to absorb micronutrients from soil with adverse chemical properties would be significantly impaired to achieve desirable concentrations in seeds. It is, therefore, important to add agronomic biofortification (i.e., fertilization) strategy to the food-based solutions addressing micronutrient deficiencies in human populations. The fertilizer strategy may also contribute to better crop yield depending on the severity of the soil deficiencies of the targeted micronutrients.

The fertilizer strategy is not an alternative or separate solution to the plant breeding approach, biofortification; they are complementary and synergistic. Combination of these agricultural tools would create additive and synergistic impacts on accumulation of micronutrients in seeds at desirable amounts for human nutrition. Certainly, the crop genotypes, which are under development and release through different breeding programs, such as under HarvestPlus breeding programs, would express their genetic capacity to the fullest extend when sufficiently available/soluble pools of micronutrients are maintained in soil solution (for root absorption) and leaf tissue (for re-translocation into seeds). Keeping high available pool of micronutrients in soil solution and in the leaf tissues can be achieved by soil and foliar application of micronutrient fertilizers.

There is published evidence demonstrating that application of micronutrient fertilizers greatly contribute to the seed density of micronutrients, such as Zn, Se and I. Here, several examples have been presented for the impact of Zn fertilization on grain-Zn levels. Readers are referred to (Lyons and Cakmak, 2012) for the examples for Se and I. In case of iron (Fe), agronomic approaches remain ineffective for sufficient accumulation of Fe in seeds to meet human needs. Both inorganic and chelated Fe fertilizers were found not to be effective in improving grain-Fe concentrations greatly when applied to soils or foliar sprays (Rengel et al., 1999; Aciksoz et al., 2011). Possibly, due to rapid conversion of Fe fertilizers into less soluble Fe forms in soil, poor penetration into leaf tissue of the foliar sprayed Fe along with limited phloem mobility and transport of Fe into grain seem to be the major factors contributing inefficiency of Fe fertilization in improving seed-Fe concentrations.

For Zn, the results published show substantial effects of foliar-applied Zn fertilizers on grain-Zn concentrations. In Turkey, where Zn deficiency is a well-known micronutrient deficiency in soils, soil-applied Zn fertilizers markedly improved grain concentrations of Zn (Figure 7) and simultaneously grain yield. Combination of soil-Zn fertilization with a foliar Zn spray was a more effective practice in increasing grain-Zn concentration (up to 3-fold) (Cakmak et al., 2010b). Positive impact of soil-applied Zn fertilizers on grain-Zn concentration is not always found, especially in soils without a Zn deficiency problem. By contrast, irrespective of soil conditions, foliar application of Zn fertilizers is highly effective in improving grain-Zn concentrations that meet human needs. In a global Zn fertilization program conducted in seven countries directed at wheat and rice production, soil-Zn application was ineffective in increasing grain-Zn concentrations, while foliar application of ZnSO4 resulted in very significant increases in grain-Zn up to 85 % in wheat (Zou et al., 2012) and 25 % in rice (Phattarakul et al., 2012) irrespective of soil conditions, management practices and cultivars used.

The timing of foliar Zn applications is a key factor in maximizing Zn accumulation in wheat grain. Foliar spray of Zn late in the growing season in wheat (e.g., at milk and dough stage) under field conditions caused much greater increases in grain-Zn concentrations when compared to the foliar application of Zn at earlier growth stages (Figure 8). Increases in the concentrations of whole grain-Zn through foliar Zn applications were similar to the increases in Zn concentrations found in various grain fractions such as the endosperm, aleurone and embryo tissues of the grain (Table 5). Since phytate (a antinutrient that inhibits Zn bioavailability to humans) concentrations in the wheat grain endosperm is very low, or not detectable (Pomeranz, 1988), the increases in Zn concentrations in the endosperm up to 3-fold by foliar Zn spray is important for human nutrition. Possibly, the Zn increased in the endosperm of wheat by foliar Zn spray is highly bioavailable due to the low levels of phytate in this grain tissue. These increases in endosperm-Zn concentrations may have highly positive impacts on human nutrition, because the endosperm is the source of white wheat flour in various countries. Experiments are needed to study the bioavailability of Zn in the grain from plants treated by foliar Zn applications.

Use of soil-applied Zn-containing fertilizers may also contribute to increasing grain-Zn concentration. In field tests conducted in India on wheat and rice, it was reported that applying urea fertilizer containing Zn up to 3 % significantly enhanced both productivity and also grain concentration of Zn (Table 6) (Shivay et al., 2008).

<u>Designing farming systems for improve nutrient output</u>

Farming systems can be designed to improve the nutrition and health of people. Improving the diversity of farming systems (including crops, livestock and aquaculture) is an important factor in providing adequate levels of nutrients to meet human needs (Graham et al., 2001). Indeed, humans require at least 43 nutrients to live and prosper (see Table 4) and these nutrients are primarily provided through farming systems. Normally, farming practices are primarily directed at improving production without much concern given to human nutrition and health as an outcome of farming. However, farming systems can be developed that promote and support human nutrition and health (McIntyre et al., 2001; Graham et al., 2007). Nevertheless, this cannot be done unless agricultural policies and programs include such thinking in their development and application (IFPRI, 2012; Haggblade, 2012). Support for integrated farming systems directed at securing household nutrient security through programs that promote a variety of foods that meet the nutritional needs of people is necessary (Frison et al., 2006; Graham et al., 2007). Using the right mix of energy-rich staple crops, animal/ fish as major sources of protein, and fruit and vegetables rich in micronutrients and beneficial health promoting antioxidants support enough nutrient output of farming systems to assure adequate nutrition for all. Including indigenous, traditional micronutrient-rich food crops could also be used to improve nutrient output (National Research Council, 1996; Tontisirin et al., 2002).

Biofortification of staple food crops to improve the micronutrient output of farming systems

Biofortification (having food crops fortify themselves with nutrients) is a relatively new world strategy focused on reducing micronutrient malnutrition in a sustainable way – using agriculture as a nutritional intervention tool (Bouis et al., 2011; Bouis et al., 2012). Biofortification is currently being developed and being deployed in the Global South (White and Broadley, 2009; Tanumihardjo SA, 2008; Bouis and Welch, 2010; Bouis et al., 2012). Biofortification is achieved through plant breeding, genetic modifications (including both transgenic and cisgenic approaches), and through agronomic approaches including micronutrient fertilizer applications (e.g., zinc). Biofortification targets resource-poor rural families in developing world regions. This strategy was selected by the Copenhagen Consensus as one of the top five investments that governments should support with a very high return on investment (Anonymous, 2008). Biofortification was listed by the World Bank as an effective tool to deliver micronutrients to rural poor (The World Bank, 2006). The HarvestPlus program (www.harvestplus.org), the Biofort Brazil program (biofort.ctaa.embrapa.br), HarvestPlus-HarvestZinc project (www.harvestzinc.org) and the HarvestPlus-China program (www.harvestplus-china.org) are examples of programs developing biofortified staple food crops. The programs focusing on breeding approach have released some biofortified staple food crops in collaboration with interdisciplinary global alliances of scientific institutions and implementing agencies in various global regions. The crops include (among others) rice, wheat, maize, beans, sweet potato, cassava and pearl millet enriched in one or more of these nutrients - vitamin A, iron, and zinc - to several regions in Africa, Brazil, China and South Asia. Success of these programs is based on three principles 1) biofortified crops must be high yielding and profitable to farmers, 2) eating the biofortified crops must measurably improve the nutritional health of people in target populations, and 3) farmers must adopt the crops and most consumers in target populations must accept and consume the crops in quantities sufficient to improve their nutritional health. Biofortification is rural-based, focused on more remote people who typically suffer from higher rates of micronutrient malnutrition. When crop surpluses are achieved, urban populations would benefit when crop surpluses are marketed in cities and urban areas (Bouis et al., 2011; Bouis et al., 2012). This strategy is a relatively low-cost sustainable strategy with low recurring costs once the micronutrient-dense crops are developed. One-time investments in plant breeding to develop biofortified crops results in micronutrient-rich crops for producers to grow throughout the world into the foreseeable future making biofortification very cost-effective. Supplementation and fortification programs require continued relatively costly long-term funding, monitoring and a dedicated support structure to assure success into the future. Biofortification complements these strategies in that it is rural based while the others are more urban focused (Pfeiffer and McClafferty, 2007; Qaim et al., 2007).

Successes have been reported for biofortification in improving the health of the rural poor in several countries. Orange flesh sweet potato (OFSP) varieties, enriched in provitamin A carotenoids, are being released in some countries in Africa (Low, 2007). OFSP crops have been shown to be efficacious and effective at improving the vitamin A status of villagers where they have been released, propagated and consumed. Yellow varieties of cassava, high in provitamin A carotenoids, are also being released in Nigeria. Nigeria's former, President Olusegun Obasanjo, has commended the International Institute of Tropical Agriculture (IITA) for successfully leading efforts in developing high pro-Vitamin A cassava varieties (http://bit.ly/IS6oRl) for that country. High-iron biofortified rice grain has been shown to be efficacious at improving the iron status of women in the Philippines (Beard et al., 2007). The Brazilian biofortification program is also releasing a number of biofortified crops. School lunch programs that promotes locally grown biofortified, nutritionally enriched, food crops in rural schools has been launched in Brazil (biofort.ctaa.embrapa.br). The HarvestPlus program predicts that it will take ten years before micronutrient-enriched biofortified crops are widely grown in the developing nations. If biofortification strategies continue to show improved nutritional health impacts for rural populations than biofortification will become a widely recognized global strategy for reducing micronutrient malnutrition.

Improving nutrient bioavailability in edible parts of staple plant foods

Not all of a nutrient in food crops can be utilized in the human body. This is because plant foods can contain inhibitor substances (i.e., antinutrients, such as phytic acid and certain polyphenolics that inhibit the intestinal absorption of some micronutrients such as iron and zinc) that reduce the amount of utilizable nutrients in these foods (Hambidge, 2010; Hotz et al., 2007; Bouis and Welch, 2010). The bioavailable amount (i.e., the amount that can be absorbed from the diet and utilized in the body) needs to be known when biofortifying staple food crops in order to inform plant breeders as to the level of micronutrient enrichment of edible portions of staple food crops that must be achieved to have nutritional impact on human health (Hotz et al., 2007; Welch and Graham, 2012). However, determining the bioavailable amount of a micronutrient in a diet is very complicated because of numerous interacting factors that can influence the absorption and utilization of micronutrients from a meal (see Figure 9). Other foods in a meal can interact to affect the bioavailable content of nutrients in a diet. Significantly, there are other dietary constituents (bioavailability promoters/enhancers factors) that can decrease the negative effects of antinutrients found in plant foods (Zhao, 2010; Welch and Graham, 2005). Once identified, these factors could be incorporated into plant breeding program to enhance the nutritional quality of these crops (Bouis and Welch, 2010; Welch, 2008).

Recent research suggests that certain microbiota in the human gut may be significant factors in determining bioavailable amounts of nutrients in diets (Brownawell et al., 2012; Murgia et al., 2012). Possibly, some beneficial bacteria (probiotics) can increase the bioavailable levels of some micronutrients, such as iron, in staple plant foods that contain antinutrients that inhibit their bioavailability (Perez-Conesa et al., 2007; Tako et al., 2007). Probiotic microbiota can be stimulated in the intestine by some non-digestible carbohydrates that occur in staple food crops as well as other plant foods. These compounds are termed prebiotics that enhance the proliferation of beneficial bacteria in the intestine (Teitelbaum and Walker, 2002). If further research establishes these possibilities in human trials, prebiotics in staple food crops could be enhanced via plant breeding or genetic engineering.

Employing biotechnology to improve the nutritional quality of staple food crops

Genetic engineering is being used to develop food crops enriched in nutrients including some vitamins (e.g., vitamins E, A, riboflavin and folic acid) and more bioavailable levels of iron and zinc (White and Broadley, 2009) (Waters and Sankaran, 2011). The Bill and Malinda Gates Foundation (www.gatesfoundation.org) is funding research (Grand Challenge #9 Grant Program) to develop transgenic staple food crops with multiple nutritional improvement traits (e.g., improved protein quality, improved bioavailable levels of iron and zinc, improved vitamin A levels, etc.) to enhance the nutritional quality of these foods with multiple limiting nutrients for the poor in developing nations. Transgenic approaches are the only way to increase some vitamins and other nutrients in certain staple food crops that cannot accumulate them in their edible portions such provitamin A carotenoids in rice grain. The genome of the rice plant does not contain the genes necessary for the production of provitamin A carotenoids in its grain which makes it impossible to breed for this trait in rice using traditional breeding techniques without genetic transformations. Thus, rice plants were transformed using transgenic approaches to accumulate β-carotene (i.e., Golden Rice) in their grain. Golden Rice has been under development for over a decade and is expected to be released to some farmers soon (Tang et al., 2009; Swapan et al., 2007). Many complications are being overcome for this to be achieved. Individual property rights, public and government acceptance and safety issues have to be addressed before Golden Rice can be released to farmers. Because of these obstacles, transgenic approaches to biofortified crops are costly and take significant amounts of time before releases to farmers are possible in many countries.

Potential agricultural strategies to reduce micronutrient malnutrition via foreign aid investments.

The United State, Canada, Australia and European Union are among the most important wheat exporting nations globally. These nations could significantly contribute to reducing the high incidence of Zn deficiency in human populations by exporting Zn-biofortified wheat grain. A significant amount of wheat grain exported from these countries is shipped to developing countries where Zn deficiency in humans is well-known. At least a part of the wheat exported to these countries could be biofortified with Zn by using a foliar-Zn fertilization strategy possibly in combination with plants bred to accumulate more grain-zinc. This high-zinc wheat grain could be shipped to the target regions of the selected developing countries where those developed countries have an existing aid program. Targeted regions could be monitored for selected nutrition and development parameters to assess the health impacts of the Zn-enriched wheat grain in those countries. If such a strategy were shown to be successful from human effectiveness trials, Zn-biofortifying programs could be extended to all nations with a high incidence of zinc deficiency in their populations.

Summary and Conclusions

Currently, maximizing crop production is usually achieved by applying modern agronomic approaches to farming such as by using innovative and useful nutrient, water and pest management practices. However, such approaches, although they are highly effective at increasing productivity, are not directed at increasing nutrient levels in edible portions of food crops to meet human needs. Indeed, only focusing on productivity of staple food crops can cause reductions in the level of micronutrients in those crops through "growth dilution" as discussed previously. Obviously, much higher concentrations of micronutrients in seeds and grains, beyond the amounts needed for high crop yields, are required to address micronutrient malnutrition in human populations. Increasing seed and grain micronutrient concentrations more than that required for maximum yields is an important challenge, and this challenge can be easily and rapidly met by applying micronutrient fertilizers at the right rate, at the right time, in the right place using the right fertilizer source (Bruulsema et al., 2012).

Agricultural production practices must be closely linked to human nutrition and health goals if we are to find sustainable solutions to malnutrition, including overt nutrient deficiencies and diet-related chronic diseases. Not only productivity goals and environmental goals must be met through agriculture but also human nutrition and health priorities need to be considered by agriculturalists and policy makers when planning for the future. Furthermore, human nutrition, health experts and policy makers must start to use agricultural tools and strategies to address malnutrition issues. Policies to improve nutrition and health need to include agricultural strategies as primary tools in finding sustainable solutions to malnutrition. Sustainable agriculture can only be achieved when agriculture can provide all the essential nutrients required for human life in adequate quantities to all throughout the year. Importantly, if agricultural systems cannot meet the nutritional needs of the societies and the people they service, than these agricultural systems will not be sustainable. Thus, linking agriculture to human nutrition and health must be accomplished to assure sustainable agricultural systems and human life.

Tables

Table 1. Micronutrients in whole cereal grains and legume seeds (pulses) (data from USDA Nutrient database at http://ndb.nal.usda.gov/).

	Plant Food	Fe	Zn	Mn	Cu	Mo	Cr	Ni
		($\mu g\ g^{-1}$ dry weight)						
Cereals	Brown rice	20	14	11	2.4	0.78	0.088	-
	Whole soft wheat	39	22	35	4.5	-	0.370	0.31
Legumes	Mung bean	87	41	14	13.0	3.20	0.251	2.04
	Black gram	139	36	19	7.9	0.16	0.530	3.43
	Cowpea	67	45	16	6.3	1.47	0.272	3.44
	Soybean	97	43	26	15.5	-	-	-
	Red kidney bean	64	30	12	6.8	-	-	-

Table 2. Effects of milling and polishing on micronutrients in rice grain (data from USDA Nutrient database at http://ndb.nal.usda.gov/).

Micronutrient	Brown Rice	Polished Rice	% Removed
Iron (mg kg^{-1})	20	5	75
Copper (mg kg^{-1})	3.3	2.9	12
Manganese (mg kg^{-1})	17.6	10.9	62
Zinc (mg kg^{-1})	18	13	30
Biotin (µg kg^{-1})	120	50	58
Folic Acid (µg kg^{-1})	200	160	20
Niacin (mg kg^{-1})	47	16	66
Pantothenic Acid (mg kg^{-1})	20	10	50
Riboflavin (mg kg^{-1})	0.5	0.3	40
Thiamin (mg kg^{-1})	3.4	0.7	80
Vitamin B_6 (mg kg^{-1})	6.2	0.4	94
Vitamin E (IU kg^{-1})[b]	20	10	50

[a]Dry weight basis.
[b]IU = International Unit.

Table 3. Some micronutrients provided by animal/fish products [modified from (Randolph et al., 2007)].

Micronutrient	Sources
Vitamin A	Dairy, liver, fish-liver oil
Iron	Meats and fish contain heme-iron and meat factors that promote iron bioavailability
Zinc	Meats and (shell)fish contain meat factors that promote zinc bioavailability
Riboflavin	Dairy, organ meats and eggs
Cobalamine (vitamin B_{12})	Animal-source foods only dietary source

Table 4. The 43 essential nutrients required for human life. The elements shown in blue are not accepted as essential but some evidence exists that suggests that they may be essential. Table modified from: (Welch and Graham, 2005).

Air, Water & Energy (3)	Protein (amino acids) (9)	Lipids-Fat (fatty acids) (2)	Macro-Minerals (7)	Trace Elements (9) (17)	Vitamins (13)
Oxygen	Histidine	Linoleic acid	Na	Fe	A
Water	Isoleucine	Linolenic acid	K	Zn	D
Carbohydrates	Leucine		Ca	Cu	E
	Lysine		Mg	Mn	K
	Methionine		S	I	C (Ascorbic acid)
	Phenylalanine		P	F	B_1 (Thiamin)
	Threonine		Cl	Se	B_2 (Riboflavin)
	Tryptophan			Mo	B_3 (Niacin)
	Valine			Co (in B_{12})	B_5 (Pantothenic acid)
				Cr	B_6 (Pyroxidine)
				Si	B_7/H (Biotin)
				B	B_9 (Folic acid, folacin)
				Ni	B_{12} (Cobalamin)
				V	
				As	
				Li	
				Sn	

*Numerous other beneficial substances in foods are also known to contribute to good health.

Table 5: Zinc concentrations of the whole grain and the bran, embryo and endosperm fractions of the wheat plants grown under field conditions with foliar spray of 0.5% $ZnSO_4.7H_2O$ at different growth stages in the Konya (a Zn-deficient location) and Adana locations in Turkey [see, for further details (Cakmak et al., 2010a)].

	Zn concentration (mg kg^{-1})							
	Konya				Adana			
Foliar Zn Treatment Stages	Whole Grain	Bran	Embryo	Endosperm	Whole Grain	Bran	Embryo	Endosperm
Control (No Zn appl.)	12	20	38	8	32	42	70	11
Stem + Booting	19	28	47	10	51	72	96	15
Milk + Dough	25	41	63	15	57	88	98	16

Table 6: Changes in grain yield and grain Zn concentrations of aromatic rice grown under field conditions in India as affected by use Zn-enriched urea (ZEU) at increasing Zn concentrations from 0 % to 3 % (Shivay et al., 2008).

Zincated Urea Application	Zn Applied	Grain Yield	Grain Zn Concentration
	kg ha $^{-1}$	ton ha $^{-1}$	mg kg $^{-1}$
Prilled Urea	-	3.87	27
0.5% ZEU	1.3	4.23	29
1.0% ZEU	2.6	4.39	33
2.0% ZEU	5.2	4.60	39
3.0% ZEU	7.8	4.76	42

Figures

Figure 1. Percent change in cereal and pulse production and in human populations from 1965 to 1999 for select countries, developing nations and world population; from (Graham et al., 2007).

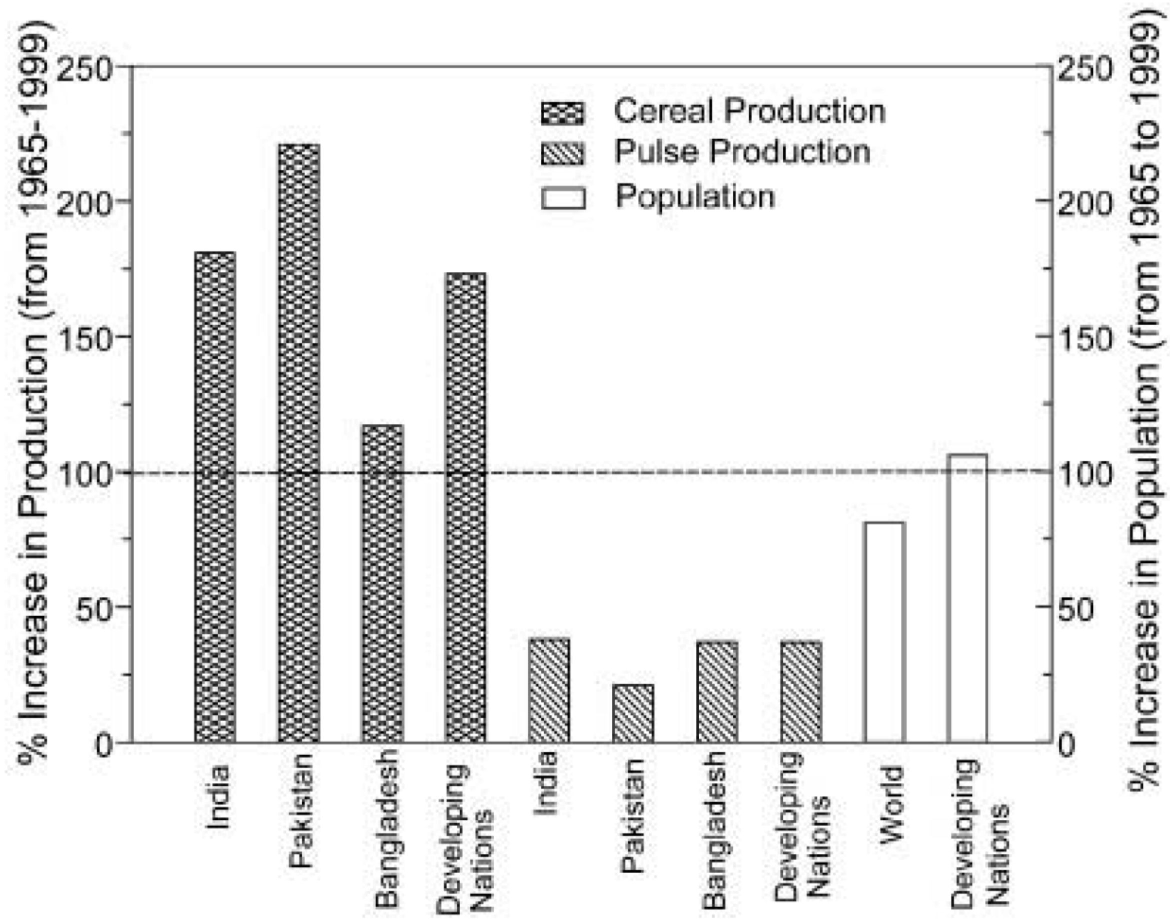


Figure 2. Historical trends in grain-iron and grain-zinc levels in hard red winter wheat varieties in USA from 1873 to 2000. Figure from: (Garvin et al., 2006).

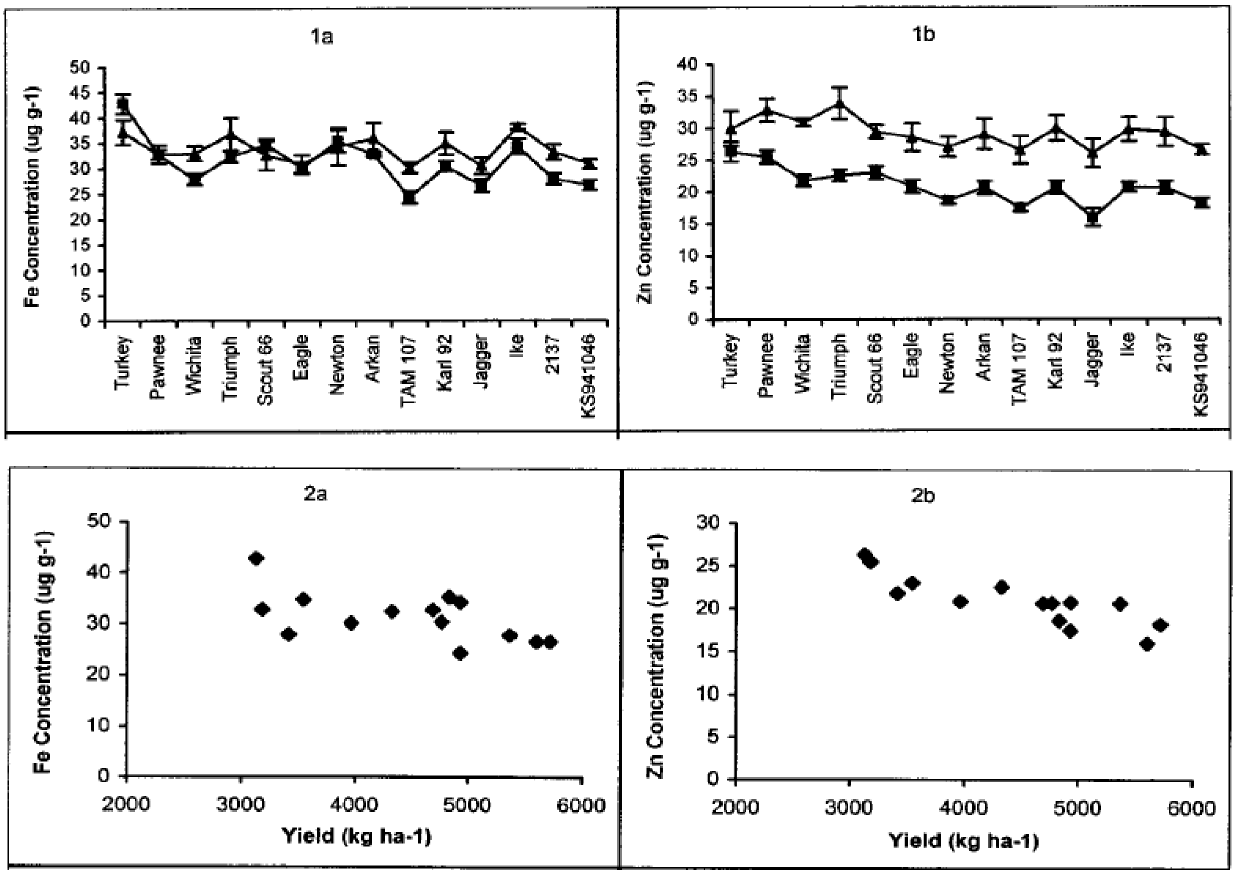


Figure 3. Zinc deficiencies in crops globally: major regions of reported deficiencies; from: (Alloway, 2008).

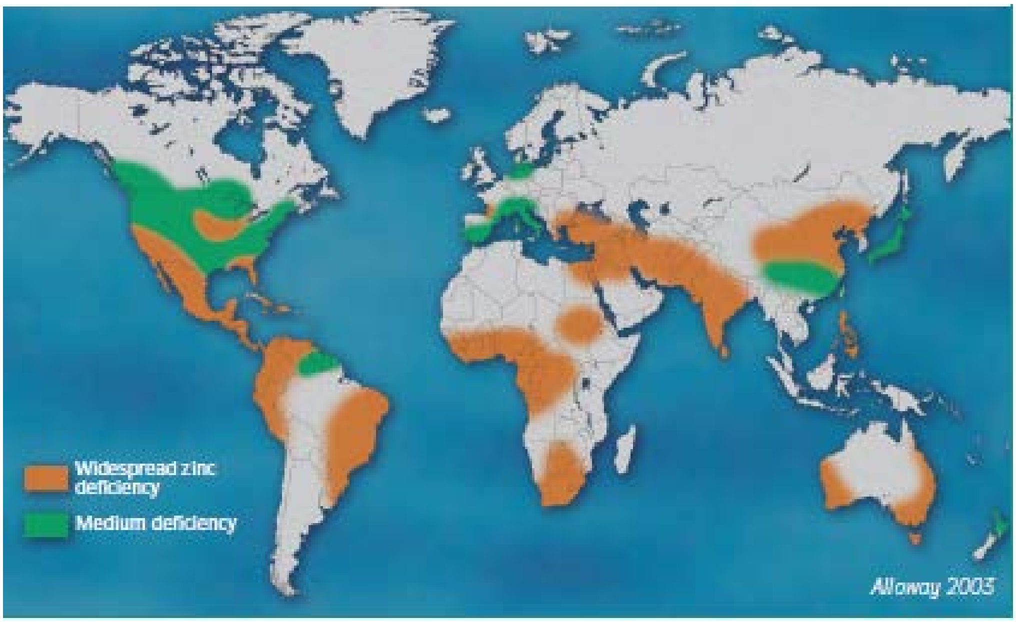


Figure 4. National risk of zinc deficiency in human populations (from A. Green presentation, 2009 from Hotz and Brown, 2004).

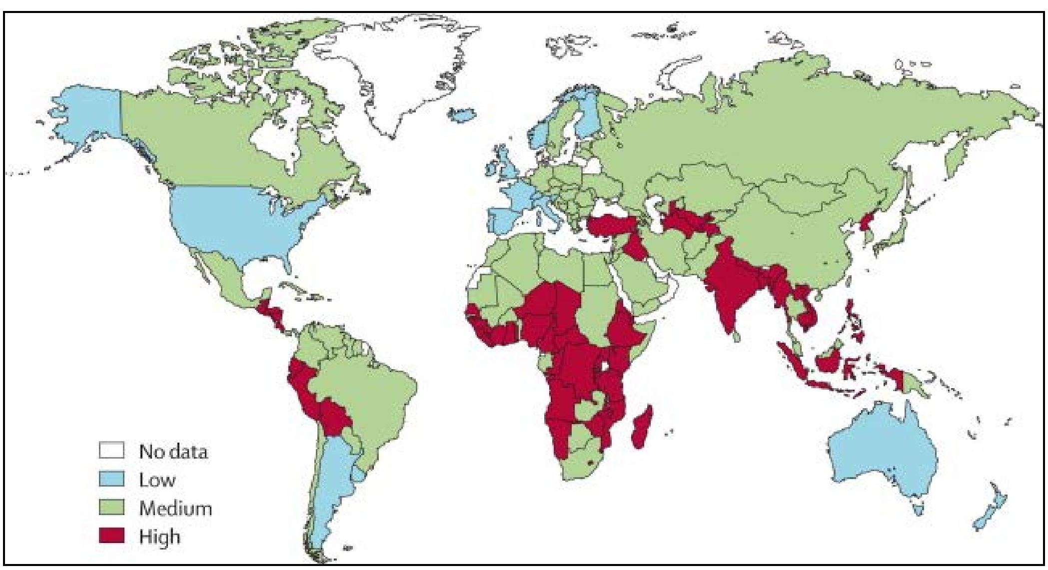


Figure 5. The historical iodine deficient goiter regions (i.e., the "Goiter Belt") in USA from two sources; from: (Schiel, Jr. and Wepfer, 1976).

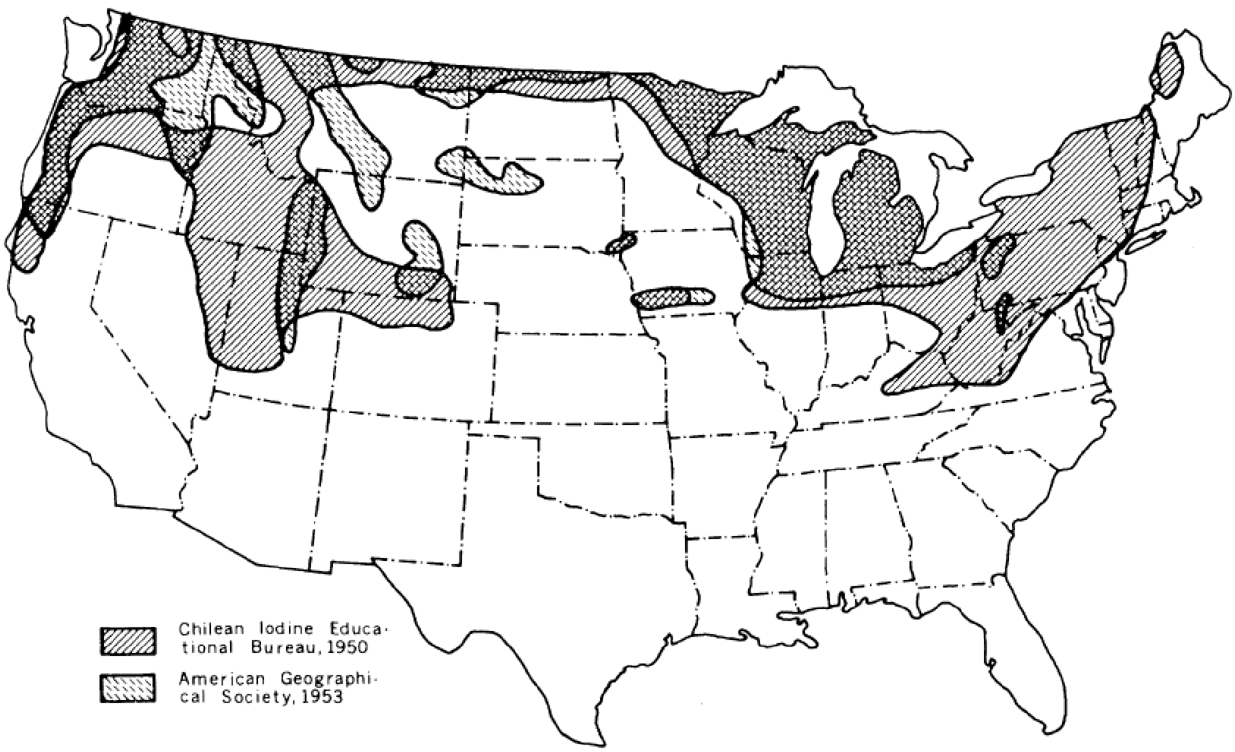
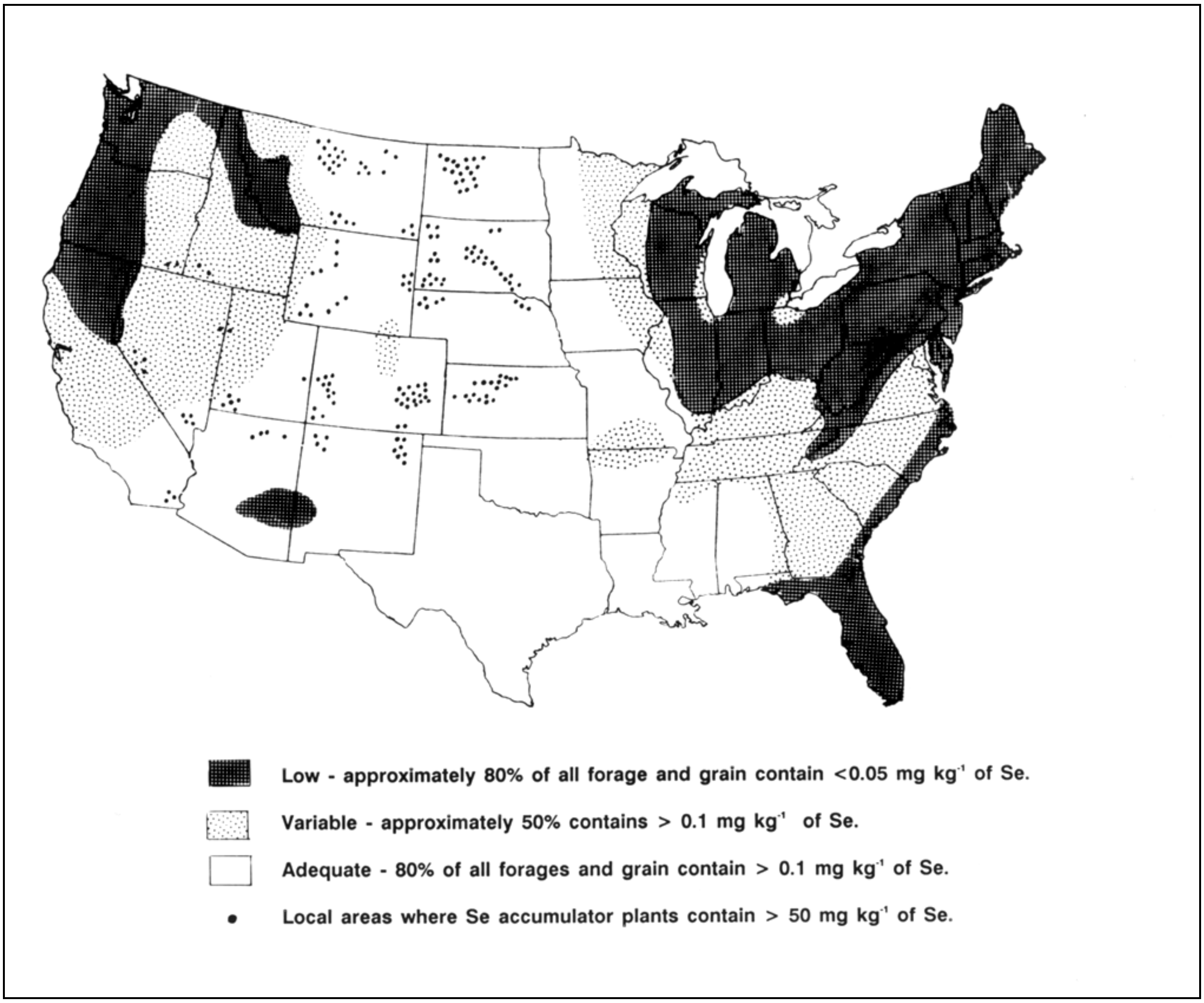


Figure 6. Map of selenium concentrations in forages of the 48 conterminous states of the USA; from: (Welch et al., 1991).



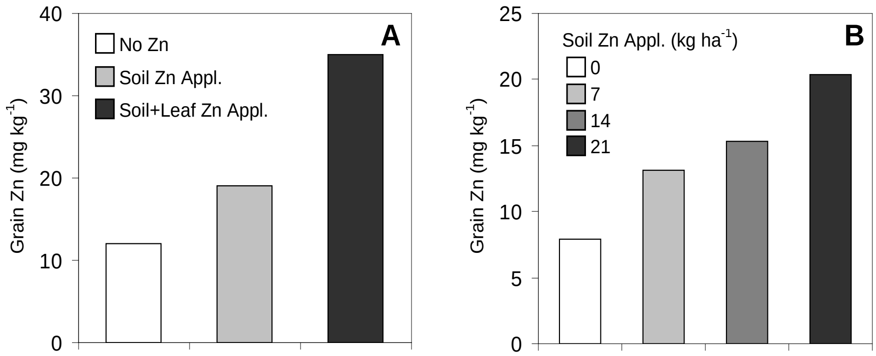


Figure 7: Grain-Zn concentrations of wheat plants treated with soil and foliar applications of $ZnSO_4$ (A) and by increasing soil application rates of $ZnSO_4$ into soil (B). Plants were grown on a highly Zn-deficient calcareous soil in the field in Central Anatolia (Cakmak et al., 2010b).

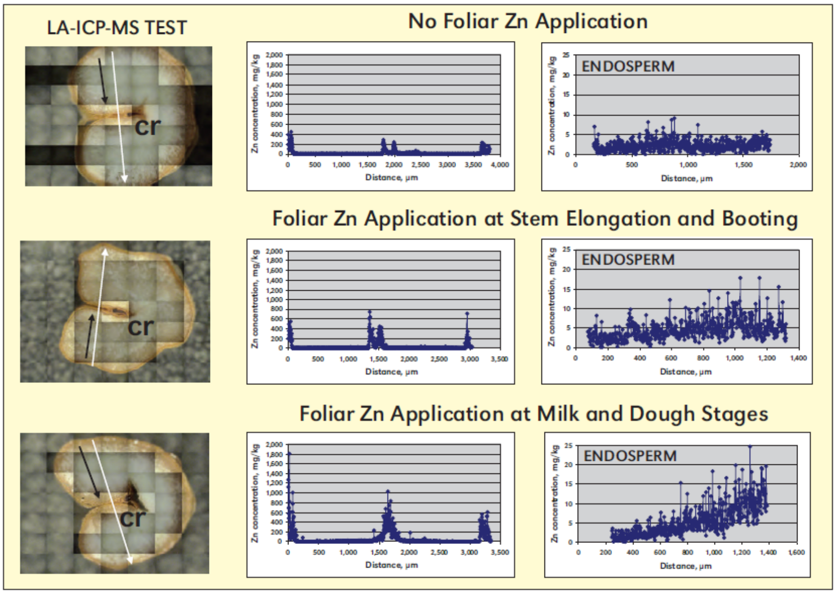
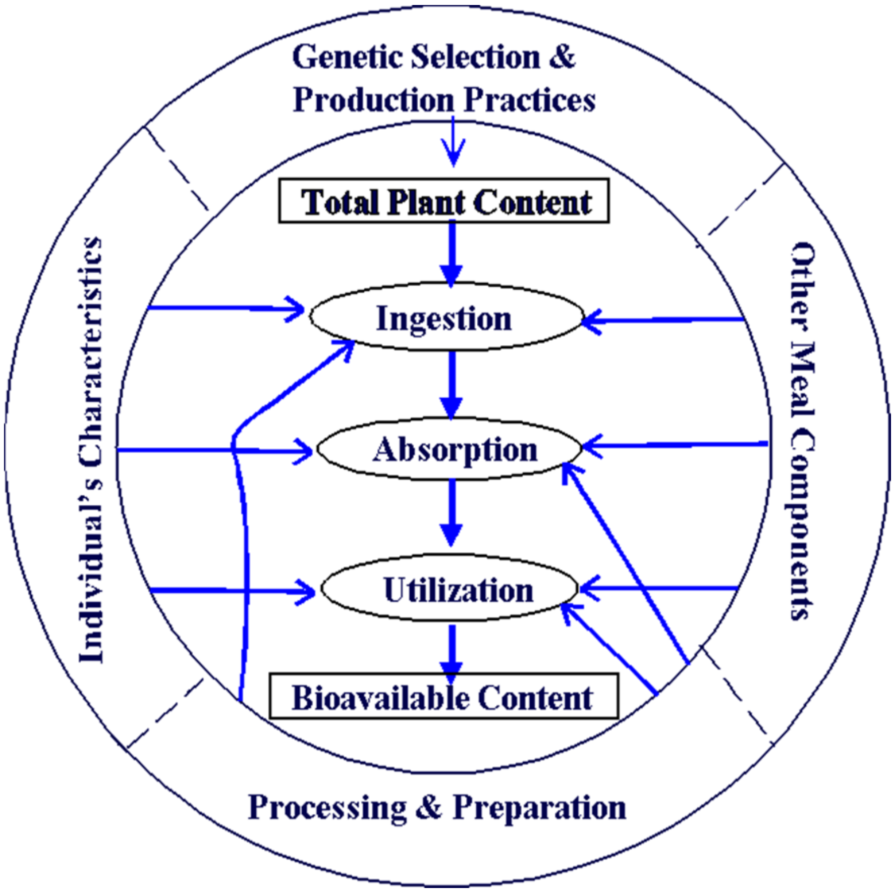


Figure 8: Changes in the Zn concentration in the endosperm of wheat seeds from plants foliar sprayed with $ZnSO_4$ at different growth stages in the field. Identifying the Zn localization in the endosperm was performed using a LA-ICP-MS (Laser Ablation Inductively Coupled Plasma Mass Spectrometry). Black arrows on the seeds (left side) show the analyzed area of the endosperm. Distance on the x-axis shows the length of the seed-endosperm section [for more detail see (Cakmak et al., 2010a; Cakmak, 2012)].

Figure 9. The complexities of determining nutrient bioavailability from staple food crops eaten in a meal [from (Welch and Graham, 2005)].



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