Plant breeding: a long-term strategy for the control of zinc deficiency in vulnerable populations[1–3]

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ABSTRACT Because trace minerals are important not only for human nutrition but for plant nutrition as well, plant breeding holds great promise for making a significant, sustainable, low-cost contribution to the reduction of micronutrient deficiencies in humans. It may also have important spinoff effects for increasing farm productivity in developing countries in an environmentally beneficial way. This article describes ongoing plant breeding research that could increase the intake of bioavailable zinc from food staple crops in vulnerable populations in developing countries. The 3 most promising plant breeding strategies toward this goal are as follows: *1*) increasing the concentration of zinc, *2*) reducing the amount of phytic acid (a strong inhibitor of zinc absorption), and *3*) raising the concentrations of sulfur-containing amino acids (thought to promote zinc absorption) in the plant. The agronomic advantages and disadvantages as well as the potential benefits and limitations of each approach for human nutrition are described. Research is currently underway to identify the optimal combination of these approaches that will maximize the effect on human zinc nutrition. *Am J Clin Nutr* 1998;68(suppl):488S–94S.

KEY WORDS Zinc deficiency, zinc, plant breeding, agriculture, interventions, developing countries, phytic acid, sulfur-containing amino acids, zinc supplementation, zinc fortification

INTRODUCTION

Designing cost-effective and sustainable strategies to improve the zinc nutriture of vulnerable groups in developing countries is a serious challenge for program planners. Both food fortification and daily individual supplementation, which are the traditional approaches, face logistic constraints and are often not cost-effective. Dietary modifications are promising, but they require behavioral changes that depend on intensive and costly education, communication, and social marketing strategies, and may be difficult to implement.

Plant breeding strategies hold great promise for making a significant low-cost and sustainable improvement in the intake of bioavailable zinc in populations. The possible improvements range from increasing the concentration of minerals such as zinc and iron in the plant to reducing the amount of antinutrients such as phytic acid to raising the concentrations of promoters of zinc absorption such as sulfur-containing amino acids.

This article describes recent findings in plant research in these 3 areas. It also discusses the potential for plant breeding strategies to help in the long-term resolution of programmatic issues related to the prevention and control of zinc deficiency in developing countries.

HISTORICAL BACKGROUND

In rich and poor countries alike, the primary objective of plant breeding at agricultural research stations is to improve farm productivity, usually by developing crops with higher yields. When crossbreeding plants with particular traits, scientists also monitor and attempt to maintain marketable characteristics such as taste, cooking qualities, and appearance. This is because such characteristics affect market prices and profitability, which motivate farmers to adopt improved varieties.

Enhancing the nutrient content of plants for human nutrition purposes has rarely been a breeding objective; in fact, the nutritional qualities of improved crops are mostly ignored during the breeding process. This is due to the presumptions that *1*) nutrient-enhanced crops will be lower yielding and so must command a higher price to be profitable, and *2*) even if the problem of identifying nutrient-enhanced products could be solved, consumers are basically unwilling to pay a premium for a higher nutrient content of a specific food.

However, as we learn more about the substantial costs of micronutrient deficiencies in people in developing countries and the similarities between trace mineral requirements in both human and plant nutrition, and as plant breeding techniques improve, it becomes clear that conventional wisdom needs rethinking. The suggestion that a plant breeding strategy could improve human nutrition as well as farm productivity was very much unexpected by scientist members of the Consultative Group on International Agricultural Research (CGIAR) when the idea of breeding micronutrient-dense seeds was first broached in 1993.

In the past 4 y, however, opinion within the CGIAR as to the wisdom of breeding for nutritional objectives has changed substantially because of the influence of recent research showing the

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importance, for plant nutrition, of the ability of particular crop genotypes to take up trace minerals from trace mineral–deficient soils (1). In the case of trace minerals, it appears that the disparate objectives of breeding for higher yield and better human nutrition largely coincide.

An international research effort is now underway to assess the feasibility of breeding for micronutrient-dense staple food crops. The nutrients emphasized are iron, zinc, and vitamin A (β-carotene) and the food crops are wheat, maize, rice, beans, and cassava (2). An independent, national-level research project concentrating on zinc in wheat is also being conducted in Turkey (3).

Some progress has been made relative to the first stage of plant breeding research, which consists of screening for genetic variability in concentration of trace minerals (4). All crops show significant genotypic variation, up to twice that of common cultivars for minerals and even more than that for β-carotene in cassava. For instance, of nearly 1000 traditional cultivars, improved commercial varieties, and elite breeding lines of brown rice that were evaluated for iron and zinc, the average iron concentration in the grain was 12 parts per million (ppm) with a range of 8–24 ppm, and zinc concentrations averaged 25 ppm with a range of 14–42 ppm. Similar ranges of iron and zinc concentrations were found in wheat; as for rice, there appeared to be more genetic diversity for zinc than for iron. In maize, the range of genotypic differences in iron and zinc concentrations in 150 improved genotypes was ≈50% of the mean value. In beans, screening of 1500 traditional varieties and wild relatives showed iron and zinc concentrations ranging from 34 to 89 ppm and from 21 to 54 ppm, respectively [D Senadhira (rice), M Banziger (maize), I Monasterio (wheat), and S Beebe (beans), personal communications, 1997]. Although encouraging, these results should be considered preliminary because much more extensive screening remains to be done.

With respect to a strategy of reducing phytic acid in seeds, Raboy (5) reported the development of low–phytic acid mutants of maize, barley, and rice. Total phosphorus concentrations in these mutants are similar to those in nonmutant seeds, but phytic acid represents a substantially lower percentage (eg, 25% compared with 75%) of total seed phosphorus. The low–phytic acid trait is easy to work with in a breeding program because it is a single-gene trait. Moreover, the unusually high free phosphate in low–phytic acid seeds provides an easily applied field assay in breeding programs.

THREE PLANT BREEDING STRATEGIES TO INCREASE BIOAVAILABLE ZINC IN DIETS

The success of any plant breeding strategy depends critically on the following 2 fundamental factors: *1*) adoption of the nutritionally improved varieties by farmers, which is dependent on the improved crops offering the necessary agronomic advantages (ie, profit incentives) to farmers, and *2*) an actual increase in intake of bioavailable nutrients in a population, which is dependent on the product being acceptable to consumers relative to cost, cultural preferences, and organoleptic properties, and containing bioavailable nutrients.

These 2 issues are addressed below for each of the 3 most promising plant breeding strategies for the control of zinc deficiency worldwide, which are: *1*) increase the concentration of zinc in the plant, *2*) reduce the amount of phytic acid, and 3) increase the concentrations of sulfur-containing amino acids. The present article focuses on zinc and touches on iron where appropriate.

Increasing the zinc concentration of staple crops

Agronomic advantages and disadvantages

This section draws on a monograph by Graham and Welch (1) that summarizes the research and available evidence showing the agronomic advantages of breeding mineral-dense staple crops. A soil is said to be deficient in a nutrient when the addition of a fertilizer containing this nutrient produces better plant growth. However, the amount of a mineral micronutrient added to a soil to produce better growth is usually small compared with the total amount of the mineral found in the soil by complete analysis. This is because most of the trace mineral in the soil is unavailable to plants because it is chemically bound to other elements in the soil. An alternative view, therefore, is that there is a genetic deficiency in the plant, rather than a mineral deficiency in the soil.

Tolerance of micronutrient-deficient soils, termed *micronutrient efficiency*, is a genetic trait of a genotype or phenotype that causes it to be better adapted to, or yield more in, a micronutrient-deficient soil than an average cultivar of the species (6). Growing zinc-efficient plants on zinc-deficient soils, for example, represents a strategy of "tailoring the plant to fit the soil" in contrast with the alternative strategy of "tailoring the soil to fit the plant" [terminology according to Foy (7)]. These efficient phenotypes exude substances from their roots that chemically release trace minerals from binding sites, thereby making the trace minerals available to the plant.

Most micronutrient efficiency traits studied so far arise from a superior ability of the plant to extract the limiting micronutrient from the soil rather than from a capacity to survive on less of that micronutrient. It is well understood that depletion of soil nitrogen takes only a few years if there is no replacement. Thus, it is pointless to breed for greater tolerance of nitrogen-deficient soils (although breeding has been effective in producing crop varieties more efficient at extracting added soluble nitrogen before it is leached and pollutes ground waters and streams). Likewise, breeding has been successful in improving tolerance to many soil mineral problems such as acidity, salinity, and other toxicities, as well as tolerance to soils low in macronutrients, particularly phosphorus.

The increased yield resulting from phosphorus efficiency results in overall improvements in cost efficiency, but phosphorus is eventually depleted from the soil. By contrast, for mineral micronutrients, depletion may take hundreds or thousands of years, or may likely never occur at all, owing to various inadvertent additions and other processes (eg, minerals carried in windblown dust) (8). It is logical, then, to concentrate some plant breeding efforts on producing micronutrient-efficient varieties for minerals that are required in low amounts and for which there are large reserves in the soil but low availability.

On the basis of several soil surveys, particularly in China, where the most extensive soil surveys were done, it can be estimated that ≥50% of the arable land used for crop production worldwide is low in availability of ≥1 essential micronutrient. Zinc deficiency is probably the most widespread micronutrient deficiency in cereals. Sillanpää (9) found that, of a global sample of 190 soils in 25 countries, 49% were low in zinc. Unlike other micronutrients, zinc deficiency is a feature common to cold

and warm climates, drained and flooded soils, acid and alkaline soils, and heavy and light soils alike.

In Turkey, for example, ≈50% of the arable soils were found to contain <0.5 mg pentetic acid–extractable Zn/kg, which is a widely accepted critical concentration indicating zinc deficiency (3). In one region (central Anatolia), where nearly 45% of Turkey's wheat production is located, >90% of the soils sampled were below the critical concentration of zinc. The actual content of zinc in soils is fairly high, ranging from 40 to 80 mg/kg, but the availability to plants is extremely low.

Why do zinc-efficient varieties have higher yields in zinc-deficient soils? There are at least 3 agronomic advantages to growing mineral-dense crops, as follows:

First, efficiency in the uptake of minerals from the soil improves disease resistance in plants and results in reduced use of fungicides. This is because good nutritional balance is as important to disease resistance in plants as it is in humans (1). Micronutrient deficiency in plants greatly increases their susceptibility to diseases, especially fungal root diseases of the major food crops (10). The picture emerging from physiologic studies of roots spanning 4 decades is that the elements phosphorus, zinc, boron, calcium, and manganese are all required in the external environment of the root for membrane function and cell integrity. In particular, phosphorus and zinc deficiencies in the external environment promote the leaking of cell contents such as sugars, amides, and amino acids, which are stimuli to pathogenic organisms. It appears that micronutrient deficiency predisposes the plant to infection, rather than the infection causing the deficiency through its effect on root pruning (11–13). Thus, breeding for micronutrient efficiency can confer resistance to root diseases that had previously been unattainable. This means a lower dependence on fungicides.

Second, micronutrient-efficient varieties grow deeper roots in mineral-deficient soils and so are better able to tap subsoil water and minerals (1). When topsoil dries, roots in the dry soil zone (which are the easiest to fertilize) are largely deactivated and the plant must rely on deeper roots for further nutrition. Roots of plant genotypes that are efficient in mobilizing nutrients from surrounding minerals are not only more disease resistant but are better able to penetrate deficient subsoils and make use of the moisture and minerals contained in subsoils. This reduces the need for fertilizers and irrigation. Plants with deeper root systems are more drought resistant.

Third, micronutrient-dense seeds are associated with greater seedling vigor that is associated with higher plant yields (14). An important function of the seed is to supply the young seedling with minerals until it has developed a root system large enough to take over this role. In nutrient-poor soils, there may not be sufficient seed reserves to last while the extra roots are developed to compensate for the low mineral supply. The result is a transient and critical period of deficiency in which the seedling is particularly vulnerable. Pathogens and weeds may gain an advantage not otherwise given and the plant may never regain lost potential.

Separate mechanisms (and different genes) control the uptake of trace minerals from soils and the translocation of trace minerals to seeds, such that plant genotypes may be zinc-efficient without having zinc-dense seeds. Research is underway to better understand the mechanisms that control the translocation of zinc within the plant to seeds (15).

Adoption of zinc-efficient staple crops with zinc-dense seeds is likely to be attractive to farmers because of the potential for higher profits under zinc-deficient soil conditions. However, incorporating additional characteristics in a plant breeding program entails extra costs (because other breeding objectives, eg, pest resistance and higher yield potential, given a fixed budget, are met at a slower pace). Plant breeders need to be convinced that the benefits for human nutrition of breeding for these characteristics in nondeficient soils are worth these extra costs.

Nutritional benefits

With the goal of improved human nutrition in mind, the main question here is whether increasing the zinc content of staple crops will result in significant increases in intake of bioavailable zinc and improve the zinc status of deficient populations. For this to happen, vulnerable groups must consume the improved varieties of staple crops in sufficient quantities and the net amount of bioavailable zinc ingested must be increased relative to traditional crops. These 2 conditions are discussed below.

Consumption of staple food crops by vulnerable groups. Staple crops provide a large proportion of the daily intake of energy and other nutrients, including micronutrients, in poor populations who have limited access to animal foods (16, 17). The main sources of zinc in these populations are staple cereals, starchy roots, tubers, and legumes, which are low either in quantity or bioavailability of zinc (18). The most potent factor reducing the bioavailability of zinc in cereals and legumes is phytic acid, which exerts a strong inhibiting effect on zinc absorption (19).

As emphasized throughout this supplement, young children and pregnant and lactating women are particularly at risk for zinc deficiency because of their higher zinc requirements for growth and reproduction and their high rates of infectious diseases. Improving the zinc content of staple crops is a sound strategy from the perspective that it is likely to effectively reach the targeted populations, ie, the poorest of the poor, who are most dependent on food staples, and women and children who consume staple foods on a daily basis.

Additionally, in many cultures there are no special weaning products available for young infants and staple foods constitute the basic ingredient of most complementary foods. Efforts to design special complementary foods for young infants usually rely heavily on the use of locally available, culturally acceptable, and inexpensive staple foods (20). Therefore, if improved staple crop varieties are made available at similar prices as traditional varieties, and if acceptable organoleptic characteristics are maintained, this approach will undoubtedly be successful in reaching its target population. An additional advantage of this approach is the issue of self-targeting, or the fact that the poorer the population, the larger the contribution of staple foods to their usual daily intake of nutrients, and hence, the greater the benefits that will accrue to the most needy.

As a rough order of magnitude of the contribution of staple foods to total trace mineral intakes, dietary studies stratified by household socioeconomic status suggest that cereals contribute up to 50% of the iron intake in the poorest households (2). In preschoolers in Malawi, 42–62% of zinc intake was found to come from cereals and an additional 21–39% from other plant products, depending on the season. Only 17–19% of total zinc intake was from animal sources (17). This means that doubling the iron or zinc density of food staples could increase total intakes by ≥50%. For this to translate to a 50% increase in the total amount of zinc absorbed, the following criteria need to be met: *1*) that heme and nonheme sources of zinc form a single pool from

which usable zinc may be drawn, *2*) that staple cereals provide 50% of total zinc intake, and *3*) that the zinc contained in the zinc-dense cereals has the same percentage of bioavailability as the zinc contained in lower-zinc varieties. This last criteria is the most crucial one, and needs to be tested before predictions can be made about the potential contribution of improved varieties to the zinc (and iron) status of vulnerable populations.

Bioavailability of zinc from improved varieties. Bioavailability of zinc depends on several factors, namely the nutrient content and composition of the diet and the nutritional and health status of the host (18). The nutrients of particular importance are phytic acid, a powerful inhibitor of zinc absorption, and sulfur-containing amino acids (such as methionine, cysteine, and lysine), thought to promote the absorption of zinc (19).

Some argue that raising the concentration of minerals, eg, iron or zinc, may not increase the amount of bioavailable minerals because these additional minerals may be captured by the large amounts of phytic acid present in the grains that are consumed as part of the diet (5). The argument is that if the zinc or nonheme iron concentration of the grain is increased two- to fourfold, there would still be ample phytic acid to bind the extra minerals.

Results based on rat models, however, show that the percentage of bioavailability tends to remain constant when traditional and zinc- or iron-enhanced crops are compared, resulting in a net increase in bioavailable minerals. Studies using marginally zinc-deficient rats fed meals containing cereals or legumes with >1% phytic acid showed that increasing the zinc concentration by 400–500% did not affect the percentage of zinc absorbed: absorption went from 77.4% when rats were fed usual pea-based diets (containing 9.0 mg Zn/kg and 1.23% phytic acid) to 74.9% with the zinc-dense varieties (containing 47.8 mg Zn/kg and 1.16% phytic acid). Similar results were obtained with improved wheat (with a fourfold higher concentration of zinc): the percentage absorption was 57.4% for the improved variety compared with 56.1% for the conventional one (21, 22). Thus, studies done with marginally zinc-deficient rats showed that the percentage of zinc bioavailability remained constant when they consumed low-zinc compared with high-zinc meals, resulting in a significantly higher net amount of zinc absorbed.

Rats, however, have substantially more intestinal phytase activity than humans (a multiple of ≈30) and, therefore, are more able to absorb iron or zinc from high-phytate foods than humans (23). Despite this limitation, it was suggested that the rat model could be useful for ranking staple foods with different combinations of zinc and phytic acid content, although in the final analysis the net percentage absorbed from the highest ranked genotypes would have to be measured in marginally zinc-deficient humans.

This proposed use of the rat model has been challenged by Reddy and Cook (24) with regard to nonheme iron absorption. Through a direct comparison of nonheme iron absorption in humans and rats by the same methodologic approach, the authors showed that rats were relatively insensitive to factors that both inhibit (eg, phytic acid in bran, tea, and soy protein) and promote (eg, meat and ascorbic acid) nonheme iron absorption in humans. Thus, they warn that extrapolation of results on nonheme iron bioavailability from the rodent model to humans should be done only with caution (24). A potential limitation of this study, however, is that the authors compare only ratios of bioavailability between control and test meals, ignoring the absolute differences in bioavailability, which actually match up reasonably well between humans and rats. It is clear that these ratios will be lower for rats as compared with humans a priori, in that the base level of bioavailability for control meals (2–7% for humans and 45–70% for rats) is substantially smaller for humans than for rats.

Plant breeding requires that large numbers, perhaps hundreds, of promising genotypes (those with high mineral density, for instance) be screened for bioavailability. Although rat models have limitations for this work, use of rats is the most cost-effective method for this initial screening. Although they are substantially more expensive, human studies testing the bioavailability of added zinc to diets under dietary and nutritional status conditions found in developing countries are urgently needed.

A strategy for increasing the zinc content of staple crops may or may not work well depending on still unknown factors relating to host factors as well as interactions among dietary components. However, this strategy may be complemented by at least 2 other plant breeding strategies that increase the probability for success, specifically reducing the concentration of phytic acid in grains, increasing the concentration of promoter compounds such as certain amino acids (methionine, lysine, or cysteine), or both.

Reducing the concentration of phytic acid in the plant

Agronomic advantages and disadvantages

Phytin is the primary storage form of phosphorus in most mature seeds and grains. It is required for early seed maturation, seedling growth, vigor, and viability (1). Phytin also plays an important role in determining the mineral nutrient reserves of seeds and as such contributes to the viability and vigor of the seedling. For these reasons, some argue that selecting for crops with substantially lower phytin contents could have unacceptable effects on agronomic performance, especially in regions of the world with low-phosphorus soils (1). However, initial results from research in low–phytic acid mutants discussed earlier suggest that these mutants perform well agronomically and there is not a noticeable decline in yields (5). More research is needed to obtain better information on the agronomic effects of lower concentrations of phytates in seeds.

Nutritional benefits

The negative effect of phytic acid on zinc absorption in humans is well documented (19). For example, addition of phytic acid to diets in amounts usually found in whole grain–based cereals reduced the absorption of zinc by one-half, from 34% to 17% (25, 26). Data compiled from various studies of zinc absorption from cereal-based meals in humans show a gradual decrease in zinc absorption as phytic acid concentrations increase (19). At concentrations of 400–500 μmol (264–330 mg) phytic acid, zinc absorption is <10% and is reduced to <5% at concentrations of 1000 μmol (660 mg). This indicates that substantial reductions in phytic acid would be necessary to significantly improve zinc absorption.

A similar and probably even more dramatic phenomenon was described for nonheme iron absorption. Research in humans showed that minimal amounts of phytic acid added to meals can produce a severe inhibition of nonheme iron absorption. Although studies do not agree on the exact cutoff point where nonheme iron is significantly improved by removal of phytic acid, some found that almost complete removal (<10 mg/meal)

was necessary (27), or that concentrations as low as 50 mg phytic acid caused a 78–92% reduction in nonheme iron absorption, depending on the protein composition of the meal (28).

To provide an idea of the order of magnitude of this phenomenon, daily intakes of phytic acid in preschool children from populations whose staple diets are based on cereals, legumes, and starchy roots and tubers are estimated to range from 600 to 1900 mg, that is 200–600 mg/meal (18). In Mexican adult men and women, intakes of phytic acid are on the order of 4000–5000 mg/d (16). Cereals such as whole wheat, corn, and millet contain ≈800 mg phytic acid/100 g cereal.

A key issue, then, is whether plant breeding can achieve the magnitude of reduction in phytic acid that may be necessary to obtain significant improvements in absorption of both zinc and nonheme iron. If, as suggested by Raboy (5), phytic acid in staple foods can be reduced by a factor of two-thirds, and if dietary phytic acid comes mainly from staple foods, it is likely that this strategy would affect the bioavailability of zinc and iron simultaneously and may also affect that of calcium, manganese, magnesium, and possibly other trace minerals.

More research is needed in iron- and zinc-depleted humans subjects and with meals typical of the diets of poor families in developing countries to understand the relation between the phytate-zinc and phytate-nonheme iron molar ratios and zinc bioavailability to guide the optimal breeding strategy. Complementary food processing, preparation, and consumption strategies may be needed to further improve mineral bioavailability (29, 30).

Increasing the concentration of promoter compounds (sulfur-containing amino acids)

Another potentially complementary approach to increasing the bioavailability of minerals (iron and zinc in particular) in staple crops is to increase the concentration of sulfur-containing amino acids that are thought to promote their absorption, namely methionine, lysine, and cysteine.

Agronomic advantages and disadvantages

Information on the agronomic advantages or disadvantages to increasing the concentration of sulfur-containing amino acids in staple foods is scant. It appears, however, that the magnitude of the increase in amino acid concentrations needed to positively affect the bioavailability of iron and zinc may be small and, therefore, unlikely to affect plant functions significantly (22).

Nutritional benefits

Both the source and the amount of dietary protein affect zinc and nonheme iron absorption in humans as well as in animals (31). The positive effects of proteins found in meat on the bioavailability of minerals was shown, but the precise mechanisms are not fully understood. Researchers question whether the so-called "meat factor" is *1*) a protein per se, *2*) specific amino acids in proteins (in particular sulfur-containing amino acids), *3*) some amino acid metabolites (namely citric acid and picolinic acid), or *4*) unidentified components in proteinaceous foods (32).

Results of a few studies in rats and in humans showed that both the amount of proteins and the concentration of cysteine, and histidine to a lesser extent, had positive effects on mineral absorption, particularly zinc (31–33). Iron and copper were less affected by sulfur-containing amino acids. The authors also found that the addition of sulfur amino acids and of protein to the diet did not produce duplicate effects, suggesting that the 2 factors had independent effects on zinc metabolism (31, 32).

More recent work with marginally zinc-deficient rats showed that diets supplemented with amino acids increased the absorption of zinc from an initial 64% to 69% with lysine, 82% with methionine, and 86% with both amino acids (34). A second experiment testing the effect of supplemental cysteine and methionine in test meals also showed an increase in the absorption of zinc from 53% and 57% initially to 73% with either amino acid added. The authors concluded that adding supplemental methionine to basal diets resulted in increases in the absorption of zinc of ≈14–35% (34). More research is needed in human subjects on the effects of protein and sulfur-containing amino acids on zinc and nonheme-iron bioavailability under the dietary and nutritional status conditions found in developing countries.

COMPARATIVE COSTS OF PLANT BREEDING STRATEGIES

A plant breeding strategy, if successful, will not eliminate the need for supplementation, fortification, dietary diversification, or disease reduction programs in the future. Nevertheless, this strategy does hold great promise for significantly reducing the recurrent expenditures required for higher cost short-term programs by significantly reducing the number of people requiring treatment.

For example, Yip (35) argues that if prevalence rates are >25%, the best approach to treating iron deficiency in developing countries is to develop programs to improve the iron nutriture of the entire population. In such situations, which are the rule rather than the exception for preschoolers and women in developing countries, this is less costly than screening for iron-deficient individuals. By increasing the iron content of food staples through plant breeding, the entire distribution curve could be shifted to the right, so that targeting a subsequently smaller group of iron-deficient persons could become feasible. Little is known about the prevalence of zinc deficiency in developing countries or about the distribution curve for biochemical indicators of zinc status. Even less is known about the cost of interventions for the prevention and control of zinc deficiency, so the following cost estimates and comparisons will be discussed with reference to iron, for which there is information.

The plant breeding effort can be seen as a 2-stage process. The first 5-y phase primarily, but not exclusively, involves research at central agricultural research stations at an estimated $2 million/y for research on 5 crops (maize, rice, wheat, beans, and cassava). During this initial phase, promising genotypes are identified and the general breeding techniques are developed for later adaptive breeding. The second phase involves shifting from research to national agricultural adaptive breeding programs.

Total costs and duration of this second phase are difficult to estimate, but will depend on the number of countries involved and the number of crops worked on in each country. Certainly, the annual cost for each country should not be more than the $2 million/y estimated for the first phase.

To provide some sense of the magnitude of the recurrent annual cost involved in iron fortification and supplementation, a lower bound estimate of the cost of iron supplementation is $\$2.65 \cdot \text{person}^{-1} \cdot \text{y}^{-1}$ when all administrative costs are taken into account (36). A lower bound estimate for iron fortification is $\$0.10 \cdot \text{person}^{-1} \cdot \text{y}^{-1}$. In India, as many as 28 million pregnant

women may be anemic in any given year out of a total population of 880 million. These figures imply that treating one-half of the anemic pregnant women in any 1 y through a well-targeted supplementation program would cost $37 million/y. A fortification program that reached one-half of the population would cost $44 million/y. Thus, the projected costs of a plant breeding strategy are relatively low. Most of the cost is the initial one-time cost of development.

One can imagine that there will be unforeseen problems and costs associated with plant breeding not mentioned here. Additionally, daily doses of iron from supplementation programs may be higher than the additional iron likely to be added to the daily intake of food staples via plant breeding. Nevertheless, whatever refinements are necessary to these comparative cost estimates, there is no argument that the base, fixed costs of plant breeding are low, and that cost considerations are overwhelmingly on the side of a plant breeding strategy compared with supplementation and fortification.

Moreover, these comparative costs do not take into account the potential benefits of improved agricultural productivity and reduced input needs that will also have a positive effect on the incomes of poor farmers. For example, in Turkey it was estimated that if existing Australian zinc-dense seed varieties were adapted to growing conditions in Turkey, Turkish wheat farmers would save $75 million/y in reduced seeding rates alone (seeding rates could be reduced from an average of 250 to 150 kg/hectare on 5 million hectares; a metric ton of wheat has sold for ≈US$150 on the world market in recent years). This does not count the benefit to yield or the potential benefit of improved zinc status in humans (2).

CONCLUSIONS

The research presented at the *Zinc for Child Health* conference constitutes a persuasive body of evidence showing the seriousness of zinc deficiency in developing countries as a public health problem. Until now, lack of such information was a major constraint that prevented action by national and international agencies. A primary constraint to immediate action continues to be that no fully tested interventions are available for immediate implementation, and designing cost-effective and sustainable strategies to improve the zinc nutrition of vulnerable groups in developing countries poses a serious challenge for program planners.

For the reasons stated in this article, it is clear that plant breeding strategies hold great promise for making a significant low-cost and sustainable contribution to improving the intake of bioavailable zinc in developing countries. Although plant breeding requires comparatively long lead times before an appreciable effect is shown, a start has been made. The pace of progress in the years ahead will depend on the support that this nontraditional approach receives from plant breeders and human nutritionists.

The feasibility of breeding plants separately for increased trace mineral density (eg, research results to date under the ongoing CGIAR Micronutrients Project) or for higher concentrations of promoter compounds (eg, quality protein maize now being disseminated widely in Ghana) in the context of high crop yields was already shown. Promising work in low–phytic acid mutants is underway as well to evaluate the agronomic characteristics of seeds that already have substantially lower amounts of antinutrients. Work has yet to begin on combining any or all of these traits in a single variety.

The key issues are not those of cost, or whether plant breeders eventually will be successful in developing micronutrient-dense seeds if the relatively modest resources required to develop them are found. Rather, they are *1*) whether the agronomic advantages of the zinc-dense seeds are sufficiently strong that national breeding programs will incorporate them into their improved lines of staple food crops so that they can be widely adopted by farmers, and *2*) whether the additional zinc contained in the seeds will be of sufficient magnitude and bioavailablity to appreciably affect zinc status. There is enough scientific evidence to be optimistic on the first issue. Additional research is needed to get a clearer picture on the second.

More broadly, in conceptualizing solutions for a range of nutritional deficiencies with zinc as a particular case, interdisciplinary communication holds great potential for better program and policy formulation. Experts in human nutrition, in general, are not aware of the extent to which the vitamin and mineral density of specific foods, as well as compounds that promote and inhibit their bioavailability, can be manipulated through plant breeding. On the other hand, plant breeders, in general, are not aware of the major influence they may have had on nutrient utilization in the past (ie, are trace minerals in modern varieties more or less bioavailable than in traditional varieties?), nor of their potential for future improvements in nutrition and health. As the world's resources for food production and other purposes become increasingly stressed, such interdependencies between agricultural systems and human nutrition will become not only increasingly obvious, but impossible to ignore in formulating solutions.

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