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PLANT BREEDING: A LONG-TERM STRATEGY FOR THE CONTROL OF ZINC DEFICIENCY IN VULNERABLE POPULATIONS

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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 low-cost and sustainable contribution to reducing micronutrient deficiencies in humans, and may have important spinoff effects for increasing farm productivity in developing countries in an environmentally beneficial way.

This paper describes ongoing plant breeding research that could increase the intake of bioavailable zinc from food staple crops among vulnerable populations in developing countries. The three most promising plant breeding strategies to achieve this goal are (1) increasing the concentration of zinc in the plant, (2) reducing the amount of phytic acid (a strong inhibitor of zinc absorption), and (3) raising the levels of sulfur-containing amino acids (which are thought to promote zinc absorption). 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 impact on human zinc nutrition.

CONTENTS

1. INTRODUCTION

Designing cost-effective and sustainable strategies to improve the zinc nutrition of vulnerable groups in developing countries constitutes a serious challenge for program planners. Food fortification and daily individual supplementation, the traditional approaches, face logistical constraints and are often not cost-effective. Dietary modifications are promising, but they require behavior changes, and thus, intensive and costly education, communication, and social marketing strategies and may be difficult to scale up.

Plant breeding strategies hold great promise for making a significant low-cost and sustainable contribution to improving the intake of bioavailable zinc in populations. The possibilities range from increasing the concentration of minerals such as zinc or iron in the seed,[1] to reducing the amount of antinutrients such as phytic acid, and to raising the levels of promoters of zinc absorption such as sulfur-containing amino acids.

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

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[1] For cassava, we are referring to the edible portion of the root.

2. 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. In crossing varieties with particular traits, scientists also monitor and attempt to maintain consumer characteristics such as taste, cooking qualities, and appearance. This is because such characteristics have a bearing on market prices, and subsequently on profitability, which motivates farmers to adopt improved varieties.

Enhanced nutrient content for human nutrition purposes has almost never been a breeding objective. For the most part, the nutritional qualities of improved crops are 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 higher nutrient content of a specific food.

However, as we learn more about the substantial costs of micronutrient deficiencies in humans, particularly in developing countries, as we discover some similarities between trace mineral requirements in both human and plant nutrition, and as plant breeding techniques improve, conventional wisdom needs rethinking. The idea that a plant breeding strategy could benefit farm productivity in addition to improving human nutrition was met with skepticism among scientists at several international agricultural research centers (members of the Consultative Group on International Agricultural Research [CGIAR]).

Over the past four years, however, opinion within the CGIAR as to the wisdom of breeding for nutritional objectives has improved substantially. The primary reason has been the influence of a relatively new body of research that provides a better understanding of the importance for plant nutrition of the ability of particular crop genotypes to take up trace minerals from trace mineral "deficient" soils (Graham and Welch 1996). That is, in the case of trace minerals, it turns out that the objectives of breeding for higher yield and better human nutrition appear to largely coincide. The reasons for this are discussed in more detail in the following section of the paper.

An international research effort is now under way to assess the feasibility of breeding for micronutrient-dense staple food crops. The nutrients emphasized are iron, zinc, and vitamin A (beta-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 undertaken in Turkey (Cakmak et al. 1996).

To date, some progress has been made relative to the first stage of the plant breeding research, which consists of screening for genetic variability in a concentration of trace minerals (Bouis 1995). All crops have shown significant genotypic variation, up to twice that of common cultivars for minerals, and even more than that for beta-carotene in cassava. For instance, of nearly 1,000 traditional cultivars, improved commercial varieties, and elite breeding lines that have been evaluated for iron (Fe) and zinc (Zn) in brown rice, the average Fe concentration in the grain was 12 parts per million (ppm) with

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[2] Additional information on this project is available in Bouis (1996).

a range of 8 to 24 ppm, and Zn averaged 25 ppm with a range of 14 to 42 ppm. Similar ranges of Fe and Zn concentrations were found in wheat, and as for rice, there appeared to be more genetic diversity for Zn than for Fe. For maize, the range of genotypic differences in Fe and Zn concentration in the grain of 150 mainly improved genotypes was around 50 percent of the mean value. For beans, screening of 1,500 traditional varieties and wild relatives showed Fe and Zn concentrations ranging from 34 to 89 ppm and from 21 to 54 ppm, respectively (personal communications with plant breeders).

Although encouraging, much more extensive screening is still to be undertaken, so these results should be considered as preliminary.

With respect to a strategy of reducing phytic acid in seeds, Raboy (1996) has reported the development of low phytic acid (*lpa*) mutants of maize, barley, and rice. Total phosphorus levels in these mutants are similar to nonmutant seeds, but phytic acid represents a substantially lower percent (e.g., 25 percent as compared with 75 percent) of total seed phosphorus. The *lpa* trait is easy to work with in a breeding program in that it is a single-gene trait. Moreover, the unusually high free phosphate in *lpa* seeds provides an easy-to-apply field assay in breeding programs.

3. THREE PLANT BREEDING STRATEGIES TO RAISE THE LEVEL OF BIOAVAILABLE ZINC IN DIETS

The success of any plant breeding strategy depends critically on two fundamental factors:

1. Whether farmers will adopt the nutritionally-improved varieties, which, in turn, depends on whether the improved crops offer the necessary agronomic advantages, and therefore profit incentives, to motivate farmers to adopt them.
2. Whether the improved varieties will actually increase the intake of **bioavailable** nutrients, in this case, zinc. This in turn will depend on whether the product is acceptable to the consumer relative to cost, cultural preferences, and organoleptic properties, and whether the zinc contained is bioavailable.

These two issues are addressed below for each of the three most promising plant breeding strategies for the control of zinc deficiency worldwide: (1) increasing the concentration of zinc in the plant, (2) reducing the amount of phytic acid, and (3) raising the levels of sulfur-containing amino acids. The present paper focuses on zinc and touches upon iron where appropriate.

INCREASING THE ZINC CONCENTRATION OF STAPLE CROPS

Agronomic Advantages/Disadvantages[3]

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 that is added to a soil to produce better growth is usually small compared to the total amount of that mineral found in the soil by complete analysis. This is because the major part of the trace mineral in the soil is "unavailable" to plants. 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 to 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 can an average cultivar of the species (Graham 1984). 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 [1983]). These efficient genotypes exude substances from their roots that chemically release trace minerals from binding sites, and so make the trace minerals available to the plant.

Nearly all micronutrient efficiency traits so far studied arise from a superior ability to extract the limiting micronutrient from the soil, rather than a capacity to survive on less

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[3] This section draws on a monograph from Graham and Welch (1996), which summarizes research and available evidence demonstrating the agronomic advantages of breeding mineral-dense staple crops.

of that micronutrient. It is well understood that, without replacement, depletion of soil nitrogen takes only a few years. Thus, it is pointless to breed for greater tolerance to 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 groundwaters 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.

Because of its high input requirements and cost, phosphorus efficiency results in overall improvements in cost-efficiency. Depletion of soil phosphorus usually results in the long term. 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 (for example, minerals carried in windblown dust) (Graham 1991). It is logical, then, to concentrate some plant breeding efforts toward producing micronutrient-efficient varieties for minerals for which there are large reserves in the soil, but low availability.

As a guide, based on a number of soil surveys, particularly in China, where the most extensive soil surveys have been done, it can be estimated that at least 50 percent of the arable land used for crop production worldwide is low in availability of one or more of the essential micronutrients for current varieties. Zinc deficiency is probably the most widespread soil micronutrient deficiency for cereals. Sillanpää (1990) found that 49 percent of a global sample of 190 soils in 25 countries were low in available zinc. Unlike other micronutrients, zinc deficiency is a common feature of both cold and warm climates, drained and flooded soils, acid and alkaline soils, and both heavy and light soils.

In Turkey, for example, approximately 50 percent of the arable soils were found to contain less than 0.5 milligrams per kilogram (mg/kg) DTPA-extractable zinc, which is a widely accepted critical level indicating deficiency (Cakmak et al. 1996). In one region (Central Anatolia), where nearly 45 percent of Turkey's wheat production is located, more than 90 percent of the soils sampled are below the critical level of zinc. The actual content of zinc in soils is fairly high, ranging from 40–80 mg/kg, but the availability to plants is extremely low.

Why are zinc-efficient varieties higher-yielding on zinc-deficient soils? There are at least three agronomic advantages to growing mineral-dense crops.

First, efficiency in the uptake of minerals from the soil improves disease resistance in plants and results in reduced use of fungicides. This is due to the fact that good nutritional balance is as important to disease resistance in plants as it is in humans (Graham and Welch 1996). Micronutrient deficiency in plants greatly increases their susceptibility to diseases, especially fungal root diseases of the major food crops (Graham and Webb 1991). The picture emerging from physiological studies of roots spanning four 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 leaking of cell contents such as sugars, amides, and amino acids, which are chematoxic 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 (Graham and Rovira 1984; Sparrow and Graham 1988; Thongbai et al. 1993). Thus, breeding for micronutrient efficiency can confer resistance to root diseases that had previously been unattainable. This, in turn, 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 (Graham and Welch 1996). 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 so make use of the moisture and minerals contained in subsoils. This reduces the need for fertilizers and irrigation. Furthermore, plants with deeper root systems are more drought resistant.

Third, micronutrient-dense seeds are associated with greater seedling vigor which, in turn, is associated with higher plant yield (Rengel and Graham 1995). 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, seed reserves may be insufficient 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 when the seedling is particularly vulnerable. Pathogens and weeds may gain an advantage not otherwise given, so that the plants never regain lost potential.

Separate mechanisms (and so different genes) control trace mineral uptake from soils and translocation of trace minerals to seeds, so 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 (Pearson 1996).

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 (a slowing down in the rate of meeting other breeding objectives, e.g., pest resistance, higher yield potential, for a fixed budget). Plant breeders need to be convinced that the benefits for human nutrition of breeding for these characteristics for **nondeficient** soils are worth these extra costs.

Nutritional Benefits

From a human nutrition point of view, the main question is whether increasing the zinc content of staple crops will, in fact, result in significant increases in intake of bioavailable zinc and improve the zinc status of deficient populations. For this to happen, vulnerable groups have to 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 two 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, among poor populations who have limited access to animal foods (Allen et al. 1992; Ferguson et al. 1989). The main sources of zinc in these populations come from staple cereals, starchy roots, tubers and legumes and, thus, are low either in quantities or bioavailability (Gibson 1994). 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 (Sandström and Lönnerdal 1989).

Young children and pregnant and lactating women are particularly at risk of zinc deficiency due to their higher 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 targeted populations, i.e., 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, thus, staple foods constitute the basic ingredient of most complementary foods. Efforts to design special complementary foods for young infants also usually rely heavily on the use of locally available, culturally acceptable, and cheap staple foods (Brown and Begin 1993). 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 more 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 percent of **iron** intakes of poorest households (Bouis 1996). Among preschoolers in Malawi, between 42 and 62 percent of **zinc** intakes were found to come from cereals, and an additional 21–39 percent from other plant products, depending on the season. Only 17–19 percent of total zinc intake was from animal sources (Ferguson et al. 1989). This means that doubling the iron or zinc density of food staples could potentially increase total intakes by at least 50 percent.

The crucial question, however, is the extent to which zinc-dense varieties will increase the amount of ***bioavailable*** zinc consumed by the targeted population. A definite answer to this question is still premature, but a discussion of some of the issues involved is presented below.

Bioavailability of Zinc from Improved Varieties. The bioavailability of zinc depends on a series of factors, namely the nutrient content and composition of the diet and the nutritional and health status of the host (Gibson 1994). 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), which are thought to promote the absorption of zinc (Sandström and Lönnerdal 1989).

Some argue that raising the concentration of minerals (iron or zinc, for instance) may not increase the net 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 (Raboy 1996). 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 animal (rat) models, however, show that the percent bioavailability tends to remain constant when traditional versus zinc- (or iron-) enhanced crops are compared, which results in a net increase in bioavailable mineral. Studies using marginally zinc-deficient rats fed meals containing cereals or legumes with over 1 percent phytic acid showed that increasing the zinc concentration by 400 to 500 percent did not affect the percentage of zinc absorbed—absorption went from 77.4 percent when rats were fed usual pea-based diets (containing 9.0 mg/kg of zinc and 1.23 percent phytic acid) to 74.9 percent with the zinc-dense varieties (containing 47.8 mg/kg of zinc and 1.16 percent phytic acid). Similar results were obtained with improved wheat (with a fourfold higher concentration of zinc): the percentage absorption was 57.4 percent for the improved variety compared to 56.1 percent for the conventional one (House and Welch 1989; Welch 1996). Thus, studies done with marginally zinc-deficient rats showed that the percentage zinc bioavailability remained constant when they consumed low versus high zinc meals, which resulted in a significantly higher net amount of zinc absorbed.

Rats, however, have substantially more intestinal phytase activity than humans (a multiple of about 30) and, therefore, are more able to absorb iron or zinc from high phytate foods than humans (Iqbal, Lewis, and Cooper 1994). Despite this limitation, it has been 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 (Reddy and Cook 1991) with regard to nonheme[4] iron absorption. Through a direct comparison of nonheme iron absorption in humans and rats using the same methodological approach, the authors showed that rats were relatively insensitive to factors that inhibit nonheme iron absorption in humans (phytic acid in bran, tea, soy protein), as well as to promoters such as meat and ascorbic acid. Thus, they warn that extrapolation of results on nonheme iron bioavailability from the rodent model to humans should be undertaken only with caution (Reddy and Cook 1991). A potential limitation of this study, however, is that the authors compare only ***ratios*** of bioavailability between control and test meals, ignoring ***absolute differences*** in bioavailability, which actually match up reasonably well between humans and rats. It is clear that ratios will be lower for rats as compared with humans, a priori, in

[4] The type of iron commonly found in plant sources versus animal sources.

that the base level of bioavailability for control meals (2–7 percent bioavailability for humans and 45–70 percent bioavailability 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 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 of 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 two other plant breeding strategies, which increase the probability for success, specifically (1) reducing the concentration of phytic acid in grains, and/or (2) increasing the concentration of promoter compounds such as certain amino acids (methionine, lysine, or cysteine). These two complementary approaches are discussed below.

REDUCING THE CONCENTRATION OF PHYTIC ACID IN THE PLANT

Agronomic Advantages/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 (Graham and Welch 1996). Phytin also plays an important role in determining the mineral nutrient reserves of seeds and, thus, contributes to the viability and vigor of the seedling. For these reasons, some argue that selecting for crops with substantially lower phytin content could have unacceptable effects on agronomic performance, especially in regions of the world that have low phosphorus soils (Graham and Welch 1996). Initial screening results, however, with *lpa* mutants discussed earlier suggest that these mutants perform well agronomically—there is not a noticeable decline in yields (Raboy 1996). More research is needed to obtain better information on the agronomic effects of lower levels of phytates in seeds.

Nutritional Benefits

The negative effect of phytic acid on zinc absorption in humans is well documented (Sandström and Lönnerdal 1989). 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 percent to 17 percent (Turnlund et al. 1984; Nävert, Sandström, and Cederblad 1985). 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 (Sandström and Lönnerdal 1989, Figure 4.1, 69). At levels of 400–500 µmol (264–330 milligrams) of phytic acid, zinc absorption is lower than 10 percent and is reduced to less than 5 percent at levels of 1,000 µmol (660 milligrams). This indicates that substantial reductions in phytic acid would be necessary to significantly improve zinc absorption.

A similar, and probably even more dramatic, phenomenon has been described for nonheme iron absorption. Research in humans has shown 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 milligrams per meal) was necessary (Hurrell et al. 1992), or that levels as low as 50 milligrams of phytic acid caused a 78 to 92 percent reduction in nonheme iron absorption, depending on the protein composition of the meal (Reddy et al. 1996).

To provide an idea of the order of magnitude, daily intakes of phytic acid among preschool children from populations whose staple diets are based on cereals, legumes, and starchy roots and tubers are estimated to range from 600 to 1,900 milligrams, that is, 200 to 600 milligrams per meal (Gibson 1994). Among Mexican adult men and women, intakes of phytic acid are in the order of 4,000–5,000 milligrams per day (Allen et al. 1992). Cereals such as whole wheat, corn, and millet contain approximately 800 milligrams of phytic acid per 100 grams of 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 (1996), 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 impact bioavailability of zinc and iron simultaneously, and potentially calcium, manganese, magnesium, and possibly other trace minerals.

Much more research is needed using iron- and zinc-deplete human subjects and meals typical of the diets of poor families in developing countries to understand the relationship between [phytate]:[zinc] and [phytate]:[nonheme iron] molar ratios and zinc bioavailability as guidance for the optimal breeding strategy. Complementary food processing, preparation, and consumption strategies may be needed to further improve mineral bioavailability (Ferguson et al. 1995; Allen and Ahluwalia 1996).

INCREASING THE CONCENTRATION OF PROMOTER COMPOUNDS (SULFUR-CONTAINING AMINO ACIDS)

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

Agronomic Advantages/Disadvantages

There is little information on the agronomic advantages or disadvantages to increasing the concentration of sulfur-containing amino acids in staple foods. 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 (Welch 1996).

Nutritional Benefits

Both the source and the level of dietary protein has been shown to affect zinc and nonheme iron absorption in humans as well as in animals (Snedeker and Greger 1983). The positive effects of proteins found in meat on the bioavailability of minerals has been shown, but the precise mechanisms are not fully understood. Researchers question whether the so-called "meat factor" is (1) a protein per se, or (2) specific amino acids in proteins (in particular sulfur-containing amino acids), or (3) some amino acids metabolites (namely citric acid and picolinic acid), or (4) unidentified components in proteinaceous foods (Snedeker and Greger 1981).

Results of a few studies in rats and in humans showed that both the level of proteins as well as the concentration of cysteine, and histidine, to a lesser extent, had a positive effect on mineral absorption, particularly zinc (Snedeker and Greger 1981, 1983; Martinez-Torres and Layrisse 1970). Iron and copper were less affected by sulfur-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 two factors had an independent effect on zinc metabolism (Snedeker and Greger 1981, 1983).

More recent work with marginally zinc-deficient rats showed that diets supplemented with amino acids increased the absorption of zinc from an initial 64 percent to 69 percent with lysine, 82 percent with methionine, and 86 percent with both amino acids (House, Van Campen, and Welch 1996). A second experiment testing the effect of supplemental cysteine and methionine added to test meals also showed an increase in the absorption of zinc from 53 and 57 percent initially, and to 73 percent with either amino acid added. The authors concluded that adding supplemental methionine to basal diets resulted in increases in the absorption of zinc in the order of 14–35 percent (House, Van Campen, and Welch 1996).

Again, more research is needed using 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.

4. COMPARATIVE COSTS OF PLANT BREEDING STRATEGIES

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

For example, in treating iron deficiency in developing countries, Yip (1994) argues that if prevalence rates are above 25 percent, the best approach is to develop programs to improve the iron nutriture of the entire population. In such situations, which for preschoolers and women in developing countries are the rule rather than the exception, this is cheaper 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. Much less 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.

The plant breeding effort generally underway can be seen as a two-stage process. The first five-year phase primarily, but not exclusively, involves research at central international agriculture research stations, at an estimated $2 million per year for research on five crops (maize, rice, wheat, beans, and cassava). During this initial phase, promising germplasm is identified and the general breeding techniques are developed for later adaptive breeding.

During the second phase, the research needs to shift to national agricultural research. 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 per year 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 per person per year when all administrative costs are taken into account (Levin et al. 1983). A lower bound estimate for iron fortification is $0.10 per person per year. In a populous country such as 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 one year through a well-targeted supplementation program would cost $37 million per year. A fortification program that reached half the population would cost $44 million per year. Thus, the projected costs of a plant breeding strategy are relatively low. The major portion of the cost is the initial one-time cost of development.

One can imagine that there will be unforseen 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 sufficiently low, and that cost considerations are overwhelmingly on the side of a plant breeding strategy as compared with supplementation and fortification.

Moreover, these comparative costs do not take into account the potential benefits to improved agricultural productivity and reduced input needs, which may also have a positive impact on poor farmers' income. For example, for 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 *annually* in reduced seeding rates alone (seeding rates could be reduced from an average of 250 to 150 kilograms per hectare on 5 million hectares; a ton of wheat has sold for about 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 (Bouis 1996).

5. CONCLUSIONS

The research presented 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 has been a major constraint preventing action by national and international agencies. However, a primary constraint to immediate action continues to be that no fully-tested interventions are available for immediate implementation. Designing cost-effective and sustainable strategies to improve the zinc nutrition of vulnerable groups in developing countries constitutes a serious challenge for program planners.

The reasons 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 have been outlined in this paper. Although plant breeding involves comparatively long lead times before it can have an appreciable impact, a start has been made. The pace of progress in the years ahead will depend to a significant extent on the support that this nontraditional approach receives from plant breeders and human nutritionists.

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 are found to develop them. Rather, the two key issues are (1) whether the agronomic advantages of the zinc-dense seeds are sufficiently strong that national breeding programs will want to incorporate this characteristic into their improved lines of staple food crops, so that they will be widely adopted by farmers; and (2) whether the additional zinc contained in the seeds will be of sufficient magnitude and bioavailability so as to have an appreciable impact on zinc status. There is much scientific evidence to be optimistic on the first issue. Additional research is needed to get a clearer picture on the second one.

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. Human nutritionists in general are not aware, for example, 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 sensitized to the major influence that they may have had on nutrient utilization in the past (are trace minerals in modern varieties more or less bioavailable than in traditional varieties?), nor to their potential for future improvements in nutrition and health. As the world's resources for food production and other purposes become increasingly stressed, not only will such interdependencies between agricultural systems and human nutrition become increasingly obvious, but also impossible to ignore in formulating solutions.

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