# *Symposium: Plant Breeding: A New Tool for Fighting Micronutrient Malnutrition*

## Plant Breeding: A New Tool for Fighting Micronutrient Malnutrition[1]

Howarth E. Bouis[2]

*International Food Policy Research Institute, Washington, DC 20006-1002*

ABSTRACT The final permanent solution to micronutrient malnutrition in developing countries is a substantial improvement in dietary quality—higher consumption of pulses, fruits, vegetables, fish and animal products that the poor already desire but cannot presently afford. Meanwhile breeding staple foods that are dense in minerals and vitamins provides a low-cost, sustainable strategy for reducing levels of micronutrient malnutrition. Getting plants to do the work of fortification, referred to as "biofortification," can reach relatively remote rural populations that conventional interventions are not now reaching and can even have benefits for increased agricultural productivity. Biofortification, thus, complements conventional interventions. The symposium articles discuss several examples of ongoing research projects to develop and disseminate nutrient-dense staple food crops and issues that remain to be resolved before successful implementation can be attained. J. Nutr. 132: 491S–494S, 2002.

KEY WORDS: • *micronutrient malnutrition* • *plant breeding* • *bioavailability* • *biotechnology* • *cost-effective*

Commercial fortification of foods is an intervention familiar to all of us. Minerals and vitamins are added to a particular food vehicle during processing, well after the food has left the farm and before it is distributed through various marketing channels for consumer purchase and consumption. What if instead, it were possible to get the plants themselves to do the work of fortification, an intervention strategy that may be referred to as "biofortification"? What are the inherent comparative advantages of such an approach?

First and foremost, biofortification would be cost-effective. Once the plants are developed and being grown by farmers, there are no costs year in and year out of buying the fortificants and adding them to the food supply during processing. Second, biofortification would be sustainable. Once the investment has been made in developing and disseminating the nutritionally improved crops, farmers will be driven by a profit incentive to continue to produce these crops. In fact, this strategy has the potential to significantly improve agricultural productivity for reasons explained in more detail below. Moreover, monitoring and maintenance costs are low and not subject to the vagaries of political will and availability of public funds. Third, biofortification could make an impact in relatively remote rural areas where food staples do not enter the marketing system or where processing facilities are relatively small, numerous and widely dispersed.

These three, key, comparative advantages of biofortification are vitally important in the fight against micronutrient malnutrition in developing countries, where the set of constraints to successful implementation of conventional interventions is much different than in developed countries, where cost, access to programs, and consumer awareness and so political will, are problems of lesser magnitude.

### *Structure of the symposium presentations*

To be successful, the biofortification strategy must address three fundamental questions: *1*) Can commonly eaten food staple crops be developed that fortify their seeds with essential minerals and vitamins?; *2*) Can farmers be induced to grow such varieties?; and *3*) If so, would this result in a significant improvement in human nutrition at a lower cost than existing nutrition interventions?

Questions 1 and 3 are linked in the sense that there are actually three breeding strategies that may be applied: increasing the mineral and vitamin content as stated in question 1; reducing the level of antinutrients in food staples that inhibit the bioavailability of minerals and vitamins; or increasing the levels of compounds that promote the bioavailability of minerals and vitamins.

The following article by Ross Welch, U.S. Department of Agriculture-Agricultural Research Service (USDA-ARS)[3] Plant, Soil, and Nutrition Laboratory discusses the comparative advantages and disadvantages of these three breeding substrategies based on the existing state of knowledge. The optimal breeding strategy for any one staple food crop may

---

[1] Presented as part of the symposium, "Plant Breeding: A New Tool for Fighting Micronutrient Malnutrition," given at the Experimental Biology 2001 meeting, Orlando, Florida, April 1, 2001. This symposium was sponsored by the American Society for Nutritional Sciences. Guest editor for the symposium publication was Howarth E. Bouis, International Food Policy Research Institute, Washington, DC.

[2] To whom correspondence should be addressed. E-mail: h.bouis@cgiar.org

[3] Abbreviations used: CGIAR, Consultative Group on International Agricultural Research; USDA-ARS, U.S. Department of Agriculture-Agricultural Research Service.

combine two or even three of these substrategies. Among other factors, the optimal strategy will depend on: impact on human nutrition, impact on plant nutrition, the difficulty and cost of breeding for each particular characteristic, and the effect on consumer characteristics (e.g., color, taste and cooking qualities).

The impact on plant nutrition is a particular concern of agriculturalists, whose first inclination may be to raise the yield potential of plants and to leave human nutrition problems to others to solve. If yield and profitability are compromised by breeding for nutrient content, farmers will not want to adopt nutritionally enhanced cultivars. Dr. Welch's article presents evidence that mineral-packed seeds will sell themselves to farmers because, as recent research has shown, these trace minerals are essential in helping plants resist disease and other environmental stresses. More seedlings survive and initial growth is more rapid. Ultimately, yields are higher, particularly in trace mineral-deficient soils in arid regions. (Biofortification will not deplete soils of trace minerals. Sufficient trace minerals are present in most soils for thousands of crops. Some soils are labeled "trace mineral-deficient" because the properties of these soils are such that the trace minerals are chemically bound and unavailable to the plant. Roots of trace mineral-efficient lines release compounds into the soil, which chemically unbind the trace minerals in the soils and make them available to the plant. Thus, a strategy of breeding for trace mineral-efficient lines makes use of an untapped and abundant resource in the soil. This is a very different situation from depletion of macronutrients in the soil, such as nitrogen and phosphorus.) Because roots extend more deeply into the soil and can tap more subsoil moisture and nutrients, the mineral-efficient varieties are more drought-resistant and require less irrigation. And because of their more efficient uptake of existing trace minerals, these varieties require fewer chemical inputs. Thus, the new seeds can be expected to be environmentally beneficial as well (1).

In addition to multiple substrategies as breeding objectives, two broad techniques to breeding are possible—classical breeding and use of molecular methods that allow transfer of genes across species. Articles three through six discuss particular applications currently in progress that are representative of the various substrategies possible and breeding methodologies available. Two use conventional breeding methods, two use molecular approaches, two seek to increase mineral and vitamin density, and two seek to increase the bioavailability of minerals by reducing the effects of phytates.

An interdisciplinary, international effort is being undertaken by the Consultative Group on International Agricultural Research (CGIAR) to evaluate the feasibility of developing mineral- and vitamin-dense varieties of rice, wheat, maize, beans and cassava using conventional breeding. (The CGIAR is a group of 16 internationally funded agricultural research institutes, most located in developing countries, which seek to raise the productivity of low-income farmers while lowering food prices for consumers in poor countries through increases in the supply of food.) These efforts are summarized in the third article by Glenn Gregorio, who is the rice crop leader for this project and based at the International Rice Institute in the Philippines. Victor Raboy, USDA-ARS National Small Grains Germplasm Research Facility, has successfully developed low-phytate lines of maize and other food staple crops, also using available conventional breeding technologies. Lowering phytate levels has the potential to increase the bioavailability of a range of trace minerals. In the fourth article, Dr. Raboy discusses the results of this research and plans for nutrition trials in Central America using human subjects.

The fifth and sixth articles describe research, presently being undertaken in Europe with the intention of applying the results to improve nutrition in developing countries, using transgenic methods. Preben B. Holm of the Danish Institute of Agricultural Sciences and coauthors present results of early efforts to introduce genes for microbial phytases into wheat and the strategies for future work. Phytases, which can raise bioavailability by breaking down phytate, have already successfully been introduced into wheat and rice but these phytases are inactivated at temperatures typically attained in domestic baking and boiling of staple foods. Development of a rice with β-carotene in the endosperm, popularly known as "Golden Rice" is described by Peter Beyer of the University of Freiburg, Germany, and coauthors. Professor Beyer is codeveloper of the Golden Rice along with Ingo Potrykus of the Swiss Federal Institute of Technology. Rice lines based on initial constructs developed in Switzerland and Germany are currently under development in Asia.

Articles two through six are written by scientists trained and working primarily in plant science. A biofortification strategy requires interdisciplinary coordination among plant scientists, human nutritionists and social scientists. In the final article, Janet King, USDA-ARS Western Human Nutrition Research Center, discusses the next steps that will need to be taken in terms of evaluating the potential effects of nutritionally improved staple foods on human nutrition.

### *The serious problem of micronutrient malnutrition in developing countries*

The articles presented in this symposium focus on plant-breeding strategies for reducing micronutrient deficiencies in developing countries through the modification of staple food crops, the only foods eaten in relatively large quantities by the poor day in and day out and, therefore, the optimal food vehicles for biofortification or commercial fortification. The final, permanent solution to micronutrient malnutrition in developing countries is a substantial improvement in dietary quality—higher consumption of pulses, fruits, vegetables, fish and animal products that the poor already desire but cannot presently afford. Meanwhile, breeding staple foods that are dense in minerals and vitamins provides a low-cost, sustainable strategy for reducing levels of micronutrient malnutrition. No single type of intervention can by itself solve the micronutrient malnutrition problem. A comprehensive strategy involving multiple types of interventions adapted to conditions in specific countries and regions is required. Biofortification complements existing strategies and has its own unique niche, as conditioned by the comparative advantages outlined in the introduction and technical characteristics, most importantly the level of the dose that biofortification can be expected to deliver. In any given day, biofortified staple foods cannot deliver as high a level of minerals and vitamins as supplements or industrially fortified foods.

To provide some background on the motivation for the research reported in this symposium, it is useful first to summarize briefly the dimensions and consequences of micronutrient malnutrition in developing countries. It is estimated that over 3 billion people in developing countries are iron-deficient (2). The problem for women and children is more severe because of their greater physiological need for iron. In poor countries, >50% of pregnant women and >40% of nonpregnant women and preschool children are anemic. Iron deficiencies during childhood and adolescence impair physical growth and mental development and learning capacity. In adults, iron deficiency reduces the capacity to do physical labor. Iron deficiency is a leading cause of death among women during childbirth.

Globally, ~3 million preschool-aged children have visible eye damage due to a vitamin A deficiency. Annually, an estimated 250,000 to 500,000 preschool children go blind from this deficiency and approximately two-thirds of these children die within months of going blind. The estimates of the subclinical prevalence of vitamin A deficiency range between 100 and 250 million. A number of clinical trials in developing countries have shown than vitamin A capsule distribution can reduce mortality rates among preschool children by 23%.

Iodine deficiency is the greatest single cause of preventable brain damage and mental retardation in the world. More than 2 billion people in the world live in iodine-deficient environments. Deficiencies in iodine that occur in late infancy and childhood have been shown to cause mental retardation, delayed motor development, growth failure and stunting, neuromuscular disorders and speech and hearing defects. Even mild iodine deficiency has been reported to reduce intelligence quotients by 10–15 points.

The World Bank (3) estimates that at the levels of micronutrient malnutrition existing in South Asia, 5% of the gross national product is lost each year due to deficiencies in the intakes of just three nutrients: iron, vitamin A and iodine. For each 50 million in population, that translates into an economic loss of $1 billion per year. Deficiencies in several other micronutrients, zinc in particular, may be similarly widespread with equally serious consequences for health. However, because there are no specific indicators to screen for deficiencies in these nutrients (other than a positive health response to supplementation), they have not received as much attention.

The remainder of this article addresses particular aspects, not addressed in the following six articles, of the three fundamental questions raised above with respect to successful implementation of biofortification. Particular emphasis is placed on the apparent cost-effectiveness of biofortification.

### *Will breeding for micronutrient-dense seeds change the processing or consumer characteristics of staple foods?*

Mineral micronutrients comprise a tiny fraction of the physical mass of a seed, 5–10 parts per million in milled rice. Dense bean seeds may contain as many as 100 parts per million. It is not expected that such small amounts will alter the appearance, taste, texture or cooking quality of foods. The dissemination strategy for trace minerals, then, would be to convince agricultural research institutes to include the mineral-density trait in as many varietal releases as possible to benefit a high proportion of the population—without having to inform consumers and to change their behavior as a condition for success, much as fluoride is added to drinking water in developed countries.

In contrast, higher levels of $\beta$-carotene will turn varieties from white or light colors of yellow to dark yellow and orange. Often white varieties are much preferred by consumers (e.g., milled rice, wheat flour, maize and cassava). Major nutrition education programs will have to be mounted to encourage consumers to switch to more nutritious varieties. If these nutrition education programs are successful, then the yellow-orange color will mark the more nutritious varieties from the less nutritious and a disadvantage will have been turned into an advantage (4).

### *Will micronutrient intakes be increased to a significant degree?*

For poor populations, food staple consumption so dominates diets (their low incomes preclude the consumption of desired levels of nonstaple foods) that primary food staples provide, for example, in the range of 40–55% of total iron intakes for lower income households. If a single food staple provides 50% of total iron intakes for a poor population (e.g., for rice in Bangladesh), then a doubling of the iron density in that food staple will result in a 50% increase in total iron intakes (5).

Iron intakes for low-income women in developing countries range perhaps between 50% and 75% of recommended daily allowances. Despite well-known difficulties with determining useful benchmarks for recommended daily allowances of iron, it would seem evident that a 50% increase in intakes of bioavailable iron would be of considerable benefit to anemic women with such low iron intakes. Some empirical evidence is available from a recently published study of a population of Bangladeshi rural women (6). This study measured the relationship between foods in the diet and blood hemoglobin. The estimated relationships suggest that a 50% increase in iron intakes from biofortified rice would reduce rates of anemia among these women by a minimum of 3% (e.g., from 53% to 50%) and perhaps as much as 6%. This is an estimate of the percentage of women who would cross above the threshold of 12 g/dL hemoglobin as a result of consuming biofortified rice. Women who remain below this threshold presumably also derive some benefit from a 50% increase in higher iron intakes.

For this same rural Bangladesh population, it also possible to estimate the percentage increase in total provitamin A intake provided by Golden Rice (1.6 $\mu$g $\beta$-carotene per gram of dry rice endosperm) (7). For this poor population, animal and fish intakes provide only 3% of total energy (5), so that retinol intakes are negligible and vegetables provide >90% of total provitamin A intakes. If the provitamin A in both vegetables and Golden Rice are converted to retinol equivalents at a rate of 26 to 1, total provitamin A intakes are increased by 23–26% for adult women and preschool children. If provitamin A in vegetables is converted to retinol equivalents at a rate of 26 to 1 and provitamin A in Golden Rice at a rate of 6 to 1, total provitamin A intakes are increased by 79–90% for adult women and preschool children. There is some speculation that the $\beta$-carotene in rice endosperm will be more easily converted to retinol than $\beta$-carotene in vegetables because of the physical characteristics of the rice endosperm matrix.

### *What are the costs and benefits of a biofortification strategy? how do these compare with supplementation and fortification?*

Although benefit to cost ratios are quite high, supplementation and fortification programs must be sustained at more or less the same level of funding year after year in any given country. If investments are not sustained, benefits disappear. Some back-of-the-envelope calculations may be made for the costs of supplementation and fortification in South Asia, which has a total population of roughly 1.25 billion people.

Although the costs of vitamin A pills themselves are low, an often-quoted cost of vitamin A supplementation, which includes the costs of delivery, is U.S. $0.50 per person per year ($0.25 per capsule) (3). If 1 in 12.5 persons in South Asia were to receive supplements (100 million people in total), this is a cost of $50 million per year, or $500 million over 10 years. An often-quoted cost of iron fortification is U.S. $0.12 per person per year (3). If a particular food vehicle fortified with iron were to reach 33% of the total (but untargeted) population in South Asia (412 million people), the total cost is again $50 million annually, or $500 million over 10 years. In absolute terms, these may seem to be large amounts of money, but they are very worthwhile investments and are actually quite small percentages of the total economic activity of the South Asian economies.

Nevertheless, in contrast, investments in plant-breeding research and dissemination are far lower. Development of iron- and zinc-dense varieties of rice or wheat might cost as much as $10 million each over 10 years, including the costs of nutrition efficacy tests, the costs of dissemination in selected regions, and the costs of a nutrition and economic impact evaluation. Moreover, such an investment of $20 million in two crops, rice and wheat, would have multiplicative effects—benefits may accrue to countries all over world, which then need only invest in adaptive breeding and dissemination costs. Moreover, benefits are sustainable at low maintenance costs—benefits from breeding advances typically do not disappear after initial investments and research are successful, as long as an effective domestic agricultural research infrastructure is maintained.

As an example of the enormous economic benefits of the biofortification strategy, a simulation model was developed for Bangladesh and India, based on development of iron- and zinc-dense varieties of rice and wheat and assumed to be adopted on only 10% of ~83 million hectares planted to rice and wheat. The somewhat conservative assumptions suggest that the returns that come on-stream during the second decade of research and development would be ~$4.9 billion on a total investment of $42 million, $1.2 billion in benefits from better nutrition and $3.7 billion in benefits from higher agricultural productivity.

A more formal economic evaluation, in which the ratio of the present value of benefits divided by the present value of costs were discounted at a 3% rate (commonly used for evaluation of social benefits), gave a benefit to cost ratio of 19 for returns to better iron nutrition in humans alone, a ratio similar to that found by Horton and Ross (8) for fortification in South Asia. This benefit to cost ratio rises to 79 if benefits to higher agricultural productivity are included. A different way of expressing the concept of discounting over time is the internal rate of return, the interest rate at which benefits equal costs plus interest if the funds were borrowed to make the investment. In this case the internal rate of return is 29% if only benefits to human nutrition are considered and 44% if both benefits to human nutrition and higher agricultural productivity are considered.

In the longer term (years 11–25 of the simulation), it is estimated that a total of 44 million annual cases of anemia will be prevented if nutritionally improved varieties are adopted on 10% of the rice and wheat areas in Bangladesh and India. This is based on a conservative assumption of only a 3% reduction in anemia among those consuming the high-iron rice (see above). This is a cost of ~U.S. $1/annual case of anemia prevented and a cost of $0.03 per person per year for those whose iron intakes increase by 50% through consumption of the high-iron rice and wheat.

## CONCLUSION

Although plant breeding involves comparatively long lead times before it can have an appreciable effect, a significant start has now been made. The pace of progress in the years ahead will depend to a significant extent on the acceptance and support that this nontraditional approach receives from the plant-breeding and human nutrition communities.

In conceptualizing solutions for a range of nutritional deficiencies, interdisciplinary communication between plant scientists and human nutritionists holds great potential. Human nutritionists need to be informed, for example, about 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. Plant breeders need to be sensitized to the major influence that they may have had on nutrient utilization in the past (e.g., are trace minerals in modern varieties more or less bioavailable than in traditional varieties?), and the potential of plant breeding 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 increasingly obvious and impossible to ignore in formulating solutions.

## LITERATURE CITED

1. Graham, R., Welch, R. & Bouis, H. (2001) Addressing micronutrient malnutrition through the nutritional quality of staple foods: Principles, perspectives, and knowledge gaps. Adv. Agronomy 70: 77–142.
2. Administrative Committee on Coordination/Subcommittee on Nutrition (ACC/SCN) of the United Nations and the International Food Policy Research Institute (IFPRI). (2000) Fourth Report on the World Nutrition Situation. United Nations, Geneva, Switzerland.
3. World Bank. (1994) Enriching Lives: Overcoming Vitamin and Mineral Malnutrition in Developing Countries: Development in Practice Series. World Bank, Washington, DC.
4. Hagenimana, V. & Low, J. (2000) Potential of orange-fleshed sweet potatoes for raising vitamin A intake in Africa. Food Nutr. Bull. 21: 414–418.
5. Bouis, H., de la Brière, B., Guitierrez, L., Hallman, K., Hassan, N., Hels, O., Quabili, W., Quisumbing, A., Thilsted, S., Zihad, Z. & Zohir, S. (1998) Commercial Vegetable and Polyculture Fish Production in Bangladesh: Their Impacts on Income, Household Resource Allocation, and Nutrition. International Food Policy Research Institute, Washington, DC.
6. Bhargava, A., Bouis, H. & Schrimshaw, N. (2001) Dietary intakes and socioeconomic factors are associated with the hemoglobin concentration of Bangladeshi women. J. Nutr. 131: 758–764.
7. Ye, X., Al-Babili, S., Kloti, A., Zhang, J., Lucca, P., Beyer, P. & Potrykus, I. (2000) Engineering the provitamin A (-carotene) biosynthetic pathway into (carotenoid-free) rice endosperm. Science 287: 303–305.
8. Horton, S. & Ross, J. (2001) The Economics of Iron Deficiency. Economics Department, University of Toronto, Toronto, Canada.