Micronutrient fortification of plants through plant breeding: can it improve nutrition in man at low cost?

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Can commonly-eaten food staple crops be developed that fortify their seeds with essential minerals and vitamins? Can farmers be induced to grow such varieties? If so, would this result in a marked improvement in human nutrition at a lower cost than existing nutrition interventions? An interdisciplinary international effort is underway to breed for mineral- and vitamin-dense varieties of rice, wheat, maize, beans and cassava for release to farmers in developing countries. The biofortification strategy seeks to take advantage of the consistent daily consumption of large amounts of food staples by all family members, including women and children as they are most at risk for micronutrient malnutrition. As a consequence of the predominance of food staples in the diets of the poor, this strategy implicitly targets low-income households. After the one-time investment is made to develop seeds that fortify themselves, recurrent costs are low and germplasm may be shared internationally. It is this multiplier aspect of plant breeding across time and distance that makes it so cost-effective. Once in place, the biofortified crop system is highly sustainable. Nutritionally-improved varieties will continue to be grown and consumed year after year, even if government attention and international funding for micronutrient issues fades. Biofortification provides a truly feasible means of reaching malnourished populations in relatively remote rural areas, delivering naturally-fortified foods to population groups with limited access to commercially-marketed fortified foods that are more readily available in urban areas. Biofortification and commercial fortification are, therefore, highly complementary. Breeding for higher trace mineral density in seeds will not incur a yield penalty. Mineral-packed seeds 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: Plant breeding strategy: Human micronutrient status:
Biofortification *v.* commercial fortification**

Taken together, mineral and vitamin deficiencies affect a greater number of the world's population than does protein–energy malnutrition. As trace minerals are important not only for human nutrition, but also for plant nutrition, plant breeding holds great promise for making a major, low-cost and sustainable contribution to reducing micronutrient, particularly mineral, deficiencies in man, and may have important spin-off effects for increasing farm productivity in developing countries in a way that is environmentally beneficial (Graham & Welch, 1996; Graham *et al.* 2001).

An underlying cause and fundamental constraint to the solution of the micronutrient problem is that non-staple foods, particularly animal products, tend to be the foods richest in bioavailable micronutrients, which the poor in many developing countries desire to eat, but cannot afford. Their diets consist mostly of staple foods, primarily cereals; in fact, *per capita* direct consumption of staple foods in the aggregate varies little by income level. For the poor, these staple foods already are primary sources of what micronutrients they are able to consume, particularly minerals.

The plant-breeding strategy seeks to take advantage of this existing human consumption behaviour by developing staple food crops that, in some sense, fortify themselves. Staple crop genotypes are bred that load high amounts of minerals and vitamins into their seeds, a strategy referred to in the present paper as 'biofortification'.

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Biofortification has several complementary advantages. No behavioural change on the part of consumers is required. Indeed, the strategy seeks to take advantage of the consistent daily consumption of large amounts of food staples by all family members. Nevertheless, any intervention to improve micronutrient status targets women and children because of their elevated needs for minerals and vitamins for reproduction and growth (for example, see Perry *et al.* 1995).

Biofortification provides a truly feasible means of reaching malnourished populations in relatively remote rural areas, delivering naturally-fortified foods to population groups with limited access to commercially-marketed fortified foods that are more readily available in urban areas. Biofortification and commercial fortification are, therefore, highly complementary.

Mineral-packed seeds will sell themselves to farmers because, as relatively recent research has shown, these trace minerals are essential in helping plants resist disease. More seedlings survive and initial growth is more rapid. Ultimately, yields are higher, particularly in trace mineral-'deficient' soils in arid regions. After the one-time investment is made to develop seeds that fortify themselves, there are low recurrent costs, which for supplementation and fortification remain constant year after year.

Micronutrient malnutrition: extent and underlying cause

Billions in the populations of developing countries suffer from micronutrient malnutrition. Even mild levels of micronutrient malnutrition may damage cognitive development, lower disease resistance in children and reduce the likelihood that mothers survive childbirth. The costs of these deficiencies in terms of lives lost and poor quality of life are staggering (Table 1).

More than two billion of the world's population are Fe deficient (ACC/SCN, 2000; Stoltzfus, 2001). Fe-deficiency anaemia is by far the most common micronutrient deficiency in the world. Fe deficiency during childhood and adolescence impairs physical growth, mental development and learning capacity. In adults Fe-deficiency anaemia reduces the capacity to do physical labour. Fe deficiency increases the risk of women dying during delivery or in the postpartum period.

Zn deficiencies have equally serious consequences for health. For example, meta-analyses of recent randomised controlled trials show that Zn supplementation can reduce morbidity from a number of common childhood infections, especially diarrhoea, pneumonia and, possibly, malaria by

one-third (Black, 1998; Bhutta *et al.* 1999, 2000; Roy *et al.* 1999; Shankar *et al.* 2000). In addition, Zn deficiency is an important cause of stunting (Roy *et al.* 1999; Brown & Wuehler, 2000; Umeta *et al.* 2000). Billions of individuals are also at risk for Zn deficiency (Brown & Wuehler, 2000).

Globally, approximately three million preschool children have visible eye damage as a result of vitamin A deficiency. Annually, an estimated 250 000–500 000 preschool children go blind from this deficiency and about two-thirds of these children die within months of going blind. Even more importantly, the last two decades have brought an awareness that vitamin A is essential for immune function. Estimates of the prevalence of subclinical vitamin A deficiency range between 100 and 250 million for preschool children. Individuals with subclinical vitamin A deficiency more often experience anaemia, impaired linear growth (Villamor & Fawzi, 2000) and morbidity from common childhood infections, such as respiratory and diarrhoeal diseases (Sommer & West, 1996), measles (West, 2000) and malaria (Shankar *et al.* 1999). Most importantly, a number of randomised controlled trials in developing countries have shown that administration of vitamin A capsules to infants and preschool children helps reduce mortality rates from all causes by 23 % (Beaton *et al.* 1993; Sommer & West, 1996) and that administration of capsules with vitamin A or β-carotene to women of childbearing age can reduce maternal mortality related to pregnancy by 40 and 49 % respectively.

The primary underlying cause of micronutrient malnutrition is poor-quality diets, characterised by high intakes of food staples, but low consumption of animal and fish products, fruits, lentils and vegetables, which are rich sources of bioavailable minerals and vitamins. As such, most of the population groups who are malnourished are those who cannot afford to purchase high-quality micronutrient-rich foods or who cannot obtain these foods from their own production (for an example from Bangladesh, see Fig. 1).

What is perhaps most alarming, however, is the upward trend in non-staple food prices, shown in Fig. 2. Cereal prices have fallen by 40 % since the early 1970s. The Green Revolution can rightly take credit for its crucial contribution to this tremendous achievement. Falling cereal prices have not only led to increased food security in terms of energy, but also allowed greater purchases of non-staples by freeing up cash. Unfortunately, however, the rate of production of non-staple foods (e.g. fruits, vegetables, lentils) has not kept pace with demand (Fig. 3), so that these micronutrient-rich food sources have become increasingly expensive for the poor.

Table 1. Extent and consequences of micronutrient malnutrition (ACC/SCN, 2000)

| Deficiency	Prevalence in developing countries	Groups most affected	Consequences
Fe	2 billion of the population	All, but especially women and children	Reduced cognitive ability, childbirth complications, reduced physical capacity and productivity
Vitamin A	250 million children	Children and pregnant women	Increased child and maternal mortality, blindness
Zn	May be as widespread as Fe deficiency	Women and children	Illness from infectious diseases, poor child growth, pregnancy and childbirth complications, reduced birth weight
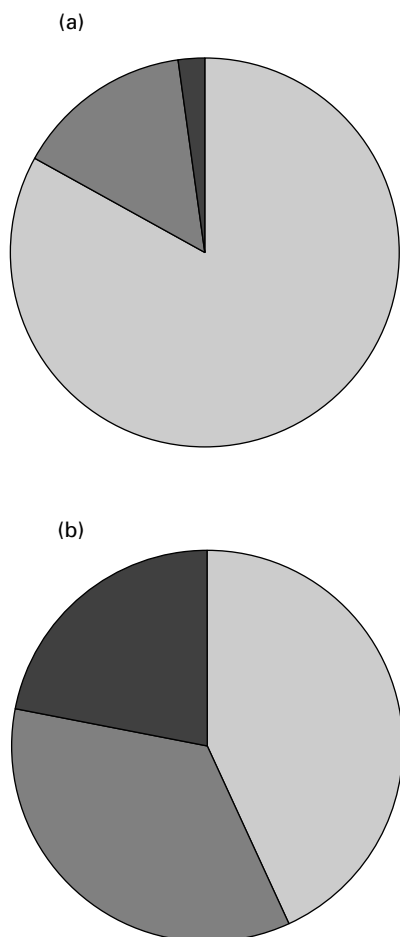
Fig. 1. Shares of energy intake (a) and food budget (b) for rural Bangladesh. The data shown are typical of diets and food expenditures for those who suffer from micronutrient malnutrition. (▦), Staple foods (in this example, overwhelmingly rice) account for 80 % total *per capita* energy intakes. (▦), Animal and fish products are dense sources of bioavailable micronutrients that the poor wish to eat but cannot afford in large quantities. They account for 25 % of the total food expenditures but only 3 % of the total energy intakes. (▦), Non-staple plant foods such as fruits, vegetables, and lentils are also rich sources of vitamins and minerals. Together, non-staple plant foods and animal and fish products account for only 20 % of the total energy intakes but 60 % of the total food expenditures. (From Bouis *et al.* 1998.)

Fig. 2. Indices of inflation-adjusted prices for Bangladesh (where the 1973–5 is taken as 100). (▦), staple; (▦), non-staple plant; (▦), animal and fish. (From Bouis *et al.* 1998.)

Fig. 3. Changes (%) in cereal and pulse production and in population between 1965 and 1999. (From Food and Agriculture Organization, 1999.)

Can a breeding strategy work?

A strategy of breeding plants that enrich themselves will be successful only if farmers are willing to adopt such varieties, if the edible parts of these varieties are palatable and acceptable to consumers and if the micronutrients incorporated can be absorbed by the human body. In examining the feasibility of a plant-breeding strategy, it was imperative to address five core questions.

Is it scientifically feasible to breed for staple food varieties whose seeds are micronutrient-dense?

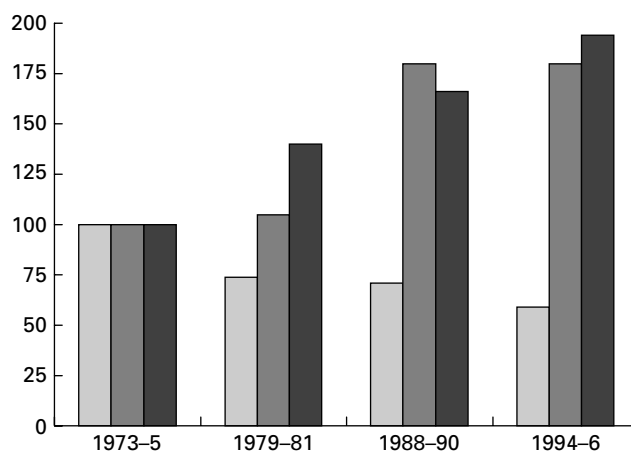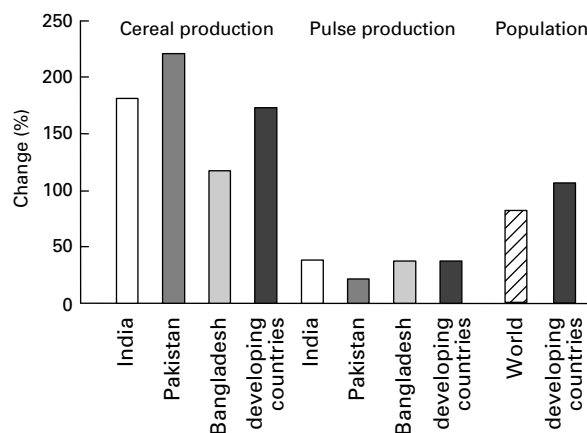At least three cases of agricultural research projects in developed countries have successfully manipulated the efficiency of mineral uptake of plants and the mineral content of plant seeds, all of which have been commercially successful. Zn-dense wheat varieties have been developed at the Waite Agricultural Research Institute of the University of Adelaide (Adelaide, Victoria, Australia) and are already being grown on a commercial basis in Australia (Rengel & Graham, 1995*a,b*). In the USA an Fe-efficient soyabean has been developed to overcome problems of Fe-'deficient' soils, and Cd levels in durum wheat have been reduced through plant breeding in order to meet quality standards in countries importing US wheat.

The Australian wheat strategy was motivated by previous more basic scientific research at the Waite Agricultural Research Institute involving the trace minerals Mn and Cu. Previous research suggested that genetic variation in the uptake and grain content of Mn, Cu and other micro-elements was associated with tolerance to low availability of the elements in the soil.

What effect will breeding for micronutrient-dense seeds have on plant yields? Will farmers adopt such varieties?

Good nutritional balance is as important to disease resistance and stress tolerance in plants as it is in man. Micronutrient deficiency in plants greatly increases their susceptibility to diseases, especially fungal root diseases of the major food crops. Efficiency in the uptake of mineral micronutrients from the soil is associated with disease resistance in plants. Breeding for micronutrient efficiency can confer resistance to root diseases that had previously been unattainable (Graham & Rovira, 1984; Sparrow & Graham, 1988; Thongbai *et al*. 1993).

Micronutrient-efficient varieties grow deeper roots in mineral-deficient soils and are better at tapping subsoil water and minerals. When topsoil dries, roots in the dry soil zone (which are the easiest to fertilise) are largely deactivated and the plant must rely on deeper roots for further nutrition. Roots of plant genotypes that are efficient in mobilising surrounding external 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. These characteristics reduce the need for fertilisers and irrigation. Plants with deeper root systems are more drought resistant.

Micronutrient-dense seeds are associated with greater seedling vigour that, in turn, is associated with higher plant yield (Welch, 1986, 1995, 1999; Graham, 1991; Marschner, 1995; Graham & Welch, 1996; Yang & Römheld, 1999).

A substantial percentage of the soils in which staple foods are grown are 'deficient' in these trace minerals, which has kept crop yields low. In general, these soils, in fact, contain high amounts of trace minerals, enough for hundreds or thousands of crops. However, because of chemical binding to other compounds, these trace minerals are 'unavailable' to staple crop varieties presently used. Depletion of soils of trace minerals may never occur, because of various inadvertent additions, such as windblown dust (Graham, 1978; Sillanpaa, 1990; Graham & Welch, 1996).

Thus, the traits of efficient uptake of trace minerals from the soil and of loading of those trace minerals into the seed are compatible with breeding for high yields. Based on a profit motive, farmers can be expected to adopt genotypes with trace mineral-dense seeds.

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

Mineral micronutrients make up a very small proportion of the physical mass of a seed, 5–10 mg/kg in milled rice. Dense bean seeds may contain as much as 100 mg/kg. Whether such small amounts will alter the appearance, taste, texture or cooking quality of foods will need to be investigated. If increased densities of Fe and Zn are not noticeable to consumers, the dissemination strategy for trace minerals, therefore, could rely on existing producer and consumer behaviour. Analogous to the addition of fluoride to drinking water in some developed countries, successful implementation would not require that farmers and consumers know that they are producing and eating more nutritious varieties, although this information would be publicly advertised and publicly available.

Increasing the seed content of β-carotene, which is associated with an orange or yellow colour, will alter its colour, which might well reduce consumer preference. However, nutrition education could turn this obstacle to an advantage, as consumers could be taught that deepness of colour is visually representative of a nutrient-dense product.

Will micronutrient intakes be increased to a marked extent? To what extent will the extra micronutrients in staple foods consumed be bioavailable?

For the poor, these staple foods are already primary sources of what micronutrients they are able to consume, particularly minerals. This situation is demonstrated by food intake data shown in Table 2 for survey populations in Bangladesh and the Philippines (Bouis & Haddad, 1990; Bouis & Novenario-Reese, 1997). Average incomes in these households range from US $45 *per capita* per year in the poorest 20 % of the households surveyed to US $250 in the richest 20 % of the households surveyed. Thus, they are typical of the middle to lower end of the income distribution in rural areas of these countries.

Not only are food staples poor (non-dense) sources of trace minerals, but anti-nutrient (e.g. phytate) levels are high, which reduces the bioavailability of overall intakes of trace minerals. Nevertheless, for poor populations such as those represented in Table 2, food staple consumption so dominates diets (their low incomes preclude the consumption of desired levels of non-staple foods) that primary food staples provide in the range of 40–55 % of the total Fe intakes for lower-income households.

If a single food staple provides 50 % of the total Fe intakes for a poor population (e.g. for rice in Bangladesh), then a doubling of the Fe density in that food staple will result in a 50 % increase in total Fe intakes, and a tripling of the Fe density will mean a doubling of total Fe intakes.

A key issue is the level of bioavailability of total Fe (or Zn) intakes and whether the percentage bioavailability will remain constant as additional Fe and Zn is added to the diet through biofortification. *In vitro* and rat studies, for example, suggest that the percentage of the Fe (and Zn) that is bioavailable remains relatively constant across cereal genotypes with high and low density (Welch *et al*. 2000; Glahn *et al*. 2002).

A second key issue is the range of genetic diversity in Fe (or Zn) density that can be identified for use in breeding programmes, which will determine the maximum level to which trace mineral density can be increased. Germplasm screening under the Consultative Group on International Agricultural Research Micronutrients Project suggests that trace mineral content of cereals can be doubled as compared with commonly-eaten cereal genotypes (Graham *et al*. 1999). This improvement would increase the Fe intakes of the populations surveyed in Table 2 by about 50 %.

Fe-deficiency anaemia is widespread among adult women in developing countries. For the lower-income households in Table 2, Fe intakes for women range between 50 and 75 % of the recommended daily allowances. Despite well-known difficulties associated with the determination of useful benchmarks for recommended daily allowances of Fe, it would seem evident that a 50 % increase in intakes of

Table 2. Percentage contributions of staple foods to food expenditures *per capita* per week and to energy and iron intakes for survey populations in Bangladesh and the Philippines

Food group	Poorest 20 % of households surveyed		Richest 20 % of households surveyed		Average for all households surveyed	
	Bangladesh	Philippines	Bangladesh	Philippines	Bangladesh	Philippines
Household food expenditure						
Rice, wheat, maize	69	45	54	24	62	33
Meat, fish	9	28	19	39	14	32
Other foods	22	27	27	37	24	35
Total	100	100	100	100	100	100
Houshold energy intake						
Rice, wheat, maize	87	84	81	70	84	79
Meat, fish	1	4	4	10	2	6
Other foods	12	12	15	20	13	15
Total	100	100	100	100	100	100
Household Fe intake						
Rice, wheat, maize	55	43	43	30	51	36
Meat, fish	3	18	6	36	5	25
Other foods	42	40	52	34	45	39
Total	100	100	100	100	100	100

bioavailable Fe would be of considerable benefit to anaemic women with such low Fe intakes. Nevertheless, studies in human subjects still need to be undertaken in order to measure the effects of increased Fe (or Zn) density in food staples on Fe (or Zn) status and consequent improvements in health and productivity.

Similar arguments apply to those staples in which pro-vitamin A content may be enriched by plant breeding (e.g. wheat, maize and cassava). Some differences apply, however, as compared with trace minerals. First, no agronomic advantages accrue to higher pro-vitamin A content, so that high density will need to be bred into varieties that are otherwise high-yielding. Second, the colour of the final food product may change so that consumers may need to be educated about the improved nutritional content. However, if education programmes are successful, the colour change becomes an advantage, in that it identifies those particular varieties of superior nutritional quality.

A breeding strategy of lowering the level of inhibiting substances (anti-nutrients, e.g. phytates) in the grain has often been suggested as a way of increasing the bioavailability of minerals already consumed (Wise, 1995; Raboy, 2002). Phytin is the primary storage form of P in most mature seeds and grains and is an important compound required for early seed germination and seedling growth (Welch, 1986). Phytin plays an important role in determining mineral reserves of seeds and, thus, contributes to the viability and vigour of the seedling produced (Welch, 1993). Selecting for seed and grain crops with substantially lower phytin content could have an unacceptable effect on production, especially in regions of the world that have soils of low P status and/or poor micronutrient fertility (Graham & Welch, 1996).

Such attempts to markedly lower the anti-nutrient content of seeds and grains require a major shift in seed or grain composition. As most of the anti-nutrients known to occur in seeds and grains are major organic constituents of these organs, they may play additional, but as yet unrecognised, beneficial roles in plant growth and human health. Thus, a breeding strategy of attempting to increase Fe bioavailability by reducing anti-nutrient content is not recommended (Graham & Welch, 1996).

Certain amino acids (cysteine and lysine, but particularly methionine) enhance Fe and/or Zn bioavailability (Hallberg, 1981). These amino acids occur in many staple foods, but their concentrations are lower than those found in meat products. A modest increase in the concentrations of these amino acids in plant foods may have a positive effect on Fe and Zn bioavailability in man. Fe and Zn occur only in micromolar amounts in plant foods, so only micromolar increases in the amounts of these amino acids may be required to compensate for the negative effects of anti-nutrients on Fe and Zn bioavailability. These amino acids are essential nutrients for plants as well as for man, so relatively small increases of their concentrations in plant tissues should not have adverse consequences on plant growth. The optimal breeding strategy from the point of view of bioavailability may be to increase levels of promoter compounds (Graham & Welch, 1996).

Are there other lower-cost more easily sustainable strategies for reducing micronutrient malnutrition?

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

The World Bank (1994) estimated 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, Fe, vitamin A and I. For a

hypothetical country with 50 million in the population burdened with this rate of malnutrition, deficiencies in these three nutrients could be eliminated through fortification programmes costing a total of 25×10^6 annually, or 50 cents per person per year. The monetary benefit of this 25×10^6 investment is quite high in terms of increased productivity, which is estimated to be $20 per person per year, or a forty-fold return on an investment of 50 cents. These benchmark numbers will be used later as a basis of comparison with the benefits of a plant-breeding strategy.

While benefit:cost values are quite high, supplementation and fortification programmes 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 will of course 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 approximately 1·25 billion.

Although the costs of vitamin A pills are low, an often-quoted cost of vitamin A supplementation, which includes the costs of delivery, is US $0.50 per person per year (25 cents per capsule; World Bank, 1994). If one in 12·5 of the population in South Asia were to receive supplements (100 million in total), this is a cost of 50×10^6 per year, or 500×10^6 over 10 years. An often-quoted cost of Fe fortification is US $0.12 per person per year (World Bank, 1994). If a particular food vehicle to be fortified with Fe were to reach 33 % of the total (but untargeted) population in South Asia (412 million), the total cost is again 50×10^6 annually, or 500×10^6 over 10 years. In absolute terms, these costs may seem to involve large amounts of money, but they are very worthwhile investments and are actually quite small percentages of the total economic activity of South Asia. Nevertheless, in contrast, investments in plant-breeding research and dissemination are far lower.

Calculation of benefit:cost for biofortification

The two fundamental reasons for expecting high payoffs to investments in breeding for Fe- and Zn-dense seeds of food staple are: (1) fixed costs of research at a central location may accrue across countries and over time at low recurrent costs; (2) not only are there nutritional benefits, but agricultural productivity may also be increased. These factors may be demonstrated empirically with a simple benefit:cost calculation for India and Bangladesh, where the two major staples are rice and wheat (total population of 1·125 billion; 55×10^6 ha rice and 28×10^6 ha wheat harvested annually).

For any single staple crop, the estimated central fixed costs over 10 years of developing Fe- and Zn-dense rice varieties are estimated to be $12·5 \times 10^6$. This estimate includes several costs not directly related to breeding, such as those of nutritional studies to establish efficacy and to demonstrate impact after adoption. Conservatively, it should be assumed that all these central fixed costs are charged to India and Bangladesh. It is further assumed that $2·5 \times 10^6$ per crop is spent on adaptive breeding specifically for growing conditions in India and Bangladesh, again over the same 10-year period.

Various rates of adoption of nutritious varieties are assumed in the simulations, and extension costs are tied to the rates of adoption, specifically $1 per adopted hectare. Thus, if adoption occurs on 10 % of the rice and wheat area ($8·3 \times 10^6$ ha), then a fixed undiscounted extension cost of $8·3 \times 10^6$ is incurred. Varieties are assumed to come on line gradually after year 10 of the simulation, e.g. in a 10 % adoption scenario, to cover 2 % of total area in year 11, 4 % in year 12, 6 % in year 13, 8 % in year 14, and 10 % of the total area in all years thereafter. Recurrent costs (such as for maintenance breeding) of $250 000 annually are assumed after the initial 10-year period of fixed investments. Thus, in a 25-year simulation, assuming a 10 % adoption rate, 42×10^6 in undiscounted costs may be incurred in total.

Nutritional benefits are tied to assumed rates in reduction of anaemia. Using an analysis by Bhargava *et al*. (2001), which provided empirical estimates of the relationship between haemoglobin levels of rural Bangladeshi women and their intakes of Fe and other nutrients and compounds, it is conservatively estimated that anaemia prevalence rates would be reduced by 3 % in those who consume the nutritious rice and wheat (e.g. a reduction of 3 % of 10 % of the population under a 10 % adoption scenario, or 3·375 million cases of anaemia averted each year). Benefits to cases of anaemia averted are those estimated by Horton & Ross (1999) for India and Bangladesh, a discounted present lifetime value of $27.50 per case.

Even these conservative assumptions of nutrition benefits well justify the investment cost (as shown in Table 3). In addition, however, as discussed, for example, in Graham *et al*. (2001) increased seed Zn density may increase rice and wheat yields substantially and lower seeding rates. Yield increases of 250 kg (8 % on a base yield of 3 tonne/ha) of unmilled rice and wheat are assumed on adopted areas, giving a net incremental undiscounted profit of about $35/ha per year.

Even though all centralised fixed costs of 25×10^6 are charged to India and Bangladesh, Table 3 suggests that nutritious varieties may reach undernourished populations at a cost of just 2–3 cents per person per year. Depending on adoption rates and the levels of Fe that can be added to food staples through breeding, anaemia may be averted for as low as 22–36 cents per case. Internal rates of return on nutrition benefits should be >25 %. If agricultural benefits are also considered, several billions of dollars of benefits can be expected on investments of tens of millions of dollars.

Conclusions

The time is long overdue for involving agricultural research directly in the fight against micronutrient malnutrition. As trace minerals are important not only for human nutrition, but also for plant nutrition, plant breeding holds great promise for making a major, low-cost and sustainable contribution to reducing micronutrient, particularly mineral, deficiencies in man, and may have important spin-off effects for increasing farm productivity in developing countries in a way that is environmentally beneficial.

Results so far obtained under the Consultative Group on International Agricultural Research Micronutrient Project (Graham *et al*. 1999) indicate that the breeding parameters are not difficult and are highly likely to be low cost. The following points are seminal:

Table 3. Simulated benefits and costs over 25 years of developing iron- and zinc-dense rice varieties for India and Bangladesh

Description of benefits and costs	Variety adoption rate (%)					
	10			20		
	Anaemia reduction rate (%)			Anaemia reduction rate (%)		
	3	4	8	3	4	8
Cost per person reached who consumes nutritious staples (undiscounted)	0·03	0·03	0·03	0·02	0·02	0·02
Cost per case of anaemia avoided (undiscounted)	0·96	0·72	0·36	0·58	0·44	0·22
Internal rate of return on nutrition benefit (%)	28·9	31·8	39·2	34·0	37·1	44·9
Total investment for research and extension ($\times 10^6$; undiscounted)	42·1	42·1	42·1	51·2	51·2	51·2
Total nutrition benefits (3 % discount rate; $\times 10^6$)	694·2	925·6	1851·2	1388·4	1851·2	3702·4
Total agricultural benefits (3 % discount rate; $\times 10^6$)	2142·7	2142·7	2142·7	4285·3	4285·3	4285·3
Total benefits (3 % discount rate; $\times 10^6$)	2836·9	3068·3	3933·9	5673·7	6136·5	7987·7
Total Costs (3 % discount rate; $\times 10^6$)	35·9	35·9	35·9	43·7	43·7	43·7
Nutrition benefits:total costs	19·3	25·8	51·5	31·8	42·4	84·7

1 adequate genetic variation in concentrations of β-carotene, other functional carotenoids, Fe, Zn and other minerals exists in the major germplasm banks to justify selection;

2. micronutrient-density traits are stable across environments;

3. in all crops studied it is possible to combine the high micronutrient-density trait with high yield, unlike protein content and yield, which are negatively correlated;

4. genetic control is simple enough to make breeding economic;

5. it will be possible to improve the content of several limiting micronutrients together, thus pushing populations towards nutritional balance;

6. bioavailability of the extra nutrient in elite breeding lines is high for rats and, where the density is high enough for the test, also to human colon cell lines. Tests on human subjects are now a high priority.

Thus, some successes in increasing the mineral content of staples can be achieved in the short term through conventional breeding techniques, because of the inherent compatibility of high yields and trace mineral density in the seeds. After feasibility and practicality are established for specific crops and nutrients using conventional breeding, the hope is that transgenic techniques can then be applied to improve the nutritional content of food staples by: (1) perhaps increasing mineral levels even further than is possible with conventional breeding techniques; (2) pursuing complementary strategies, such as adding β-carotene and heat-stable phytase genes in rice, which are not possible using conventional breeding techniques (for a discussion of the application of biotechnology, see Bouis, 2000; also, see Beyer *et al.* 2002; Holm *et al.* 2002).

The final permanent solution to micronutrient malnutrition in developing countries is a substantial improvement in dietary quality, i.e. higher consumption of pulses, fruits, vegetables, fish and animal products, which the poor already desire but cannot presently afford. Achieving this objective will require several decades and involve billions of dollars of investments in infrastructure and research to increase the production of non-staple foods. Meanwhile, breeding staple foods that are dense in minerals and vitamins provides a low-cost sustainable strategy for helping to reduce levels of micronutrient malnutrition. Biofortification complements conventional interventions.

The two key issues on which success will turn are:

(1) will staple varieties with mineral-dense seeds be widely adopted by farmers in developing countries, either because of agronomic advantages on trace mineral-deficient soils or through this characteristic being bred into the highest-yielding varieties;

(2) will the additional nutrients contained in the seeds be of sufficient magnitude and bioavailability that they will have an appreciable impact on micronutrient status?

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