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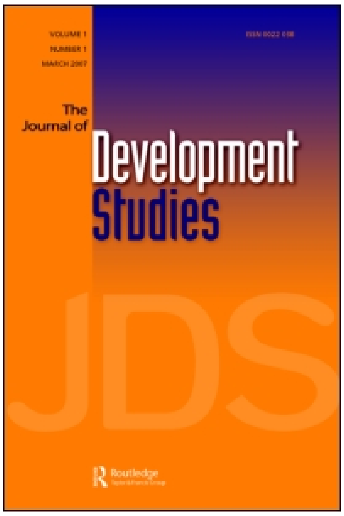

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The Potential of Genetically Modified Food Crops to Improve Human Nutrition in Developing Countries[1]

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ABSTRACT *Because of poor dietary quality and consequent widespread micronutrient malnutrition in low income countries, children and their mothers, who have higher requirements for vitamins and minerals due to rapid growth and reproduction respectively, have higher mortality, become sick more often, have their cognitive abilities compromised for a lifetime, and are less productive members of the workforce. Their quality of life and aggregate economic growth are unnecessarily compromised. One way that biotechnology can help to improve the nutrition and health of consumers in developing countries is by increasing the vitamin and mineral content and their bioavailability in staple foods.*

I. Introduction

This essay discusses the potential of biotechnology to improve the health and nutrition of consumers in developing countries. In the relatively wealthy countries of Europe, North America and elsewhere, consumers spend perhaps 10 per cent of their income on food. For the most part consumers in developed countries are free of classical nutrient deficiencies, although over-consumption is a problem for some. Also in relatively wealthy countries there is, in general, good access to affordable medical care to meet health needs, and most consumers in rich countries have access to a relatively inexpensive supply of safe and healthy food. In these settings, the possibility that biotechnology might reduce the price of food or make food more beneficial to health is a relatively minor concern. Rather, public debate about genetically modified foods (GMFs) appears to have focused on the potential for harm to either the environment or health without a clear definition of benefit to the consumer.

The situation is quite different in poor countries, where malnutrition and ill health are frequent. Poor consumers typically spend 70 per cent of their incomes on food, and diets consist primarily of staple foods, which lack the vitamins, minerals, and very likely other food components necessary to sustain good health and minimise the

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risk of adult onset diet-related chronic diseases. In addition, low incomes typically exclude the poor from access to adequate health care.

There are three broad ways that biotechnology may benefit consumers in developing countries. First, biotechnology offers a powerful new tool to improve crop productivity, both by making conventional breeding faster and more efficient and, more controversially, by the insertion of novel genes in a crop species, by use of transgenic methods. This includes the ability to bring new lands with unfavourable growing environments, such as those with highly saline soils, under production. Second, pesticide applications may be reduced through adoption of *Bt*-containing crops (that is, crops with insect resistance owing to the introduction of the *Bacillus thuringiensis* [*Bt*] gene encoding an insect-specific toxin). Reducing pesticide use can improve the health of farmers, in addition to lowering input costs. Third, transgenic methods may be used to improve the micronutrient content and/or bioavailability of commonly eaten foods in developing countries.

The first pathway, that is, improving crop productivity, is associated with an often-asked question: Does feeding the world depend on the use of biotechnology? The answer largely depends on perceptions of the current situation. Countries around the world are already using most of the arable land available for agriculture. As populations continue to grow, increasing the supply of food to meet future world food needs will depend on increasing yields. This, in turn, requires investments in agricultural research to increase the yield potentials of specific food crops as well as fish and livestock production.

Conventional breeding of cereals has been especially successful over the past three decades. Through research and extension efforts associated with the 'Green Revolution', the rate of increase of production of rice, wheat, and maize in developing countries has outpaced population growth and other factors associated with increased demand (such as higher household incomes), such that the inflation-adjusted prices of rice and wheat fell by 30–40 per cent between 1970 and 1997 (World Bank, 1990–99).

World supplies and prices of cereals are interconnected through international trade. Advances in conventional breeding in Australia, Europe, and North America have also contributed to falling cereal prices. Continued low prices of cereals are likely as long as investments in agricultural research continue, although a worrisome trend is that funds for public research in agriculture have been declining (Rosegrant et al., 2001).

It is often said that there is enough food in the world to feed everyone. Except for some pockets of extreme poverty and dislocations owing to natural disasters and civil strife, this is largely the case for cereals. Cereals (and roots and tubers) provide the cheapest sources of energy to meet requirements for poor populations. The availability of affordable staple foods prevents explicit hunger, as defined narrowly in terms of energy requirements.

However, a range of non-staple foods, such as animal and fish products, fruits, pulses, and vegetables, are foods rich in bioavailable vitamins and minerals, or micronutrients, and possibly other food components, which are necessary for good health and a productive life. As discussed in more detail below, micronutrient undernutrition is widespread in poor countries, affecting more than one-half of the population in the developing world. This situation is due primarily to diets of low nutritional quality. The poor want to eat larger amounts of non-staple foods, and most often these foods are available in local markets. However, such non-staple foods are simply too expensive to be eaten by the poor in large quantities owing to a combination of high prices and low purchasing power. The inflation-adjusted prices of non-staple foods have not been declining; in some cases they have been increasing over the past 30 years.

Because of poor dietary quality and consequent micronutrient malnutrition, some people, especially children and their mothers, who have higher requirements for vitamins and minerals, have higher mortality, become sick more often, have their cognitive abilities compromised for a lifetime, and are less productive members of the workforce than might otherwise have been the case. Their quality of life and aggregate economic growth are unnecessarily compromised. To make matters worse, the adverse synergy between undernutrition and infection results in nutrition requirements above those that characterise the needs of well-nourished populations.

In developing countries, demand for non-staple foods is growing faster than demand for cereals, as ever-richer households purchase more non-staple foods than cereals, with consequent pressure on non-staple food prices to increase. In addition, increasing the productivity of non-staple foods through agricultural research (and so lowering prices) is much more expensive than increasing the productivity of staple foods, because of the far larger number of non-staple foods involved.

From this perspective, then, the world is already failing to provide an adequate supply of non-staple foods for a large proportion of its population, and prospects are somewhat bleak for short- to medium-term improvements. Biotechnology affords a powerful new tool to help increase the supply of food produced in the world and redress, in part, situations characterised by poor dietary quality.

A third pathway through which biotechnology can improve the nutrition and health of consumers in developing countries is through increasing the vitamin and mineral content and bioavailability of staples and other foods, an approach which is the focus here.

Although it is obviously important to provide an accounting of the range of specific efforts being developed to improve the nutritional content and health-enhancing properties of particular foods, it is also necessary to place these activities in the context of alternative interventions (that is, interventions that do not involve the use of biotechnology) that might solve these malnutrition and health problems in other ways. This is accomplished by (i) examining the relative costs of nutrient supplementation and commercial nutrient fortification programs that are already being implemented to reduce micronutrient malnutrition; and (ii) examining the recent history of attempts to improve the micronutrient content of staple food crops – efforts that involve use of both biotechnology and conventional plant breeding. Recent developments in efforts to breed iron- and beta-carotene dense rices are described in this essay as a concrete example, illustrating several key generic issues associated with the use of biotechnology to breed for characteristics that have direct benefits for consumers.

It is important to keep in mind that the final, sustainable solution to micronutrient malnutrition is a substantial improvement in dietary quality by higher consumption of pulses, fruits, vegetables, fish, and animal products, which the poor need and already desire, but cannot presently afford. Realisation of this goal of high quality diets will require (i) substantial investments by farmers, private businesses and public agencies to build the infrastructure to produce and bring to market the requisite supply of non-staple foods; (ii) sound government policies to stimulate agricultural and economic growth; and (iii) considerable increases in the incomes of the poor during the course of economic development over many decades; or (iv) other strategies (for example, subsidies) designed to enhance the accessibility of these products to wider populations. Meanwhile, breeding staple foods that are dense in minerals and vitamins can provide a low-cost, sustainable, although as yet unproven strategy for reducing existing levels of specific micronutrient undernutrition.

Sections II to V (below) discuss, in some detail, iron- and beta-carotene dense rice, as an example of the development of a GMF crop of potential importance in developing countries.

II. Potential Contribution of GM Technology: A Case Study on Breeding of Iron- and Beta-carotene Dense Rices to Help Alleviate Malnutrition

Background to the Problem of Micronutrient Malnutrition in Poor Countries, its Economic Costs and Costs of Present Interventions to Address the Problem

It is only relatively recently that nutritionists working in developing countries have demonstrated conclusively that, during times of relative economic and political stability, many children and adults, particularly women in their child-bearing years, suffer more from a lack of essential vitamins and minerals in their diets than from a lack of energy. People, for the most part, are not aware that their diets lack such trace nutrients and so do not associate these deficiencies with listlessness, poor eyesight, impaired cognitive development and physical growth, more frequent and severe bouts of illness, and high mortality. For this reason, the general problem of poor dietary quality has been dubbed ‘hidden hunger’.

It is useful to summarise very briefly the scale and consequences of micronutrient malnutrition in developing countries. It is estimated that over three billion people in developing countries are iron-deficient (Administrative Committee on Coordination, Subcommittee on Nutrition, and International Food Policy Institute, 2000). The problem for women and children is more severe because of their greater physiological need for iron. In poor countries, more than half of pregnant women and more than 40 per cent of non-pregnant women and preschool children are anaemic. Iron deficiencies during childhood impair physical growth, mental development and learning capacity. In adults, iron deficiency reduces the capacity to do physical labour. Severe iron deficiency is a leading contributor to death among women during childbirth, owing to low haemoglobin levels in the light of physiological blood loss.

Globally, about three million children of preschool age have visible eye damage owing to a vitamin A deficiency. Annually, an estimated 250,000 to 500,000 preschool children go blind from this deficiency, and about two-thirds of these children die within months of going blind. Estimates of the subclinical prevalence of vitamin A deficiency range from 100–250 million. A number of clinical trials in developing countries have shown that vitamin A supplementation, as capsules distributed biannually in high doses, as weekly distributed low doses (consistent with levels attainable through food), or as a fortified product in diets can reduce mortality rates among preschool children on average by 23 per cent (Beaton et al., 1993).

Deficiencies in several other micronutrients, in particular zinc (Hotz and Brown 2004), may also be widespread, with equally serious consequences for health. However, because for some of these micronutrients, specific indicators are lacking to screen for deficiencies, they have not received as much attention as iron, vitamin A and iodine deficiencies.

The World Bank (1994) estimates that at the levels of micronutrient malnutrition existing in South Asia, 5 per cent of gross national product is lost each year due to deficiencies in the intakes of just three nutrients, namely iron, vitamin A and iodine. For each 50 million in population, this translates into an economic loss of US$1 billion per year.

Some general cost calculations can be made for interventions to relieve iron and vitamin A deficiencies by supplementation and fortification in South Asia, which has a total population of roughly 1.25 billion people. The costs of vitamin A pills themselves are low: an often-quoted cost of vitamin A supplementation, which includes the cost of delivery, is US$0.50 per person per year (that is, US$0.25 per capsule; World Bank, 1994). If one in every 12.5 people in South Asia were to receive supplements (that is, 100 million people in total), this would cost US$50 million per year, or US$500 million over 10 years. An often-quoted cost of iron fortification is US$0.12 per person per year (World Bank 1994). If a particular food vehicle fortified with iron were to reach 33 per cent of the total (but untargeted) population in South Asia (that is, 412 million people), the total cost would, again, be US$50 million annually, or US$500 million over 10 years. In absolute terms, these nutrient-specific interventions may seem to be large amounts of money, but they are very worthwhile investments and actually represent quite small percentages of the total economic activity of the South Asian economies.

The Micronutrient Initiative (MI) estimates that 1 billion vitamin A pills have been distributed worldwide since the inception of vitamin A distribution programmes up to the end of 2000 and that 500 million supplements are now given out annually (UNICEF, UNU, WHO and MI, 1999). A conservative estimate of the annual, recurrent cost of global vitamin A supplement programmes is, therefore, US$125 million.

Although benefit–cost ratios 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 disappear.

Investments in plant breeding research and dissemination are far lower (see Section III(ii)) and potentially longer lasting. Benefits of agricultural research at a central location can be leveraged throughout the world and across time. Breeding for staple plants with high bioavailable micronutrient content in their seeds, hereinafter referred to as ‘biofortification’, treats the underlying cause of micronutrient undernutrition. Although plant breeding can involve relatively long lead times of eight to ten years before nutritious varieties can be developed and their adoption by farmers can be initiated, such a strategy is sustainable once breeding has been completed, and seeds have been disseminated and adopted by farmers. Biofortification has the potential to provide coverage for remote rural populations, which supplementation and fortification programs may not reach, and it inherently targets the poor who consume high levels of staple foods and little else.

However, efficacy and effectiveness trials and other studies have yet to be undertaken to determine both the degree to which nutritionally dense varieties can improve micronutrient status and whether there are unintended negative effects.

According to an expert group convened to consider micronutrient supplementation and fortification with iron, iron overload disorders and haemochromatosis are rare, even in those populations of European origin most susceptible to them; therefore, the use of fortification and supplementation as public health interventions for preventing and controlling iron deficiency should not be constrained (UNICEF, UNU, WHO and MI, 1999). It is safe to assume that the same conclusions would apply to biofortification. If biofortification eventually were to replace supplementation in some areas, there is the possibility that biofortification might lessen risks of overdosing, such as that recently reported in India, where toxicity associated with a mass distribution of a vitamin A concentrate to children was thought, possibly, to have been the result of a changed delivery routine (Sharma, 2001).

Improving the Nutrient Content and Bioavailability of Minerals and Vitamins in Staple Food Crops Through Biofortification

Breeding strategies. There are three breeding sub-strategies that may be applied individually or in various combinations. These are (i) reducing the level of antinutrients in food staples, which inhibit the bioavailability of minerals and vitamins; (ii) increasing the levels of nutrients and compounds that promote the bioavailability of minerals and vitamins; and (iii) increasing the mineral and vitamin content. Experience with increasing the mineral and vitamin content of rice is discussed in some detail in section II(iii).

Reducing antinutrients. A breeding strategy of lowering the level of antinutrients, such as phytic acid, which binds metals in grain, has often been suggested as a way to increase the bioavailability of minerals already consumed.

Phytin is the primary storage form of phosphorus in most mature seeds and grains and is an important compound required for early seed germination and seedling growth (Wise, 1995). 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).

Graham and Welch (1996) argue that selecting for seed and grain crops with substantially lower phytin content could have an unacceptable effect on production, especially in regions of the world where there are soils of low phosphorus status and/or poor micronutrient fertility. Such attempts to lower the antinutrient content of seeds and grains significantly require a major shift in seed or grain composition. Because most of the antinutrients known to occur in seeds and grains are major organic constituents of these organs, they may play beneficial roles in plant growth and may have other unidentified roles in human health. Therefore, Graham and Welch argue against a breeding strategy that attempts to increase iron bioavailability by reducing antinutrient content. Antinutrients may also reduce absorption of potentially toxic trace minerals such as cadmium and other heavy metals (McLaughlin et al., 1999).

However, Raboy (2002) has developed low phytic acid (or *lpa*) mutant varieties of maize, rice, and barley. The phytic acid content of *lpa* seeds is reduced by 50 per cent to 80 per cent compared with non-mutant seeds. The total amount of phosphorus remains the same – phytic acid is replaced by inorganic phosphorus, which does not bind a range of trace minerals.[2] These mutations typically have little observable effect on other seed or plant characteristics. These mutants are presently being tested for agronomic performance and effects on micronutrient status in humans.

A related strategy is to increase the level of phytase. Phytase can break down phytates, thus increasing bioavailability of minerals. Phytases have been used successfully in animal feeds (Nelson et al., 1971; Rimbach and Pallauf, 1993; Yi et al., 1996). Phytase is present in the endosperm of rice, for example, but is destroyed when rice is boiled for eating. Heat-stable phytase may be introduced in food staples through genetic transformation (Holm et al., 2002).

Increasing levels of compounds that improve absorption and utilisation of nutrients. Certain amino acids, such as cysteine, enhance iron and/or zinc 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 positive effects on iron and/or zinc bioavailability in humans. Iron and zinc 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 antinutrients on iron and zinc bioavailability. These amino acids are normal constituents of plants, so relatively small increases in their concentrations in plant tissues should not have adverse consequences on plant growth (Graham and Welch, 1996).

An additional possibility is that as intakes of beta-carotene (converted to vitamin A after ingestion) are increased, the utilisation of absorbed iron may be promoted and vice-versa. That is, there are possible synergies between increasing intakes of these two nutrients (Garcia-Casal et al., 1998). There is already considerable evidence for synergism between vitamin A and zinc intakes (Smith, 1996).

Feasibility. Will famers adopt nutrient-rich varieties?

Impact on plant nutrition is a particular concern of agriculturalists, whose first priority may be to raise the yield potential of plants rather than to address human nutrition problems. If yield and profitability are compromised by breeding for nutrient content, farmers may not adopt nutritionally enhanced cultivars. However, relatively recent research has shown that mineral-dense seeds assist plants in resisting disease and other environmental stresses (Welch and Graham, 1999; Graham et al., 2001). More seedlings survive and initial growth is more rapid. Ultimately, yields are higher, particularly in trace mineral 'deficient' soils in arid regions.[3]

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; for example, 5–10 mg/kg (ppm) in milled rice, and as much as 100 mg/kg in micronutrient-dense bean seeds. It is not known whether such small amounts will alter the appearance, taste, texture, or cooking quality of foods. The dissemination strategy for trace minerals, then, would be to include the mineral-density trait in as many varietal releases as possible, in order to benefit a high proportion of the population, without having to rely on behavioural change as a condition for success. This would be much the same approach as adding fluoride to drinking water in developed countries. As with the example of fluoride, information on increased nutrient content would be made publicly available.

However, increasing levels of beta-carotene will turn varieties from white or light colours of yellow to dark yellow and orange. Often white varieties are much preferred by consumers (for example, milled rice, wheat flour, maize, cassava). Major nutrition education programs will probably be necessary to encourage consumers to switch to more nutritious varieties. However, if these nutrition education programs are successful, the yellow–orange colour will mark the more nutritious varieties from the less nutritious, and a disadvantage will have been turned into an advantage (Hagenimana and Low, 2000).

Increasing Micronutrient Content in Rice

Conventional breeding. In a survey of traditional and modern varieties of rice, Graham et al. (1999) reported that iron density in unmilled rice varied from 7–24 mg/kg (ppm) and zinc density from 16–58 mg/kg. Nearly all the widely grown 'green revolution' varieties were similar, at about 12 and 22 mg/kg for iron and zinc, respectively. The best lines discovered in the survey of the existing germplasm collection were, therefore, twice as high in iron and 1.5 times as high in zinc as the most widely grown varieties. These ratios, therefore, are benchmarks for iron and zinc density, which seem to be reasonably attainable using conventional breeding.

Expression of micronutrient-density traits has been tested over a wide range of environments, and although the environmental effect itself is strong, the genotype effect is consistent across environments (implying that the genotype–environment interaction is not serious), a finding that is sufficient to encourage a breeding effort. Environmental factors considered by one or more crop programs include acid soils, alkaline soils, saline soils, acid-sulphate soils, iron-deficient soils, time of planting, field site, season, nitrogen fertilisation, phosphorus fertilisation, potassium status, elevation and drought stress (Graham et al., 2001).

Transgenic methods.

Increasing iron. Ferritin is an iron-storage protein, and forms of it are found in animals, plants, and bacteria. Ferritin is used by both plants and animals as the storage form of iron (Theil et al., 1997). The ferritin gene has been isolated and sequenced from a number of plants, including soybean, French bean, pea, and maize. Orally administered ferritin, in non-transgenic foods (Beard et al., 1996) or from transgenically-derived ferritin-rich rice (Murray-Kolb et al., 2002) has been demonstrated to provide a source of iron for treatment of iron deficiency in rats.

Human studies with extrinsically radiolabelled animal ferritin have indicated that, when added to a meal, iron from ferritin is only about half as well absorbed as iron from vegetables (Martinez-Torres et al., 1976; Taylor et al., 1986) and iron as ferrous sulphate (Skikne et al., 1997). However, a recent study has shown that intrinsically radiolabelled iron in soybeans is highly bioavailable (27 per cent) to iron-deficient women (Murray-Kolb et al., 2003). About 50 per cent of the iron in the soybeans was ferritin; the remaining iron, ferric phytate, is not thought to be highly bioavailable.

Goto et al. (1999) report improving the iron content of rice by transferring the entire coding sequence of the soybean ferritin gene into Japonica rice. The introduced ferritin gene was expressed under the control of a rice seed-storage protein glutelin promoter, to mediate the accumulation of iron specifically in the grain. The transgenic seeds stored up to three times more iron than normal seeds. Iron levels in the whole (unmilled) seeds of the transformants varied from 13–38 mg/kg (ppm); pooled mean values were 23 mg/kg for transformants and 11 mg/kg for non-transformants. The average iron content in the endosperm was 3.4 mg/kg in the transformant and 1.6 mg/kg in the non-transformant.

This underscores the importance of determining where in endosperm the iron (and other trace minerals) are deposited and how mineral levels are affected by milling. Trace minerals cannot be synthesised by plants and must be transported from the soil, through the plant and to the seed. Several processes and genes may be involved. The authors speculate that the amount of iron accumulation is restricted by transport of iron to the ferritin molecule, rather than simply by levels of ferritin protein. Thus, it may be possible to store larger amounts of iron in the ferritin molecule by co-integrating the ferritin gene and the iron reductase-like transporter gene. Robinson et al. (1999) report a newly discovered ferric-chelate reductase gene, which allows plants to absorb more iron from the soil, thus introducing the possibility of widening the scope of rice varieties with high iron uptake.

A doubling of the iron content in rice using a ferritin gene derived from *Phaseolus vulgare* has been reported (Gura, 1999). Metallothionine was also expressed in the rice grain, increasing the cysteine content seven-fold.

The ongoing work of exploiting the sequence of the rice genome is also proving invaluable to the acceleration of our understanding of the internal iron transport processes and should open up new options for iron accumulation in the rice endosperm (Gross et al., 2003; Koike et al., 2004).

Introducing a gene which codes for heat-stable phytase. Phytic acid or phytate is present predominantly in the aleurone layers of the rice grain, and while most of these tissues are removed during polishing of the grain, remaining amounts of phytate may have some effects on the bioavailability of iron (and other micronutrients). The level of phytase, which breaks down phytic acid, is normally low in milled rice. Several studies have already demonstrated the usefulness of adding phytase to the rice diets of poultry (for example, Adrizal et al., 1996; Munaro et al., 1996; Farrell and Martin, 1998; Martin et al., 1998; Teichman et al., 1998). The phytase that does exist in rice seeds will hydrolyse the phytic acid present at lower pH levels, if seeds are left to soak until germination in water. However, boiling destroys the phytases that occur naturally in rice.

In one study, an amino acid was changed in the protein sequence to make the phytase heat stable (Pasamontes et al., 1997). The phytase was active under the pH conditions of digestion and degraded phytic acid in a very short time, during model *in vitro* digestion.

Lucca et al. (2001) reported the introduction into rice of a transgene for this particular heat-stable phytase from *Aspergillus fumigatus*; the transgene increased the level of phytase activity 130-fold. Unfortunately, after expressing the gene in the grain, the phytase was no longer stable to heat and lost its activity on boiling.

A new approach is now under investigation in which the *A. fumigatus* phytase gene would break down phytate during seed maturation (when pH levels [6–7] would be conducive to phytase activity). Fusing the globulin promoter to the phytase gene, which tests have shown is expressed only in the endosperm of rice, which is consumed after milling, should prevent seed germination being compromised (after harvesting and replanting) owing to low phosphorus content. The hope is that the phosphorus in the outer layers of the seed (which is milled away for consumption but not for planting) would remain unaffected (Lucca et al., 2002).

Increasing levels of compounds that improve absorption and utilisation of nutrients. Levels of lysine, which is an important, essential and limiting amino acid in rice and which might promote the uptake of trace minerals, can be improved by transgenic methods (Datta and Bouis, 2000). Introduction of two bacterial genes, expressing DHSPS (dihydrodipicolinic acid synthase) and AK (aspartokinase) enzymes, encoded by the *Corynebacterium dapA* gene and a mutant *Escherichia coli lysC* gene, have enhanced lysine levels about five-fold in canola and soybean seeds (Falco et al., 1995). More recent work shows that a single novel storage protein can lead to significant increases in the rice endosperm (Sun and Liu, 2004). The private sector has been successful in increasing the lysine content of maize and this product has entered regulatory review in a number of countries.

Adding beta-carotene. Beta-carotene, a precursor of vitamin A, does not occur naturally in the endosperm of rice. Ye et al. (2000) originally reported generating transgenic plants that produce grain with yellow-coloured endosperm by inserting three genes to complete the biosynthetic pathway for carotenoids, including one gene taken from daffodil. Biochemical analysis confirmed that the colour represented beta-carotene. The reported level of total carotenoids in one gram of the dry, uncooked transformed rice (Golden Rice) was 1.6 μg/g. More recently, Paine et al. (2005) have reported substantial increases in these levels (37 μg/g total carotenoids and 31 μg/g provitamin A carotenoids, 84 per cent of which are beta-carotene), by replacing the gene from daffodil with a gene from maize. In addition, only one other gene, the phytoene reductase, had been shown to be also necessary – the level of endogenous lycopene cyclase (added originally as the 'third gene' in the Ye et al. work) has been shown to be sufficient in the rice endosperm to drive the pathway to the provitamin A carotenoids (Schaub et al., 2005). A discussion on the degree to which vitamin A intakes may be improved by the use of Golden Rice in the rural Bangladesh context is provided below (Section III(i)).

III. Outcomes and Impacts of Breeding for Iron- and Beta-carotene Dense Rice

Impact on Iron and Beta-carotene Intakes

For poor populations, food staple consumption so dominates diets that primary food staples can provide in the range of 40–55 per cent of total iron intakes (Bouis et al., 2000). If a single food staple provides 50 per cent of total iron intakes for a poor population, then a doubling of the iron density in that food staple will result in a 50 per cent increase in total iron intakes. It would seem evident that a 50 per cent increase in intakes of iron, if it were to be as bioavailable as iron already in the diet, would be of considerable benefit to anaemic women with such low iron intakes. With respect to rice, rural Bangladeshi women consume an estimated 400 grams of milled rice per day. If the level of iron in rice can be increased by (say) +10 mg/kg, which seems feasible (Gregorio et al., 2000; Graham et al., 2001), this represents an increased intake of +4 mg of iron a day on a base intake of 6–8 mg iron per day (Bhargava et al., 2001).

With respect to vitamin A intake from Golden Rice for these same Bangladeshi rural women, 400 grams of rice times a density of 31 μg/g beta-carotene gives a daily intake of 12,400 μg/day. Reducing this figure by 25 per cent to take account of loss of beta-carotene due to boiling (presumed to be an overestimate of losses), and converting Retinol Equivalents (RE) using a ratio of 12 μg beta-carotene per RE, gives an intake of 775 RE. The WHO/FAO recommended daily intake (RDI) is only 500 RE. This is over and above present sources of vitamin A in the diet, which already provide an estimated 50 per cent of the RDI for adult women. Thus, adult women would consume twice the RDI each day if they switched exclusively to Golden Rice.

Rice intakes for non-breastfed pre-school children are about half those for adult women, so that vitamin A intakes from Golden Rice may be estimated at 387 RE, as compared with a WHO/FAO recommended daily intake of 450 RE for four to seven year-olds. This is over and above present sources of vitamin A in the diet, which already provide an estimated 25 per cent of the RDI for preschool children. Thus, four to seven year-olds would consume approximately 10 per cent more than their RDI each day if they switched exclusively to Golden Rice.

Costs and Benefits of a Biofortification Strategy

Development of iron- and zinc-dense varieties of rice or wheat using conventional breeding might cost as much as US$10 million each over ten years, including the costs of nutrition safety and efficacy tests, the costs of dissemination in selected regions, and the costs of an evaluation of nutritional and economic impact (Hunt, 2002). As indicated above (Section II(i)), such an investment (of US$20 million in two crops, rice and wheat) is projected to have far-reaching impacts if efficacy and effectiveness are achieved. Under such conditions, it would be reasonable to extrapolate benefits to countries around the world, as countries would need only to invest in adaptive breeding and dissemination costs. Moreover, benefits should be sustainable at low maintenance costs. Benefits from breeding advances typically do not disappear after initial investments and research have been successful, as long as an effective domestic agricultural research infrastructure is maintained.

A simulation model developed for Bangladesh and India based on development of iron- and zinc-dense varieties of rice and wheat, which were assumed to be adopted on only 10 per cent of approximately 83 million hectares planted to rice and wheat, supported the expectation of enormous economic benefits from a biofortification strategy (Hunt, 2002). Total costs were estimated to be US$42 million which, in addition to the US$20 million in central development costs for rice and wheat, included costs of adaptive and maintenance breeding and extension costs. These conservative assumptions suggest that the returns that come on-stream during the second decade of research and development would be about $ 1.2 billion in benefits from better nutrition.

A more formal economic evaluation of biofortification in Bangladesh and India, in which the ratio of the present value of benefits to the present value of costs was discounted at a 3 per cent rate (commonly used for evaluation of social benefits), gave a benefit-cost ratio of 19, for returns, simply for better iron nutrition in humans; a similar ratio was found by Horton and Ross (1998) for fortification in South Asia. A different way of expressing the concept of discounting over time is the internal rate of return, in which the interest rate is calculated at which benefits would equal costs plus interest, if the funds were to be borrowed to make the investment. In this case the internal rate of return would be 29 per cent, measured as benefits to human nutrition (Hunt, 2002).

In the longer term (years 11–25 of the simulation model) it was estimated that a total of 44 million person-years of iron deficiency would be prevented if nutritionally improved varieties were to be adopted on 10 per cent of rice and wheat areas in Bangladesh and India. This was based on a conservative assumption of only a 3 per cent reduction in the prevalence of iron deficiency among those consuming the high-iron rice. Thus, costs would be about US$1 per case of anaemia per year prevented and US$0.03 per person per year for those whose iron intakes would be increased by 50 per cent through consumption of iron-dense rice and wheat.

These estimates have been made for conventional breeding. It is not known whether transgenic methods would be more or less costly than conventional breeding methods, in part because the higher costs of meeting stricter regulatory procedures for transgenic crops are not yet known. These higher regulatory costs for transgenic methods may be offset by the greater costs and time of backcrossing involved with conventional techniques. However, the relative costs of transgenic and conventional methods are of secondary importance, in the sense that, even if total costs for either method doubled the assumed costs for conventional breeding of $10 million over ten years, biofortification would still be a very cost-effective proposition. For example, the very conservative benefit calculations above included only benefits for India and Bangladesh, while the varieties developed under full development cost assumptions could be used in other countries around the world as well. It is very difficult to predict benefits and breeding costs ex ante, so that it is important to make conservative estimates of benefits.[4] Extrapolations are made on the assumption of specified levels of efficacy and effectiveness for interventions characterised by uncertainties that result from incomplete knowledge.

There is no a priori reason to believe that research costs will be higher or lower for a widely grown crop (for example, for a cereal such as rice) than for a 'minor' crop (for example, pulses). Given constant costs, benefits in agricultural research will always be higher for the more widely grown crop. Thus, there is a bias in research investments toward those crops and, consequently 'minor' crops lag behind in terms of productivity increases. If the costs of developing transgenic crops are high owing to the need to meet regulatory procedures, the tendency to undertake research only on the more widely grown crops will increase. On the other hand, if biotechnology can lower the costs of undertaking agricultural research by making the process more efficient, this tendency will be mitigated.

IV. Knowledge Gaps in Breeding for Iron- and Beta-carotene Dense Rice

The Genotype Factors that Optimally Determine Bioavailability

Bioavailability to humans of micronutrients in plant foods depends on a myriad of factors, which interact to determine the ultimate bioavailability of a particular micronutrient to an individual, eating a mixed diet, within a given environment (Fairweather-Tait and Hurrell, 1996; Welch 2002). These factors include the combination of nutrients, antinutrients, and absorption enhancers present in the nutrient enhanced rice and the meal in which it is eaten. Because of this complexity, the data obtained using *in vitro* systems, animal models and test meals are always ambiguous (House, 1999; Van Campen and Glahn, 1999). Only data obtained on reducing the prevalence of micronutrient deficiencies using feeding trials in test populations under free living conditions can delineate the actual efficacy of using micronutrient-enriched varieties of plant foods as an intervention tool. However, it is impractical to test, in this way, the bioavailability of selected micronutrients, in the numerous genotypes of staple plant foods that can be generated in plant breeding programs (Graham and Welch, 1996; Graham et al., 2001). The ultimate proof of the biofortification strategy will lie in effectiveness studies undertaken in areas where nutritionally improved varieties are introduced.

Consumer Acceptance

There are various potential barriers to the adoption, for example, of Golden Rice.

- It is yellow in colour, whereas Asian consumers who stand to benefit the most from its introduction are used to eating white rice.
- There may be consumer acceptance issues, potentially related to safety, ethics and localisation of the decision-making process in agricultural development and associated processes.
- There may be concerns that technological solutions used in isolation will exclude alternative approaches, including for example, failure to harness technology to social policy.

Whether public health education initiatives can address all these concerns is open to question. Examples of successes in programs encouraging consumers to switch from white to yellow or orange varieties of staple food crops provide some encouragement (Hagenimana and Low, 2000).

Relative Efficiency of Transgenic and Conventional Breeding Methodologies

Much experience has been accumulated with conventional breeding and it continues to become more efficient, in part owing to new techniques developed through the use of biotechnology. Yet, clearly the capability to move genes across species holds great potential, as demonstrated by the examples presented above for rice, to accomplish goals that cannot be attained with conventional breeding. As experience is gained with biotechnology, development of transgenic varieties will become more efficient and cost-effective. It is difficult if not impossible to determine how investments should best be allocated between conventional breeding, which will give benefits now, and transgenic methods, which will generate future benefits.

V. Conclusions

The following lessons may be drawn concerning the potential usefulness of biotechnology in helping to provide more nutritious foods in developing countries.

- To be of value, plant breeding has to be demonstrated to be safe (see below) and more cost-effective than alternative interventions already in place to reduce micronutrient undernutrition. Such cost-effectiveness is anticipated, in large measure because of the far-reaching impacts of plant breeding. A relatively small, fixed, initial investment in research could benefit the health of millions of poor people all over the world, and at the same time improve agricultural productivity on lands that are presently among the least productive. Nutrient dense varieties of crops can be developed for a fraction of the recurrent estimated annual costs of supplementation programmes in developing countries (for example US$1.65 billion for vitamin A supplementation programmes) and can reach far more people, as the benefits can be extended across countries and time.
- There should be aspects of the breeding strategy for which biotechnology is superior to conventional breeding techniques. For rice, this is the case for adding beta-carotene-related and heat-stable phytase genes. In the long run, as more is understood about the factors driving translocation of minerals in plants, biotechnology may also be a more efficient way to increase trace mineral density.
- Where biotechnology is superior to conventional plant breeding, it must be recognised that the same conditions that apply to products developed through conventional plant breeding, must also be met, as follows:
    - there should be no serious, negative agronomic consequences of the characteristic being added;
    - any noticeable changes in the colour, taste, texture, cooking qualities, and other features associated with the characteristic being added should be acceptable to the consumer;
    - the characteristic being added should result in a measurable improvement in the nutritional status of the malnourished population; and
    - there should be no unacceptable nutritional effects.

The conditions, relating to safety, acceptability and efficacy, in particular, have yet to be firmly established. Nutritionally improved transgenic foods have not been fully developed and tested for their potential to improve micronutrient status, even using *in vitro* techniques and animal models, let alone in human subjects with micronutrient deficiencies.

Definitive proof of the benefit of nutritionally improved, transgenic foods obviously depends on further development, release and eventual impact evaluation, all of which are many years into the future. Nevertheless, in the shorter term, lessons learned through initial experiences with conventional breeding efforts show just how cost-effective a biofortification strategy can be. Clearly, the nutritional quality of staple foods can be substantially improved using transgenic methods compared with what can be accomplished using conventional breeding. Knowledge in the area of nutritional genomics should expand rapidly in the future, and more efficient techniques for producing transgenic plants will be developed. There are potentially substantial benefits to the poor in relation to costs.

Characteristics of food, such as appearance, taste, and colour, which are important to consumers in both developed and developing countries, can also be improved through biotechnology; however, such research currently probably benefits wealthy consumers in developed countries more than poor consumers in developing countries.

Ultimately, good nutrition depends on adequate intakes of a range of nutrients and other compounds, in combinations and levels that are not yet completely understood. Thus, the best and final solution to eliminating undernutrition as a public health problem is to provide increased consumption of a range of non-staple foods. By reducing the cost of producing food, biotechnology will, perhaps, make its most important contribution to reducing malnutrition. However, this will require several decades to be realised, informed government policies, and a relatively large investment in agricultural research and other public and on-farm infrastructure.

In conceptualising solutions for a range of nutritional deficiencies, interdisciplinary communication between plant scientists and human nutrition scientists 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 modified through plant breeding. Plant breeders need to be aware of both the major influence that agricultural research may have had on nutrient utilisation in the past (for example, the bioavailability of trace minerals in modern varieties versus bioavailability in traditional varieties), and the potential of plant breeding for future improvements in nutrition and health.

Notes

1. This essay is a modified version of Bouis et al. (2003). Permission granted by Elsevier Press is gratefully acknowledged.
2. When such mutants are used as animal feeds, this also avoids what has become a serious pollution problem – excretion of unutilised phytic acid.
3. Biofortification will not deplete soils of trace minerals. Sufficient trace minerals are present in most soils for thousands of crops. Some soils are labelled ‘trace mineral-deficient’ because the properties of these soils are such that the trace minerals are chemically bound and so 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. This is a very different situation from depletion of macronutrients in the soil, such as nitrogen and phosphorus (Graham and Welch, 1996).
4. There are agronomic benefits associated with high zinc seed density which are not discussed here (Graham et al., 2001). Possible higher crop yields are not counted as possible benefits nor benefits to better zinc nutrition. During germplasm screening, a high correlation between iron and zinc density in rice and wheat seeds has been found; therefore breeding for both characteristics simultaneously is feasible.

References

Administrative Committee on Coordination, Subcommittee on Nutrition, and International Food Policy Research Institute (2000) *Fourth Report on the World Nutrition Situation* (Geneva, United Nations).

Adrizal, P. E. P. and Sell, J. L. (1996) Utilization of defatted rice bran by broiler chickens, *Poultry Science*, 75(8), pp. 1012–7.

Beard, J. L., Burton, J. W. and Theil, E. C. (1996) Purified ferritin and soybean meal can be sources of iron for treating iron deficiency in rats, *Journal of Nutrition*, 126, pp. 154–60.

Beaton, G. H., Martorell, R., Aronson, K. J., Edminston, B., McCabe, G., Ross, A. C. and Harvey, B. (1993) *Effectiveness of Vitamin A Supplementation in the Control of Young Child Morbidity and Mortality in Developing Countries* (ACC/SCN State of the Arts Series, Nutrition and Policy Discussion Paper No. 13) (Geneva: Administrative Committee on Coordination, Subcommittee on Nutrition), accessed at: http://www.unsystem.org/scn/

Bhargava, A., Bouis, H. and Scrimshaw, N. (2001) Dietary intakes and socioeconomic factors are associated with the haemoglobin concentration of Bangladeshi women, *Journal of Nutrition*, 131, pp. 758–64.

Bouis, H., Graham, R. and Welch, R. (2000) The Consultaive Group on International Agricultural Research (CGIAR) Micronutrients Project: justification and objectives, *Food and Nutrition Bulletin*, 21(4), pp. 374–81.

Bouis, H., Chassy, B. M. and Ochanda, J. (2003) Genetically modified crops and their contribution to human nutrition and food quality, *Trends in Food Science and Technology*, 14, pp. 191–209.

Datta, S. and Bouis, H. E. (2000) Application of biotechnology to improving the nutritional quality of rice, *Food and Nutrition Bulletin* (United Nations University Press), 21(4), pp. 451–6.

Fairweather-Tait, S. and Hurrell, R. F. (1996) Bioavailability of minerals and trace elements, *Nutrition Research Reviews*, 9, pp. 295–324.

Falco, S. C., Guida, T., Locke, M., Mauvais, J., Sanders, C., Ward, R. T. and Webber, P. (1995) Transgenic canola and soybeans seeds with increased lysine, *Biotechnology*, 13, pp. 577–82.

Farrell, D. J. and Martin, E. A. (1998) Strategies to improve the nutritive value of rice bran in poultry diets. III. The addition of inorganic phosphorus and a phytase to duck diets, *British Poultry Science*, 39(5), pp. 601–11.

Garcia-Casal, M. N., Layrisse, M., Solano, L., Arguello, F., Llovera, D., Ramirez, J., Leets, I. and Tropper, E. (1998) Vitamin A and β-carotene can improve nonheme iron absorption from rice, wheat and corn by humans, *Journal of Nutrition*, 128, pp. 646–50.

Goto, F. T., Yoshihara, T., Shigemoto, N., Toki, S. and Takaiwa, F. (1999) Iron fortification of rice seed by the soybean Ferritin gene, *Nature Biotechnology*, 17, pp. 282–6.

Graham, R. D. and Welch, R. M. (1996) *Breeding for Staple-food Crops with High Micronutrient Density: Long-term Sustainable Agricultural Solutions to Hidden Hunger in Developing Countries* (Agricultural Strategies for Micronutrients Working Paper 3) (Washington, DC: International Food Policy Research Institute).

Graham, R. D., Senadhira, D., Beebe, S. E., Iglesias, C. and Ortiz-Monasterio, I. (1999) Breeding for micronutrient density in edible portions of staple food crops: Conventional approaches, *Field Crop Research*, 60, pp. 57–80.

Graham, R. D., Welch, R. M. and Bouis, H. E. (2001) Addressing micronutrient malnutrition through enhancing the nutritional quality of staple foods: principles, perspectives and knowledge gaps, *Advances in Agronomy*, 70, pp. 77–142.

Gregorio, G., Senadhira, D., Htut, H. and Graham, R. D. (2000) Breeding for trace mineral density in rice, *Food and Nutrition Bulletin*, 21(4), pp. 382–6.

Gross, J., Stein, R. J., Fett-Neto, A. G. and Fett, J. P. (2003) Iron homeostasis related genes in rice, *Genetics and Molecular Biology*, 26, pp. 477–97.

Gura, T. (1999) New genes boost rice nutrients, *Science*, 285, pp. 994–5.

Hagenimana, V. and Low, J. (2000) Potential of orange-fleshed sweet potatoes for raising vitamin A intake in Africa, *Food and Nutrition Bulletin*, 21(4), pp. 414–8.

Hallberg, L. (1981) Bioavailability of dietary iron in man, *Annual Review of Nutrition*, 1, pp. 123–7.

Holm, P. B., Kristiansen, K. N. and Pedersen, H. B. (2002) Transgenic approaches in commonly consumed cereals to improve iron and zinc content and bioavailability, *Journal of Nutrition*, 132(Supplement), pp. 514–6.

Horton, S. and Ross, J. (1998) *Economic Consequences of Iron Deficiency* (Ottawa, Canada: The Micronutrient Initiative).

Hotz, C. and Brown, K. (eds) (2004) Assessment of the risk of zinc deficiency in populations and options for its control, *Food Nutrition Bulletin*, 25, pp. S189–95, accessed at: http://www.izincg.ucdavis.edu/publications/FNBv25n1supp2zinc.pdf

House, W. A. (1999) Trace element bioavailability as exemplified by iron and zinc, *Field Crop Research*, 60, pp. 115–41.

Hunt, J. M. (2002) Reversing productivity losses from iron deficiency: the economic case, *Journal of Nutrition*, 132(4, Supplement), pp. 794–801.

Koike, S., Inoue, H., Mizuno, D., Takahashi, M., Nakanishi, M., Mori, S. and Nishizawa, N. K. (2004) OsYSL2 is a rice metal-nicotianamine transporter that is regulated by iron and expressed in the phloem, *Plant Journal*, 39(3), pp. 415–24.

Lucca, P., Hurrell, R. and Potrykus, I. (2001) Genetic engineering approaches to improve the bioavailability and the level of iron in rice grains, *Theoretical and Applied Genetics*, 102, pp. 392–7.

Lucca, P., Hurell, R. and Potrykus, I. (2002) Fighting iron deficiency anemia with iron-rich rice, *Journal of the American College of Nutrition*, 21(3), pp. 184S–90S.

Martin, E. A., Nolan, J. C., Nitsan, Z. and Farrell, D. J. (1998) Strategies to improve the nutritive value of rice bran in poultry diets. IV. Effects of addition of fish meal and a microbial phytase to duckling diets on bird performance and amino acid digestibility, *British Poultry Science*, 39, pp. 612–21.

Martinez-Torres, C., Renzi, M. and Layrisse, M. (1976) Iron absorption by humans from hemosiderin and ferritin, further studies, *Journal of Nutrition*, 106(1), pp. 128–35.

McLaughlin, M. J., Parker, D. R. and Clarke, J. M. (1999) Metals and macronutrients – food safety issues. *Field Crop Research*, 60, pp. 143–63.

Munaro, F. A., Lopez, J., Lopez, S. E. and Rutz, F. (1996) Effect of phytase on boiavailability of phosphorus in diets with defatted rice bran for broiler chickens, *Revista da Sociedade Brasileira de Zootecnia*, 25(5), pp. 932–43.

Murray-Kolb, L. E., Welch, R. M., Theil, E. C. and Beard, J. L. (2003) Women with low iron stores absorb iron from soybeans, *American Journal of Clinical Nutrition*, 77, pp. 180–4.

Murray-Kolb, L. E., Takaiwa, F., Goto, F., Yoshihara, T., Theil, E. C. and Beard, J. L. (2002) Transgenic rice as a source of iron for iron-depleted rats, *Journal of Nutrition*, 132(5), pp. 957–60.

Nelson, T. S., Shieh, T. R., Wodzinski, R. J. and Ware, J. H. (1971) Effects of supplemental phtase on the utilization of phytate phosphorus by chicks, *Journal of Nutrition*, 101, pp. 1289–94.

Paine, J. A., Shipton, C. A., Chaggar, S., Howells, R. M., Kennedy, M. J., Vernon, G., Wright, S. Y., Hinchliffe, E., Adams, J. L., Silverstone, A. L. and Drake, R. (2005) A new version of Golden Rice with increased pro-vitamin A content, *Nature Biotechnology*, 23, pp. 482–7.

Raboy, V. (2002) Progress in breeding low-phytate crops. *UNKNOWN*.

Rimbach, G. and Pallauf, J. (1993) Enhancment of zinc utilization from phytate-rich soy protein isolate by microbial phytase, *Zeitschrift für Ernahrungswissenschaft*, 32, pp. 308–15.

Robinson, N. J., Procter, C. M., Connolly, M.L. and Guerinot, M. L. (1999) A ferric-chelate reductase for iron uptake from soils, *Nature*, 397, pp. 694–7.

Rosegrant, M. W., Paisner, M., Meijer, S. and Witcover, J. (2001) *Global Food Projections to 2020: Emerging Trends and Alternative Futures* (Washington, DC: International Food Policy Research Institute).

Schaub, P., Al-Babili, S., Drake, R. and Beyer, P. (2005) Why is Golden Rice golden (yellow) instead of red?, *Plant Physiology*, 138(May), pp. 441–50.

Sharma, D. C. (2001). UN vitamin A campaign in India under fire, *Lancet*, 358(9295), p. 1791.

Skikne, B., Fonzo, D., Lynch, S. R. and Cook, J. D. (1997) Bovine ferritin iron bioavailability in man, *European Joural of Clinical Investigation*, 27(3), pp. 228–33.

Smith, J. C. (1996) The vitamin A-Zinc connection, in H. E. Bouis (ed) *Micronutrients and Agriculture* (Washington DC: Federation of American Scientists).

Sun, S. M. and Liu, Q. (2004) Transgenic approaches to improve the nutritional quality of plant proteins, *In Vitro Cellular and Development Biology – Plant*, 40(2), pp. 155–62.

Taylor, P. G., Martinez-Torres, C., Romano, E. L. and Layrisse, M. (1986) The effect of cysteine-containing peptides released during meat digestion on iron absorption in humans, *American Journal of Clinical Nutrition*, 43, pp. 68–71.

Teichmann, H. F., Lopez, J. and Lopez, S. E. (1998) Effect of phytase on the bioavailability of phosphorus in diets with rice bran for broilers, *Revista Braasileira de Zootechnia*, 27(2), pp. 338–44.

Theil, E. C., Burton, J. W. and Beard, J. L. (1997) A sustainable solution for dietary iron deficiency through plant biotechnology and breeding to increase seed ferritin control, *European Journal of Clinical Nutrition*, 21(4, Supplement), pp. S28–31.

UNICEF, UNU, WHO, and MI Technical Workshop (1999) *Preventing Iron Deficiency in Women and Children: Background and Consensus on Key Technical Issues and Resources for Advocacy, Planning and Implementing National Programmes* (Boston, MA: International Nutrition Foundation).

van Campen, D. R. and Glahn, R. P. (1999) Micronutrient bioavailability techniques: accuracy, problems and limitations, *Field Crop Research*, 60, pp. 93–113.

Welch, R. and Graham, R. (1999) A new paradigm for world agriculture: meeting human needs, productive, sustainable nutritious, *Field Crop Research*, 60, pp. 1–10.

Welch, R. M. (2002) Breeding strategies for biofortified staple plant foods to reduce micronutrient malnutrition globally, *Journal of Nutrition*, 132(Supplement), pp. 495–9.

Wise, A. (1995) Phytate and zinc bioavailability, *International Journal of Food Science and Nutrition*, 46, pp. 53–63.

World Bank (1990–99) *Commodity Markets and the Developing Countries. A World Bank Quarterly* (Washington, DC: World Bank), accessed at: www.worldbank.org/prospects/gcmonline/index.htm

World Bank (1990–99) *Global Commodity Markets* (Washington, DC: World Bank), accessed at: www.worldbank.org/prospects/gcmonline/index.htm

World Bank (1994) *Enriching Lives: Overcoming Vitamin and Mineral Malnutrition in Developing Countries* (Development in Practice Series) (Washington, DC: The World Bank).

Ye, X., Al Babili, S., Kloeti, A., Zhang, J., Lucca, P., Beyer, P. and Potrykus, I. (2000) Engineering the provitamin A (β-carotene) biosynthetic pathway into (carotenoid-free) rice endosperm, *Science*, 287, pp. 303–5.

Yi, Z., Kornegay, E. T. and Veit, H. P. (1996) Supplemental microbial phytase improves zinc utilization in broilers, *Poultry Science*, 75, pp. 540–6.