

ENGINEERING SOLUTIONS TO MALNUTRITION

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Some 40% of the world's people suffer from micronutrient deficiencies. The 'solution' to this problem is now being promised through genetic engineering. In the face of growing resistance to the first generation of genetically modified foodstuffs, Vitamin A or 'golden rice' provides a golden opportunity to restore biotechnology to public acceptability. Not only will it address a global public health problem, but it is being promised free to farmers. Monsanto has also been developing high beta-carotene mustard which it is targeting – for free – to poor farmers in the South. These nutrient-enhanced crops are receiving a good deal of attention, particularly in delivering the promise of genetic engineering in the guise of humanitarian cause. Too good to be true? Technical fixes such as these will only treat the symptoms of micronutrient deficiency and propagate the problem, which is caused by declining diversity in the food being produced and consumed.

Despite improvements in global food supplies, malnutrition and hunger remains one of the most devastating problems facing society. Malnutrition caused by deficiencies in specific vitamins and minerals afflict some 40% of the world's population, especially women and children. Ironically, the largest numbers of people suffering from micronutrient malnutrition live in South Asia, where a high diversity of micronutrient sources, such as fruits and vegetables, exist.

Vitamin A deficiency (VAD) is one of the leading causes of micronutrient malnutrition in developing countries. Historically, vitamin A was recognised to be important for the prevention of blindness. More recently, its role in helping to fight infections has come to light. Vitamin A helps prevent diseases such as diarrhea, respiratory ailments, tuberculosis, malaria and ear infections, and helps prevent transmission of Human Immunodeficiency Virus from mother to child. According to the World Health Organisation (WHO), around 2.8 million children under five years of age currently exhibit a severe clinical manifestation of vitamin A deficiency known as xerophthalmia. It has been demonstrated that vitamin A could lower childhood mortality by about one-third in many parts of the developing world. VAD is considered a serious public health problem and several high level initiatives have been launched with the goal of eliminating VAD in 2000. Progress has been made, but the goal is still a long way off.

Deficiency of a single micronutrient seldom occurs in isolation. In many countries, malnutrition with significant health consequences results from deficiencies in zinc, vitamins C and D, folate, riboflavin, selenium and calcium, in addition to the three micronutrients to which so much attention is now given (vitamin A, iron and iodine). VAD is mostly prevalent amidst poverty, environmental deprivation and social disparity. It is considered as one of the components – and a

minor component at that - of the syndrome of undernutrition. Hence, in the context of multiple nutrient deficiencies and inter-relationships of nutrients, the use of a single nutrient to combat micronutrient malnutrition does not make sense.

Vitamin A or retinol, is present exclusively in animal foods such as liver, milk and eggs. Fruits and vegetables contain provitamin A, such as beta-carotene and other carotenoids, which first need to be converted into retinol before the body can utilise them (see example in the table below). The origins of vitamin A deficiency in childhood can be traced to poor nutrition status of the mother during pregnancy and lactation, and inadequate intake of foods rich in either preformed or provitamin A by the infant after weaning and thereafter. A logical approach then to the prevention of vitamin A deficiency must seek to address these basic causes and not rely on technological fixes. Fortunately, the abundance of natural foods in the South should make such dietary improvements possible.

Farms not pharmacies!

Three measures are currently being employed worldwide to control vitamin A deficiency: supplementation, food fortification and dietary diversification. Most of the current strategies worldwide rely heavily on health interventions - usually the administration, at periodic intervals, of massive oral dosages of synthetic vitamin A supplements to children under three years of age. This strategy was pioneered in India in the late 1960's. What was originally envisaged as a short-term measure to dietary improvement has become the centerpiece of many current programs. UNICEF estimates that half of the children in the world at risk of vitamin A deficiency received at least one dose of vitamin A in 1998. The ease of supplementation has left research into and promotion of dietary measures in the background.

This 'drug-based approach' to synthetic vitamin A distribution has received wide criticism, even from the very individuals who have pioneered the work. Some of the limitations cited based on the 30- year experience of India are: ineffectiveness in correcting VAD (especially in populations where milder signs of deficiency are widespread), the limited shelf-life of vitamin A and logistical problems in ensuring supply. Supplementation programs are often expensive and unsystematic, and coverage may be poor. There have been many calls for an alternative approach, addressing the root causes of the problem rather than treating the symptoms. The World Declaration and the Plan of Action on Nutrition, adopted by 159 countries, at the International Conference on Nutrition jointly organized by the UN's Food and Agriculture Organisation (FAO) and WHO in 1992, states that strategies to combat micronutrient malnutrition should: "Ensure that sustainable food-based strategies are given first priority particularly for populations deficient in vitamin A and iron, favouring locally available foods and taking into account local food habits."

The fortification of butter, margarine and sugar with vitamin A is already being implemented in some countries. It too has drawbacks. In most instances, food fortification is only feasible in countries that possess well-developed, efficiently monitored and properly regulated pharmaceutical and food processing sectors. Like supplementation, fortification does not lead to awareness building and changes in dietary habits, and its impact is limited to those who can access these fortified products. Dietary diversification, on the other hand, requires minimal foreign currency; it promotes the intake of a whole range of micronutrients other than vitamin A; it is sustainable; it fosters community and individual involvement; and it can even help stimulate the local economy.

The Green Revolution: feast and famine

The prevalence of micronutrient deficiencies now far exceeds protein and calorific malnutrition in Asia. Despite substantial increases in cereal supplies, which have contributed to increased intake of calorie- and protein-rich foods, the supply and consumption of foods rich in micronutrients have not increased proportionally, and in many cases have actually declined. Only 30 crops 'feed the world,' providing 95% of dietary energy and protein requirements. More than half of these come from wheat, rice and corn alone. For this reason, these three crops served as the cornerstone of the Green Revolution in the 1960's. Monocultures of these crops were encouraged, which resulted in the growth of a food supply that provided more macronutrients but did not provide the much-needed micronutrients, which were already in short supply. In some cases, the availability of and access to micronutrient rich food crops actually decreased for millions of poor people. Today, more than 2 billion people consume diets that are less diverse than 30 years ago, leading to deficiencies in micronutrients, especially iron, vitamin A, iodine, zinc and selenium.

Varietal replacement of traditional varieties in the field, which is reported to be the major cause of genetic erosion around the world, also had its impact in home gardens. A farm household survey in the Republic of Korea, for example, revealed that out of 143 crops cultivated in home gardens in 1985, only around 26% of landraces remained cultivated by 1993. These results are disturbing since such home gardens have traditionally been important not only as conservation sites especially for vegetable crops, but also an important source of vitamins and minerals.

A significant and consistent decline in per capita consumption of green leafy and yellow vegetables had been noted in Philippines. The same is true for vegetables, fruits, pulses and spices in Bangladesh (see graph above). This situation caused the Director of the Horticultural Research Center of Bangladesh Agricultural Research Institute to suggest that "Food patterns could have been changed and we could have attained self sufficiency in food and nutrition much earlier with 300 g cereal/capita per day as against achieving food self sufficiency today with 500 g cereals."

It is becoming evident that the Green Revolution represented a trade-off between quantity and quality in peoples' diets, especially amongst the poor. Even the International Rice Research Institute (IRRI) admits that the Green Revolution may have actually increased micronutrient malnutrition among the poor. But IRRI can not look beyond the Green Revolution model for a solution to this problem, and is looking to genetic engineering to get it out of the hole it has dug for itself. Like many other international organisations involved in agricultural development, IRRI sees the answer to micronutrient malnutrition in engineering the missing elements back into Green Revolution crops. Some of the most advanced research in this arena is on engineering vitamin A into rice and mustard plants. These vitamin A crops are being hailed as evidence that genetic engineering holds promise for the poor as well as the rich, and that transgenic crops can benefit humanity as well as generating profits for the gene giants. This new approach is expected by many to supplant existing strategies for dealing with VAD, hopefully overcoming their limitations.

Engineering vitamin A into crops

Vitamin A rice was showcased in *Science* in August 1999. This genetically-engineered rice produces beta-carotene in its endosperm, giving it the distinct yellow colour that affords it the name 'golden rice.' The rice was developed with funds from the Rockefeller Foundation and the European Commission. Since it has been developed outside the private sector, 'golden rice' has become a much-needed and timely public relations tool for the promoters of genetic engineering. At the same time, Monsanto had been developing a high beta-carotene mustard plant which it planned to offer to poor subsistence farmers around the world. Through the Global Vitamin A partnership and local stakeholders, Monsanto promised to develop appropriate varieties of crops for those areas in greatest need. This donation allowed Monsanto to make a strong case for the relevance of agricultural biotechnology to the problems faced by the world's poorest, to get the technology adopted on the grounds of >public good, and to counter the very bad reputation it had earned itself, particularly in Europe and India.

'Golden rice' is the product of two German research teams under the direction of Dr Ingo Potrykus of the Swiss Institute of Technology in Zurich, and Dr Peter Beyer of the University of Freiburg. The idea of genetically engineering beta-carotene into rice emerged nine years ago, in the light of UNICEF and WHO reports on the high incidence of VAD in countries where rice serves as a staple food. The researchers engineered a laboratory variety of japonica rice (Taipei 309, adapted to temperate weather in Europe) to convert a naturally-occurring hormone precursor into beta-carotene. The team has added three genes, two of which are new to genetic engineering and come from daffodils (*Narcissus pseudonarcissus*). The third comes from a bacterium, *Erwinia uredovora*, which has been already used by Kirin Brewery. The teams are also working to cross this new line with another rice line to increase its iron content.

The amount of hype given to 'golden rice' seems a little premature given that only a handful of genetically engineered seeds have so far been developed. All that is certain is that some of the transformed seeds contain beta-carotene in the endosperm, but it is not yet clear whether or not it is available for absorption. Even if the rice proves to be a success, the beta-carotene trait still needs to be transferred to the indica rice varieties, the types grown in Asia. This work will be done by several of the International Agricultural Research Centres (IARCs), including the Philippine-based IRRI, the India-based ICRISAT and the Colombia-based CIAT where further cross-breeding and field testings will be done. IRRI, together with the Philippine Rice Research Institute, is set to transfer the golden trait to widely-grown varieties such as IR64.

Vitamin A rice has a long way to go still. Success in the laboratory means little in the field. Transgenic plants which perform well in laboratories often fail in nature, especially if they contain not one, but three added gene-constructs. Environmental impact can only be speculated on at this point, and issues such as palatability and public acceptance may also pose problems. The whole project does not seem to have been thought through very well. Potrykos' and Beyer's teams contacted international institutions with experience in VAD, such as UNICEF, FAO and the WHO, only after the project was well underway. Had they done so prior to undertaking the research, the project might well never have happened. The research team has consisted of plant scientists and a nutritionist, and issues related to extension and public acceptance have not been addressed. Consumers may very well react against a rice which is yellow instead of white. If public education is needed, wouldn't it be better to use such efforts to promote dietary diversification which would improve overall nutrition rather than simply supplement a single vitamin?

While the development of vitamin A rice seems to be well-intentioned, if perhaps misdirected, Monsanto's beta-carotene mustard comes from more questionable roots. Calgene, which was bought by Monsanto in 1996, first developed rapeseed (*Brassica napus*) with elevated carotenoid levels because it contained higher proportions of fatty acids, making it potentially more profitable. Unlike the 'golden rice' initiative, the objective was purely commercial. Transferring the technology to mustard (*Brassica juncea*), a close relative, was an afterthought.

It seems unlikely that it is pure coincidence that Monsanto's idea to create beta-carotene mustard has come at a time when mustard, which is the most important oil crop in South Asia, is being pushed into the marketplace. Monsanto is present in the Indian seed market through its agreements with Mahyco and its ownership of Cargill. Monsanto's donation appears within the context of mustard's transformation into an international trade commodity and the company's desperate attempts to gain credibility and support for its transgenic crops in India. Although the company is ready to share the technology with any interested party, only the new Delhi-based TATA Energy Research Institute is mentioned by Monsanto as a potential partner – hardly one of the "local stakeholders" it talks about. It may take more than beta-carotene mustard for local farmers to trust the corporation they see as at least partially responsible for their own hardships.

Monsanto's new R&D center at the Indian Institute of Science in Bangalore is responsible for transferring the beta-carotene technology from rapeseed into mustard varieties, which it hopes to do by the end of 2000. Field testing will take a further 2 to 3 years. Meanwhile, many questions remain. Since beta-carotenes are fat-soluble, Monsanto expects that the oil from its transgenic mustard will be readily absorbed by the human body. However, heat destroys beta-carotene, and mustard oil is most often consumed after cooking, so the beta-carotene needs to be stabilised somehow. Another drawback is that the modified rape seed oil is orange, which could affect public acceptance.

Tangled up in patents

Despite all the publicity, the promises of 'golden rice' and Monsanto's rapeseed are still far from being realised. One issue that has been largely beyond the scope of the press debates is that of intellectual property rights associated both to the Monsanto rapeseed and, perhaps less evidently, to the 'golden rice'. In the case of Monsanto, the company owns – through Calgene – the patent on the beta-carotene rapeseed (WO9806862), and on the promoter (napin promoter: US 5,420,034). It is bound to pay royalties to the developers of the transformation method it has used to produce the transgenic rapeseed and to Kirin Brewery for the carotenoid biosynthesis genes from the bacterium *Erwinia uredovora* (EP0393690).

Monsanto has announced that it aims to provide the high beta-carotene mustard free of charge to poor and subsistence farmers "not fully participating in the world economy." However, what this means is not clear. What will be the limit for the sale of the rapeseed or its oil? How would such limitations affect the availability of the beta-carotene oil to the poor? Will they affect the purchase of the seeds or oil by large national or international corporations? Sources from Monsanto's R&D Institute say that while the project is philanthropic, the company has no clear policy to answer these questions.

In the case of the 'golden rice,' its developers claim that it will likely be given free of charge to the farmers. Whether this claim will be realised is still up in the air given the patent hurdles it faces. Despite being funded by public sector, the 'golden rice' is to a large extent the product of private companies.

The development of the rice has involved patented processes, genes and promoters, which amount to at least six previous patents (see table opposite). On top of these, the teams of Zurich and Freiburg have filed a patent application covering the insertion of the metabolic pathway to produce beta-carotene in seeds. The scientists involved claim this was to prevent other parties (corporations) from patenting the technology. If this is really the case, it would have been enough just to release the information into the public domain. Applying for the patent turns the Rockefeller Foundation and the European Commission into potential for-profit institutions. According to Beyer, the patent application that has been filed covers the insertion of the new

metabolic path in any crop, not only rice. Rice will be the only crop freely available to farmers, and only under certain circumstances as specified in a contract between the 'inventors' and the IARCs transferring the genes for the 'golden rice' into tropical varieties.

This is not the first agreement between private sector companies and IARCs to use and distribute patented materials. Ciba-Geigy (which merged with Sandoz to form Novartis) made Bt genes available to IRRI to develop rice, and the rice produced with this gene is freely available to rice producers in all countries except Australia, Canada, Japan, New Zealand, United States, and members of the European Patent Convention as of 1994. Plant Genetic Systems has provided the Centro Internacional de la Papa (CIP) with Bt genes and technologies, and the results of collaborative research are freely available for developing countries, provided the recipient does not appropriate them unfairly or seek profit through their commercialisation in industrial countries. The control must remain, after all, in the hands of the patent holder.

The teams behind the 'golden rice' believe that, if only for the sake of their public image, no company will prevent them from using their patented processes, genes or promoters to make rice freely available for the poor. But it is a complicated arena because a conflict of interest could easily arise for the companies involved, particularly given that they have only made their technologies freely available for use under certain circumstances. However philanthropic the intentions of the project, the products of genetic engineering are so entangled in IPR issues and directed towards the profit motive, conflicts are almost certain to arise. Charitable initiatives may easily be corrupted and derailed because of the private sector's ownership of key genes and patents.

Will biotech solve the problem?

The unveiling of 'golden rice' is giving impetus to the application of genetic engineering to combat micronutrient malnutrition. But it is highly unlikely that poor people stand to benefit from this strategy. This 'band aid' approach will merely perpetuate the declining quality of food grown under the industrial agricultural system at the expense of fruits, vegetables, and underutilized and wild crops. Without shifting the focus of nutrition efforts towards a more diverse agricultural base, there is no doubt that micronutrient deficiency will persist. The real impacts of vitamin A crops will be:

- Reducing dietary and nutritional diversity Focusing on engineering micronutrients into staples instead of promoting natural sources will further skew agricultural research and development and consequently food availability further away from diversity. It will perpetuate the commodity bias towards staples or a limited range of so-called functional foods such as high beta- carotene oil. This will exacerbate genetic erosion, decimate farming systems and reduce nutritional diversity.

- Decreasing overall nutritional status The very narrow target of just providing a single micronutrient such as vitamin A into commonly consumed crops will do little to overcome micronutrient deficiencies. The transfer of an exotic gene into a monoculture crop can do little to make up for the dietary deficiencies of those suffering from monoculture malnutrition. The nutritional value of a combination of rice and Moringa (drumstick) leaves is far greater than that of the 'golden rice'. Providing only a single micronutrient via food to a population which is deficient in a whole range of nutrients could be considered unethical, especially where the whole range can easily be obtained easily from locally-available fruits and vegetables and in wild and underutilised crops.
- Perpetuating the problem The claim that 'golden rice' or beta-carotene mustard will help eliminate VAD in the South has great appeal. Yet the genetic engineering approach erroneously assumes that VAD exists due to a general lack of vitamin A food sources. This type of intervention tends to maintain the status quo, where rice remains to be the predominant food in poor peoples' diets, instead of encouraging people to diversify their food sources. Instead of solving the problem, it merely masks the shortcomings of the Green Revolution and perpetuates the problem.
- Promoting technical fixes again This one-dimensional technical fix approach to VAD is reminiscent of the Green Revolution paradigm. This was another techno-fix solution to a complex problem: that of poverty and hunger. 'Golden rice' is another simple, universal solution to the problems of the poor decided upon and developed by scientists from the North. It comes as no great surprise that the Rockefeller Foundation, one of the main architects of the Green Revolution, has been financing this approach to solve a problem which it helped to create in the first place.
- Accessibility and equity The "poor" are a major target for vitamin A crops. Yet many of the poor, particularly women, have not benefited from Green Revolution crops, so it is unlikely they will benefit from the next wave. Any direct benefit to the poorest, who by definition have little purchasing power thus generate little of a market, is to be generated as a side effect, or an exception to the rule, upon which the poor do not have any control. Scarce resources should be directed, instead, to policies that have the poor as their main objective, not as incidental beneficiaries.
- Dietary diversification or uniformity? Although improved dietary habits, particularly the increased production and consumption of beta-carotene-rich foods, have long been advocated as the only acceptable long-term solution to combat VAD, very few concrete steps have been taken in this direction in the past twenty years. In the words of the 1991 laureate of the World Food Prize, Dr. Nevin Scrimshaw: "It is ironic that some of the worst concentrations of xerophthalmia and blindness due to vitamin A deficiency occur in populations surrounded by abundant sources of the vitamins and minerals in local vegetables and fruits, yet, no country has yet mounted a successful campaign to solve the Vitamin A problem in this way".

Breaking the cycle

Supplementation and fortification programmes treat the symptoms but not the underlying cause of micronutrient malnutrition. Poor quality diets consisting primarily of staple foods are the underlying cause of micronutrient malnutrition. 'Golden rice' is merely an extension of the supplementation approach and also fails to address the cause. Even worse, it actually perpetuates malnutrition because it fails to address peoples' requirements of other minerals and vitamins, which would be met by adopting a dietary approach to VAD.

Improving dietary diversity by stimulating the production and consumption of micronutrient-rich foods is the only sane and sustainable approach to overcoming micronutrient deficiencies. There is a great scope for improving direct household supplies to such foods in rural and urban areas (see box on p 17). The real cause of VAD is that vulnerable populations are not empowered enough to access these natural sources of vitamin A. This should be the starting point of any strategy to combat VAD. Diversity is the basis of balanced nutrition. Agricultural and nutritional policies should promote the availability of micronutrient-rich foods and targeted nutrition education programs should help increase their consumption. Only by providing a diversity of food sources in the field and by increasing awareness of food's relevance not just to fill the bowl with calories but to improve nutritional well-being, can we break away from the vicious cycle of hunger and malnutrition.

Main Sources

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