Biofortification: the nutrition problem and ways of intervention

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Human health is at the crossroads regarding demography and the food supply. Populations are at once growing in number (although not uniformly, with some in decline) and aging and food resources are being developed in often nonsustainable ways. The capacity to live longer and healthier lives, however, is never more clearly in evidence. For this to be achieved requires not only adequacy of energy intake for a population whose size may stabilize at 10 billion or so by about 2050 but also nutritional quality (nutrient- and food-component-dense foods and diets) to allow good health and well-being. Global "dysnutrition" can be overcome, in part, through biofortification, whether by cultivar selection and plant breeding or by genetic modification. At the same time, the ultimate goal of food variety for all and sustainability through biodiversity is a stimulus for eco-nutritional science.

Ongoing deficits in energy intake for much of the world's population mandate an approach to poverty and hunger by way of staple foods, which are principally grains (grasses) and root vegetables (Serageldin 2002). It is generally not sustainable to contemplate animal-derived foods, meats, and fish as the principal energy source for large populations. Because of the location of human habitats and the nature of food trade, a few select grains and tubers have accounted for most population expansion (Diamond 1999, Wahlqvist 1992).

Scientific efforts have increasingly complemented these trends in the food-population relationship, most recently through molecular biology (Cantrell and Reeves 2002). The landmark publication (Kennedy 2002) of both rice genomic sequences (Goff et al 2002, Yu et al 2002) and the human genome (Venter 2001, Lander et al 2001) underscores the significance of plant foods, and rice in particular, in human development. So does the genome sequence of *Arabidopsis thaliana*, a weed linked to the cabbage and mustard family (Cantrell and Reeves 2002).

What these developments leave to examine are the nutritional quality of the plant foods on which so many depend. Indeed, there is concern that a loss of many nutritious cultivars of grains, especially rice and maize, and of tubers has been taking place. This is highly relevant to micronutrient deficiencies and to chronic diseases. Hence, a renewed interest has arisen in measuring and promoting the nutritional quality of individual foods and diets.

Biofortification through cultivar selection and breeding is an important approach to both adequacy and quality of the human diet (Welch 2002, Bouis 2002).

Food-related world health needs

Most of the world's population, the economically disadvantaged (EcDis), still suffers from nutritional deprivation, and associated infectious disease, whereas those with an adequate (or excessive) energy intake, the economically advantaged (EcAdv), may or may not have the food quality to ensure optimal health. If not, they may experience a range of so-called chronic diseases. Others, in transitional economies (EcTrans), may experience the succession of nutritional deprivation followed by relative energy excess in the one lifetime, manifesting a double burden of nutritionally related disease themselves, within their family, or within their community (Fig. 1) (Popkin et al 2001, Wahlqvist and Kouris-Blazos 2002).

While nutritional deprivation is generally and understandably thought of as a child health problem, it can have life-long effects, even when corrected in the early years, and can continue to operate to varying degrees (loss of well-being, chronic ill health, and clinically evident disease) at any age (Wahlqvist et al 1999a,b, Barker 1993a,b). More than health, it represents social deprivation (Wahlqvist 1988) and economic handicap as well (Sachs 2001).

Foods and food components: critical factors in nutrition

The concept of "nutritional quality" for food is evolving from one focused on energy or macronutrients, along with micronutrients (vitamins and minerals), to one that embraces other nutritionally beneficial components of food, especially of plant food, by way of phytochemicals not classified as essential nutrients (e.g., carotenoids, polyphenolic compounds, sulfur-containing isothiocyanates, and sulfuraphanes) (Wahlqvist and Briggs 1998).

Nutritional quality is best expressed as the amount of an essential nutrient, or other biologically advantageous food component, per unit energy of that food, that is, nutrient or food component density (ND or FCD):

$$\text{ND (or FCD)} = \frac{\text{Mass of nutrient (or food component) (e.g., mg)}}{\text{Unit energy (e.g., 100 kJ)}}$$

Phytonutrient density, PD, could be expressed in the same way.

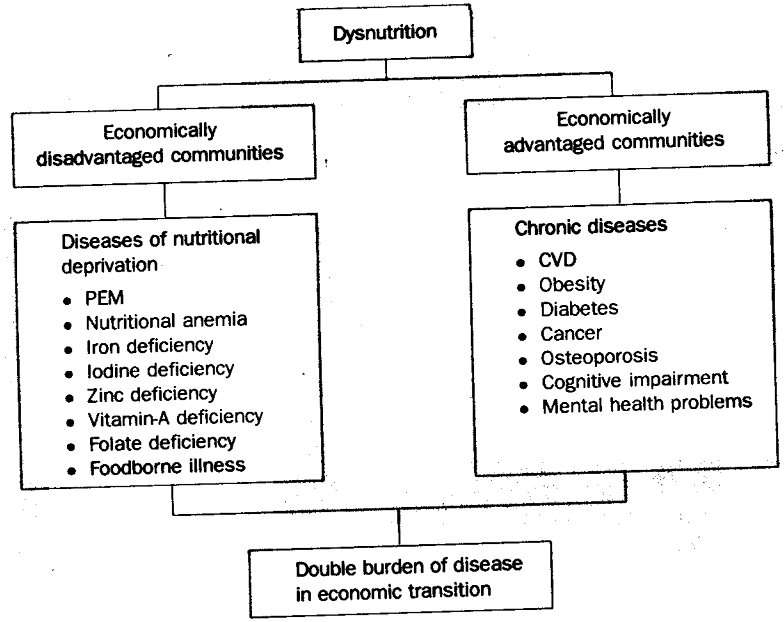

Fig. 1. Global nutritional disorders (dysnutrition).

By contrast, the energy density (ED) of a food is

$$\text{ED} = \frac{\text{Energy (cal or kJ)}}{\text{Mass of food (g, kg)}}$$

The ND (or FCD) of a food can be related to the recommended intake (e.g., RDI) as the RND (recommended nutrient density) of a diet (Wahlqvist and Flint 1989, Mertz 1990, Wahlqvist et al 1998).

Phytochemicals (or phytonutrients) are increasingly recognized to play a role in disease prevention and they probably ameliorate the effects of some micronutrient deficiencies. For example, grains, fruits, vegetables, and nuts can protect against the development of CVD (cardiovascular diseases), diabetes, osteoporosis, and certain cancers and some of their sequelae (Wahlqvist 2002). They might also have a sparing effect on the requirements for certain micronutrients, such as (1) anti-inflammatory factors in certain culinary herbs, for n-3 fatty acids, and (2) antioxidant phytochemicals for vitamin C and E and for selenium.

Again, the interaction and synergy between established micronutrients can be used to advantage in food-based strategies to deal with nutritional problems, such as

(1) adjusting intakes of competitive divalent cations (Fe^{++}, Ca^{++}, Mg^{++}, Zn^{++}, Cu^{++}, etc., Nielsen 1996) and (2) ensuring adequate vitamin-A intake to ameliorate iron deficiency (Schultink and Gross 1996).

Enhancing food and its nutritional quality

There are several ways in which the nutritional utility of a food could be enhanced.

1. *Selection* in favor of a more nutrient (a food component)-equivalent food within the same commodity group, for example, for grains, wheat instead of rice since it has, overall, a superior ND, at least with currently grown cultivars; and, for root crops, colored sweet potato rather than potato because it has more carotenoid (pro-vitamin A).

   The problems with this approach are (1) agricultural feasibility, (2) cultural acceptability, (3) individual tolerance, for example, gluten sensitivity with wheat, but not rice, and (4) processing capability (e.g., to make flour or bread).
2. *Explore the range of cultivars* for nutritionally enhanced varieties. This may mean retrieving discarded cultivars from another food culture, or from a germplasm library. It requires the availability or compilation of food compositional data for many cultivars.

   This is the basis of current biofortification strategies for iron-, zinc-, and vitamin-A (carotenoid)-dense rice (Bouis 2002).

   The advantages of the strategy are many and they have been documented by Bouis et al (2002). They include bioequivalence, associated intake of complementary food components, a food-based approach, acceptability, and sustainability.
3. *Genetic modification* of an existing cultivar (GMF, genetically modified foods). The advantages of biofortification, through elite cultivar selection, have to be established for each GMF, such as Golden Rice with carotenoid enrichment (Beyer et al 2002).
4. *Fortification postharvest.* For each of the major micronutrient deficiencies (iron, iodine, zinc, vitamin A, folic acid), postharvest fortification has utility and attractive economics (Mason et al 1999, Bouis and Hunt 1999). However, some management and quality problems could allow this approach to falter.
5. *How the food is eaten.* Various changes to the food grown may influence its relevance to nutrition problem solving:
   a. Processing, for example, fermentation, as with rice (like tapai in Malaysia).
   b. Cooking, for example, lycopene bioavailability increases with cooking.
   c. With what is eaten:
      - Vitamin C (increases iron bioavailability)
      - Soy sauce may be fortified with iron (an added micronutrient source) (China) (Chen 2000)
      - Spices and condiments (may supply intrinsic and fortified components to enhance a food's nutritional value) (Nguyen 2000)
6. *Dietary diversity.* The most nutritionally sound way to ensure the adequate intake of essential and desirable food components is to achieve dietary diversity (Wahlqvist and Specht 1998, Hodgson et al 1991, 1994, Wahlqvist et al 1989, Hsu-Hage and Wahlqvist 1996, Savige et al 1997). This is because, apart from certain especially nutritious foods (liver, eggs, wheat germ, sprouts, yeast, and human breast milk in the first 6 months of life), we need a range of foods to cover the spectrum of required food components. The evidence points to at least 20, and up to 30, biologically distinct foods over the course of a week being required (Savige et al 1997). The problem is that, unless the consumer hunts and gathers, or acquires, through economic advantage and trade, or is assiduous in an urban environment to obtain a range of foods, such dietary diversity is not usually achieved. In such circumstances, recourse to nutrient-dense animal-derived foods (as above) is required, or plant foods may require fortification (biofortification or postharvest fortification).

Overcoming health problems with characterized and formulated foods

The global current and emerging health problems that may be tackled by well-characterized traditional and/or novel foods are set out in Table 1 (Wahlqvist 2000). Several of these problems could be tackled through biofortification using nutritionally enhanced cultivars and improved plant-breeding techniques.

Clinical nutrition trials (CNTs) and clinical outcomes

Randomized clinical trials are generally regarded as level 1 (highest) evidence for clinical decision-making and, to some extent, this applies to nutrition decision-making. The limitations of CNTs are

1. Only a few (usually not more than 3 or 4) variables can be tested.
2. The time frame of the CNT is limited—usually weeks or months and at the most 3–4 years.
3. It is difficult to do a double-blind study with food.
4. Food cultural considerations that may influence the outcome or extrapolation are rarely taken into account.
5. They are usually not undertaken in representative populations.

Thus, although CNTs are still important and attractive in comparing one cultivar with another, population-based data and cohort studies are also usually required for public health nutrition policy (Wahlqvist et al 1999a).

Public health outcomes

Although the essential nutrient or food component deficiencies of individuals are obviously important, the broader public health significance of endemic (and often multiple) deficiencies requires attention.

Table 1. Examining food-health relationships with food.

Health category	Food characteristics
1. Disease related to environmental degradation and methods of food production	Eco-sensitive foods (e.g., produced in sustainable ways; biodegradable or edible packaging; identifiable biosecurity for animal-derived foods; nature of genetic material)
2. Food shortage and PEM (protein energy malnutrition)	Technologies that minimize postharvest loss, increase shelf life, and maintain palatability
3. Disease related to protein quality, fat quality, and micronutrient status	Nutrient-dense foods; fish or its plant or microbial food surrogates
4 Physical inactivity and health (especially overweight, also loss of lean mass, particularly muscle)	Food of low energy density and high nutrient density
5. Phytochemical-deficiency disorders including menopause, macular degeneration, osteopenia	Greater emphasis on plant-derived foods and their variety
6. *Diseases of changing demography*	
Aging	Antiaging foods, especially ones to delay body compositional change (bone, muscle, and fat); loss of sensory function; decline in immune function; proneness to neoplastic disease; decline in cardio-respiratory function; decline in cognitive function; and anti-inflammatory foods
Rapid loss of traditional food culture and acquisition of new food cultures	Maintenance of traditional foods in convenient, affordable, and recognizable form
7. New psycho-social stressors and mood change	Food that favorably affects mood
8. Foodborne illness and microbiological safety of foods	Pre- and pro-biotic foods; immune-system-enhancing foods
9. Illness related to chemical safety of foods (e.g., pesticide residues)	Regional origin and certification of foods

Another consideration is that there may be unintended consequences of a public health intervention, whose unfolding may take time, even years. The introduction of new crops into particular locations is illustrative of this, such as the potato, with population increase, and maize, with pellagra (Wahlqvist 1992).

Increasingly, a knowledge of the genetic predisposition of a population (and its prevalence) and its changing demography to nutritionally related disease will influence the required evidence and its management. Thus, biofortification strategies, at best, take account of population genetic polymorphisms (Stover and Garza 2002).

Risk analysis, management, and communication in biofortification

Risk science now allows increasingly good analysis of risk-benefit and cost-benefit. It can be applied when a problem is defined, in the amount of study to try to solve it, and in implementation strategies.

Most important, the community increasingly requires the opportunity to consider risk and benefit. Not to communicate this may reduce the value of the findings to the community, if, for example, unwarranted concern arises or overly confident action is taken.

Biofortification and sustainability

There will be a need to consider the short- and long-term consequences of the agricultural production of biofortified crops. Well-managed, these crops ought to contribute to optimal biodiversity and sustainability of the food supply (Wahlqvist and Specht 1998).

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