

Review Article

National food fortification: a dialogue with reference to Asia: policy in evolution

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Food fortification generally refers to the addition of micronutrients and other favourably bio-active food components to food-stuffs where there are recognised deficiencies in the target population. Each fortificant has had or could have regulatory implications. It is understandable, although arguable, in the face of a limited food supply skewed, for the majority, in the direction of starchy staples of low essential nutrient density. Efforts, with plant breeding, to biofortify such foods are underway and likely to be safer, more sustainable and affordable than chemical additions. Unfortunately, with an increasingly refined and naturally tasteless food supply (salty, fatty, sugary and starchy), and where energy requirements are falling because of physical inactivity, micronutrient fortification is being used as a nutritional 'fix-it' strategy. In Asia, there are several critical micro-nutrients. No one national fortification program can deal with all deficiencies is likely to be highly selective for the nutrients which have the greatest advocacy or are most recognisable. They also leave the other health promoting food properties like intactness, nutrient spectrum, and phytonutrient content un-addressed. A variety of food-stuffs, with different biological origins, is the preferred approach. Where an optimal food system is not in place, there may be justification for fortification if there is regular monitoring and surveillance of the food supply and health outcomes occurs; is a clear cost-risk-benefit advantage in such a strategy; are programs in place to improve the nutritional value of the basic food supply and is an 'exit strategy' for the fortification program.

Key Words: Optimal nutrition, food diversity, criteria, single nutrients, vitamin D, iodine, folic acid

WHAT IS FORTIFICATION?

Fortification is a food-based approach to optimize nutrition where there is dependence on staples and a narrow range of foods.¹⁻³ Fortification is not all the same and may be:

- Chemical fortification (e.g. Blending)
- Biofortification (e.g. Plant breeding)
- A recipe approach where the ingredients are the fortificants

OPTIMAL NUTRITION

Although intuitive, increasing evidence points to the need for food and not simply nutrients to achieve optimal nutrition. This may be partly because all that is required for optimal nutrition is yet to be defined, whether by way of food constituents or its physico-chemistry or because of the patterns of consumption. However, in brief it may be said that there must be:

- An adequate food intake to meet energy needs
- A variety of food-stuffs, with different biological origins, as the preferred approach for dietary quality
- Sufficient energy throughput with levels of physical activity which allow enough to be eaten without excessive gain in body fat

FOOD DIVERSITY CONFERS WIDE NUTRITIONAL BENEFITS

The human species is probably the one which requires the

greatest diversity in its diet for its own short, medium and long-term needs and because it has roamed over many habitats and eco-systems to achieve planetary dominance. It has dispensed with some biological abilities to make essential chemicals, resulting in the need for 'essential nutrients', its sheer numbers mean it cannot live with only one kind of food supply, and its exploitation of its habitats puts it at perpetual risk of destroying the eco-systems of which it is part. Although quantitation of the environmental biodiversity and food variety needs of humans is imperfect, there would appear to be limits below which we cannot safely go.^{4,5} However, although not optimal, survival is possible on formula feeds, as used in enteral and parenteral (so-called 'total') nutrition for extended periods of time. These feeds increasingly contain all the known essential macro- and micro-nutrients. They inspire nutrition scientists and caregivers to believe that, eventually, it will be possible to optimize human health with 'designer foods'.

These will not have the ability to fulfil the socio-cultural roles and meet the related health benefits of the species. Nevertheless, for reasons of availability and affordability of

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preferred food-stuffs, increasingly formulated or, at least fortified, foods may be required. With the advent of human settlement and staple crops and the consequent explosion in population numbers, much as Malthus argued, there has been an increasing mis-match and tension between *Homo Sapiens sapiens* and its food supply.⁶ Wherever possible, food diversity eases this tension because of:

Sustainability

Not only are the usual seasonal rhythms and climatic perturbations catered for to a greater extent through diversity, but the risks of longer-term adverse climate change reduced with environmental advantage.

Safety (nutritional, microbiological and toxicological)

There is a reduction of adverse component effects by dilution and the securing of favourable effects from various food components.

The collective role of selenium, vitamin C, polyphenolics, carotenoids and vitamin E isoforms, derived from various sources, in anti-oxidant and detoxifying pathways, along with other properties of these multi-function compounds, including ones with potential anti-pathogen and immune-system enhancing potential, is an example.

Security

With less dependency on a single source of nutrients, food security is more achievable. Not only is blight of a single crop or disease in a particular breed of farm animal less critical, but it is less likely in the first place because of environmental 'buffers'.⁴ There are many historical examples of the relevance of this principle which discourages mono-culture and limited farm animal species, ranging from potato blight to poultry disease. The relevance now of these concepts is even greater with the shrinkage in spectrum of food plant and animal varieties and breeds.

However, for many of the world's population, these dilemmas are not readily soluble and recourse to 'second best' approaches to enough food of sufficient quality may be required.

One of the most promising transitional strategies to food and nutrient security is *biofortification*.² This is the use of more micronutrient-rich staple crops, obtained through selective plant breeding, to address highly prevalent and intransigent deficiencies. The food matrix is likely to be a much more physiological approach with biofortification than with fortification by additions.

FOOD DIVERSITY, MORBIDITY AND MORTALITY

The measurement or estimation of food diversity allows the evaluation of its contribution to health. It reduces morbidity,⁷⁻⁹ all-cause and disease-specific mortalities.¹⁰

Using food diversity or cuisine measures, like the Mediterranean diets score, foods & meal patterns are found to predict morbidity & mortality better than nutrients.¹¹ This has relevance for single factor, or even multi-nutrient, approaches to dietary improvement.

When it comes to survival amongst older people, and most likely various morbidities like obesity, cardiovascular disease and diabetes, then pulses or legumes confer advantage in various food cultures. In north-east and

south-east Asia, this means soy. In South Asia and the Mediterranean, it means lentils and chickpeas. In Scandinavia and Australia, it means beans of various kinds.¹²

CRITERIA FOR FOOD FORTIFICATION

Against a background of understanding of what probably constitutes an optimal diet, it is possible to formulate criteria and caveats for appropriate food fortification. These might be:

- Population nutrient deficiency
 - Micronutrient
 - Macronutrient component
 - e.g. dietary fibre, n-3 fatty acid, oligosaccharides
 - Phytonutrients
- Severity of health problem
- Efficacy
- Effectiveness
- High benefit-risk ratio
- Attractive cost-benefit ratio
- No feasible and timely alternative

NATIONAL FOOD FORTIFICATION

The merits of national food fortification are predicated on several considerations:

Population needs versus Individualization

Nutrigenomics can help sort out the relative benefits to the population as a whole and to individuals in particular, by identifying polymorphisms and their frequencies.

Cost-effectiveness: The individual approach is likely to be more costly to the individual, but not necessarily per individual when applied across a population.

Human rights: The right to food is part of the United Nations Charter and, it must be assumed, if food quality is jeopardized, fortification if safe and effective, is part of the right. Who assumes responsibility for it would ordinarily be the government of the jurisdiction in which the vulnerable persons or population resides. The reality is that this will often not obtain and that international agencies or the international community will need to consider their positions. A growing concern in this regard is the plight of the unborn child, the more we learn about maternal nutritional especially under-nutrition, and the life-long consequences for the child.

Public good: An enlightened society, and one informed by scientific evidence, will be concerned about the importance of nutritional deficiencies for individuals, the community-at-large and how it functions. It will seek to have leadership and governance in place which can weigh up the various priorities for resource allocation. Evidence-based nutrition policy will need to align with nutritional and health economics to argue the case for the best available strategy to achieve optimal nutrition, by food-based methods.

Policy issues

- Efficacy and effectiveness both need to be satisfied in determining the public good of fortification.
- Whether the fortification program is mandatory or voluntary will depend on the level of confidence of the policy makers and the receptivity of the public as well as the support of producers.

- Food labeling of the fortificant will nearly always be required in enlightened societies where policy makers accept responsibility for education about the products and where the trust of consumers is expected.
- Arrangements with manufacturers are the outcome of negotiations to secure commitment, motivation, good manufacturing practice with QA (quality assurance) and effective reliable distribution.
- Monitoring and surveillance of product and target population are basic, but not often in place.
- The tenure of a fortification program should be limited by a sun-set clause and only continued on the basis of evidence of benefit.

Regulatory implications

Fortification programs require a regulatory framework to avoid failure and harm and optimize benefit.

This will take account of

- Consumer characteristics
e.g. nutrition & health literacy, health status
- Nutrient and health claims
- Equivalence
- Representation of food-stuff as nutritious counterpart of preferred item
e.g. wholegrain/ wholesome
- Representation as superior product to usual product
- Bioavailability
- Shelf-life considerations
- Monitoring and surveillance

Relevant food component deficiencies

The *current issues in fortification* relate to the micronutrient deficiencies of poverty (e.g. especially iron, zinc, iodine, vitamin A, B₁¹³), certain universal micronutrient deficiencies (e.g. folate and B₁₂ especially in relation to H. Pylori gastritis) and to re-emergent micronutrient deficiencies irrespective of economic development. (e.g. iodine, Mg, Ca?, vitamin D)

Insofar as macro- and phyto-nutrients are concerned, fortification has accompanied the advent of Dietary Guidelines to reduce the burden of so-called chronic disease by macronutrient adjustments. This has, in turn, focussed attention on indices of food nutritional quality reflected in phytonutrient density. The inadequacy of dietary fibre/ NSP (non-starch polysaccharide) and oligosaccharide remains in many circumstances. As does that of n-3 fatty acids, polyphenolics, anthocyanins, glucosinolates and pro-vitamin A carotenoids.

The food matrix, its structure and composition, is relevant for all of these nutrients e.g. fish for n-3, D, Ca, ubiquinone. Further, a culturally-based food cluster, like beans and grains, or fruit and yoghurt might benchmark fortification approaches and require assessment in terms of relative availability, affordability and sustainability.

IODINE DEFICIENCY RE-EMERGES¹⁴

The persistence of iodine deficiency in many areas and its re-emergence in advanced economies has puzzled and disappointed public health nutritionists.¹⁴ Most likely, in countries like Australia it results from effective campaigns to reduce salt intake because of hypertension, and inadvertently reduce iodized salt intake. It may also repre-

sent people still living in deficiency areas and not having a sufficiently diverse food intake from traded food items.¹⁵

What can be done about iodine?

- Iodised salt has problems for Na intake and hypertension, but could be used in a more limited way with higher iodine concentration.
- Iodophores have been removed as cleaning agents in the milk industry and probably should not be re-introduced. But some dairy herds could have defined diets including seaweeds with iodine as happens in countries like Korea. This would require careful definition and control.
- Food sources of iodine are limited to aquatic foods (fish, algae), eggs and land plants depending on source, but their place in iodine deficient diets could be reviewed subject to questions of sustainability.
- Iodine replete food ingredients can be used in recipes and meals, but monitoring for excess is required.

VITAMIN D DEFICIENCY RE-EMERGES

There are several reasons why vitamin D deficiency is re-emerging, even in sun-drenched countries like Australia.¹⁵⁻¹⁷

- Reduced sun exposure to avoid skin cancer with climate change
- Increased requirements in ageing populations (skin and renal functions)
- Low intake of foods which modulate the vitamin D receptor
- Reduced intake of the few Vitamin D rich foods on advice from Cardiovascular clinicians and public health workers (organ meats, eggs)

Is food fortification the answer to vitamin D deficiency?

There is de facto fortification in some margarine. This could be reviewed as a more formalized strategy with careful consideration of the homology with naturally synthesized vitamin D in animal-derived foods and in vivo in humans since there are questions about vitamin D supplements and atherogenesis (perhaps because of different isomers). Irradiated mushrooms have their ergosterol partially converted to ergocalciferol, which may be a more acceptable approach for vegetarians. The crucial ability to have sufficient sunlight exposure whilst minimising UV skin damage may itself be enhanced by nutritional means.

The multifunctionality of micro-nutrients like vitamin D makes the dilemma to fortify or not more poignant.¹⁵ Vitamin D and the nutritional regulation of its receptor, by food factors like soy isoflavones, have several wide-ranging biological roles beyond musculo-skeletal health.

KNOWN AND EMERGING FUNCTIONS AND TOXICITIES OF MICRONUTRIENTS

The concern about micronutrient deficiencies has grown with the realization that they are seen in conjunction with the characterizing NRDs of advanced economies, as well as lesser developed economies. An important example is *hyperhomocysteinaemia* with vitamins B₆, B₁₂ and folacin deficiencies as a risk factor for osteoporosis and for athero-thrombotic cardiovascular disease (CVD). However, supplementary vitamins and, probably, fortificants, do not seem to protect against CVD events in those at risk.

There has been strong advocacy *for folic acid fortification to prevent NTDs*.

Strategies like those in the USA and Australia have had to consider:

- That NTDs are not the only rationale
e.g. CVD, bone health related to homocysteinaemia
- The impact with and without nutrition education in regard to the background diet and nutritious food choices
- The resultant intakes with and without supplements
- The often inadequate base-line data

The Australian experience was one of intense political and scientific debate during 1997-1998 until an extraordinary ministerial power was invoked to allow voluntary folate fortification despite the lack of baseline data. Mandatory fortification of wheat flour received inter-ministerial support in 2007, at a time of new evidence which casts doubt on the acceptability of the risk analysis.

British nutrition scientists have now shown that the *inactive folic acid used in fortification*, as opposed to the naturally occurring polyglutamyl folacin can readily saturate liver and appear in peripheral blood in the free form.¹⁸ This has the potential for toxicity.¹⁹ The concerns are that folic acid fortification may:

- Induce B₁₂ deficiency
- Result in twinning, perhaps through rescue of a blighted twin, but with increased risk of maternal and perinatal mortality. It is noted that
 - the risk is greater than expected with IVF²⁰
 - is evident with supplements in sickle cell anaemia²¹
 - there are genotype rescue-ethical considerations
- Increase cerebrovascular events in homocysteinaemia (with supplements)²²
- Increase risk of colonic cancer in susceptible individuals²³
 - risk probably depends on MTHFR polymorphism & colonic microflora

THIAMIN DEFICIENCY CONTINUES 100 YEARS LATER WHERE IT WAS FIRST DISCOVERED

There should be a high level of professional awareness of the risk of thiamin deficiency in rice-eating communities. In Indonesia here the vitamin deficiency was first recognized by Eijkman. He earned the first Nobel prize for Medicine and Physiology in the Asian region. A renowned research institute, named after him, has grown from his laboratory. Yet, 100 years after his discovery, anaemia, thiamin and, possibly, vitamin B₁₂ deficiencies are prevalent in the elderly living in Indonesia.⁷ Why? Improved techniques are available for B₁ retention in rice although there is reluctance to eat more wholegrain rices and other grains which are better sources of B₁. Is it the food habits or nutrient handling of older people? Would food fortification or nutrient supplementation be the answer? And what of the health outcomes, which are evident as neuropathies, and with risk of CNS (central nervous system) and cardiac sequelae.

PARTICULAR CONCERNS WITH USE OF SINGLE NUTRIENTS

The experience with use of single nutrients, without a food context, has not been particularly rewarding for health outcomes. Some examples are:

- NSP vs. Dietary Fibre - a refined 'nutrient' (bowel tumours depending on background diet)²⁴
- β -carotene^{24,25}
- Folic acid (see above)
- Selenium with possible anti-cancer properties, but a low safety margin which food sources can obviate.
- Iron (uncertain prevalence of iron storage disorders)
- B₆ (sensory neuropathy)
- Potassium (in renal impairment and with medication)

Isolated food chemicals (synthetic or natural) may be more hazardous or toxic than when in food, and even when re-introduced into food. This is because:

- Isomers may differ
- Physical structure has nutritional value
- The food matrix alters bioavailability and dose-response
- Food components are synergistic

ADVERSE EFFECTS OF SINGLE NUTRIENT FORTIFICATIONS AS ADDITIONS

These may result from:

- Errors in fortified food production as documented with iodine and vitamin A
- Poor QA as with iodine
- Inadvertent fortification with carotenoid food colorants? This could conceivably happen with β -carotene and tumour risk.²⁶
- Toxicity due to genetic susceptibility and narrow safety margins for intake as with iron and selenium
- Fortification and safety margins may be low as with selenium and vitamin B₆, yet high as with B₁ and B₁₂
- Trade-offs between reduced lead and iron overload in iron storage disease
- Nutrient imbalance as with Na/K molar ratios and effects on blood pressure
- Pregnancy outcomes eg. twinning with folate

Single nutrient approaches usually represent a 'patchwork quilt approach' to nutrition and health where one problem is dealt with and then others are recognized or created in a relentless effort to solve what are basic food problems.

Multiple fortifications may be more justifiable. It is noteworthy that:

- No one national fortification program can deal with all marginal nutrient states, yet usually such programs are highly selective for the nutrients which have the greatest advocacy or are most recognisable
- Foods are more than nutrients
- 'Single nutrient deficiencies are rarely seen'
e.g. scurvy is more than vitamin C deficiency; vitamin D is pluri-potential and its deficiency modulated by UV light and food components other than vitamin D
- Inherited metabolic abnormalities for which increased single nutrient intakes need to be increased are not usually wide-spread in the population
- Dietary patterns may accentuate or create single nutrient deficiencies

e.g. vitamin B₁₂ in hygienic vegans; B₂ in rice eaters who have no dairy foods; high sodium diets for K⁺ and Ca⁺⁺; alcohol increases risk of B₁, folate, zinc, Mg and more

- Geographic location where soils are deficient may be low in several minerals eg. iodine, selenium, zinc

MICRONUTRIENT DEFICIENCY IS NOT ALWAYS AN INTAKE PROBLEM

There is often an assumption that micronutrient deficiency is an intake problem when it may be attributable to malabsorption, decreased bioavailability, excessive turnover, loss or misdiagnosis. Examples are:

- Iron with GI blood loss (helminthiasis); probably the most common cause of iron deficiency world-wide
- Malabsorption (as with *H. Pylori* infestation or with HIV/AIDS)
- Ca turnover, often more dependent on vitamin D and Na than on calcium intake
- Decreased bioavailability with anti-nutrients (as with zinc, iron and Ca in regard to phytate, dietary fibre, amino acids or oxalate)
- Misdiagnosis as with nutritional anaemia when a haemoglobinopathy may appear like a deficiency

It is important to deal with the underlying cause wherever possible. There may, otherwise, be un-met nutritional needs with fortification. Also, other health promoting food factors and properties like intactness, nutrient spectrum, and phytonutrient content might not be recruited. The psycho-social role of food may be contributory and offer solutions. The economic benefits of local food production and food trade of a wider range of food commodities may also be over-looked.

NON-OPTIMAL FOOD SYSTEMS AND NATIONAL FORTIFICATION CAVEATS

Basically, fortification is a strategy for widespread nutrient deficiency in a population where individuals cannot be expected to readily, affordably or sustainably access foods sufficiently nutritious for their needs. Wherever this need is defined, biofortification rather than nutrient additions is likely to be a safer and more secure alternative, but it still requires much development.

There are caveats to apply for fortification to be undertaken:

- Regular monitoring and surveillance of the food supply and health outcomes occurs
- A clear cost-risk-benefit advantage in such a strategy
- Programs in place to improve the nutritional value of the basic food supply
- An 'exit strategy' for the fortification program

As with most complex human and planetary problems, nutrient deficiencies are part of a bigger spectrum of NRDs, societal and environmental problems to be understood and solved with multi-faceted approaches.

AUTHOR DISCLOSURES

Mark L Wahlqvist, no conflicts of interest.

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