Review Article

Micronutrient restoration and fortification: Communicating change, benefits and risks

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Food fortification has played a significant role in the current nutritional health and well-being of populations in industrialized countries for over 70 years. A relative lack of a concentrated food processing chain, less developed commercial markets, and relatively low consumer awareness and demand have hindered the same application of the intervention in the transitional, and even more, in the least developed countries until quite recently. The present paper reviews fortification of foods with micronutrients in advantaged (industrialized), transitional (developing) and least developed countries briefly, including reference to bio-fortification, examining some of the public health issues involved. There are different needs and challenges in getting this technology accepted and making it sustainable. Primary constraints in reaching poor target populations are adequate availability, accessibility, and quality assurance/quality control. The paper then examines some issues of risk and benefit and the communication of these, and finally looks towards the future and draws some conclusions. Despite these issues there has been an enormous increase in fortification programmes over the last couple of decades in developing countries. Along with dietary diversification, supplementation and related public health and private sector interventions, this has resulted in considerable progress in reducing the prevalence of vitamin A and iodine deficiencies, but much less so with iron, even as zinc and folic acid deficiencies have emerged as significant public health problems. Food fortification based on sound principles and supported by clear policies and regulations will play an increasingly large role in the progress towards the prevention and control of micronutrient malnutrition. Success and sustainability require clear communication of the small risks involved and the substantial benefits, particularly to populations with significant levels of micronutrient malnutrition, as a complementary approach with other public health measures, in reducing the prevalence of deficiencies and their health consequences.

Key words: communication, fortification, iodine deficiency disorders, iron deficiency anaemia, micronutrient malnutrition, risk, risk management, vitamin A deficiency.

Introduction

Food fortification has been in use for over 70 years in industrialized countries as a means to prevent and mitigate public health problems of micronutrient deficiencies.[1,2] More recently, fortification has also proven its worth in the prevention and control of micronutrient malnutrition in less industrialized economies, especially Latin America.[2–5] This is more true of transitional than the least developed economies. The remit for the present paper was to examine micronutrient restoration and fortification, and to consider questions of communication, change, benefits and risk.

For public health, as well as for most other purposes, the world can be considered from three perspectives: developed/advantaged; transitional; and underdeveloped economies. Clearly, these are artificial, changing and even potentially damaging arbitrary definitions. However, they are also useful in public health nutrition terms, somewhat permitting disaggregation that allows planning, and, in the current context, to address the very different experiences with fortification and its potential. For the purposes of the present paper, countries will be classified according to the World Bank 2000 gross national income (GNI) categories. (Economies are divided according to 2000 GNI per capita, calculated using the World Bank Atlas method. The groups are: low income, $755 or less; lower middle income, $756–$2995; upper middle income, $2996–$9265; high income, $9266 or more.) This results in 52 high-income economies ('advantaged'), 92 in the 'transitional' (upper and

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Paper presented at the FAO Centre of Excellence/WHO Meeting 'Novel Foods in Nutrition, Health and Development: Benefits, Risks and Communication' on 11–14 November 2001, Metung, Victoria,

lower middle together), and the low-income category defined here as 63 'developing' countries. However, because the United Nations Economic and Social Council list of least developed countries also incorporates weak human resources and a low level of economic diversification, we use that list of 49 countries (Appendix 1) as the developing countries.[6] Many smaller countries have little or no commercial food processing taking place within their borders and so are passive participants in fortification through trade. With increasing globalization, the fortified foods that they are likely to import will be determined using Codex Alimentarius as the default standards in the absence of national regulations.

Public health issues

In public health terms how might the economic categories advantaged/developed, transitional, and developing, be characterized? Developed countries tend to be those in which the incidence of many food-related diseases have plateaued but in which non-communicable diseases (NCD) such as cardiovascular disease, cancer and violence/accidents are the commonest causes of death. Mortality from ischaemic heart disease has been declining over the last 10–30 years, while cancer, obesity, hypertension and diabetes type II have increased. Ageing and low fertility are established trends, and life expectancy is over 75 with women living longer but perhaps having less robust health. Obesity, smoking rates and mortality from chronic or NCD are all greater in lower socioeconomic groups. Micronutrient deficiencies are relatively rare, except for iron deficiency anaemia, and again are worse in the less well-off. Micronutrient fortification is widespread in a variety of commercially processed foods, especially breakfast cereals, and vitamin and mineral supplements are taken by up to two-thirds of the adult population, at least in the USA.[7] Fortification is now increasingly used to target specific groups and conditions, such as folate for women of reproductive age.

Transitional countries are characterized as increasingly bearing the burden of both chronic and infectious disease, often in the same communities. These countries are seeing a shift in morbidity and mortality patterns. In 1999, 60% of deaths globally and 43% of the global burden of disease were from NCD and this will increase to 60% of the global burden of disease by the year 2020, with 79% of cardiovascular deaths already occurring in these transitional countries.[8] The burden of cardiovascular disease alone is now greater in India, or in China, than in all the developed countries added together.[8] The increasingly accepted fetal origins of adult disease theory would predict a massive future problem for countries such as India.[9,10] In many cases the better off and urban populations bore the early brunt of chronic disease, but it has now shifted to the lower socioeconomic strata in adult populations. Whereas childhood malnutrition, especially stunting, remains a serious problem, childhood obesity is also increasing in some more affluent groups.[11,12] While iodization of salt has been a considerable success in most of these countries, iron deficiency anaemia remains common, and in the younger and less well-off vitamin A deficiency disorders (VADD) and other micronutrient deficiencies such as zinc and folate are being recognized as significant problems. Although industrial and other capacity to support fortification is often present, there are still limited successes in this area, partly because of a relative lack of experience with private/public sector activities, and largely because of inadequate quality assurance monitoring and evaluation capabilities, and enforcement.

The least developed countries have higher levels (at least in sub-Saharan Africa) of mortality from infectious diseases but chronic diseases are emerging as public health problems of significance. Life expectancy remains low, and malnutrition in the sense of inadequate energy and protein and key micronutrients remains common. In such settings malnutrition plays a role in over half of all children's deaths from infectious diseases. It has been estimated that vitamin A deficiency may contribute up to as much as 23% of the childhood mortality in these countries. Micronutrient deficiencies such as iodine deficiency, iron deficiency and zinc, and often others, are highly prevalent. Although many of these countries tend to be predominantly rural (sometimes with urban megalopolises), those migrating to urban areas are not always better off in terms of growth, and particularly in terms of micronutrient malnutrition.[13–15] Because of poorly developed transport structures, and lack of commercial development, along with difficulty of both access and availability, and poor buying power of those likely to be most deficient, fortification has not thus far played a significant role, except where heavily promoted by donor and public sector support.

In summary, in the least developed countries, and in pockets of poverty in transitional and even developed economies, the populations have higher overall mortality rates, significantly less life expectancy and higher under-5 child mortality rates, resulting, at least partly, from infant, child, and often female undernutrition, including micronutrient malnutrition. Over 2000 million people, or more than 1 in 3 individuals throughout the world, are at risk of iron, vitamin A or iodine deficiency.[16] Zinc, folic acid and other micronutrients are also increasingly being recognized as public health problems in many disadvantaged populations.

The International Food Policy Research Institute (IFPRI) projects that under the most likely scenario 132 million children under 5 years of age will be malnourished in 2020.[17] Hence 1 in 4 children in developing countries will still be malnourished in 2020 compared with 1 in 3 in 1995. While deficiency disorders such as iodine (IDD) and vitamin A (VADD) prevalence levels are showing encouraging decreases, iron deficiency anaemia levels appear not to have improved at all, and along with the other micronutrients mentioned, seems likely to be a significant problem in the future as part of undernutrition. These projections indicate that the category of developing countries and problems of malnutrition and poverty are not going to disappear any time soon. In fact, reduced levels of investment in agricultural research, female education, rural infrastructure, and safe

water could increase the numbers of malnourished children in 2020 to 175 million.[17]

There is also evidence that the gap between rich and poor, both between and within countries is worsening.[18] Without a massive change in international priorities, the trends that are loosely defined as globalization will aggravate this.[19] In contrast, as globalization moves forward, transnational food and tobacco industries have demonstrated the possibilities of wider reach, to places previously considered quite remote and inhospitable.[20] Nevertheless with such depressing projections as those aforementioned, the poor diets that most of these populations will be consuming will be micronutrient poor; so the question will become, what interim approaches can be used to reach the diets of such populations? Fortification is a promising answer, and is cost-effective, but many challenges remain.

Fortification experience, needs and challenges

Figure 1 shows one paradigm for increasing coverage of micronutrient adequacy in populations.[5] Assuming that the curve represents the needs of a total population for a particular micronutrient, the tail area to the right of the curve represents the most affluent portion of the population who will receive their more than adequate share of that same micronutrient from their diet, and because of reduced demands for the micronutrient because of their good health. The tail on the left represents the poorest segments of society whose diets and living conditions are so poor that they will probably only get enough of the micronutrient by supplementation. The largest section in the middle is the target population for fortification, where it is presumed the diet and health are good enough for a basis for adequacy but, because of poor dietary patterns, limited availability or accessibility, cultural reasons or whatever, the intake is marginal. Building on a dietary base, the extra coming in through the fortification is targetted to move most of this population into adequacy. In Indonesia, for example, it has been found that whereas commercial foods reach large parts of the population, coverage of the same foods fortified is related to socioeconomic status and urban/rural location.[21]

For example, Bangladesh studies have shown that only approximately 50% of the RDA for vitamin A is supplied by the diet. Currently supplements are enhancing dietary provision but there still remains a gap. Those who are most poor need home gardening approaches and supplements. Those who are marginally better off might be addressed by a combination of dietary approaches, fortification and supplements,[21] and in fact it is now accepted that it is always better to have an integrated approach addressing dietary approaches, of which fortification might be considered one, along with supplementation and public health measures, including socio-political moves towards poverty reduction. Likewise, because micronutrient malnutrition affects people throughout the life cycle, including infants, young children, and women of reproductive age (especially when pregnant or lactating), but also schoolchildren and adolescents, some approaches are clearly more suitable for some groups than others. Fortified foods reach urban populations more easily than remote rural populations and may also fail to reach those worst off, although perhaps not so much for condiments such as salt and sugar, which are less dependent on socioeconomic status for consumption levels,[21] and staple foods when accessible. The questions then become those of the present paper: is the political, economic and transportation structure sufficient to get fortified foods to poor areas, is there a public or private willingness and capacity to fortify; and are people willing and able to buy the sort of foods that might be fortified? First, the question of fortification and restoration.

Restoration, fortification and development

Fortification is defined by *Codex Alimentarius* as 'the addition of one or more essential nutrients to a food, whether or not it is normally contained in the food, for the purpose of preventing or correcting a demonstrated deficiency of one or more nutrients in the population or specific population groups'.[22] The fortification vehicle can be either a staple food, or a more processed commercially available food, and many have been used. The requirements for a potential food vehicle for fortification are well established.[22] Fortification can be with one or more fortificants, most often micronutrients.

While most experience and emphasis is with fortifying foods in the food processing chain, there is also now some renewed attention to biofortification: fortifying food at source by growing micronutrient-enhanced foods. Biotechnological tools have opened up the possibilities to introduce micronutrients to staple foods, such as vitamin A in rice, but also to enhance the efficacy of traditional breeding approaches. Gene mapping has enabled the identification of those varieties within a crop that have high micronutrient content and the relevant genes. This then speeds up the conventional breeding process to produce agronomically viable micronutrient-dense varieties. For example, as a result of these exercises it is known that aromatic rice varieties tend to be higher in iron content than non-aromatics.

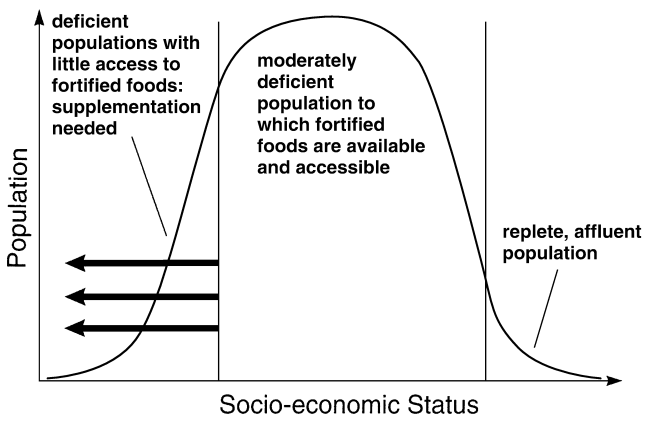

Figure 1. Paradigm for increasing micronutrient intakes in deficient populations.[5]

Restoration, on the other hand, is the replacement of nutrients, usually micronutrients, to preprocessing levels, where nutrients have been lost or destroyed in the processing. Where a new or alternative food has come to largely replace a food in the diet that previously supplied significant amounts of a micronutrient (e.g. vitamins A and D in butter), these have been 'restored' to the substituting food, margarine, an early fortification measure to control xerophthalmia and rickets in middle and northern parts of Europe last century.[23] Although this is clearly a nutritionally appropriate thing to do, this article will concentrate on fortification rather than restoration. Restoration has more or less the same costs involved as fortification but without the presumed added benefit of addressing deficiencies. It would seem to be primarily appropriate for the advanced countries, and is in fact often mandated as such by law. Latin American countries chose to restore ('enrich') iron levels in wheat flour but now generally fortify although the type of iron used for fortification has limited bioavailability.[24] Given the ongoing relatively high levels of anaemia,[25] fortification is more appropriate. With the usually acceptable levels of risk (briefly addressed later), fortification would seem to be the best approach where there is any likelihood of a public health micronutrient deficiency problem that is unlikely to be addressed by dietary changes.

A further perception that argues against restoration in countries with likely micronutrient deficiencies of public health proportions comes from the globalization discussion. This is paraphrased from Sobal, whereby peripheral or developing countries supply raw food commodities, which the agri-industrial complex of the core or advantaged nations process and sell back to developing nations as manufactured, including restored or fortified, food products.[26]

Reaching the targetted populations

One of the factors critical to fortification with micronutrients is that the fortified foods must reach those who need it. At least three major factors are involved: (i) availability: will the food get to the people (logistics/infrastructure, urbanization); (ii) accessibility: will they be able to afford it; and (iii) quality assurance/control (QA/QC): will the food be adequately fortified? The answer to these three fundamental questions will determine success or otherwise, and provide different challenges according to the stage of development.

Little further will be said at this point about the advantaged industrialized countries where fortification has been long widely practised, except where technological or other lessons might be transferred. The key issues in these countries are communication about perceived and real, benefits, risks, need and sustainability. Cost–benefit is an important factor influencing what is fortified and how. Affluent countries can afford to target less common health problems in their populations, even pre-emptively, where a problem has not been actually demonstrated. Finland, for example, fortifies with selenium, although there is not strong evidence of selenium deficiency-related public health problems.[27] Australia has fortified flour with thiamin, although the population as a whole is not clearly deficient but, with some of the highest levels of Wernicke–Korsakoff syndrome in the world, presumably related to thiamin deficiency and high alcohol consumption, it was considered to be a preventive measure even though the proportion concerned is less than 1% of the population.[5] The recent fortification of flour with folic acid in the USA (which is planned in the UK), is aimed to prevent neurotubal defects in fetuses, and so is targetted at only women of reproductive age despite the relatively low birth rate, although the impact of homocysteine levels and their possible relationship to cardiovascular diseases has widened the potential benefit.[28]

Availability

Availability of processed, fortifiable foods remains a constraint for many affected areas. Globalization of markets, in a sound policy environment, may help address this problem. Different transnational companies have shown that it is possible to send almost any commodity out to the most remote places and one has only to go to small stores in the highlands of Papua New Guinea, or in Indonesia or Niger to see the limited, but often surprising, range of goods there. Nevertheless availability of processed, fortifiable foods remains a constraint for many affected areas. Fortified monosodium L-glutamate (MSG) in Indonesia, although it was not successful for various reasons,[29] demonstrated the feasibility of small fortified sachets reaching small *sari sari* stores. Indonesia has a considerable variety of fortified foods on the market such as milk (powdered, condensed and flavoured), margarine and lemonade powder, lollies, snacks, complementary foods and infant formula.[30] Instant noodles reach nearly 100% of even the rural population in South Sulawesi.[21] Opportunities are being recognized, including by the private sector, in West Africa where there is high market penetration with soup/bouillon cubes to village markets. The core issues may therefore become whether the marginally nourished person can then afford, and will buy, the fortified food, and whether distribution channels can reach the poorest and neediest populations located in more remote rural areas, rather than finding candidate foods for fortification.

Where there is inadequate penetration, public sector support may need to be provided. This may be in the form of public support to the food industry to ensure that there is no price differential for fortified foods, or that the proposed fortification has the public investment needed for start-up, especially for staple foods such as wheat flour. Often a donor has been found to be essential at this phase.[2] Fortification of staple foods has traditionally been the public health approach in the developing countries, for example iodate in salt, vitamin A in sugar, iron in flour, usually with a single micronutrient. Although this has had a measure of success, particularly vitamin A in sugar in Central America and salt iodization, it has often required a substantial funding input from donor countries, especially the United States Agency for International Development (USAID), which has long seen fortification as consistent with its thinking, presuming that over time it will move from the donor/public sector to

the private sector, and hence be sustainable. (It is interesting that it appears to have supported an apparently opposite logic with supplementation.) Recent examples have included vitamin A fortification of sugar in Zambia, vitamin A and iron in the Philippines and vitamin A in Morocco and Nicaragua, along with other bilateral and multilateral donor partners.

Possible constraints to such approaches are well documented[2,5] and include lack of appropriate staple, lack of centralized processing, lack of QA/QC facilities, poor legal enforcement (including border controls to stop non-fortified staple foods, especially if cheaper, coming into the country), lack of transport and market/retail outlets, and cost of setting up. These remain formidable constraints although there is increasing international experience that is being shared (e.g. from the Guatemala experience with sugar fortification to Zambia). There remain problems of access to marketed staples because the majority of the poor are subsistence farmers with little opportunity for fortification of locally grown and consumed staple foods. At-home fortification, as in the Japanese experience with thiamin-fortified kernels added to the family rice bowl before cooking, has not been tried, although a similar approach with fortified rice kernels or fortified artificial kernels has been promoted by the Micronutrient Initiative and the non-governmental organization, Program for Appropriate Technologies (PATH), with UltraRice®, and by the Food and Nutrition Research Institute of the Philippines with iron-fortified rice kernels. Despite encouraging small efficacy and effectiveness trials this approach is not currently working at any national level, and has involved considerable donor support for development.

More local approaches such as fortifying maize meal at the village level when subsistence maize is taken to a community-based hammermill flour mill and the fortificant bought and added there, is also at the effectiveness trial stage. There are some encouraging early results.[31,32] Again this development is requiring substantial donor involvement (mainly Canadian in this case). The issues of QA and QC have not been seriously addressed and may, in fact (at a community level) be less relevant in a cost-effective sense. Other innovative approaches to reach poor communities include fortified drinks in Argentina, the Philippines and Tanzania, sweets/candies in Indonesia, and fortified biscuits in Andean Latin America.

Bio-fortification may make an important contribution to fortifying staple foods consumed by those in the most remote rural areas, generally the poorest and most malnourished, where markets fail to reach, given that they are largely sustained by subsistence agriculture. There have been a number of advances through traditional breeding, which are now under cultivation or in human field trials. A vitamin A-rich sweet potato has been disseminated in Kenya with a high adoption rate. However, to have significant impacts on vitamin A levels, intensive nutrition education and promotional activities were necessary. Using partial sweet potato flour replacement in some processed foods, together with specially prepared weaning foods, vitamin A deficiencies could be reduced through this approach. Similar varieties are now been widely disseminated in Mozambique and in parts of West Africa.

Quality protein maize developed by Centro Internacional de Mejoramiento de Maiz y Trigo (CIYMMT) is now being widely grown in several countries, including China, El Salvador, Guatemala and Mexico, and the area cultivated is expected to reach 2 million ha by 2002. High rates of adoption are easily achieved given that the yield is up to 1 ton/ha higher than the conventional hybrids improving overall food security and income generation. The higher levels of lysine and tryptophan, together with better balances among other amino acids, have also increased bio-absorption rates for iron and zinc. They are also focusing on the variability of zinc and iron across the different grains in wheat, trying to increase the overall levels and reduce variability across grains. Animal trials have already indicated success in increasing zinc content in a bio-available form. The International Rice Research Institutes have also developed a rice variety with high iron and zinc content. It is currently in human consumption field trials to establish human bioavailability (previous animal trials confirmed bio-availability in rats). Thus these approaches represent a very real step forward and are expected to be available in the relatively near future.

These approaches are non-controversial, unlike those that produce transgenic crop varieties (the transference of genes from one plant to another, often called genetically modified organism (GMO) or novel foods). The most commonly relevant example would be that of golden rice where genes from a daffodil were inserted into rice, with the help of a bacterium, to produce a grain with vitamin A. These crops are unlikely to be available for broad-based dissemination for at least 5 years. Transgenic approaches clearly expand the possibilities for bio-fortification substantially. However, the 'transgenic' approach brings with it major issues with regard to acceptability to consumers, policy makers and donors that will be resolved only by further scientific evidence of lack of harm, and appropriate communication and sound, credible, risk management.

A new consortium, led by the Consultative Group on International Agricultural Research (CGIAR) Centres and focused on 'seeds for health', believes that within 4 years seeds will be available and released to farmers with micronutrient levels in core staples (beans, cassava, maize, rice, sweet potato and wheat) up to 40% higher than currently available and 80% higher by the end of a 10-year breeding and adaptation programme.

Accessibility

Although the relatively minor incremental costs of fortification are often quoted favourably (e.g. as only 1 cent more per tonne), the very poor are acutely sensitive to any margin at all. On the whole, poor people do not buy similar goods where one is more expensive.

In two sites in Indonesia, urban (South Kalimantan) and rural (South Sulawesi), approximately 100% of households

were consuming instant noodles in the week preceding the survey. However, the proportion consuming fortified instant noodles was much higher in urban areas (65%) than in rural areas (29%).[33] It would be interesting to know if this was because of distribution (because instant noodles were reaching the households), or cost-related (were the fortified noodles more expensive?). In both sites the proportion of households taking fortified noodles was higher in higher socioeconomic status households.[33] The potential vehicles not related to socioeconomic status in these communities were the condiments sugar, salt, and MSG, which were universally consumed and available. Because there is experience with all three (including MSG), they could be possibilities, but would require significant public sector and donor involvement.

In transitional societies it is presumed that communication, and information that such and such a food is better for one's family/self because it is fortified, will encourage people to pay any incremental cost of fortification (and this would then contribute to sustainability). However, there is limited evidence of this. It is likely that the producer or processor will have to bear the initial costs (with 'gain' being to capture a market share). Governments can encourage this by reducing the risk the company has to bear by abolishing tariffs on imported fortificants, and by paying or loaning for the initial fortificant which, while only incrementally more expensive, will still run into hundreds of thousands of dollars for initial runs.

In developing countries accessibility will continue to be a problem, especially in much of Africa. Urbanization that is proceeding at a rapid pace in the non-industrialized world will help availability if not always accessibility. Although it continues to be important to encourage the fortification by the private sector/food industry of such foods as do reach rural consumers, it is likely that the public sector will need to take the lead in public/private sector partnerships in these countries. This is because the economic risk will probably not be accepted by the private sector, and also because of the uncertainty of the size and profitability of the market. Suppliers' perceptions of benefits (returns on investment) is perhaps the greatest factor affecting supply and distribution of new commercial and health technologies. Few suppliers are interested in developing technologies for people unlikely to be able to pay much for them,[34] and this appears true of fortification technology and investment as well.

Consequently governments will continue to play a major role, along with bilateral donors and civil society in assessing the problem, identifying suitable food vehicles, running the trials and reducing start-up costs. Costs of supplying fortified staple foods can be increased or offset by local tax and subsidy policies, including assistance for research and development programmes. However, such policies usually require a stable government and established legal and money lending systems, which are not always in place in many countries. Structural support such as sufficiently skilled labour, material inputs, credit, and law to enforce contracts and quality control measures and tax collection and to prohibit corruption and a stable distribution network,[34] are all needed to initiate a successful national programme to fortify a staple food item. The public sector/governments may also need to supplement the cost of the fortified foods, at least initially, so that they remain much the same as non-fortified foods (or even cheaper). They can also help by assuring producers of a firm market, for example by ensuring that all boarding schools, the armed forces and other public institutions, use basic staples such as flour, sugar etc., that have been fortified.

Another complementary approach is to look at innovative ways of getting the micronutrients to wider, and isolated populations. This might be through multiple fortification (e.g. triple fortification of salt). Others include the use of drink mixtures as in Philippines and Tanzania,[35] using food-to-food fortification by use of red palm oils and by modifying cooking methods, in both of which the efficacy has been demonstrated in Malaysia, South Africa and Tanzania[36] and other countries. Vietnam has had some initial success with fortifying biscuits with vitamin A and iron,[37] and putting iron (ethylenediamine tetraacetic acid (EDTA)Fe) in fish sauce and, in China, with soy sauce.[38,39] In the Philippines vitamin A has been added to hard margarine and is used by poorer consumers because it does not require a refrigerator, although rural penetration has not been confirmed.[40] There are many other examples.[2,32]

Quality assurance/quality control

An important part of a successful fortification programme is the confidence a consumer has that the food his or her family is eating is safe, and also has been modified in this way to enhance benefits to the consumer. The latter is often expressed as reduced sickness in children or optimizing a child's development in intellectual abilities and hence probable success at life and school. Similarly, local and national authorities need some assurance of the safety and benefit of the programme. The food processors need to be assured that all competitors are facing the same control measures and any added costs. However, the costs in terms of functioning laboratories, enough food inspectors and the timely and accurate reporting of results, and the resources for government authorities to do something about it, are often missing in many of the transitional and least developed countries.

This has led to reliance on simple QA methods by which the industry regulates itself, with goodwill and self-interest being the motivating factor. There are certainly anecdotal pieces of information to suggest that this is not always enough, but is an area not adequately assessed and evaluated in current programmes. Where this has been done (e.g. with the salt iodization programme) it has found to be essential because of wide variation, and because urinary iodine levels have been found to be creeping up in some countries. This is even a stretch for many of the world's wealthiest countries where surveillance and survey data have indicated a need to modify the fortificant levels (Australia, Switzerland and the USA, among others). The risks in terms of litigation, and

loss of reputation, consumer confidence and hence sales, have proven sufficiently strong in industrialized countries to maintain good QA. But these are not in place in most countries, and remain a constraint to a successful, sustainable programme. Some recent donor and non-governmental organization emphasis on capacity building is starting to address this, but it is ultimately a question of resources and the adequate funding of the QC part of the whole fortification process.

Risk, benefits and development

Although there is increasing information about risks involving food systems and nutrition, there is far less on fortification compared with food safety. This increase over the last few years has been largely because of debates on bovine spongiform encephalopathy (BSE), transgenic foods and general perceptions of risks from hormones and antibiotics and other contaminants in food, although the risks of diarrhoea and childhood mortality in developing and transitional countries far outweighs these risks. The scientific perception is that such (non-diarrhoeal) risks are few, although not non-existent. However, public perception is not always the same, although fortification in general does not seem to be considered a high risk except in special circumstances.

The advantaged countries appear not to see excessive risk in fortification, perhaps because of the relatively long history and ubiquity of the practice, along with a high acceptance of supplement taking. However, this would seem more so in the North American countries than in Europe. Norway for example is actively resisting a WTO instruction that its breakfast cereals be fortified (A Orshaug, pers. comm. 2001). The acceptability of risk has been reported to be crudely proportional to the third power of the benefits (real or imagined), although this is based on US data[41] and would conceivably be very different in a different social, cultural and economic setting. The social acceptance of risk is directly influenced by public awareness of the benefits of an activity, as determined by advertising, usefulness, and the number of people participating.[41]

In looking at risk in food systems, several problems exist. One is the complexity of foods and food systems and the very commonness of food and traditional diets. There is the inherent difficulty of assessing risk in food systems, which is why most interest has so far been on carcinogens. Here the assumption is made that any risk to human or animal is absolute by that substance, after exposure to which, cancer will occur (although it is understood that this is not the case, the so-called Delaney resolution, implying the possibility of non-risk, remains in place in the USA).[42] Further complexity is provided by the cultural, socioeconomic and environmental conditions in which foods are eaten. Risk is the measured or estimated probability of injury, disease or death and is not the same as 'safe', which is usually taken to mean 'without risk', although dichotomy does not exist and it is not possible to label foods simply as 'safe/unsafe'. Familiarity with particular foods and a long history of cultural use increases the perception of safety.

Given that all 'chemicals can be made to produce some form of toxicity under some conditions of exposure'[42] and that many of the micronutrients used are known to be unsafe in certain circumstances (e.g. iron overdose in children, teratogenicity of vitamin A and iodine), some concern is warranted. A recent review of where the world stands with respect to iodine deficiency has shown that many previously iodine-deficient parts of the world now have median urinary iodine concentrations well above 300 μg/L, which is excessive and carries the risk of adverse health consequences.[43] An example of this was in Zimbabwe, and later Congo, where several reports of salt fortification of iodine in communities with chronic iodine deficiency led to fatal cases of Jodbasedow or iodine-induced hyperthroidism (IIH) disease.[44,45] These were found to be due to poor or absent monitoring, a common set of circumstances in many developing and transitional economies, and the sudden introduction of overly fortified salt coming in from surrounding countries.[46]

The ultimate conclusion about safety (risk management) is a policy judgement about the degree of risk to be tolerated, or, stated in more common functional terms, what level of exposure results in residual risks so small as to be of no public health concern, and what, if any, controls are needed on the substance to ensure safety?[42] Despite the attempted harmonization of such risk management through the WTO, the policy judgement is likely to be different depending on the disease profile, economic well-being, and public structures, within a particular country.

The degree of acceptable risk to a specified target group depends, in public health terms, on the benefits that would be brought to the greatest number of beneficiaries, and the alternative technological and other possibilities available to a population, given socioeconomic and other circumstances. If there is less need (i.e. there is not a micronutrient deficiency problem of public health significance), then less risk is expected and acceptable. Notwithstanding this, developing countries may not want differentiated interventions for those originally proven, and still in place, in the developed countries, no matter how different local health, need and circumstances actually are (e.g. the use of iodate *vs* iodine in the fortification of salt). There was a continuing debate in the early days of the universal iodization of salt campaign as to why developing countries should be using iodate when the western world had used iodine for such a long time, although there were valid environmental and storage reasons for why iodate was a more appropriate fortificant in the often tropical environment and storage and packaging options available. Perception is highly important, and so issues of how benefits, and the rationale for a particular fortification, are communicated to those consuming the fortified product become of prime importance.

A pertinent example currently getting a lot of attention is the effort to increase micronutrient intakes of staple grain foods by the transgenic 'fortifying' of grains so that they have higher concentrations of existing low levels of a particular micronutrient, or more extreme, a nutrient that has not

'traditionally' been found in such a species. In discussion of who benefits and who loses, extravagant claims have been made on both sides, but both have elements of some truth. It would be likely that, successfully done, the process could contribute helpfully to reducing hunger and malnutrition by increasing yields. However, it is also likely, unless closely monitored and controlled, that attempts at monopolization would take place. What has been interesting in this argument is that it has been those with least risk of deficiency, and the health consequences of this in terms of increased mortality of women and children, who have come out most strongly against the risks. (In contrast it is probably good that they are, considering the powerlessness of third world consumers and farmers.) Nevertheless, it must ultimately be up to developing countries to analyse the risks to their populations of malnutrition and the cost–benefits of other alternatives, if they exist.

Communication of risks and benefits and development

Given the demonstrated great need, and the difficulty of ensuring adequate intakes through socio-political change, and the small risk but high benefit, why is risk communication in fortification being addressed? Virtually any health programme has less chance of sustainability if there is not community involvement and consumer acceptance. It was previously considered that one of the prime advantages of fortification was the fact that the consumer did not need to be involved. Although this remains largely true of the actual consumption side (and presuming that basic tenets of fortification have been met such as no change in organoleptic properties or price), sustainability has been found to be compromised in countries in which the public does not have information and endorsement of the intervention.

Clearly there are other factors that can mitigate against sustainability of health interventions, especially where it is less clear sometimes that it is indeed a health intervention, such as fortification. Nevertheless, fortification is a potentially powerful tool for helping reduce deficiencies, if the fortified foods reach those most in need. To get consumer support, communication, including risk communication, is essential. It could be argued that the reaction to transgenic foods, and to globalization, in general has been so negative in so many quarters, sometimes unexpectedly, largely because of a lack of consideration of the need for people to know, especially where it concerns food that they will be eating. It has been essentially a failure of risk communication (along with a degree of misplaced arrogance by the industrialized country-based multinational firm developing and promoting such innovative interventions, for example in the early development of seeds).

Perceived risk must take into account people's extreme aversion to some hazards, their indifference to others, and the discrepancies between these reactions and experts' recommendations.[47] Scientists and regulators are increasingly aware of the apparent difference between what they consider to be the 'real risk' in relation to concern over food safety, and the perception that consumers have of that risk.[48] This may be more an issue that gets attention in advantaged countries than in poorer countries.[49] But, even within these advantaged economies, people of the USA seem to have more willingness to accept what is added to their food than in Europe, where the proposed labelling provisions are currently being strengthened.[50,51] Consumer attitudes to risk and government approaches to food safety and quality vary significantly from country to country.

While it could be argued that there is no point having food labelling and other information if there are not the facilities to ensure that the actual contents and amount reflect what is on the label, experience has shown that it is most unwise to underestimate the power of the public, including in developing countries, if concern takes hold. The reaction to transgenic seeds, especially those bred to be sterile, was significant in countries such as India and certainly influenced policy. Likewise, iodine fortification has been put on hold in India because of legal action by consumers (in this case probably more affluent consumers who want the option of buying non-iodized salt). This is despite the evidence (probably not communicated adequately) that this reduced availability will likely impact on the poor, who will preferentially consume cheaper non-iodized salt if available.

However, it is not just the consumers who have a right to and need for information and communication. This must be equally (and early in the process) a concern of policy makers in ministries and governments. Dary has described how on three occasions, the government in Guatemala has tried to abolish the requirement of sugar being fortified with vitamin A, despite the proven effectiveness of the measure.[52] Because of good communication and information from a concerned partnership, this was overturned. Now another risk is perceived to be globalization and the role of recent *Codex* decisions, which have been suggested to 'reflect political compromises designed to promote international trade, not the best science to protect consumers'.[53] Given that trust is the prime determinant in communicating risk, and that 'consumer trust in government and food industry scientists is low',[48] then there is clearly progress to be made.

Although there are clear advantages to harmonization of standards (e.g. in fortification levels, or the fortificant used) in terms of mobility across borders, costs and consistency of information, there is also concern that parts of the 'Agreement on the Application of Sanitary and Phytosanitary Measures' regulations may be used to actually prohibit countries from fortification in terms of trade, even when a proven problem exists. Article 3 of the Agreement provides that a national health standard for food is presumptively legal if it conforms to a standard, guideline, or recommendation established by Codex. A national standard that provides a greater level of protection than Codex (and this conceivably includes fortification) is a 'trade barrier' unless the WTO decides that the stricter national standard is based on a proper 'risk assessment' that demonstrates that the Codex standard, guideline, or recommendation does not provide sufficient protection, or that the country maintaining the stricter standard has other scientific justification.[53] An

example might be where a country that fortifies a particular staple food is forced to accept the importation of the same food unfortified and cheaper from another country, or not be in compliance with WTO regulations.

Risks should always be communicated in the context of the accompanying benefits. There is considerable information and experience on the benefits of reducing micronutrient deficiencies, and in the effectiveness of fortification in doing this. One of the most effective has been the frequently quoted statement that correction of iodine deficiency protects 85 million neonates from mental retardation annually, which was reached by extrapolating the 13.5 points of IQ reduction with iodine deficiency to populations at risk for iodine deficiency (Bleichrodt and Born 1994, quoted in Delange *et al.* 2001).[43] Given that fortification is in a relatively clear position vis a vis benefit versus risk, it would seem important to give users (consumers, government, civil society, donors and the private sector) much more information. This will require the allocation of a greater proportion of budgets to doing this than currently is the case. The other frequently quoted advocacy is the World Bank's estimation of micronutrient interventions, and food fortification in particular, as among the most cost-effective of all health interventions.[54] This has been heard by the donor community more clearly than the affected countries themselves and this needs to be addressed.

Sustainability

One of the stated advantages of fortification is the presumed sustainability of the intervention, particularly where costs can be passed on to the consumer (without affecting the poorer, and probably needier, consumer). Commercial fortification of retail foods has shown good sustainability in the industrialized countries and requires little government involvement, presumably a factor in its sustainability. However, the public sector remains important in quality control, standards, and increasingly, in the 'health claims' area.[51] Strong partnerships at the national level are essential, not least to protect the local food/miller industry. It is suggested that one of the reasons that locally made complementary foods did not succeed was that local industry could not compete with the multinational companies involved in infant and young child feeding.

Where the fortification is addressing a specific issue it has been found necessary to monitor fortificant levels, as well as the levels of the communities' biological indices, as in Switzerland where the IDD programme still continues to need constant monitoring and where levels were recently adjusted, in particular in response to importation of prepared food made with non-iodized salt.[55] In the USSR severe IDD had been eliminated by effective control measures as early as the 1940s–1960s, but government programmes were discontinued after 1970 and IDD are now common again in the Newly Independent States and the Russian Federation.[56] However, the perception of where the risk lies is dependent on the national environment. A recent health article in Ireland warned that a 'low iodine diet will put people at a greater risk in the event of a nuclear disaster',[57] clearly a different perception of the risk compared with that of a developing country where suboptimal brain development is likely to be the main concern.

There is little information on sustainability of programmes in the transitional economies, except in Latin America where fortification has had a relatively longer history. Dary contends that the Guatemala fortification program of sugar with vitamin A has been very successful precisely because it was a closed market.[52] However, as noted, the government has three times enacted legislation that fortification is no longer necessary, in order to allow non-fortified sugar to be imported. A civil society alliance with INCAP, UNICEF, WHO etc. protested the proven impact on vitamin A deficiency and it was re-enacted. Two years later the government tried again but more carefully legally. This time, little could be done but the private sector declined to take advantage, thus demonstrating an important private/public partnership where the leadership was provided by the private sector and strongly supported by civil society alliances. It had also happened in the earlier days of sugar fortification, and a resultant increase in vitamin A deficiency was recorded when fortification ceased. He concludes that '. . . it is essential to have effective and reliable enforcement mechanisms, and that the consumer be aware about the existence of these programmes and be ready to defend them'.[52]

A similar saga is being played out in India now, where the universal iodization of salt, considered essential for success, has been revoked. A strong counter campaign means that it is likely that it will become a State issue but there is concern that some States will react considerably more responsibly than others. As stated by Delange *et al.*, 'Iodine deficiency is a disease of the soil that will relapse soon after the preventive measures are abandoned.' Guatemala, and to a much larger extent, Russia and the Commonwealth of Independent States offer spectacular examples of this point.[43] The same is true, to a greater or lesser degree, of all the micronutrients, and so adequate diets and reducing the drain on stores by controlling disease, have to remain ongoing concerns of households, communities and governments.

Sustainability is likely to be low in the least developed countries, and particularly where there is civil strife. In Sierra Leone iodized salt coverage declined from 75% to 8% in 1999 due to the civil war.[45] Where there is little or no QC there can be little incentive for companies to pay the added costs of fortifying, promoting and monitoring that fortification entails. A further factor, besides very weak infrastructure, is the competition for resources, not least trained personnel, in the face of competing threats in many of these countries, such as the AIDS epidemic.

Looking ahead

The IFPRI has projected that child malnutrition will decline by only 20% over the next 20 years. India will remain home to one-third of all malnourished children and the numbers will actually increase in sub-Saharan Africa by 18%, unless new action is taken.[17] Given such gloomy predictions, and the current clear lack of willingness of most affluent nations

to make the serious financial transfers needed, or to allow the international structural changes to happen that would help relieve such inequity, piecemeal interventions, but of proven effectiveness, will continue to be needed, and expanded.

Some important elements of this will be addressing rural infrastructure, agricultural research and development, and innovative local fortification such as hammermills and additions to drinks and foods. In fortification, even more than other micronutrient interventions, the private sector will need to be partners in a way that recognizes the different agendas but concentrates on the overall goal of a healthy, consuming population. As in the industrialized world, an increasingly wide spread of fortified foods will help address the bulk of the population (the large central part under the curve in Fig. 1).

The evidence suggests that single-element micronutrient deficiencies are the exception rather than the rule. It has been suggested that it would therefore seem logical to develop multimicronutrient interventions, at the same time aiming for a better understanding of the interactions involved. As Huffman *et al.* have shown, women in developing countries often consume diets of poor bio-availability and limited micronutrient content, leading to concurrent deficiencies of iron, vitamin A, zinc, folic acid, vitamins B6 and B12 and occasionally other vitamins and minerals.[58] Such deficiencies have important consequences for women's own health, pregnancy outcomes and their breast-fed children's health and nutritional status.[58]

This multiple micronutrient approach has been the general experience in a lot of fortification anyway, both in more processed foods, such as breakfast cereal foods, but also in wheat flour fortification. In Thailand a small sachet containing spices and multimicronutrients is marketed along with instant noodles.[59] Ready-made mixtures of commercial fortificants are marketed with a variety of combinations of vitamins and minerals. Citing folate and its possible effect on elevated levels of homocysteine and the risk of cardiovascular disease, and the relationship between intakes of vitamins B6 and B12 in reducing homocysteine levels, the Kellogg Company now makes a 'structure function' claim linking folic acid, vitamins B6 and B12 and cardiovascular health on the packaging of a number of its adult breakfast cereals in the USA.[60] This is probably somewhat in front of current scientific certainty.

In terms of QA/QC most developing countries (and many transitional countries) do not have the financial or technical resources for the laboratory facilities necessary for proper monitoring. This will continue to be one of the major challenges.

The increasing levels of urbanization, both in the least developed countries and transitional countries, represents an enormous challenge in terms of nutrition. The increasing urbanization will mean increased needs for infrastructure such as transport, the supply of clean water and garbage removal, but at present it is likely to result in increased malnutrition and greater health risks if people's access to adequate and safe food is not improved.[61] The causes of malnutrition and food insecurity in urban and rural areas are not the same because of factors that are unique to, and exacerbated by, urban living.[14] In many developing countries less than 40% of food production enters the market beyond the rural village, whereas urban people buy 90% of their food from the market.[13] Between 1975 and 2000 the developed countries' markets had to accommodate an additional 175 million customers, while at the same time developing markets had to accommodate an extra 1.2 billion, under considerably more difficult conditions.[13] However, this global trend may also be an opportunity for fortification as an intervention because the availability of processed foods is greater to urban populations, if they can afford them.

Globalization will be a major factor regardless of which way it ends up being played out. It is becoming increasingly easy to transfer information and technology between countries with the expansion of the Internet and online health training programmes, including the growth of information about the relative effectiveness of different technologies, and some aspects of the liberalization of trade. However, appropriate health technologies, and one might include methods of fortification in these, may become more unequally distributed than ever.[34] There are issues of purchasing power, technological capability, purchasers' priorities, and unequal information. This is where a different form of risk comes in. More importantly concern is widely held that the benefits of globalization are not being shared fairly, and that world inequalities have increased as globalization has increased.[20] As indicated, the public sector must continue to take an active role in promoting fortification, facilitating the mitigation of risk to suppliers in non-distorting ways, and ensuring that there is enabling legislation backed by adequate QA and QC.

Conclusion

During the last two decades there have been impressive results in reducing the prevalence of vitamin A and iodine deficiencies, but considerably less so with iron deficiency.[62] Much experience has been gained and this must be built upon, taking into account the factors mentioned here. Innovative proposed solutions are increasingly global in concept although the poorer, rural areas will need to look to local community-based solutions at the same time. The Global Alliance for Improved Nutrition (GAIN), a global alliance for the improvement of nutrition, but targetted to fortification interventions to prevent and control micronutrient deficiencies, is a partnership among the Gates Foundation, Food and Agriculture Organization of the United Nations System (FAO), UNICEF, World Bank, WHO, bilaterals such as Canadian International Development Agency (CIDA) and USAID, international non-government organizations such as the Micronutrient Initiative, and the private sector. This should help direct added resources to work with national governments, where increased global trade is not addressing the problem.

The United Nations (UN) has recently developed, with wide input, a series of nutrition, health and other goals for

children, for the special session of the UN on Children (UNGASS) held in May of 2002. This follows the utility of the previous World Summit and FAO/WHO International Conference on Nutrition micronutrient goals, and their partial achievement. It is notable that in the new recommended goal, more than a decade after the original micronutrient goal, fortification is specifically mentioned as an intervention strategy. The goal is to 'achieve sustainable elimination of iodine deficiency disorders by 2005 and vitamin A deficiency by 2010; reduce by one-third the prevalence of anaemia, including iron deficiency, by 2010; and accelerate progress towards reduction of other micronutrient deficiencies, through food fortification and supplementation'. These are not impossible goals but will require increased commitment by all concerned, whether in developing, transitional or developed economies. However, the power and the resources to facilitate this happening are largely with the last of these three global economies.

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Appendix 1. Least developed countries

Afghanistan	Madagascar
Angola	Malawi
Bangladesh	Maldives
Benin	Mali
Bhutan	Mauritania
Burkina Faso	Mozambique
Burundi	Myanmar
Cambodia	Nepal
Cape Verde	Niger
Central African republic	Rwanda
Chad	Samoa
Comoros	Sao Tome and Principe
Democratic Republic of Congo	Senegal
Djibouti	Sierra Leone
Equatorial Guinea	Solomon Islands
Eritrea	Somalia
Ethiopia	Sudan
Gambia	Togo
Guinea	Tuvalu
Guinea Bissau	Uganda
Haiti	United Republic of Tanzania
Kiribati	Vanuatu
Lao PDR	Yemen
Lesotho	Zambia
Liberia	