

# Ending Hidden Hunger: The History of Micronutrient Deficiency Control

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## **1. Introduction**

There has been a tremendous investment in the control of micronutrient deficiencies during the last 15 years. Agencies, governments, scientists and private industry have been brought together to work on micronutrient issues in a way that has been quite unique in the history of malnutrition. The purpose of this paper is to review the history of the present focus on micronutrient interventions. It starts with a summary of the events that changed the focus of nutrition interventions from protein malnutrition to protein energy malnutrition, then to energy deficiency, and to the present emphasis on ending “hidden hunger” by controlling micronutrient deficiencies. Subsequent sections provide more in-depth information on events that influenced decisions about the control of iodine, vitamin A, and iron deficiency, and on factors that affected the success of these programs. The review ends with an intentionally provocative section on the possible future of micronutrient deficiency control and how it fits within the global nutrition situation.

Information in this narrative was obtained from interviews of key individuals in agencies and the academic community, as well as from reports and other publications, and personal experience. This narrative is intended as a basis for discussion of the issues and does not pretend to be an authoritative document.

## **2. The era of protein energy malnutrition**

Between 1933 and about 1965 the main focus was on severe protein malnutrition. Impetus for the emphasis on protein deficiency was provided by the following events. In 1933 Cicely Williams diagnosed kwashiorkor as a nutritional disease "in which some amino acid or protein deficiency cannot be excluded". Because the condition was prevalent in rural Africa - in part because of the low protein content of starchy complementary foods - kwashiorkor and milder forms of protein deficit were assumed to be common in the developing world in general. Changes in serum protein and amino acids in kwashiorkor supported the picture of protein deficit. Awareness of the malnutrition caused by World War II gave additional impetus to research on protein deficiency and starvation. Dean and Platt, based in the Medical Research Council unit established in Uganda in the early 1950s, conducted some of the earliest studies of human malnutrition, again working in an area where kwashiorkor was common. Most of the animal studies during this period and into the early 1970s were designed to test the effects of protein deficiency, or less often protein and energy restriction, on metabolism and function. In the late 1950s the official position of WHO and FAO was that the single most important nutrient deficiency was protein. In 1959, Jelliffe coined the term “protein-calorie malnutrition” recognizing that protein deficiency was not the only cause of malnutrition and essentially contradicting the WHO/FAO position. However, throughout the 1960s investigators such as Cravioto in Mexico and Guatemala, Birch and Richards in Jamaica, and Monckeberg in Chile, continued to work with protein deficiency as the paradigm.

A number of large and important research projects, such as the Guatemalan longitudinal study that was conceptualized in 1967-69 and started in 1969, were designed primarily to assess the effects of adding supplemental protein to the diet. When the project was eventually funded

there was already a great deal of evidence that protein might not be the limiting nutrient. However, the investigators retained the original design, comparing the efficacy of a high protein-high energy formulation to that of a low protein, low energy control. Later, however, Lechtig could show that birthweight response was proportional to the amount of energy consumed because many pregnant women consumed large amounts of the control supplement and thus quite high amounts of energy, but low amounts of protein. While some effort was made to match the micronutrient content of the two supplements there was no real attention paid to micronutrient issues, and energy and micronutrient intakes covered. The confounding effects of anemia on mental and motor development were not considered to be sufficiently important at that time. The Bacon Chow study in Taiwan, and others, were confounded in a similar way.

In the 1960s and early 1970s UNICEF was heavily invested in primary health and in alleviating emergency situations. The UN agencies attempted to consolidate activities such as food supplementation programs, nutrition rehabilitation and nutrition education under the umbrella of "Applied Nutrition Programs". Because it had been insisted that UNICEF must rely on WHO and FAO for technical expertise, UNICEF had been an important advocate of the need to set up the Protein Advisory Group, later the Protein Calorie Advisory Group, in 1955. The PAG was created to "help WHO advise FAO and UNICEF on the safety and suitability for human consumption of new protein foods". It became intensely occupied with solving the perceived protein gap. It was also instrumental in the development of specifications for improved weaning foods, which assisted UNICEF in its complementary feeding activities. The emphasis was on protein quality, with concern about micronutrients largely limited to preventing clinical symptoms of deficiency.

In 1974 Donald McClaren, concerned about the lack of attention to marasmus, wrote "The Great Protein Fiasco" (McClaren, 1974) in which he claimed that the role of protein deficiency in PEM had been greatly over-emphasized, by the Protein Advisory Group of the UN in particular. His article was the natural outcome of years of doubt that protein deficiency was the main problem. He also noted that recommended intakes of dietary protein had been lowered progressively for years, thus closing the protein gap "unwittingly". The mathematical calculation by Joy and Payne on the critical protein content of diets compared to world food availability drastically changed estimates of the diets that were inadequate in protein; by their calculations these would be limited to those based on cassava and yams. Some years before Sukhatme had already observed that few Indians who consumed adequate amounts of energy had lower protein intakes than were recommended. In their article "The Protein Gap", Waterlow and Payne argued that "the concept of a worldwide protein gap, derived from the diagnosis of kwashiorkor as a protein deficiency state, is no longer tenable" (Waterlow & Payne, 1975).

The World Bank's main effort in nutrition was focused on operations, with some work on related economic and policy issues. Economists accepted the protein-energy deficiency paradigm through the 1980s. A seminal econometric analysis of the link between malnutrition and work productivity was conducted by Taylor (MIT) and Selowsky (The World Bank). This included a cost-benefit analysis of investments in nutrition, and the elasticity between increments in protein-energy intake and increments in IQ. In 1973 Reutlinger and Selowsky

authored the report “Malnutrition and Poverty” for The World Bank, which focused almost exclusively on the world calorie deficit.

UNICEF and the World Bank both supported and participated in the evolution of the PAG into the UN's Administrative Coordination Committee's Subcommittee on Nutrition (ACC/SCN) in 1977. UNICEF's Heyward chaired the SCN from 1977 to 1982. The improvement of breastfeeding practices, and maternal and child malnutrition including supplementary feeding programs, received much attention from UNICEF during this time but little was done specifically in the area of micronutrient deficiencies. Nevertheless it was well-known that anemia was widespread, that iodine deficiency was the cause of endemic goiter and a serious problem in some parts of the world, and that vitamin A was the leading cause of preventable blindness.

### **3. Emergence of the present focus on “hidden hunger” and micronutrient deficiencies**

As described above, in the early and mid 1970s the nutrition community began to realize that protein deficiency, or PEM, was not the major cause of malnutrition. This was followed by a shorter period of interest in whether energy deficiency was the main problem. In 1977 the conclusion of a prestigious group of nutritionists and economists was that “on a worldwide basis inadequate intake of energy because of inadequate intake of food appears to rank ahead of all other types of malnutrition”. However, they also agreed that “when the total of intake of food and thus energy is low, the intake of many nutrients is low as well” (National Academy of Sciences, 1977). This perspective led to the Nutrition Collaborative Research Support Program (Nutrition CRSP, funded by USAID). A series of seminars was held over a year examining the association between energy deficiency and functional performance. This activity was very influential in documenting current knowledge about the functional consequences of undernutrition but micronutrient deficiencies were not considered. The 1982-1986 CRSP studies in Egypt, Mexico and Kenya revealed that dietary quality, especially the intake of animal products, was the main predictor of functional outcomes, while dietary energy intake met requirements and protein intakes were more than adequate. The co-existence of multiple micronutrient deficiencies in each country was demonstrated, as was the association of several of these with impaired function (Allen, 1993). Interestingly the Nutrition CRSP has been criticized because it was not an intervention study - but if it had been, it is quite possible that the wrong interventions would have been tested.

In the early 1970s many countries developing their national plans for nutrition were certainly already aware that iron, vitamin A and iodine deficiencies were more widespread problems than PEM (e.g. Thailand, Indonesia and the Philippines). But at that time they were concerned mainly about the clinical manifestations of these deficiencies (fatigue, blindness, and goiter and cretinism) and were unaware of their adverse effects on child mortality and morbidity, and motor and mental development.

The 1977 Alma Ata meeting on primary health care brought together the main agencies, including UNICEF, the World Bank and WHO, to improve child health and survival. They agreed to collaborate to reduce child mortality, and chose the areas in which each agency would focus. Out of this meeting came support for UNICEF's GOBI initiative (growth

monitoring, oral rehydration therapy, breastfeeding and immunization) and other strategies to improve child survival. One impetus for these activities was the growing concern that little progress was being made in addressing PEM. The task of dealing with the underlying sociopolitical and ideological determinants of PEM was overwhelming, as were the complexities of the role of infection and other factors in its etiology. There had been relatively little emphasis on targeting interventions. Beaton & Ghassemi's 1982 review of supplementary feeding programs for young children concluded that they were expensive compared to their relatively small measured impact (Beaton & Ghassemi, 1982). There was a need to show an impact on at least some forms of undernutrition.

Micronutrient issues started to receive the serious attention of the international nutrition community in the mid-1980s. The impetus was renewed interest in iodine deficiency, with the recognition that this affected a wide range of functions in the syndrome "iodine deficiency disorders" (IDD) rather than causing only cretinism and goiter. Importantly, there appeared to be options (especially salt iodization) for essentially eliminating IDD on a global scale.

At the same time Sommer's group at Johns Hopkins University demonstrated in Aceh, Indonesia, that vitamin A supplementation of preschoolers reduced mortality by 34% (Sommer et al., 1986). This was a pivotal finding, supported later by other studies. It prompted concern that vastly more individuals may be functionally impaired by vitamin A deficiency than was formerly assumed, and led to interest in the use of oral vitamin A capsules to reduce the problem.

As described below, there were strong champions of the need to eliminate IDD and vitamin A deficiency. They presented UNICEF and other agencies involved in Child Survival with an opportunity to have a significant impact on child health and survival. James Grant, then the Executive Director of UNICEF, envisioned that to elevate national priorities on the health, welfare and survival of children it was necessary to gain the attention of policy makers at the highest level. At the 1990 World Summit for Children, which was convened by governments and facilitated by the United Nations, 71 Heads of State and senior policy makers from 80 other countries discussed how to improve the situation for children. The World Summit was supported by UNICEF and the World Bank as well as by WHO, FAO, UNDP, CIDA and USAID. Three of the 27 goals announced at the Summit related to the elimination or significant reduction of micronutrient deficiencies - iodine, vitamin A, and iron - by the year 2000. This has been the impetus for much of the action since that time. Agencies such as UNICEF, the World Bank, WHO and USAID were now provided a basis on which to work with governments to honor the commitments made by their leaders. There was a remarkable amount of consensus across UN agencies, governments, bilateral funding agencies and NGOs/PVOs, and the topic promoted collaboration with the private sector. The agenda also received a great deal of publicity and was easy to explain and understand. Donors and governments now had access to simpler approaches to improving nutrition in a relatively short time frame and with less dependence on political change. The multi-sectoral nutrition planning approach popular in the previous decade had largely failed to mobilize other health and development sectors for nutrition purposes. Now the nutrition community was more interested in carrying out its own programs without inter-sectoral collaboration.

Related meetings soon followed the World Summit, including the Conference on "Ending Hidden Hunger" in Montreal in 1991. The meeting was convened by UNICEF and WHO with support from FAO, UNDP, the World Bank, USAID and CIDA. It was attended by more than 300 people - ministers, scientists and policy-makers - and over 50 representatives of intergovernmental, bilateral and non-government agencies. The main purpose was to discuss ways to succeed in the micronutrient agenda. Attendees agreed on the formation of the Micronutrient Initiative (MI) which would focus on addressing gaps and constraints in program implementation. The MI started in 1993 with initial support from Canada, and has since provided a strong impetus to the development of national programs integrating fortification and supplementation, and improving dietary quality.

In 1992, at the FAO/WHO International Conference on Nutrition (ICN), representatives of 159 countries reaffirmed the goals of the World Summit for Children and pledged to eliminate iodine and vitamin A deficiencies by the Year 2000. Following this conference UNICEF and WHO organized a series of consultations with scientists to establish indicators and assessment methods that would enable countries to assess the prevalence of these deficiencies and progress towards their elimination. UNICEF was also a leader in setting the Mid-Decade Goals, which were process-oriented targets to be achieved by 1995. These included iodization of all salt where iodine deficiency is a public health problem, and ensuring that at least 80% of all children under 2 years of age receive adequate vitamin A through a combination of breast-feeding, dietary improvement, fortification and supplementation. Together with WHO, bilateral agencies and NGOs, UNICEF offered national institutions and governments major assistance with training, field work, improving laboratory capacity and disseminating data on the prevalence of iodine and vitamin A deficiency (Alnwick 1998). Iron deficiency control was not included as a Mid-Decade Goal.

The World Bank's 1993 World Development Report provided data on the cost-effectiveness of supplementation and fortification with iron, iodine and vitamin. As a follow-up to these estimates, its publication "Enriching Lives" (World Bank, 1994), was important in showing that micronutrient interventions are among the most cost-effective for improving human capital. This perspective fit well with the Bank's concept of DALYs (disability-adjusted life-year gained) and helped their nutrition group to compete for resources. In "Enriching Lives" the statement was made that although the World Bank had not formerly been a major donor of micronutrients, recent investments in salt iodization, inclusion of micronutrients in basic health packages, and nutritional social marketing, had created a niche for micronutrient activities within the bank. It was perceived that attention to micronutrients attracted political support and effected cross-sectoral policy reforms, and that fortification strategies helped to build bridges between private and public sectors. The aim was to include a micronutrient intervention in every Bank project where micronutrient malnutrition exists. The extent to which this stated aim has been achieved is unclear; the 1998 Update on World Bank Lending for Nutrition specifically mentions micronutrient activities as being part of nutrition program projects in 7 countries. The Bank has also supported efforts to understand how behavior change can improve acceptance of supplements and food-based strategies, and has made large investments in IDD elimination in China and Indonesia. In addition, a sizable proportion of Bank-supported Maternal-Child Health programs and other health delivery projects include iron-folic acid, and often vitamin A, supplements.

Other organizations have also been important supporters of investment in micronutrient programs. USAID lent considerable impetus through its VITAL program, and then through its Opportunities in Micronutrients Initiative (OMNI). The latter provided both direct programmatic assistance and support for a research agenda. The agenda evolved in part through the input and participation of nutrition scientists from academia and the food industry. OMNI has now been replaced by MOST which has a more programmatic emphasis. USAID also funded the intervention trials that demonstrated the reduction in child morbidity and maternal mortality that resulted from vitamin A supplementation. Sommer and others were instrumental in obtaining the long-term Congressional support for vitamin A research. Helen Keller International has been an important participant especially in the reduction of vitamin A deficiency. The Program Against Micronutrient Malnutrition provides expertise and training to developing countries, especially for the eradication of iodine deficiency. WHO has been particularly supportive in setting criteria for the definition of these micronutrient deficiencies, indicators for their assessment and monitoring, and recommended levels of fortification and supplementation, as well as delivering vitamin A through the Expanded Program on Immunization (EPI). The ACC/SCN's Reports on the World Nutrition Situation, first published in 1987, document regional prevalences of anemia, iodine and vitamin A deficiency.

Over the past decade investment in micronutrient programs has reaped tremendous benefits, reinforcing activities and financial support to end hidden hunger. The global campaign to iodize all edible salt in the world has had spectacular success in reducing IDD, and improving the survival, mental and physical development of millions of children. About 70% of all salt is now iodized. There were virtually no large-scale programs to reduce vitamin A or iron deficiency at the start of this decade. Now about half the countries in the world have vitamin A programs with a high coverage of young children and women, and major benefits for survival and reduced mortality have been demonstrated. While solutions for reducing iron deficiency and anemia have been more difficult to find, iron fortification of staple foods and condiments is now accepted as a cornerstone and is being undertaken as a part of many national programs. Until relatively recently the term "micronutrients" was rarely used outside of academia. Now the importance of micronutrients is widely recognized across the world and the elimination of deficiencies regarded as generally feasible by many organizations, planners and governments.

#### a) Iodine deficiency disorders

UNICEF recognized the importance of iodine deficiency and promoted the use of iodized salt from its earliest days. During the 1960s it provided iodization equipment and consultants. However, the impact of these efforts was minor.

The first PAHO meeting on iodine deficiency and mental function was held in 1969. Stanbury, Bautista and others demonstrated in Bolivia and other locations that iodine deficiency was associated with mental delays (Stanbury, 1969). In the late 1970s the long-recognized fact that iodine deficiency resulted in goiter and cretinism was modified to recognize that there is a spectrum of iodine deficiency disorders (IDD). IDD were shown to

encompass a range of compromised physical and mental deficits from severe manifestations to subtle ones that affect many more millions of people (Hetzel, 1983). It had become evident from the work of Hetzel, Ma, Pharoah and others that correction of IDD (in earlier research, by iodized oil injections), could improve the productivity, cognitive and motor performance, and general development of entire communities. This was the vision that was recognized at the formation of the International Coordinating Committee on Iodine Deficiency Disorders (ICCIDD) in Kathmandu in 1986.

The formation of the ICCIDD, and the higher estimates of the number of people affected by IDD, were critical to focusing attention on the elimination of IDD. Basil Hetzel, with guidance and support from Rolf Carriere, a senior Program Officer in UNICEF in the South Asia office, brought together a group of nutritionists, endocrinologists, epidemiologists, salt technologists, communicators and economists to publicize the problem and the cost effective solution of salt iodization. Basil Hetzel's enthusiasm and force of personality is considered to be a key factor in the success of ICCIDD. Other important participants in the ICCIDD include J. Stanbury, J. Dunn, C. Pandav, V. Ramalingaswami, T. Ma, F. Delange, and C. Thilly. The ICCIDD is supported by UNICEF and The World Bank, as well as AusAID, CIDA, the MI, the Netherlands Ministry for Development Cooperation, the Swedish International Development Agency, USAID, WHO and others.

It had been known since the early 1920s that salt iodization would prevent IDD, and the technology had been used and applied in several industrialized countries since that time. In the 1950s salt iodization technology was transferred to developing countries but essentially failed because the salt industry was not organized into large processing units. Today salt production in many countries still occurs in small coastal enterprises. Even where it was not such a problem, countries such as Peru, for example, had a law that mandated salt iodization from 1969 but there was virtually no enforcement of this regulation.

By the early 1980s so little benefit had occurred that many experts were unwilling to invest further in salt iodization as a serious option for eliminating iodine deficiency. In the mid-1980s, Hetzel and others approached Venkatesh Mannar who became a major participant in the global effort to reduce IDD by salt iodization. His belief was that the salt industry had not been informed of the significance of salt iodization and therefore the failure of iodization was largely due to the industry's lack of motivation. He proposed a systematic study of the salt industry in many countries - including locations of producers and distribution and consumption of the product - to serve as the basis of country plans for iodization. Other important recommendations were that governments should make iodization of salt mandatory and that they should conduct public awareness campaigns on the importance of using iodized salt. Producers were to be provided with technical assistance and support, and advised of the importance of iodization. In 1988 the ACC/SCN and the ICCIDD collaborated on the influential report "The prevention and control of iodine deficiency disorders" (Hetzel, 1988).

While UNICEF had been an important player in the 1985 Kathmandu meeting, and had supported the formation of the ICCIDD, it subsequently became much more seriously committed to salt iodization a few years later. In 1987 Hetzel, Stanbury and Mannar met with James Grant to brief him on the ICCIDD's goals and the probable success that could be

obtained with salt iodization. In 1990 the UNICEF Executive Board adopted the virtual elimination of IDD as a goal for the year 2000 and Grant included this in UNICEF's goals for the World Summit for Children. Since then UNICEF has been a strong advocate and supporter of national programs to eliminate IDD. Grant's leadership in these endeavors is widely-recognized as having been a crucial factor. In 1994 Kiwanis International were convinced by Alnwick at UNICEF, Mannar and others to make IDD elimination their global service project. To date Kiwanis has contributed about \$35 million to support national IDD elimination programs through UNICEF.

One of the first countries to receive UNICEF support for IDD elimination was Bhutan, where the plan was implemented in 1984-5. By 1990, encouraged by evidence that the prevalence of IDD in Bhutan was declining rapidly, UNICEF started to improve iodization programs in India, Bangladesh and Nepal, followed soon after by Indonesia, Thailand, Burma, Vietnam, the Philippines, Laos and China. The World Bank has made a large investment in salt iodization in China, based in part on a UNICEF-funded study by Mannar that documented the extent of the deficiency problem in that country. In 1993, in the Great Hall of the People and in the presence of representatives of UNICEF and the World Bank, the Premier of China announced that his nation promised to eradicate IDD by the end of this century. This meeting marked the first major commitment of the World Bank to eradicating IDD. It has since made a major investment in IDD control in Indonesia. AusAID is also especially supportive of efforts to end IDD in China. WHO has helped to increase awareness of IDD and to achieve scientific consensus on standards for levels of salt iodization, administration of iodized oil in pregnancy, and indicators for evaluating and monitoring iodine status.

There has also been a major reduction in IDD in Latin America, especially in Bolivia, Ecuador and Peru which were among the world's most afflicted nations in the mid 1980s but where new cases of cretinism are now rare. In Africa iodization efforts are relatively new but 37 countries have mapped their iodine deficiency prevalence and have a salt iodization program.

By the mid-1990s there was already considerable progress toward ending IDD, described in the influential ICCIDD book "S.O.S. for a Billion" (Hetzel & Pandav, 1994). Evidence of the progress that has taken place over the past 8 years includes: over 50% of the world now has access to iodized salt and in many countries practically all salt is iodized; over 12 million cases of mental retardation in infants are being prevented annually; more than 90 governments include funds for IDD elimination in their national budget; and public and private investment in the iodized salt industry amounts to billions of dollars. One side-benefit of the wide-scale success of efforts to eliminate IDD is the increased confidence that other micronutrient deficiencies might also be eliminated if sufficient effort is brought to bear on the problem. However, it is perhaps true that it is easier to eliminate IDD than it is the other micronutrient deficiencies.

There has been a recent move to accept approaches other than universal salt iodization for resolving IDD. These include iodization of drinking water (Thailand and Malaysia), and of irrigation water (in China, thereby benefitting crop and animal production as well as human health).

## b) Vitamin A deficiency

It has long been recognized that vitamin A deficiency causes blindness. Based in part on a resolution by the World Health Assembly to give high priority to vitamin A deficiency control and at the request of the SCN, DeMaeyer of WHO presented a 10-year plan on the control of vitamin A deficiency at their 1985 meeting in Nairobi. The plan summarized the prevalence and importance of the problem and described programs in Indonesia and India that were successful and appeared feasible to expand to other countries. WHO accepted the responsibility of being the lead organization for forwarding this plan to the ACC and for its implementation. Two years later, when there had been little progress toward implementation, West and Sommer conducted a review for the ACC/SCN on the feasibility of oral doses of vitamin A to reduce blindness (West & Sommer, 1987). However, WHO at that time stated that it was unable to support a Geneva-based focus on the elimination of vitamin A and that it had delegated this responsibility to its regional offices. The SCN continued to have a working group on vitamin A that reported on key developments in the area.

While some individuals, including Barbara Underwood and Guillermo Arroyave, had long argued that subclinical vitamin A deficiency must have detrimental effects on health, it was not until it was demonstrated that vitamin A supplementation reduced mortality and morbidity that agencies became seriously involved with reducing vitamin A deficiency. The landmark initial project in this regard was that by Sommer et al., who showed in a USAID-funded project that vitamin A supplementation of Indonesian children reduced child mortality substantially. A series of studies on mortality then followed in different countries, culminating in the meta-analysis by Beaton and Martorell that was published in 1993. This meta-analysis, encouraged by the ACC's Advisory Group on Nutrition (AGN) and the SCN, and supported by the Canadian International Development Authority (CIDA), showed that vitamin A reduced mortality from measles by an average of 23% (Beaton et al., 1993). In 1992 a consensus on the prevention of mortality by oral vitamin A was reached in the Bellagio Brief organized by Helen Keller International (Sommer, 1992).

This key finding reduced concerns about the apparent inconsistencies in results among trials and brought further impetus to UNICEF and other agencies to move forward to program implementation. UNICEF has provided the major programmatic thrust supported by funding and technical support by CIDA through the MI. Ernest Loevinsohn, the Director of CIDA, is very committed to the elimination of vitamin A deficiency and is key to the continued priority of vitamin A interventions within CIDA. The distribution of vitamin A supplements (to 300 million children in the past 5 years) has been facilitated greatly by UNICEF and WHO's efforts to provide the supplements with immunizations (WHO's Expanded Program on Immunization) on National Immunization Days. Underwood's term at WHO was important in moving forward the delivery of vitamin A through the EPI.

Sommer also had a major influence through his successful lobbying of the US Congress, which generated funds for continuing research on the efficacy of interventions. Through these funds USAID provides major support for vitamin A research, and its long-term commitment to major field trials continues to produce evidence of the value of vitamin A supplementation.

For example, the recent report by West et al. suggesting that early (preconception) vitamin A or B-carotene supplementation reduces maternal mortality supports the need to refocus our attention to the nutritional status of pregnant women. Planned trials by the Johns Hopkins group in Bangladesh and by Helen Keller International in Indonesia will provide more information on the benefits of supplementation with vitamin A, and other micronutrients, in pregnancy. Helen Keller International has been the main NGO involved in reducing vitamin A deficiency, primarily through dietary interventions including gardening.

The International Vitamin A Consultative Group, backed by USAID, has played a key role in furthering and presenting the science behind the effects of vitamin A deficiency and the impact of interventions. Martin Forman of USAID was an important supporter of IVACG and an influential advocate for micronutrient programs. The IVACG meetings gained substantial attention starting in the mid-1980s. Until then they were relatively small meetings predominantly focussed on research and methods for assessment of vitamin A status, although the early meetings provided crucial documentation on how to proceed from a scientific base to policy and programs. Today the IVACG meetings are major events that bring together scientists, agencies and individuals involved with programs and policies, help to provide strong technical leadership and to focus some of the best public nutritionists on this issue. IVACG's many publications have provided useful programmatic information to program planners and managers. The 1999 theme of IVACG's meeting was the interaction of vitamin A with other micronutrients, recognizing the often-overlooked fact that vitamin A deficiency does not occur in isolation.

In 1995 the MI and PAMM convened the Ottawa Forum on Public-Private Partnerships to pull in private partnerships to support micronutrient activities, including vitamin A. UNICEF and other partners including the MI and the International Sugar Organization are actively promoting the fortification of sugar in Africa and Asia. Other vitamin A-fortified foods have been developed by the food industry, including Star margarine in the Philippines. A joint global advocacy group has been formed between UNICEF, CIDA, USAID, Johns Hopkins University, WHO, the MI and others.

There is substantial potential for vitamin A deficiency to be eliminated by dietary intervention strategies. The World Bank supported a food-based program to control vitamin A deficiency in Indonesia, which was successfully implemented on a large scale by Marcia Griffiths. Underwood has been a champion of this approach, raising the important issue of the extent to which the current focus on micronutrient interventions adversely impacts the desire and ability of countries to mount support for dietary approaches. Other prominent supporters of a non-capsule, dietary approach include Reddy and Gopalan in India. West and de Pee have raised the important question of the bioavailability of provitamin A from some plant sources; it had previously been assumed that the promotion of any carotene-rich foods could be effective at reducing vitamin A deficiency. There seems to be an emerging consensus that fruits are a better source of absorbable carotene than many vegetables, and that there is still considerable potential to invest in effective dietary approaches to prevent vitamin A deficiency.

USAID continues to make vitamin A a strong priority, predominantly through its support for research. CIDA has contributed over \$100 million for vitamin A programs through the MI. UNICEF has made support of national vitamin A programs, and their integration with other health programs, a priority. The integration of vitamin A delivery with the EPI, based at WHO, has created an additional opportunity in recent years but this may soon be impacted by the phasing out of polio vaccinations.

A UNICEF/MI/USAID meeting in New York, November 1997, identified some key ideas for the reduction of VAD in the future:

- The promotion of vitamin A sufficiency as a vital child health and survival issue
- Until dietary interventions are in place, success with supplementation and the integration of capsule delivery with immunizations can make these strategies acceptable to cover children under 5 years and women postpartum.
- There will be an increased emphasis on vitamin A fortification of staple foods such as oils and fats, flour, milk and dairy products. At least 30-40 countries can have national vitamin A fortification programs over the next 5-10 years.
- Dietary approaches should be expanded to include eggs, red palm oil and other foods in addition to fruits and vegetables.

Possible interactions between vitamin A status and HIV, and malaria, may influence future investments in the prevention of vitamin A deficiency. There is a perceived need to pay more attention to the assessment and prevention of vitamin A deficiency in Africa, where information on the prevalence of subclinical deficiency is still limited.

#### c) Iron deficiency

In the 1960s, M.S. Read, then head of the Nutrition Section at NICHD, started a series of conferences on undernutrition and its consequences for children. At the second of these, sponsored jointly by NICHD and PAHO in Puerto Rico in 1970, the first evidence was presented of a link between anemia and mental performance (Sulzer et al., 1973). The study was conducted in low income Head Start children in the USA. In 1974 Pollitt and Leibel published "Iron Deficiency and Behavior", the first comprehensive review of the potential mechanisms by which anemia and iron deficiency might affect behavior. This was soon followed by several studies showing that iron supplements improved motor and mental development, and school performance of anemic infants and children. Notable investigators in this arena include Aukett, Oski, Pollitt, Lozoff and Walter (Pollitt et al., 1989; Nokes et al., 1998).

Compared to the major investments in control of IDD and vitamin A deficiency following the reports of their impacts on human function, these earlier demonstrations of the functional effects of iron deficiency anemia attracted relatively little attention. Reflecting on the reasons for this, one investigator in this area felt that with notable exceptions, research on iron

deficiency and development has been dominated by nutritionists and biochemists who have had relatively little training or experience in child development or psychology. For example, although the Bayley Motor and Mental Scales are often used to assess the impact of iron deficiency on infant and young child development, they may not be the best tools for this purpose. Perhaps the adverse impact of iron deficiency anemia on development has been relatively ignored because the assessment tools have been too simple. It is frightening to reflect that in many respects they are a carbon copy of tools formerly used in research on the effects of protein deficiency on development.

In the early 1970s there was also a flurry of research on the effects of anemia on productivity. Anderson in 1970, and Edgerton in 1972, reported relationships between iron deficiency anemia and physical performance (Edgerton et al., 1972). In a 1975 World Bank publication Basta & Churchill described the adverse effects of iron deficiency anemia on the productivity of adult males in Indonesia. In 1979 Basta et al. reported the improved work performance of anemic Indonesian tea pickers after iron supplementation (Basta et al., 1979). This report was influential to the extent that Scrimshaw, a co-author, could use it to advocate investments in research and action on iron deficiency. In addition, Basta's work formed the basis of a system that delivered iron to 10,000 plantation workers in the World Bank's first Indonesian project. An expanded version of this program still continues without external support. In 1985 Levin authored an important World Bank paper showing the favorable benefit:cost ratio for anemia reduction.

Although we have known about the adverse effects of iron deficiency anemia on human function since the early 1970s, and iron is the most prevalent micronutrient deficiency, relatively little progress has been made towards its control. DeMaeyer at WHO was responsible for several of the earlier collaborative efforts to deal with the anemia problem. The World Summit set the goal of reducing anemia by only one third, a target that was subsequently excluded in the Mid-Decade Goals. For several reasons iron deficiency is perceived as being more difficult to eliminate. These include: iron supplements have to be taken daily or at least weekly, causing difficulties in supply, compliance, and increased dependence on the health system; fortification has been problematic in some respects; there is uncertainty about appropriate doses, side-effects, and the consequences of mild anemia; and there are some problems with iron status indicators. Importantly, the benefits from iron supplementation are less obvious to recipients, governments and donors than benefits from iodine and vitamin A interventions.

Concern is increasing about the fact that traditional programs for the daily supplementation of pregnant women with iron have not been very effective in reducing the prevalence of anemia. To a certain extent this reflects the predictable lack of response of anemia that is caused by factors other than iron deficiency (such as malaria, helminth infections and other micronutrient deficiencies), and the very high iron demands of pregnancy. However, there is general agreement that the major problem lies with non-delivery of supplements, poor compliance and other program-related obstacles (Gillespie et al., 1991; MI/UNICEF, 1998). In recognition of this problem, in late 1998 a consensus meeting was held at UNICEF and sponsored by UNU, UNICEF, WHO and the MI (UNICEF/UNU/WHO/MI, 1999). The purpose of this meeting was to reach consensus on issues that can accelerate and expand

national programs for the prevention of iron deficiency. The conclusion of the participants was that there are available, sustainable and affordable interventions to reduce the prevalence of iron deficiency and anemia in developing countries, and that a stronger, better-focused commitment is needed to ensure that they are implemented.

The fact that weekly supplementation with iron can be effective for improving iron status, especially in situations where delivery is supervised, offers a new option for programs to reduce iron deficiency. Since the early 1990s a series of field studies on the efficacy of weekly supplementation has been spear-headed by Viteri and Scrimshaw with support from the UNU, WHO, UNICEF, IDRC and the MI. A recent MI-supported meta-analysis compared the efficacy and effectiveness of the daily and weekly trials (Beaton & McCabe, 1999). The analysis showed that daily supplementation is more effective for reducing anemia, especially in pregnancy when iron requirements are high and the window for intervention is short. However, weekly supplementation in other age groups produced encouraging results. It is likely that the total amount of iron consumed over time is the most important predictor of hemoglobin response and that the frequency of consumption is less critical. Weekly supplementation may provide a programmatic approach that could be highly effective in schools, for example. The MI, together with WHO, UNICEF and PAHO, sponsored a recent meeting on the implications of daily and weekly supplementation programs for program planners. The "daily or weekly" debate has stimulated much-needed research and discussion about the prevention and treatment of iron deficiency.

There are relatively few food-based opportunities for improving iron status, because plants have a low content of absorbable iron. A USAID-funded review of this situation showed that in addition to the need for a more rational approach to iron fortification of staple foods and condiments, other opportunities include the development of cereals and legumes low in phytate and high in iron (as heme or ferritin), increased production and consumption of small animals, and fermentation of cereals or legumes to reduce phytate content (especially for complementary feeding) (Allen & Ahluwalia, 1996). USAID's INACG (International Nutritional Anemias Consultative Group) organized some of the first work that investigated the qualities of Fe-EDTA as an iron fortificant, and now ILSI and the MI are promoting this Fe-EDTA because it is not bound by dietary phytate. Many of these food-based approaches would also improve the intake or absorption of other minerals, notably zinc. Iron-fortified salt could lower the prevalence of iron deficiency, and this strategy was initiated by USAID in India in the late 1960s. However, this approach conflicts with salt iodization because the presence of iron makes the iodine less stable. For example, the World Bank was encouraging iron fortification of salt in India, after trials by the National Institute of Nutrition. However, UNICEF persuaded the government to focus only on iodized salt. A long-awaited "double fortified" (iodine and iron) salt has now been developed through the support of the MI, and although the mix of fortificants is more stable in relatively pure salt this strategy could provide another way to control iron deficiency.

There is a need for further promotion of the evidence that iron deficiency and anemia have adverse consequences for human capital and economic development. At the recent INACG meeting in S. Africa (held for one day at the end of the IVACG meetings and well attended), it became apparent that many members of the audience were not aware of the functional

consequences of iron deficiency anemia, or felt that they were irreversible. A conference on this topic is planned in 2000. Investment in the treatment and prevention of anemia is highly cost effective (MI/UNICEF, 1998). In many countries there is still a lack of good information on the prevalence and distribution of iron deficiency/anemia, its cause, and the extent to which benefits can be obtained from iron supplementation or iron fortification programs. There are almost no repeated surveys to show trends in prevalence. As mentioned above, there is an urgent need to understand how daily or weekly supplementation programs can be made more effective. Cut-offs for hemoglobin and other iron status indicators certainly need revision, especially for infants, young children and pregnant women. A recent (May, 2000) WHO/INACG meeting on this topic concluded that there is a need for more research on the association between iron deficiency anemia and risk of functional impairment, especially in mild anemia.

In 2001 there are plans for a major international conference on effective strategies to combat iron deficiency. This is a welcome event given that only the UNU and The World Bank seem to have targeted control of iron deficiency as their micronutrient priority. The relative inactivity of INACG until recently has been unfortunate. In part this situation resulted from the general perception that there was a lack of effective programmatic strategies to control iron deficiency. We have lacked charismatic entrepreneurs and advocates for the control of iron deficiency. Opportunities for scientists, agencies and governments to work together to solve the programmatic obstacles are needed urgently. Many of these obstacles are the same as those that will jeopardize the effectiveness of other nutrient supplements that need to be delivered daily or weekly.

#### **4. The current situation and implications for the future**

We should have learned long ago about the complexity of the undernutrition problem. It is rarely caused by a single nutrient deficiency, with the possible exception of iodine. In most areas of the world it is highly improbable that undernutrition can be treated by providing a single nutrient. Yet the present focus is on the efficacy of single nutrient interventions, popularized by the success of vitamin A capsule interventions and salt iodization.

Despite clear evidence (from Bangladesh, India, Indonesia, and Viet Nam, for example) that food-based approaches can work to reduce vitamin A deficiency, virtually all agencies have down-played support for this approach and made supplementation and fortification their major emphasis. FAO is ideologically committed to a food-based approach, as are HKI and WHO although perhaps less strongly. Some informants interviewed believe that the focus on supplementation has diverted our attention away from dietary approaches to preventing micronutrient malnutrition, and that we must pay more attention to improving dietary quality and diversity if such deficiencies are to be prevented in the longer-term. Supplementation is a "top-down" intervention developed in First World contexts and often requires dependency on nutrients manufactured and supplied by industrialized countries. It has been suggested that "while ... micronutrient (and breast-feeding) activities are unquestionably important, the present unbalanced preoccupation with them may have the effect of signaling a reduced commitment to the major needs of calorie deficient populations and, in turn, may risk moving nutrition back to the periphery of the development process" (Levinson & McLachlan, 1999).

Supplementation can be another version of "nutrition isolationism" if not well integrated with other sectors.

Considerable concern was voiced that massive campaigns for supplementation with single micronutrients are unsustainable. In the case of vitamin A the proposed discontinuation of polio vaccinations in the near future will reduce the opportunity to distribute capsules through the EPI. Micronutrient supplements cannot be targeted to everyone who needs them. In the case of iron, for example, the majority of infants, children, adolescents and all women of childbearing age may benefit from interventions to reduce the prevalence of this deficiency. To some extent this is also true of vitamin A, because vitamin A capsules are targeted only to children less than 5 years of age and postpartum women. A renewed emphasis on identifying and quantifying the social benefits of food-based approaches might be helpful. Genetic selection and engineering have tremendous potential to increase the vitamin A and iron content of staple foods. The efficacy of high-iron varieties for improving iron status must be tested in fairly long intervention trials; there is concern about whether the iron is bioavailable, and whether the content is high enough to really reduce anemia. In general, the implications of introducing these strategies into developing countries and their coordination with other approaches to micronutrient deficiency control merit considerable discussion. The World Bank and USAID (through its Global Livestock CRSP) have made investments in improved animal production, one stated purpose of which is to increase consumption of bioavailable micronutrients. This strategy can provide multiple benefits and deserves more attention.

So far, investment has been almost exclusively in the control of iodine, vitamin A and iron deficiencies. These deficiencies are indeed highly prevalent, and particularly in the case of iodine and vitamin A, their adverse consequences (and therefore the benefits of their eradication) are clear. What is the strategy to be for other nutrient deficiencies as they begin to be recognized? For example, while there has been considerable and justifiable interest in zinc deficiency, for both ethical and practical reasons it is now very unlikely that programs would ever be mounted as a stand-alone zinc intervention. Is it then appropriate to make large investments in research on the benefits of zinc supplements?

There is currently a move toward formulation, testing and programmatic interventions with multiple micronutrients. On one hand this makes eminent sense given the poorly-understood co-existence of multiple micronutrient deficiencies in many, if not most, situations. These supplements are likely to include at least zinc, riboflavin, vitamin B-12, vitamin D in some regions, and other nutrients for which the prevalence of deficiency is still uncertain. It has been pointed out that "past interventions have focused on single micronutrients, thus missing opportunities to coordinate and leverage scarce human and financial resources across funding agencies and the programs they conduct" (Institute of Medicine, 1998). Nevertheless, the additional benefits (including functional outcomes) of this strategy compared to iron-folate supplements need to be demonstrated. For example, there is not one published report that compares the efficacy of multiple micronutrients for reducing anemia to that of iron-folate alone. Before either iron or multiple micronutrient supplementation can be successful there is clearly a need to invest in operational research, and to find ways to improve the delivery and consumption of supplements that need to be taken at least several times a week. Our experience with iron supplementation provides many examples of the problems that will be

encountered with multiple micronutrient supplementation, although a multiple micronutrient strategy may have cost-effectiveness and advocacy advantages over providing just iron-folate. Another concern is how to coordinate micronutrient intervention programs. For example, some infants and preschoolers might be presented with cereals fortified with one or more micronutrients, improved complementary foods, a multiple micronutrient mix that can be added to these foods by the mother, vitamin A capsules, fortified salt and sugar, and daily or weekly multiple micronutrient supplements. In the case of iodine and vitamin A deficiency control there is a relatively unified agency approach to the problem. It would be highly desirable to pursue a similar unified approach to the question of how to deal with multiple micronutrient deficiencies.

Dietary approaches (and for some nutrients, fortification) are currently the only way to meet the micronutrient requirements of a large percent of the world's population. Lip service is paid to the fact that supplements are intended to fill the short-term need, while the diet gradually improves through education, a better economic situation and fortification. There is a need to define a complementary strategy that identifies how this long-term need for micronutrients will be filled for different population groups, using a mix of programmatic interventions. The responsibilities of the private sector and governments in these activities need to be appraised. Major challenges include making the elimination of micronutrient deficiencies more consumer-driven, and supporting appropriate behavior change.

Although micronutrient control has had remarkable success, it is inevitable that many other nutrition problems need to be tackled. The problem of low birthweight is unlikely to be solved with micronutrients, although much-needed trials are underway to assess the benefits of micronutrients for pregnant women. We still do not understand the causes of poor pregnancy outcomes such as low birth weight, or how best to prevent them. Clearly more attention needs to be paid to improving the pre-conceptional nutritional status of women. Hunger, stunting, anemia and delayed development in young children are still rampant, and have hardly improved at all. We do not know how to prevent growth stunting. Although we believe that stunting is in part a consequence of micronutrient deficiencies rather than energy deficiency (or PEM), we cannot say to what extent this is true in different regions. There have been remarkably few demonstrated benefits of either food-based or micronutrient interventions during the period of complementary feeding.

Obviously we need integrated programs that pay attention to micronutrient deficiencies while providing for the other nutrient needs of children and their mothers and reducing the nutritional impact of the many deprivations that they face. One viewpoint is that "the attention of the nutrition community and the resources of donors are more attracted by the glamour of micronutrients, a largely technical and often top-down solution (as close to a quick fix bullet as we are likely to get in this field), than by the politically sensitive business of poverty alleviation, people's empowerment, and equity, necessary to ensure that mothers and children have access to health and educational services and adequate food to eat" (Schuftan et al., 1998). There is sentiment that the nutrition goals and programs of some countries have become too narrowly focussed on the alleviation of one or more micronutrient deficiencies while other problems are being neglected. This concern is likely to be voiced more often as we move beyond the micronutrient goals that were set for the Year 2000. It is certainly timely

to discuss the complementarities and contradictions of focussing on a micronutrient agenda with more holistic approaches to addressing malnutrition. The micronutrient focus has provided an unprecedented opportunity for collaboration among agencies, scientists, governments and the food industry. Importantly, it has provided powerful examples of the improvement in the global nutrition situation that can be achieved when partners combine their expertise and efforts. It is hoped that active decisions will be taken to ensure the continuation of this collaboration, both for the control of micronutrient deficiencies as well as in other approaches to reducing malnutrition.

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