Food Fortification as a Public Health Strategy

Food industries add vitamins and minerals to the products they manufacture for several reasons: to bring back the micronutrients that are lost during production (restoration), to imitate the nutritional value of natural products that are replaced (equivalence), and to incorporate nutrients that are absent or present in lower amounts in the natural ingredients (enrichment). In all such cases, the end results are fortified foods. Read more on p. 6
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Locally Produced Ready-to-Use Food (RUF)
RUFs are a recent addition to the toolbox in the fight against malnutrition, revolutionizing the treatment and care of severe and moderate acute malnutrition.

Monitoring Anemia-Control Programs
As iron deficiency affects all populations of the world irrespective of race, culture or ethnic background, it is important that iron status is correctly monitored and the effects of iron treatment correctly interpreted.

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Welcome

Social Innovation not only for Economic Recovery, but also for Combating Hidden Hunger and Poverty

As the world struggles to come to grips with the realities of a global recession led by the most progressive economic democracies, influential thinkers and policy makers have started to look upon the idea of social innovation as a new guiding principle for economic recovery efforts.

In the United States, the Obama Administration has created an Office of Social Innovation in the White House. The Organization for Economic Cooperation and Development (OECD), meanwhile, has had a Forum on Social Innovations under its Local Economic and Employment Development (LEED) program since 2000.

According to the working definition used by the OECD framework, “[social innovation] can concern conceptual, process or product change, organizational change and changes with stakeholders and territories.” It goes on to state that social innovation seeks new answers to social problems by identifying and delivering new services, processes, competencies, jobs, and forms of participation that improve the quality of life of individuals and communities. Social innovation is distinguished from economic innovation because “it is not about introducing new types of production or exploiting new markets in itself but about satisfying new needs not provided by the market (even if markets intervene later) or creating new, more satisfactory ways...of giving people a place and a role in production.”

SIGHT AND LIFE’s fight against micronutrient deficiencies over the last 22 years originated under a charitable mindset, characterized by the fact that no financial returns to the giver are calculated to justify the giving. Indeed, in many areas of assistance, charity remains the dominant motivation simply because the moral case is overwhelming, and the calculation and extraction of tangible returns for the provision of often critically needed resources to population groups deemed incapable of paying for those resources would be considered unethical.

Nonetheless, charity alone cannot create sustainable solutions to complex health and social problems, whose roots are embedded within equilibrious but inequitable distribution systems and economic infrastructure that need a major ‘re-invention.’ While charity has a place in providing short- to medium-term relief to under- or unserved populations – and SIGHT AND LIFE will continue to support charitable efforts as we have done for over two decades – we do support efforts to foster social innovation approaches that result in lasting public, private and community partnerships to create new and sustained ways of solving social problems and meeting social needs – particularly in addressing the global crisis of hidden hunger and its consequences, including nutritional anemia and the double burden of malnutrition.

As a knowledge-creating and knowledge-diffusing platform in the field of micronutrient deficiencies and programmatic solutions to these, SIGHT AND LIFE seeks to increase its role in helping to develop social innovations that deliver on our mission as a philanthropic initiative. As a start, since 2007, we have actively initiated, built on and expanded partnership activities between our parent company, DSM, its Nutrition Improvement Program, and the United Nations World Food Programme (WFP) aimed at developing, producing and distributing new and more effective multiple micronutrient product formulations targeted to population groups at the bottom of the socioeconomic pyramid. In the near future, we also intend to promote pilot- or small-scale social innovations in the projects we assist through new grant-making and donation-giving policies.

In a world facing the greatest recession in recent history as well as unbridled urbanization and ‘modern’ lifestyles that amplify the frightening consequences of an unhealthy lifestyle and diet, we clearly need to invest in the most effective strategies in the fight against malnutrition and poverty. That includes both charity-driven approaches that bridge resource gaps and meet urgent needs in the short- and medium-terms, as well as social innovation approaches that
allow cost reductions and long-term sustainability in the production and distribution of public goods and services.

If our editorial on social innovation has sparked your interest, we recommend the enclosed SIGHT AND LIFE Annual Report 2008 for further reading, which features this as emerging topic as its theme.

This edition of the Magazine also includes a contribution on Food Fortification as a Public Health Strategy, aptly prepared by our long-term correspondent Omar Dary (p. 6). Among other strategies, such as dietary improvement and supplementation, food fortification plays an important role as a public health intervention to close nutritional gaps in essential micronutrients.

In her paper on the Role of Micronutrients in the Developmental Origins of Health and Disease, Christine Stewart reviews the effects of maternal micronutrient status on risk factors for chronic disease and poses questions for further research (p. 16).

Veronika Scherbaum and colleagues describe what it takes to develop and locally produce a cereal-based Ready-to-Use Food (RUF) for moderately and mildly wasted children in Indonesia (p. 29). RUFs are a recent addition to the toolbox in the fight against malnutrition, revolutionizing the treatment and care of severe and moderate acute malnutrition.

Sadly, the scientific community and public at large have lost two of our most distinguished scientists. We pay tribute to Norman I. Krinsky and John L. Beard, who made major contributions in advancing the field of micronutrients. Norman Krinsky led carotenoid and vitamin A research to unexplored heights (p. 50) and without John Beard, our knowledge of iron in the brain and neurobehavioral function would still be significantly shallower (p. 54).

For this edition of the Magazine, our Day in the Life feature meets the SIGHT AND LIFE team in Kaiseraugst, which has grown recently (p. 56). Our recent ‘addition,’ Jee Rah, and Anne-Catherine Frey and Svenia Sayer-Ruehmann talk about their specific roles within SIGHT AND LIFE.

Last but not least, as a platform for the exchange of programmatic and scientific information, we would like the SIGHT AND LIFE Magazine to remain ever-evolving and adaptive to the new realities of the micronutrient field. We are, therefore, currently conducting a survey to gather our readers’ opinions.

We would very much appreciate it if you could participate in our reader survey, and share with us your views on the Magazine and your suggestions for ways to improve it through the short questionnaire. More information about the survey is included on p. 37.

With best regards
Food Fortification as a Public Health Strategy and the Contributions of A2Z

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Background

Food industries add vitamins and minerals to the products they manufacture for several reasons: to bring back the micronutrients that are lost during production (restoration), to imitate the nutritional value of natural products that are replaced (equivalence), and to incorporate nutrients that are absent or present in lower amounts in the natural ingredients (enrichment). In all such cases, the end results are fortified foods.

Three types of food fortification have been identified: mass (staples and condiments that are promoted by governments as public health measures), targeted (complementary foods and products aimed at specific population groups), and market-driven (a strategy of the food industry to attract consumer attention to the improved nutritional value of its products).1 The increase of micronutrient intakes through these and other nutritional interventions (e.g. supplementation) should be sufficient to complement the usual diet for attaining the required daily needs (or estimated average requirements, EAR) for most individuals of the population. However, fortification levels should be regulated so individuals of the same population are not exposed to intakes above the tolerable upper intake levels (UL). Thus, to be effective and safe, food fortification should be planned, regulated, and well supervised.

A justifiable, safe, efficacious, cost-efficient, and sustainable food fortification program requires the integrated efforts of various actors in real partnerships. These efforts are the responsibility of the research, public, private, and social sectors.

Figure 1 illustrates the various activities needed in food fortification programs. The essential and logical sequence of these activities is often not fully appreciated because this strategy is frequently promoted as the simple introduction of a fortified product or as an effort focused mainly on enacting mandatory fortification standards. Consequently, food fortification projects are often ineffective.

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<th>MAIN PLAYERS</th>
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<td>Economists, Statisticians</td>
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<td>Researchers, Statisticians, Food and Biochemical Laboratories</td>
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<td>Food Industry: Marketing Dept./Gov. Guidance</td>
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<td>Food Control from MOH and M. of Economy/Food Labs</td>
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| Implementation and Production of Fortified Food |
| Implementation and Production of Micronutrient Premixes |
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**Figure 1:** Components and players in public health food fortification programs
The steps in Figure 1 suggest that, for the good implementation of each activity, it is important to have adequate support of the instruments and actions from the prior steps. Nevertheless, a program of this type does not end when effectiveness is demonstrated. The top step becomes the base of the following cycle, because food fortification programs should be conceptualized as dynamic and under permanent evolution, responding to modifications in the dietary pattern, environmental health conditions, and advances in scientific knowledge, technology and programmatic experience. Figure 2 shows the continuous rotation of the functional components of a food fortification program.

Premises for nutritional and health impact

The impact of any food fortification program is associated with the supply of adequate amounts of bioavailable micronutrients to the target populations. Successful programs are those that: (a) provide sufficient additional intake of the required micronutrients (size of the provision) in response to (b) a nutritional gap of specific micronutrients (magnitude of the need), with the capacity to (c) reach a significant proportion of the target population (extension of the intervention, or coverage). Rarely does one fortification vehicle fill all these requirements. However, in most cases, adding micronutrients to foods will almost always satisfy some of the nutritional needs of a proportion of the population. The magnitude of an individual’s benefit depends on the dietary habits of the population, which determine both the degree of the deficiency (among other causes, the basal provision of micronutrients by the usual diet) and the potential of the fortified food to deliver an important amount of the needed micronutrient (which is a function of the consumed amount of the fortification vehicle and its micronutrient content). How the population benefits is in direct proportion to the market penetration of the fortified products. In most circumstances complementary measures should be simultaneously implemented to reach the public health goal. Thus, to make suitable programmatic combinations, a strong assessment, and monitoring and evaluation components are always essential. Research institutions should assume these roles but are generally absent in many current food fortification and nutritional intervention efforts.

Beyond the scientific basis of food fortification programs, the success depends on industries manufacturing high quality products following adequate standards that are well enforced by the government, and on consumer awareness of the product’s benefits when combined with good life habits and healthy diets.

Evidence

Several case studies of food fortification provide evidence that well-planned and managed fortification programs can help reduce micronutrient deficiencies.

Salt iodization

The results from several countries with salt iodization programs demonstrated that: 1) they can achieve high coverage; and 2) salt used at the household level can contain adequate iodine (20–40 mg/kg) to improve iodine intake (usually 150–200% EAR for the average person) at current patterns of salt consumption (5–10 g/day), to prevent goiter and other iodine deficiency disorders. Salt can continue being a good iodine-delivery vehicle even when its daily consumption should decrease in response to programs for the prevention of chronic diseases, where it is only necessary to proportionally increase the iodine content.2

Sugar fortification with vitamin A

In Central America, the coverage of vitamin A-fortified sugar is high (> 75%). The fortificant level provides, on average, > 150% of the EAR. At this level of coverage and vitamin A supply, the population intake was adequate to address vitamin A deficiency for the population aged 36 months and older. Preventive supplementation is still used for children aged 6–24 months to complete the provision and coverage of the
sugar fortification program. Nicaragua reduced the prevalence of low serum retinol in pre-school aged children through preventive supplementation and sugar fortification. Based on the actual retinol serum levels, Nicaragua can claim that vitamin A deficiency in the country is controlled.

Flour fortification with folic acid

Data from programs in Canada, Chile, Costa Rica, South Africa and the USA showed that, after flour was fortified with folic acid, the prevalence of neural tube defects plateaued at about 7–10/10,000 – a decrease of 20–85% in direct proportion to the magnitude of the prevalence at baseline. Folate intakes increased, on average, 50–200% EAR, which, in general – with the exception of Chile – is far from levels that would increase the risk of some individuals reaching current UL values. In the USA, intakes are near or above the UL values because of the simultaneous use of folic acid supplements rather than by the additional intake of folic acid received from fortified cereal flours. Therefore, if the folic acid content is chosen according to flour consumption, establishing a safe and efficacious fortification program with folic acid is possible.

As with other examples, effectiveness is closely associated to a significant increase of the micronutrient intake through fortified food consumption and its accessibility to the population at large. It is important to emphasize that the biological impact depends on the size of the micronutrient provision to individuals and the population coverage, and is not due to the simple presence of fortified foods in the market.

Food and condiment fortification with iron

Recent fortification trials suggest that it is possible to use some food vehicles to provide sufficient iron to improve iron status. The fortification of maize flour in Kenya and fish sauce in Viet Nam improved the biomarkers associated with iron status. In Cambodia, a similar effect was obtained by combining ferrous sulfate and citric acid in fish sauce. In Thailand, snacks made with wheat flour, sugar, margarine, and different types of iron were also found efficacious to improve iron-status biomarkers. In all cases, the biological impact appears to be independent of the iron type. The important fact is to supply sufficient iron, depending on the specific bioavailability of each iron compound, to provide 60–90% of the corresponding EAR. Iron compounds with good bioavailability are more likely to create efficacious programs because the iron intakes that are needed are lower and, hence, easier to incorporate into food matrices than those required for less-bioavailable iron forms.

Regrettably, the iron contents necessary for reaching good iron provisions are very difficult to attain in most flour fortification programs because of sensorial incompatibility between the iron compounds and the food matrices. In any case, iron bioavailability of the diet is the factor that most influences a successful iron fortification program.

Goal

The goal of food fortification is to increase the micronutrient intake from the diet and provide a public health benefit without the risk of excess intake. Well-designed programs will help reduce malnutrition and, in turn, improve health, lessen morbidity and decrease child mortality. The A2Z Project is committed to promoting comprehensive fortification projects that address all food fortification components. Focused on strengthening public sector capacities – usually the weakest components – A2Z emphasizes integrated monitoring and evaluation systems for all nutritional interventions so effective and sustainable public health nutrition programs are carefully designed, implemented and evaluated.

Strategy

Optimal implementation of fortification programs involves coordinating closely with research, pub-
lic, private, and consumer organizations and institutions. A2Z provides technical assistance to design and analyze policies and strategies; and develop standards, guidelines, and practical tools for quality control, enforcement, and monitoring. The project shares lessons learned and facilitates experience exchanges among countries through technical workshops and training sessions. A2Z also disseminates informational materials, including documented cases, to the international community to increase knowledge, improve programming practices, and strengthen global support for micronutrient programs.

**A2Z’s contributions in food fortification**

A2Z’s global and country activities in food fortification support and inform each other and contribute to results at both levels. A2Z has built institutional capacity to design and implement program components as summarized below.

**Science and assessment**

*A practical method to identify candidate food vehicles and formulations for mass fortification:* Precise determinations of the nutritional gap and identification of potential food fortification vehicles are commonly lacking in food fortification programs. A2Z collaborated with Emory University researchers\(^{11}\) to use the information gathered through household income and expenditure surveys to establish a practical procedure to assess the need for and the potential benefit of mass fortification. The method uses purchasing data and household composition to estimate individual food intake in terms of adult equivalents. The total amount of food purchased by the family is divided by the total energy requirement of every member of the family, expressed as proportion of the energy requirement of the adult male (i.e. the ‘adult equivalent’). Thus, for example, an adult woman represents 0.79 of the energy requirement of an adult male, and a child aged 1–3 years is 0.45 adult equivalents. The probable food intake of each member of the family is then estimated by multiplying the ‘adult equivalent intake’ for the proportion of the corresponding adult equivalent values.

The World Bank, the Inter-American Development Bank, and the Pan-American Health Organization (PAHO) are using the method in some projects. In partnership with GAIN, the World Food Programme, and Makerere University in Uganda, A2Z is validating this method against traditional food consumption surveys. A2Z plans to use the same method for other countries in East, Central, and Southern Africa (ECSA). The method was used in Cambodia to assess the potential impact and coverage of food fortification vehicles for sugar and fish sauce as described in Figure 3.

**Literature review and case studies:** The A2Z project advanced the understanding of food fortification through a published literature review of food fortification for managing nutritional anemia.\(^{16}\) Technical feasibility, cost, and experience of rice fortification in Costa Rica, China, the Philippines, and the USA were also reviewed. The rice fortification report\(^ {18} \) was prepared with the Institute of Food Technologists of the United States.

![Figure 3: Coverage and potential impact (in terms of estimated average requirement, or EAR) if sugar is fortified with vitamin A and fish sauce is fortified with iron in Cambodia. The blue segment in the pie chart shows the maximum coverage possible based on food use. The dark purple segment illustrates the proportion of consumers that use the food vehicle, but which might not be fortifiable because of production/trade conditions. The column illustrates the average additional intake of the added micronutrient for those individuals who have access to the fortified food; a food that supplies 20% EAR or more of a specific micronutrient is considered a good source of that micronutrient.](image-url)
The report has been translated into Spanish by PAHO and is now being used in rice fortification feasibility studies in Nicaragua and Panama.

National policies

**ECSA guidelines on food fortification:** A2Z supported several workshops in the ECSA region to establish common policies for mass fortification (salt, oil, sugar, and wheat and maize flours) based on estimated consumption patterns of staple foods. Malawi, Kenya, and Uganda have used these regional guidelines to formulate their national standards and regulations.

Standards and regulations

**The food fortification formulator:** This spreadsheet tool\(^9\) is available in English on the websites of A2Z and ECSA, and in Spanish on the website of the World Food Programme for Latin America. It ensures both the safety and maximum efficacy of micronutrient levels in mass fortification, and predicts the potential public health impact of fortified foods. The tool can currently be applied to salt, oil, sugar, two types of wheat flour, and three types of maize flour.

The minimum information required is an estimation of the per capita consumption and the proportion of the population consuming the potential food vehicle. The Formulator calculates the probable food intake of the different gender and age groups based on the principle of adult equivalency, described earlier. Three to four fortification formulations are suggested in accordance with the consumption pattern. The formulator presents results of intake in terms of percent of EAR, the Recommended Nutrient Intake (RNI), and in absolute amounts. Users can select the fortification levels that best meet the nutritional objectives and the allowable cost. Once the fortification levels have been selected, the formulator computes the quality control and regulatory parameters. The tool also allows the user to formulate the micronutrient content of premixes for different dilution factors.

Training sessions to promote the use of the Formulator have been offered in some ECSA countries. Similar training activities were held in Central and South America in workshops sponsored by FANCAP and PAHO/WHO, respectively.

Production of micronutrient premixes

**ECSA regional certification procedure:** Quality – and the expected effectiveness – of food fortification depends heavily on the micronutrient premix quality. In most countries, regulation and control of fortified food products are absent. To address the problem, A2Z is supporting ECSA to establish a regional system to certify micronutrient premixes.

Production of fortified foods

**Collaboration to implement and improve national food fortification programs:** A2Z collaborates with other institutions to introduce fortification practices in food industries. Examples include the wheat flour fortification project sponsored by GAIN in Uganda, and salt iodization under UNICEF leadership in Cambodia and HKI leadership in Guinea. A2Z works directly with the Palestinian Authority in the West Bank on wheat flour and market-driven fortifications.

**Advocacy for sugar fortification in Malawi and Ecuador:** A2Z collaborated with the Malawian offices of UNICEF and USAID, and with PAHO and the Ecuadorian Institute of Food and Nutrition to promote sugar fortification with vitamin A. Both countries have started specific actions to introduce this intervention.
Advocacy for wheat and maize flour fortification in Tanzania: A2Z and the ECSA Health Secretariat (HS) work together with the National Working Group of Food Fortification in Tanzania to introduce wheat and maize flour fortification by large industries in the country.

Improving oil and wheat flour fortification programs in the Philippines: A2Z built on previous projects with the Filipino government to strengthen oil and wheat flour fortification.

Quality control and assurance (QC/QA)

Training food industry employees: A2Z provided technical instructions to the oil industry of Uganda and the wheat flour industry of the West Bank to strengthen their quality control and assurance activities. Some training was also given to the oil and wheat flour industries of the Philippines.

Manuals for food control for fortification programs: A2Z worked with the ECSA HS to produce several food control manuals to cover the different stages of the fortification process of several fortified products: salt, oil, sugar, wheat flour, and maize flour. INCAP and UNICEF/Guatemala translated these manuals into Spanish for Central America.

Governmental inspection

Manuals for inspecting and auditing fortified foods: The food control manuals included food inspection at factories, importation sites, and retail stores and the most common analytical assays used in mass fortification. Many manuals, translated into Spanish by INCAP and UNICEF/Guatemala, have been adapted and validated for Central America. Training workshops using these manuals have been held in Malawi, Kenya, and Tanzania.

Food control rounds in Uganda: A2Z sponsored and provided technical assistance to use the food control manuals of oil, salt, and maize and wheat flours in Uganda. Three rounds of the system (auditing and collecting samples from factories, inspecting retail stores, examining imported products, and determining the micronutrient content in the collected fortified foods) have been done, covering most provinces of the country. This experience will serve as a model for other countries in the ECSA region.

Laboratory proficiency testing (LPT) exercise in the ECSA region: A2Z and the ECSA HS conducted two rounds of proficiency testing exercises in a network of laboratories that support food fortification programs in Kenya, Malawi, Tanzania, Uganda, and Zambia. The testing aimed to improve the analytical reliability of national laboratories involved in governmental inspection activities. The Ugandan Industry Research Institute (UIRI) of the Ministry of Industry and Economy coordinated the activity. The exercise examined the iodine content in salt; vitamin A in oil, sugar, and flours; and iron in flours. The exercise revealed that some laboratories are performing well, while others need to improve their equipment and personnel capabilities. Figure 4 shows some results of the second round.

Social marketing and education

Branding: The A2Z office in the Philippines continued working with the national authorities to use and disseminate the Sangkap Pinoy seal to identify approved fortified products in the country. Uganda also uses a seal to identify fortified products, because mass fortification is voluntary. In both cases, consumer awareness is important.

Impact assessment

Dietary and biochemical assessment of micronutrients in the West Bank: A2Z assisted the Palestinian Authority to analyze food/micronutrient survey data conducted in communities of Hebron and Gaza in...
2005 with the support of researchers from Iowa State University and the Palestinian AlQuds University in Jerusalem. The results provide a situational assessment of nutrition at that time. The data might support the review and readjustment of the fortification formulation of wheat flour, introduce complementary programs, and design a permanent nutrition surveillance system. Figure 5 shows the preliminary results of the micronutrient adequacy of women of child-bearing age in Hebron and Gaza, and the potential benefit expected through wheat flour fortification. Results of the food control system in Uganda determined that in 2008, > 90% of vegetable oil in retail stores contained vitamin A, and > 40% had vitamin A levels above 20 ppm (mg/kg) (Figure 6). These data show that the program has a large penetration and is relatively successful in the country.

Cost-effectiveness analysis

Cost analysis of oil and sugar fortification in Uganda: The last step of a food fortification program is evaluation by an external and independent entity. A2Z developed tools, procedures and forms, and carried out a cost analysis of the oil and sugar fortification initiatives in Uganda.

Program monitoring and evaluation

Performance and effectiveness monitoring in Uganda: A2Z is initiating an activity with the IMPPaCt project of the Centers for Disease Control to design, plan, and introduce a system for monitoring and evaluating food fortification programs in Uganda to determine intervention quality and coverage as well as changes in impact indicators.

Monitoring and evaluation workshops: In July 2006, A2Z and other institutions organized an inter-institutional meeting to discuss general monitoring and evaluation (M & E) concepts and a framework for food fortification programs. A subsequent meeting to analyze the importance of measuring food intake for diagnostic assessment and food fortification program M & E was held in August 2007.

Future directions

A critical analysis of current programs indicated several gaps, both for specific micronutrients as well as for operational issues. The A2Z project will work with other partners to find solutions to overcome some of the identified limitations. Future directions are visualized as follows:

• The importance of industrially processed foods increases with urbanization. Salt, as a condiment, is hidden in these foods. Therefore, determining how much salt is being supplied through processed foods is critical to support programs to reduce salt intake and to adjust salt iodine levels. While salt is the vehicle of choice for delivering iodine, it is important to consider alternative vehicles when salt fails – mainly because of production under non-industry settings – to guarantee the provision of iodine to every individual in the population. Iodine delivery should be assured by using all the mechanisms that are available.

• Providing vitamin A through the diet and several interventions (mass, targeted and market-driven for-
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Fortification, as well as periodical supplementation) should be carefully measured. The potential risks of adverse effects from excessive intakes should be reduced to ensure safe, efficacious and widely accepted vitamin A programs.

- Neural tube defects have been associated with folate and vitamin B₁₂ deficiencies. In developing countries, both deficiencies may be equally important. Therefore, programs to prevent neural tube defects should establish the magnitude of the nutritional gaps of both micronutrients as one of their requirements. Serum folate and biomarkers associated to vitamin B₁₂ status seem to be relatively straightforward for this objective.

- The low bioavailability of minerals in most developing country diets demands a serious review of the actual food fortification policies supported. New iron interventions may be necessary to improve the iron status of needy populations in those countries. Furthermore, impact is closely associated to the quality of iron compounds with good bioavailability. Special efforts to assure that the food industry is using the recommended compounds would require improved analytical capabilities within these countries – a costly but worthy investment.

- Zinc is a mineral that is highly inadequate in the diet. Incorporating zinc into fortification formulas is generally feasible and simple. Although plasma/serum zinc is a good indicator to evaluate zinc status and intervention impact in populations, evidence of biological impact is the main limitation in justifying the use of zinc. This area deserves more attention and should be developed simultaneously with the efforts to correct the nutritional gap.

- Many negative consequences of micronutrient deficiencies are not only due to inadequacies of the above-mentioned micronutrients; many others are also involved. In the absence of biomarkers of status for most micronutrients, correcting deficient intakes would be a good way to start the overall improvement of the human diet in the developing world. Therefore, practical methods to measure micronutrient intakes through the diet should be introduced, validated and extended.

- The world population growth, the reduction of food availability for human consumption, and natural disasters are creating conditions leading to further reduced diversity in diets. Micronutrient status should be constantly surveyed simultaneously, with attention paid to sufficient food supply. The study of the evolution of the population nutritional status will increase in importance in the years to come. It is critical to identify which population sectors consume fortified foods in order to channel the resources and

Box 1: Roundup of A2Z food fortification activities

- Systematize data analysis of the Household Income and Expenditure Surveys (HIES) to identify food fortification vehicles and possible consumption patterns, and to propose fortification formulas for specific countries.

- Prepare articles and reports recognizing the importance of the additional intake, bioavailability, and bioefficacy to predict the impact of food fortification programs.

- Publish documents that describe the importance of doing a comprehensive technical and economical assessment before promoting wide-scale fortification programs (e.g., rice fortification).

- Develop a food fortification formulator to disseminate principles and tools that support design, regulation, implementation, and control of food fortification programs.

- Advocate the extension of food fortification in developing countries: oil in Uganda and the Philippines; sugar in Malawi and Ecuador; flours in the West Bank, Tanzania and the Philippines; and rice in Nicaragua and Panama.

- Develop tools (manuals) and training to strengthen food control actions by the food industries and governmental authorities.

- Facilitate field experiences at the national level to implement food inspection and improve laboratory reliability.

- Raise awareness for social marketing campaigns of fortified products to promote awareness about the importance of fortified foods, while at the same time preventing exaggerated and misleading messages.

- Promote global discussion to agree on M & E terms and concepts, emphasize the importance of assessing micronutrient intake as an important component of the food fortification programs, and encourage use of performance (process) and effectiveness (impact) M & E of food fortification programs.
attention to those who really need them.

• Overweight and obesity are rapidly increasing around the world, including developing countries. Many fortification vehicles are foods whose consumption should not be raised. This situation prompts special attention to health claims and social-marketing messages associated with mass and market-driven fortification programs to avoid deceiving and misleading messages prompted only for profit interests. Establishing and enforcing regulations and standards for labeling and advertising are priority areas in food fortification.

• Experience from several countries reveals that many standards and regulations are confusing and cause conflicts because the food industry and the government interpret them differently. Industry interprets minimum values as averages, while the government uses them as absolute cut-off points. Furthermore, decisions are often based on analytical assays using a very low number of samples. These issues need to be urgently addressed.

• The evolution of human nutrition and health must be assessed continually. A comprehensive, integrated, and constant surveillance system should be implemented in all countries and regions to make appropriate and timely decisions. Any nutritional intervention should be justified and based on an assessment of the epidemiological situation. The performance of implemented programs should also be well documented and shared. The improvement, appreciation, and permanence of food fortification programs as part of public health strategies may depend on timely, transparent, and well-distributed reports. Technical papers are also needed to share experiences and lessons learned.

### References


The Role of Micronutrients in the Developmental Origins of Health and Disease

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Introduction

Undernutrition and micronutrient deficiencies continue to be a problem worldwide. An estimated 2 billion people suffer from at least one form of micronutrient deficiency. There is also a growing epidemic of chronic disease, particularly in developing countries, where estimates show 80% of the burden of chronic diseases may be felt. Many developing countries are experiencing a double burden of disease with concurrent childhood malnutrition and adult obesity, sometimes even within the same household.

The field of research referred to as the developmental origins of health and disease (DOHaD) has highlighted how malnutrition during pregnancy or early childhood may influence chronic disease risk decades later. One of the most widely cited theories to explain this is that of the ‘thrifty phenotype hypothesis,’ which proposes that exposure to a deprived intrauterine environment may stimulate fetal adaptations to the growth rate, organ development, and metabolic pathways that may offer immediate survival benefits, but that may result in a greater risk of cardiovascular disease or type II diabetes in later life, particularly if exposed to a more affluent postnatal environment.

The DOHaD hypothesis is of particular relevance and concern to developing countries rapidly entering the epidemiologic and nutritional transition. Over the course of one generation, many societies are experiencing rapid changes in diet and physical activity, so that populations that may have experienced undernutrition as infants and young children may go on to become overweight as adults.

To date, much of the literature has focused on how size at birth is associated with blood pressure, insulin resistance or body composition in later life. Yet, size at birth alone does not tell us how adequate the mother’s diet was throughout gestation. Deficiencies in micronutrients, in particular, have been found to impact length of gestation, cognitive development, and organ development, and a number of well-written reviews have examined the effects of micronutrients on birth weight.

There have been a number of randomized controlled trials or observational studies of maternal calci-
Iron deficiency is the most common nutritional deficiency around the globe and is the most common cause of anemia. Anemia in pregnancy (defined as Hb < 11 g/dL) is an observed risk factor for low birth weight and preterm delivery. Animal studies have demonstrated that iron restriction during pregnancy causes elevation in the offspring’s blood pressure and altered cardiovascular development, but these findings have not been consistently observed in humans.

Some epidemiologic studies have noted a small negative association between child blood pressure and maternal iron intake or hemoglobin concentration during pregnancy, while others have observed either no association or a positive association. These studies are summarized in Table 1. Two studies of 4-year-old and 9–11-year-old British children found no significant association between maternal hemoglobin concentration and child blood pressure. In a small study from Kingston, Jamaica, following 77 children through 10–12 years of age, each g/dL fall in maternal hemoglobin during pregnancy was associated with a rise in mean systolic blood pressure of 2.6 mm Hg (95% CI: 0.5, 4.6), but this effect disappeared after adjusting for the mother’s triceps skinfold thickness during pregnancy. In this study, maternal skinfold thickness at 15 weeks gestation was strongly inversely associated with child blood pressure, with an increase of 10.7 mm Hg (95% CI: 5.8, 15.5) in systolic blood pressure for each log mm decrease in skinfold thickness. Therefore, it is likely that overall maternal nutritional status played a much more important role than anemia alone in predicting the child’s blood pressure.

In contrast, a study of 518 5–9-year-old children from Argentina noted an increase of 1.6 mm Hg (95% CI: 0.5, 2.7) in child systolic blood pressure with each standard deviation increase in maternal hemoglobin concentration during pregnancy. A study of American 3-year-old children was unable to document any association between maternal hemoglobin concentration or mean corpuscular volume during pregnancy and child blood pressure. However, less than 3% of the women involved in the study were anemic during pregnancy, so the authors argue that more extreme iron deficiency may be needed for measurable effects to occur.

Finally, a recent study of 7-year-old children in the UK concluded that child systolic blood pressure was associated with maternal anemia during the first or second trimester (-2.0 mm Hg; 95% CI: -3.6, -0.4) and third trimester anemia (-1.1 mm Hg; 95% CI: -2.1, -0.1), but the effect was attenuated after adjustment for household (social economic status), breastfeeding, maternal age at pregnancy, education, parity, height, pre-pregnancy BMI, history of hypertension and smoking.

A few of these studies have also examined maternal iron intake during pregnancy, as summarized in Table 2. Among 3-year-old American children, systolic blood pressure increased by 0.4 mm Hg (95% CI: 0.1, 0.7) for every 10 mg increase in maternal first trimester iron intake, but was not associated with second trimester iron intake. In contrast to this study, maternal iron supplement usage was found to be inversely associated with child blood pressure among 7-year-old British children. However, when restricted to iron-only supplements, this association disappeared after adjustment for confounding factors, including household SES, breastfeeding, and maternal factors during pregnancy. Similarly, maternal dietary iron intake was unassociated with child blood pressure.
It is possible that other components of the multivitamin supplements may have had a greater effect on child blood pressure than iron alone. Our group has conducted a randomized controlled trial of maternal micronutrient supplements in rural Nepal and have recently completed a follow-up with ~94% of the surviving offspring between the ages of 6–8 years. We did not observe any effect of maternal iron-folic acid supplementation on mean child blood pressure, risk of hypertension, or insulin resistance relative to the controls. To our knowledge, this is the first study that has examined maternal iron supplementation in a developing country setting and the only one to have utilized a randomized controlled trial design.

Although there is a strong suggestion from animal studies that iron deficiency during fetal development may program later hypertension, the evidence from human studies is inconsistent. Most of the studies have been conducted among developed country populations or among women in urban clinic settings, so it is possible that few of the women experienced a level of deficiency that was great enough to produce adverse effects in the offspring. Additionally,
### Difference in Systolic Blood Pressure (mm Hg)

<table>
<thead>
<tr>
<th>Crude Difference (95% CI)</th>
<th>Adjusted Difference (95% CI)</th>
<th>Factors Included in the Adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.9 (-0.4, 6.3)</td>
<td>2.2 (-1.3, 5.7)</td>
<td></td>
</tr>
<tr>
<td>2.6 (0.5, 4.6)</td>
<td>0.0 (-1.9, 1.8)</td>
<td>Current weight, gender, maternal triceps skinfold at 15 wks gestation, maternal weight gain from 15–35 wks gestation</td>
</tr>
<tr>
<td>Data not presented</td>
<td>No association:</td>
<td>Current weight, gender, maternal triceps skinfold at 15 wks gestation, maternal weight gain from 15–35 wks gestation</td>
</tr>
<tr>
<td>Hb &lt; 10.5: 106.9 mm Hg</td>
<td>Hb 10.5–11: 106.9 mm Hg;</td>
<td></td>
</tr>
<tr>
<td>Hb 11.1–11.6: 107.9 mm Hg</td>
<td>Hb 11.7–14.4: 104.3 mm Hg</td>
<td></td>
</tr>
<tr>
<td>Data not presented</td>
<td>No association:</td>
<td>Child age and sex</td>
</tr>
<tr>
<td>Change in MCV -14 to -2: 105.2 mm Hg</td>
<td>MCV -1 to 0: 106.0 mm Hg</td>
<td></td>
</tr>
<tr>
<td>MCV 1 to 2: 104.9 mm Hg</td>
<td>MCV 3–12: 108.5 mm Hg</td>
<td></td>
</tr>
<tr>
<td>1.6 (0.5, 2.7)</td>
<td>1.3 (0.4, 2.3)</td>
<td>Child BMI, height, sex, age, and maternal calcium supplementation status during pregnancy</td>
</tr>
<tr>
<td>0.4 (-0.3, 1.0)</td>
<td>0.5 (-0.2, 1.1)</td>
<td>Blood pressure measurement conditions ( extremity used, cuff size, state, position, measurement order), child gestational age, sex, current age, height and weight</td>
</tr>
<tr>
<td>Not presented</td>
<td>-1.6 (-5.0, 1.8)</td>
<td></td>
</tr>
<tr>
<td>Not presented</td>
<td>0.3 (-1.7, 2.3)</td>
<td>All models adjusted for child age and sex. Adjusted models additionally included SES, family social class, maternal education, breastfeeding, age at childbirth, parity, maternal height, pre-pregnancy BMI, maternal history of hypertension, and maternal smoking during pregnancy</td>
</tr>
<tr>
<td>-2.02 (-3.60, -0.44)</td>
<td>-1.36 (-3.18, 0.46)</td>
<td></td>
</tr>
<tr>
<td>-1.09 (-2.12, -0.05)</td>
<td>-0.49 (-1.71, 0.72)</td>
<td></td>
</tr>
</tbody>
</table>

status; CI, confidence interval; Mo, months; Yr, years

because most of these data are from observational studies, the potential for confounding by other factors cannot be ruled out. Further, most of the studies reviewed here had high losses to follow-up, so biased estimates are also a possibility. Thus, although there are many important reasons for adequate maternal iron intake during pregnancy, there is insufficient evidence at this time to suggest that maternal iron intake is a strong predictor of child blood pressure.

### Calcium

Increased calcium intake appears to reduce blood pressure among adults and children, and has been suggested as a preventive measure for preeclampsia during pregnancy among deficient populations. Calcium supplementation to pregnant women has not been found to have a strong effect on mean birth weight in most studies. However, data from a study in rats has suggested that calcium restriction during pregnancy is associated with an increase in offspring blood pressure that becomes progressively greater as the animals age.

A few studies in humans have also suggested an association between maternal calcium intake during pregnancy and offspring blood pressure, as summarized in Table 3. A systematic review concluded that there was evidence of an association, yet small sample sizes and methodological problems...
in the five papers that were reviewed limit the strength of the evidence. To date, four randomized controlled trials of maternal calcium supplementation have assessed blood pressure in the offspring during childhood.27-30

In the first study, blood pressure was measured in ~500 5–9-year-old children in Argentina born to mothers who had participated during their pregnancy in a randomized trial of calcium supplements for the prevention of hypertensive disorders. Children born to women in the intervention group had a non-significant reduction in mean blood pressure (-1.4 mm Hg; 95% CI -3.3, 0.5), which did not change after adjustment for child age, sex, and birth weight, but the risk of high systolic blood pressure was significantly reduced in the calcium group (11.4%) relative to the control group (19.3%) (RR: 0.59; 95% CI 0.39, 0.90). The effect was strongest among children who had a body mass index greater than the median.27

In the second study, 497 healthy, nulliparous young women in Portland, Oregon, were invited to participate in a randomized controlled trial of antenatal calcium supplements to prevent preeclampsia.28 There was no effect on offspring systolic blood pressure at

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study population</th>
<th>N</th>
<th>Exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Belfort et al</td>
<td>3-year-old children from Massachusetts, USA</td>
<td>1,167 of 1,579 eligible children</td>
<td>Maternal iron supplement intake (per 10 mg; all iron containing supplements)</td>
</tr>
<tr>
<td>200819</td>
<td></td>
<td></td>
<td>Maternal dietary iron intake from food (per 10 mg)</td>
</tr>
<tr>
<td>Brion et al</td>
<td>7-year-old children from Bristol, UK</td>
<td>7,638 of 13,678 eligible children</td>
<td>Maternal iron supplement intake (all iron-containing supplements)</td>
</tr>
<tr>
<td>200820</td>
<td></td>
<td></td>
<td>Maternal iron supplement intake (iron-only supplements)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Maternal iron intake (per 50 mg/wk)</td>
</tr>
</tbody>
</table>

Abbreviations: SBP, systolic blood pressure; BMI, body mass index; SES, socioeconomic status; CI, confidence interval; mo, months; yr, years

Table 2: Results from studies of the association between maternal iron intake during pregnancy and child blood pressure

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study population</th>
<th>N</th>
<th>Intervention</th>
<th>Crude Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Belfort et al</td>
<td>3-year-old children from Massachusetts, USA</td>
<td>1,167 of 1,579 eligible children</td>
<td>2 g Ca</td>
<td>-1.4 (-3.3, 0.5)†</td>
</tr>
<tr>
<td>200819</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brion et al</td>
<td>7-year-old children from Bristol, UK</td>
<td>7,638 of 13,678 eligible children</td>
<td>2 g Ca</td>
<td>At 3 mo old: -2.2 (-5.5, 1.1) At 2 yrs old: -4.8 (-9.2, -0.3)</td>
</tr>
<tr>
<td>200820</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hiller et al</td>
<td>4–7-year-old children in South Australia</td>
<td>179 of 414 eligible children</td>
<td>1.8 g Ca</td>
<td>-0.1 (-2.4, 2.3)‡</td>
</tr>
<tr>
<td>200729</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hawkesworth</td>
<td>5–10-year-old children in rural Gambia</td>
<td>389 of 519 eligible children</td>
<td>1.5 g Ca</td>
<td>-0.1 (-1.9, 1.7)</td>
</tr>
<tr>
<td>200930</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

†Adjustment for child age, sex, and birth weight or ‡current BMI, current calcium intake, calcium intake during pregnancy, and small for gestational age did not alter the results

Table 3: Results from randomized placebo controlled trials of maternal calcium supplementation during pregnancy and child blood pressure
DOHaD and Micronutrients

3 months of age (-2.2 mm Hg; 95% CI -5.5, 1.1), but a significant 4.8 mm Hg reduction (95% CI -9.2, -0.3) at 2 years of age in the calcium group compared to the controls. However, the losses to follow-up were substantial; only 260 infants and 57 toddlers were measured at follow-up. Data were not presented on the differences between participants and non-participants, and no attempts were made to control for potential differential losses to follow-up, so the potential for bias or confounding cannot be ruled out.

A third study conducted among 456 nulliparous women in South Australia found that maternal calcium supplementation had no overall effect on offspring blood pressure at 4–7 years of age. Finally, recent data from a study of 5–10-year-old offspring of mothers who participated in a randomized controlled trial of calcium supplementation during pregnancy in the Gambia found no impact of supplementation on child blood pressure, although the full results of this study have yet to be published.

Observational data have provided mixed results, and are summarized in Table 4. Maternal calcium intake during pregnancy has been inversely associated with systolic blood pressure in children at 1 month of age ($r = -0.28$, $p < 0.01$) and diastolic blood pressure at 6 ($r = -0.27$, $p < 0.01$) and 12 months of age ($r = -0.24$, $p < 0.05$). It should be noted however that, in this American study population, more than 85% of women consumed amounts of calcium in excess of 1,200 mg/day.

In a more recent study of pregnant women and their children in Massachusetts, maternal calcium intake during pregnancy has been inversely associated with offspring blood pressure at 6 months of age with an estimated 3.0 mm Hg reduction (95% CI: -4.9, -1.1) in systolic blood pressure per every 500 mg increment in maternal supplemental calcium consumed. The effect was confined to calcium consumed in the form of supplements but not from food sources. However, this effect was not maintained through the age of 3 years.

Finally, one small study of twin pairs from Tasmania found that, at 9 years of age, children whose mothers reported taking supplemental calcium during pregnancy had lower levels of total and LDL cholesterol, lower triglycerides, but no difference in blood pressure, fasting glucose, insulin, or HDL cholesterol. It is unfor-

<table>
<thead>
<tr>
<th>Difference in systolic blood pressure (mm Hg)</th>
<th>Crude Difference (95% CI)</th>
<th>Adjusted Difference (95% CI)</th>
<th>Factors included in the adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.4 (0.1, 0.7)</td>
<td>0.4 (0.1, 0.8)</td>
<td>Blood pressure measurement conditions (extremity used, cuff size, state, position, measurement order), child gestational age, sex, current age, height and weight</td>
<td></td>
</tr>
<tr>
<td>-0.1 (-1.0, 0.9)</td>
<td>0.2 (-0.8, 1.2)</td>
<td>All models adjusted for child age and sex. Adjusted models additionally included SES, family social class, maternal education, breastfeeding, age at childbirth, parity, maternal height, pre-pregnancy BMI, maternal history of hypertension, and maternal smoking during pregnancy</td>
<td></td>
</tr>
<tr>
<td>-0.72 (-1.14, -0.31)</td>
<td>-0.58 (-1.06, -0.10)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-1.03 (-2.28, 0.22)</td>
<td>-0.19 (-1.58, 1.20)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-0.41 (-1.12, 0.30)</td>
<td>0.40 (-0.45, 1.26)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
tunate that in this study, the dosage of supplementation is unknown and other dietary factors during pregnancy were not assessed. Further, it is unclear how these data from twins can be generalized to singleton pregnancies.

In conclusion, there is little evidence of an association between maternal calcium intake and offspring blood pressure. The studies among humans, both randomized controlled trials and observational studies, have not yielded strong or consistent results. However, large losses to follow-up and other methodologic considerations limit the ability to draw firm conclusions.

### Other micronutrients

**Vitamin A**

Studies of vitamin A-deficient rats or retinoic acid receptor knockout mice have demonstrated the essential role that vitamin A plays in numerous aspects of fetal pulmonary, renal, and cardiac morphological development. Moderate vitamin A deficiency will result in reductions in the relative weight of fetal lungs, heart and liver, kidney development, and pancreatic development. However, there have not yet been any published studies in humans that have explored the effects of vitamin A deficiency during pregnancy on these long-term outcomes in the offspring.

**Zinc**

A recent review suggested that zinc may play an important role in the fetal origins of disease through epigenetic mechanisms. However, only one study utilizing a rat model found that moderate maternal zinc deficiency results in elevations in offspring blood pressure, a reduction in the number and size of nephrons, a decrease in the glomerular filtration rate and an increase in renal oxidative damage. The damage could not be overcome by returning rats to the control diet, post-weaning. More research is needed to better understand the effects of maternal zinc status during pregnancy on long-term chronic disease risk in the children.

### Table 4: Results from observational studies of maternal calcium intake during pregnancy and child blood pressure

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study population</th>
<th>N</th>
<th>Exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>McGarvey et al 1990</td>
<td>Children from Providence, Rhode Island, USA. Children followed at 2–4 days, and 1, 6, and 12 months of age</td>
<td>212 newborns (2–4 days); 184 at 1 mo; 114 at 6 mo; 70 at 12 mo</td>
<td>Dietary calcium intake</td>
</tr>
<tr>
<td>Morley et al 2004</td>
<td>9-year-old children from Tasmania, Australia</td>
<td>294 children (147 pairs) of 406 eligible children</td>
<td>Calcium supplement consumption (yes/no)</td>
</tr>
<tr>
<td>Gillman et al 2004</td>
<td>Children from Massachusetts, USA. Two follow-up visits: 1) at 6 mo old and 2) at 3 years old</td>
<td>936 infants at 3 mo and 1,173 3 year olds of an eligible 1,579 children</td>
<td>Calcium consumption from foods (per 500 mg)</td>
</tr>
<tr>
<td>Bakker et al 2008</td>
<td></td>
<td>212 newborns (2–4 days); 184 at 1 mo; 114 at 6 mo; 70 at 12 mo</td>
<td>Calcium consumption from supplements (per 500 mg)</td>
</tr>
</tbody>
</table>

Abbreviations: SBP, systolic blood pressure; BMI, body mass index; SES, socioeconomic status; CI, confidence interval; mo, months; yr, years
Folic acid and vitamin B₁₂

Epigenetic alterations to DNA methylation, histone modifications, or changes in DNA-binding proteins have been explored in the context of the DOHaD hypothesis. The term ‘epigenetics’ refers to the study of heritable changes in gene expression potential that are not caused by changes in DNA sequence. Folic acid and the B-vitamins play an important role in DNA methylation, a process that occurs early in embryonic development. In animal models, dietary restriction in the methyl donors of folate, vitamin B₁₂, and the amino acid methionine around the time of conception can induce alterations in DNA methylation, increased adiposity, insulin resistance and elevated blood pressure in offspring. Further, protein deficiency during pregnancy may induce cardiovascular dysfunction and high blood pressure in the offspring, which can be reversed with the supplementation of folate, possibly via improved maternal uterine blood flow or changes in DNA methylation.

Recent observational studies in humans have suggested that high folate concentrations during pregnancy were associated with a greater degree of insulin resistance and fat mass in 6-year-old children. In particular, children born to mothers with a high folate and low B₁₂ status had the greatest degree of insulin resistance in childhood, suggesting that an imbalance in these two nutrients during pregnancy will predispose the offspring to a greater risk of insulin resistance. This observation warrants confirmation in other studies.

Multiple micronutrients

With the recognition that many women in developing countries suffer from several micronutrient deficiencies during pregnancy, there has been a recent interest in

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### Difference in systolic blood pressure (mm Hg)

<table>
<thead>
<tr>
<th>Crude Difference (95% CI)</th>
<th>Adjusted Difference (95% CI)</th>
<th>Factors included in the adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Data not shown</td>
<td>Correlation between calcium intake and SBP</td>
<td>Observer, sleep/activity status, cuff size, child age, and body weight (at 6 &amp; 12 mo)</td>
</tr>
<tr>
<td>-0.8 (-4.2, 2.6)</td>
<td>-0.7 (-4.1, 2.7)</td>
<td>Maternal education, pair birth order, child age, and sex</td>
</tr>
<tr>
<td>At 6 mo: -0.3 (-1.4, 0.7)</td>
<td>At 6 mo: -0.02 (-1.1, 1.0)</td>
<td>Crude models adjusted for maternal energy intake and BP measurement conditions. Three-year crude models also adjust for child age and sex</td>
</tr>
<tr>
<td>At 3 yrs: -0.3 (-1.0, 0.5)</td>
<td>At 3 yrs: -0.2 (-1.0, 0.6)</td>
<td>6 month adjusted models additionally adjusted for maternal race/ethnicity, education, number of previous pregnancies, marital status, prepregnancy BMI, 3rd trimester SBP, and infant age, sex and BMI</td>
</tr>
<tr>
<td>At 6 mo: -3.4 (-5.3, -1.4)</td>
<td>At 6 mo: -3.0 (-4.9, -1.1)</td>
<td>3-year adjusted models additionally adjusted for maternal race/ethnicity, education, prepregnancy BMI, 3rd trimester SBP, and paternal BMI, and child BMI</td>
</tr>
<tr>
<td>At 3 yrs: -0.1 (-1.5, 1.3)</td>
<td>At 3 yrs: -0.1 (-1.4, 1.2)</td>
<td></td>
</tr>
</tbody>
</table>
studying the potential benefits that supplementation with multiple micronutrients may have for the mother and child. However, to date, only one study has published data on the effects of maternal supplementation on the health of the offspring beyond infancy. This study, conducted in Janakpur, Nepal, followed 2–3-year-old children born to mothers enrolled in a randomized controlled trial of a multiple micronutrient supplement, containing 15 micronutrients, compared to iron-folic acid as the control. Children whose mothers had received the multiple micronutrient supplement had a reduction in systolic blood pressure of 2.5 mm Hg (95% CI: 0.5, 4.6) relative to the controls. In contrast, in a similar population in rural Nepal, children aged 6–8 years whose mothers had been enrolled in a randomized controlled trial of multiple micronutrients had no difference in blood pressure relative to controls (Stewart CP, Christian PC, Schulze KJ, LeClerq SC, West KP, and Khatry SK, unpublished).

Conclusions

While there is strong evidence from animal studies that micronutrient deficiency during fetal development may have consequences well beyond the neonatal period, there is much to be learned in terms of understanding the effects in humans as well as the potential mechanisms of action. Data on long term cardiovascular risk from human studies is equivocal or lacking for many micronutrients. Much of the literature that does exist comes from observational data, which may suffer from confounding due to both measured and unmeasured factors. Further, the majority of studies have followed-up with subjects as children or adolescents, which may be too young to demonstrate measurable effects.

Micronutrient deficiencies are prevalent in women from both the developed and the developing worlds, but the full consequences of these deficiencies have yet to be fully understood. While there have been many randomized trials that have explored the short-term effects of micronutrient supplementation on birth weight, infant growth, and morbidity, much could be gained by following these children forward in time to determine what, if any, are the latent benefits of supplementation.

Acknowledgement:

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References


Systematic Reviews of Zinc Intervention Strategies

A Technical Summary from the International Zinc Nutrition Consultative Group (IZiNCG)

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Introduction

Adequate zinc nutrition is critically important for children’s health and the achievement of their full growth potential. The Lancet series on maternal and child undernutrition concluded that zinc deficiency increases the risk and severity of common childhood infections, thereby contributing to excess morbidity and mortality in lower income countries,1 and the recently updated Copenhagen Consensus on priorities for advancing global welfare named zinc supplementation as one of the top-ranked interventions for reducing malnutrition and improving overall welfare.2 Despite these compelling conclusions, there has been surprisingly little effort worldwide focused on the prevention of zinc deficiency, in part because of the limited information that has been synthesized to assess the impact of different zinc intervention strategies on child health outcomes.

To address this information gap, the Steering Committee of the International Zinc Nutrition Consultative Group (IZiNCG) has just completed a 2nd IZiNCG technical document, which compiles and systematically examines information on the intervention strategies that have been developed to control zinc deficiency. The document was published in the Food and Nutrition Bulletin (Food Nutr Bull 2009;30(1):S3–S186) and can be downloaded for free at: http://www.foodandnutritionbulletin.org/downloads/FNB_v30n1_Supplement_izinc.pdf and www.izincg.org.

Separate chapters of the new IZiNCG technical document present the latest information on the expected health and nutrition results that can be achieved through zinc supplementation, fortification, and diet-based intervention strategies. The chapter on preventive supplementation includes meta-analyses of its impact on morbidity, mortality, growth and zinc status among infants and children,3 based on the results of 55 intervention trials in which the effects of zinc supplements, with or without other micronutrients, were compared with the results obtained from the same preparations when zinc was excluded. The section on therapeutic zinc supplementation examined the severity and duration of selected infections, such as diarrhea, pneumonia, and malaria,4 in rela-
Zinc Intervention Strategies

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tion to whether or not zinc supplements were included in the treatment regimen. The document also systematically reviews current evidence on the effects of zinc supplementation during pregnancy, the impact of zinc fortification, and the results of dietary interventions to increase zinc intake.

Zinc supplementation in children

The results of available studies indicate that preventive zinc supplementation reduces the incidence of diarrhea by approximately 27% among young children aged > 12 months and decreases the incidence of acute lower respiratory tract infections by approximately 15%. Overall, zinc supplementation reduces child mortality by approximately 6%. The impact of preventive zinc supplementation on child mortality seems to be restricted to children aged > 12 months, in whom the mortality reduction is approximately 18%.

Some evidence further suggests that zinc supplementation may reduce mortality among small-for-gestational-age infants, but the number of studies is still too small to draw definitive conclusions. Preventive zinc supplementation also increases linear growth and weight gain in young children, thereby contributing to reduced rates of stunting and underweight.

Importantly, available research has found no evidence of adverse effects on the status of other micronutrients or of any functional abnormalities when preventive zinc supplements are provided in the recommended doses. Thus, preventive zinc supplementation of children at risk of deficiency is both safe and efficacious for a variety of health and nutritional outcomes.

The newly completed meta-analyses of therapeutic zinc supplementation confirm that provision of zinc supplements as adjunctive treatment for diarrhea reduces the duration of acute episodes by ~0.5 days and of persistent episodes by ~0.7 days. The results therefore support the recommendation by the World Health Organization (WHO) and the United Nations Children’s Fund (UNICEF) to include therapeutic zinc supplementation in diarrheal disease control programs.

Zinc supplementation during pregnancy

Preventive zinc supplementation was also examined among pregnant and lactating women. An earlier meta-analysis concluded that zinc supplementation during pregnancy reduced the rate of preterm births by 14%. Most studies found no significant impact of maternal zinc supplementation on infant birth weight but a subset of studies conducted among underweight or zinc-deficient women suggests there may be a positive effect of zinc supplementation in such women. Nevertheless, the number of relevant studies is limited, and more information is needed to confirm these observations. The impact of maternal zinc supplementation during pregnancy on infant postnatal growth and risk of infection is variable, and too few studies are available to permit reliable conclusions, especially with regard to longer term effects during the second half of infancy and later childhood.

Zinc fortification

Despite the positive effect of zinc fortification on total zinc absorption, only a few studies have found positive impacts of zinc fortification on serum zinc concentrations or functional indicators of zinc status. Nevertheless, because of the desirability of increasing zinc intake in populations at high risk for zinc deficiency, the documented increase in total zinc absorption that occurs following zinc fortification, the absence of any adverse effects of zinc fortification, and the relatively low cost of adding zinc to existing fortification programs, public health planners should consider including zinc in mass and targeted fortification programs in such populations. Because of the limited available information on program impact, it will be important to evaluate the outcomes of such programs.

Dietary diversification or modification

A number of dietary intervention strategies have the potential for improving zinc status. Breast milk is an important potential source of zinc for infants and young children, and current international guidelines for the promotion and support of breastfeeding should be viewed as appropriate programmatic components to support adequate zinc nutrition of young children. Other interventions to increase the availability, acces-
sibility, and consumption of animal-source foods, increase the zinc content of plant-source foods, or increase zinc absorption from these foods should enhance the consumers’ zinc status. However, rigorous evaluations of large-scale dietary approaches are still lacking. In the future, biofortification also holds promise as a sustainable approach to improve the zinc content and/or bioavailability of staple food crops.

Conclusion

There is now clear evidence of the benefit of selected interventions to reduce the risk of zinc deficiency, and a global commitment is urgently needed to: 1) conduct systematic assessments of population zinc status, and 2) develop interventions to control zinc deficiency in the context of existing public health and nutrition programs. Such interventions, if implemented at scale and attaining high coverage, would have a direct impact on achieving several Millennium Development Goals, including reducing child morbidity, mortality, and restricted growth.

References

Local Produced Ready-to-Use Food (RUF)

Piloting in Mild and Moderately Wasted Children, Nias Island, Indonesia

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Introduction

Nias Island in Indonesia was severely affected by the 2004 Indian Ocean tsunami and a consequent earthquake some months later. A 2005 survey led by the United Nations Children’s Fund (UNICEF) found a high prevalence (12.8%) of wasting (defined as < -2 Weight-for-Height Z-score, or WHZ) among children aged below five years in South Nias, which is also one of the poorest sub-districts in Indonesia.¹

About two years later, Church World Service Indonesia (CWS) reported as many as 11.9% of children were still wasted in its intervention area on Nias Island,² and began piloting a newly developed Ready-to-Use Food (RUF) to reduce the prevalence of wasting.

The nutritional products used in this study, such as cereal/nut/legume-based RUTF-Nias biscuits and peanut/milk paste (PMP-Nias), were originally designed for severely wasted children but were nonetheless used in the interests of a conservative approach in moderately wasted children. This article reports some of the preliminary findings from a larger, ongoing research project entitled ‘Effectiveness of Locally Produced Ready-to-Use Foods (Part I) and Home-Based Foods (HBF) Fortified with Micro-
nutrient Powder (Part II) for Wasted Children in Nias, Indonesia.’

Objectives

The objectives of the study were to:

• Develop new recipes of cereal-based RUF, in the form of biscuits, for local production and consumption by wasted children aged 6 to 60 months.
• Compose a new vitamin and mineral premix that would make the micronutrient specifications of the RUF-Nias biscuits comparable (but not identical) to that of Plumpy’nut™ and reference data of WHO, WFP, UN-SCN, UNICEF.3
• Explore baking time and temperature yielding the lowest loss of micronutrients; compare the micronutrient content of the baked biscuits with the calculated ones; and study the stability of the micronutrient content of the biscuits after 3–4 weeks of storage at room temperature.
• Calculate the number of RUF-Nias biscuits needed to meet approximately 50–60% of the daily energy requirements of children aged 6 to 60 months.
• Compare the costs of locally produced PMP-Nias and cereal/nut/legume-based RUF-Nias biscuits.

Methodology

Product development and evaluation

Nine new recipes of RUF biscuits using local (Nias) and national (Indonesian) food sources were developed in Germany4 and their nutrient composition was analyzed at the Institute of Biological Chemistry and Nutrition, University Hohenheim. The goal was to make the macro- and micronutrient content of the biscuit similar (but not identical) to that of Plumpy’nut™. A vitamin and mineral premix which would enable this was finally produced by DSM Nutritional Products, Singapore, for use in the production of RUF biscuits on Nias Island.

In Nias, data on the constant availability of ingredients to produce the biscuits were collected through a market survey and in-depth interviews with key CWS staff. Based on this information, four of the RUF recipes were used to produce biscuits that were field-tested in seven feeding centers. The biscuits were examined for appearance, color, texture, consistency, smell and taste under given local climate conditions. This organoleptic evaluation was repeated after two to three weeks to fulfill the demands of weekly RUF distribution programs. The two recipes for biscuits most favored by wasted children and their caretakers were selected and locally produced.

Based on this experience, a new intervention area was established in another district, where caretakers did not participate in the local production of PMP-Nias during the first month. Later, after the product had been accepted and the caretakers observed the benefits for their children (increased appetite and weight gain), they even started to voluntarily assist in the production of the PMP-Nias. In contrast to the original problems with PMP-Nias, RUF-Nias biscuits were readily accepted and liked by the children and their caretakers.

Micronutrient stability test

Laboratory examination was performed to analyze the nutrient composition of the biscuits using High Performance Liquid Chromatography (HPLC) for vitamins A, E, C, and B₁, and Atomic Absorption Spectrophotometry (AAS) for iron and zinc.

The composition of micronutrients before baking and their deterioration during baking and storage were examined. Baking times and temperatures were investigated under the following conditions using an electric oven:

- 170°C, 20 minutes; 170°C, 25 minutes; 180°C, 15 minutes; 180°C, 20 minutes
A feeding trial was conducted among children aged 6–60 months in the CWS project area, followed by an intervention study that compared the results (e.g., mean weight gain, average duration of stay, and anthropometric and health data) from among 230 children who were given locally produced RUF-Nias biscuits versus locally produced PMP-Nias biscuits. Children discharged from this study (Part I) were admitted into the HBF with Micronutrient Powder (MNP) intervention study (Part II). Both studies included participatory nutrition education interventions, based on the FAO Family Nutrition Guide, in randomly selected areas.

After final discharge, children are followed for six months to assess the long-term effects of the above-described interventions. Further description of the groups and their characteristics (sample size calculations, mean age, sex, and other family background information) goes beyond this publication and will be presented elsewhere.

### Results and discussion

Recipes and nutritional composition

PMP-Nias and the new RUF-Nias biscuits were made from local ingredients produced either nationally (peanuts, milk powder, palm oil, sugar, wheat flour) or on Nias Island (soybeans, seeds, eggs). Originally, the nine newly designed recipes used ingredients such as rice, wheat, manioc, groundnut, cashewnut, coconut, sesame seed, soybean, kidney bean, mungbean, fish flour, milk powder, sunflower oil, palm oil, eggs, and sugar. The ingredients of the two recipes finally selected are shown in Table 1.

It was critical to select the best quality (and more expensive) nationally produced peanuts to minimize microbiological contamination caused by improper post-harvest handling. The taste and flavour of whole milk powder were originally disliked in the project

### Table 1: Recipes of locally produced peanut/milk paste (PMP-Nias) and RUF-Nias biscuits

<table>
<thead>
<tr>
<th></th>
<th>PMP-Nias with skimmed milk powder</th>
<th>PMP-Nias with whole milk powder</th>
<th>RUF 1 –Nias biscuit* with soybean</th>
<th>RUF 8 –Nias biscuit* with mungbean</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ingredients</strong></td>
<td><strong>Weight (g)</strong></td>
<td><strong>Weight (g)</strong></td>
<td><strong>Weight (g)</strong></td>
<td><strong>Weight (g)</strong></td>
</tr>
<tr>
<td>Peanut flour</td>
<td>26</td>
<td>Peanut flour</td>
<td>Wheat flour</td>
<td>25</td>
</tr>
<tr>
<td>Skimmed milk powder</td>
<td>25</td>
<td>Whole milk powder</td>
<td>Peanut flour</td>
<td>25</td>
</tr>
<tr>
<td>Palm oil</td>
<td>34</td>
<td>Palm oil</td>
<td>Soy bean flour</td>
<td>9</td>
</tr>
<tr>
<td>Refined sugar</td>
<td>27</td>
<td>Refined sugar</td>
<td>Palm oil</td>
<td>20</td>
</tr>
<tr>
<td>Vitamin-mineral premix</td>
<td>2.7</td>
<td>Vitamin-mineral premix</td>
<td>Refined sugar</td>
<td>18</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>114.7 g</td>
<td>119.7 g</td>
<td><strong>TOTAL</strong></td>
<td>109.7 g</td>
</tr>
<tr>
<td>Energy (per 100 g)</td>
<td>569 kcal</td>
<td>Energy (per 100 g)</td>
<td>Energy (per 100 g)</td>
<td>536 kcal</td>
</tr>
<tr>
<td>Fat</td>
<td>63%</td>
<td>Fat</td>
<td>Fat</td>
<td>58%</td>
</tr>
<tr>
<td>Protein</td>
<td>10%</td>
<td>Protein</td>
<td>Protein</td>
<td>10%</td>
</tr>
<tr>
<td>Carbohydrate</td>
<td>27%</td>
<td>Carbohydrate</td>
<td>Carbohydrate</td>
<td>32%</td>
</tr>
</tbody>
</table>

*RUF 1 and 8 Nias biscuits were selected based on local acceptability from nine recipes developed in Germany.

<table>
<thead>
<tr>
<th>Micronutrients</th>
<th>WHO, WFP, UN-SCN, UNICEF (for 100 g)</th>
<th>Plumpy’nut™ (in 100 g)</th>
<th>RUF 1-Nias biscuits</th>
<th>RUF 8-Nias biscuits</th>
<th>Premix</th>
<th>RUF 1-Nias (for 100 g)</th>
<th>RUF 8-Nias (in 100 g)</th>
<th>RUF 8-Nias (in 100 g)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Min</td>
<td>Max</td>
<td>Min</td>
<td>Max</td>
<td>No added premix</td>
<td>No added premix</td>
<td>(for 100 g)</td>
<td>(in 100 g)</td>
</tr>
<tr>
<td><strong>Vitamins</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitamin A µg</td>
<td>800</td>
<td>1100</td>
<td>800</td>
<td>1,200</td>
<td>49.0</td>
<td>40.8</td>
<td>930.0</td>
<td>979.0</td>
</tr>
<tr>
<td>Vitamin D µg</td>
<td>15</td>
<td>20</td>
<td>15</td>
<td>18</td>
<td>0.3</td>
<td>0.2</td>
<td>16.2</td>
<td>16.5</td>
</tr>
<tr>
<td>Vitamin C mg</td>
<td>50</td>
<td>-</td>
<td>50</td>
<td>132</td>
<td>0.3</td>
<td>0</td>
<td>54.0</td>
<td>54.3</td>
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<tr>
<td>Thiamine B1 mg</td>
<td>0.5</td>
<td>-</td>
<td>0.5</td>
<td>0.8</td>
<td>0.1</td>
<td>0.1</td>
<td>0.8</td>
<td>0.9</td>
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<tr>
<td>Riboflavin mg</td>
<td>1.6</td>
<td>-</td>
<td>1.6</td>
<td>2</td>
<td>0.1</td>
<td>0.1</td>
<td>1.8</td>
<td>1.9</td>
</tr>
<tr>
<td>Vitamin B6 mg</td>
<td>0.6</td>
<td>-</td>
<td>0.6</td>
<td>0.7</td>
<td>0.1</td>
<td>0.1</td>
<td>0.6</td>
<td>0.7</td>
</tr>
<tr>
<td>Vitamin B12 µg</td>
<td>1.6</td>
<td>-</td>
<td>1.6</td>
<td>2</td>
<td>0.1</td>
<td>0.1</td>
<td>1.8</td>
<td>1.9</td>
</tr>
<tr>
<td>Niacin mg</td>
<td>5</td>
<td>-</td>
<td>5.0</td>
<td>5.9</td>
<td>4.0</td>
<td>3.5</td>
<td>7.7</td>
<td>11.7</td>
</tr>
<tr>
<td>Biotin µg</td>
<td>60</td>
<td>-</td>
<td>60</td>
<td>72</td>
<td>3.1</td>
<td>2.6</td>
<td>62.9</td>
<td>66.0</td>
</tr>
<tr>
<td>Folic acid µg</td>
<td>200</td>
<td>-</td>
<td>200</td>
<td>230</td>
<td>52.0</td>
<td>53.4</td>
<td>203.8</td>
<td>255.8</td>
</tr>
<tr>
<td>Vitamin K µg</td>
<td>15</td>
<td>30</td>
<td>15</td>
<td>25</td>
<td>8.0</td>
<td>6.9</td>
<td>20.3</td>
<td>28.3</td>
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<tr>
<td>Vitamin E mg</td>
<td>20</td>
<td>-</td>
<td>20</td>
<td>25</td>
<td>3.9</td>
<td>3.2</td>
<td>16.2</td>
<td>20.1</td>
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<tr>
<td>Pantothenate mg</td>
<td>3</td>
<td>-</td>
<td>3</td>
<td>3.7</td>
<td>0.7</td>
<td>0.6</td>
<td>3.3</td>
<td>4.0</td>
</tr>
<tr>
<td><strong>Minerals</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcium mg</td>
<td>300</td>
<td>600</td>
<td>300</td>
<td>600</td>
<td>58.0</td>
<td>32.3</td>
<td>287.9</td>
<td>345.9</td>
</tr>
<tr>
<td>Iron mg</td>
<td>10</td>
<td>14</td>
<td>10</td>
<td>14</td>
<td>3.1</td>
<td>1.8</td>
<td>10.8</td>
<td>13.9</td>
</tr>
<tr>
<td>Iodine µg</td>
<td>70</td>
<td>140</td>
<td>70</td>
<td>140</td>
<td>0.9</td>
<td>0.8</td>
<td>119.9</td>
<td>120.8</td>
</tr>
<tr>
<td>Zinc mg</td>
<td>11</td>
<td>14</td>
<td>11</td>
<td>14</td>
<td>1.6</td>
<td>1.1</td>
<td>13.3</td>
<td>14.9</td>
</tr>
<tr>
<td>Sodium mg</td>
<td>-</td>
<td>290</td>
<td>-</td>
<td>290</td>
<td>16.0</td>
<td>14.8</td>
<td>0</td>
<td>16.0</td>
</tr>
<tr>
<td>Potassium mg</td>
<td>1,110</td>
<td>1,400</td>
<td>1,100</td>
<td>1,400</td>
<td>353.0</td>
<td>202.5</td>
<td>600.9</td>
<td>953.9</td>
</tr>
<tr>
<td>Magnesium mg</td>
<td>80</td>
<td>140</td>
<td>80</td>
<td>140</td>
<td>69.0</td>
<td>44.4</td>
<td>22.6</td>
<td>91.6</td>
</tr>
<tr>
<td>Phosphorus mg</td>
<td>300</td>
<td>600</td>
<td>300</td>
<td>600</td>
<td>206.0</td>
<td>141.8</td>
<td>144.7</td>
<td>350.7</td>
</tr>
<tr>
<td>Copper mg</td>
<td>1.4</td>
<td>1.8</td>
<td>1.4</td>
<td>1.8</td>
<td>0.5</td>
<td>0.3</td>
<td>1.8</td>
<td>2.3</td>
</tr>
<tr>
<td>Selenium µg</td>
<td>20</td>
<td>40</td>
<td>20</td>
<td>40</td>
<td>0</td>
<td>0</td>
<td>30.6</td>
<td>30.6</td>
</tr>
</tbody>
</table>
area. More expensive skimmed milk powder was therefore introduced during the initial months of the PMP-Nias production. Once the children and caregivers became familiar with the taste of PMP-Nias, both skimmed and whole milk powders were used, depending mainly on price and availability in the different project areas. Palm oil was the only available type of oil on Nias Island and was therefore used as the oil source for PMP-Nias and RUF-Nias biscuits.

Selection of biscuits for use in daily and weekly intervention programs

Of the nine newly designed RUF recipes, RUF-1 and RUF-8 biscuits were selected on the bases of the constant availability and accessibility of the ingredients on Nias Island; the high acceptability of the biscuits by children aged 6 to 60 months and their caregivers; and the stability in taste, color, consistency and texture after baking and up to three weeks of storage under local weather conditions (on average 30°C). The composition of the RUF-1 and RUF-8 selected biscuits, with and without the vitamin/mineral premix, is shown in Table 2.

Laboratory examination of RUF 1-Nias biscuits

As shown in Figure 1, a baking temperature of 180°C for 15 minutes resulted in the lowest loss of vitamins while the greatest loss was observed at 170°C for 25 minutes and 180°C for 20 minutes. Heat-sensitive micronutrients should be added in slightly higher amounts in the vitamin-mineral premix to make up for losses during the baking process.

Storage at room temperature for two to three weeks produced no further loss of the investigated micronutrients. In some trials, the vitamin content was even slightly higher after two to three weeks. This can only be explained by the fact that the premix was probably not well mixed into the dough. Therefore, for local production, we recommend producing smaller amounts of biscuits (a maximum of 1 kg was mixed in Nias), more regularly and according to the demand.
Iron and zinc content in the RUF biscuits after baking was similar to the calculated amounts, confirming that the right amount of these essential minerals had been mixed into the dough.

It is important to note that a kerosene stove was used in Nias which cannot keep exact temperature. Therefore, the CWS staff was advised to bake the RUF-Nias biscuits until they were light brown (which took about 20 minutes at about 170–180°C).

Feeding recommendations

The RUF-Nias biscuits were mainly developed as an alternative to locally produced PMP-Nias for wasted children aged 6–60 months during the rehabilitation phase. For younger children, especially infants aged 6–12 months, the biscuits were crushed into small quantities of boiled drinking water and offered by the spoonful. Mothers/caretakers were instructed to offer the biscuits between family meals and after breastfeeding. Caretakers were informed that the biscuits are supplementary foods designed to support weight and height gain in malnourished children. Originally, the recommended number of biscuits per day was calculated to cover about 50% of the daily energy requirements of individual children, based on the child’s weight. Energy requirements were taken from FAO/WHO/UNU recommendations for children’s dietary energy intakes.7

After field testing, the number of biscuits to be consumed was increased by 10% to cover 60% of the daily energy requirements of children, in line with Indonesian guidelines.8 The increase takes into consideration the possible sharing of the biscuits within families. Children aged 6–24 months, with a weight of about 6–10 kg received 4–7 biscuits per day (50–90 g); children aged 2–5 years, weighing 10–15 kg, were given 7–11 biscuits (90–150 g) per day.

As the locally produced PMP-Nias quickly sours under local temperatures of about 30°C, it was produced and distributed on the same day with close supervision. The same holds true for commercially produced Plumpy’nut™, which can be used for only one day after the packaging is opened.9,10 (In the Uganda experience, a local substitute of Plumpy’nut™ was produced on a weekly basis because it could be stored in a refrigerator.)5 For a child aged 6–24 months, with a weight range of 6–10 kg, half to one portion of PMP-Nias (50–100 g) was distributed each day; children aged 2–5 years, weighing about 10–15 kg, received 1–1.5 portions per day (100–150 g).

Cost estimation

The costs of the RUF1-Nias biscuits and PMP-Nias were calculated according to local prices for the ingredients (Table 3). In general, prices are higher on Nias Island compared to other parts of Indonesia, mainly because transportation costs are exacerbated by uneven deliveries resulting from bad weather.

Table 4 presents an overview of the calculated costs per 100 g of two locally-produced PMPs (Uganda and Nias) and the RUF1-Nias biscuits. The cost of the PMP produced in Uganda is included to illustrate the variability of local production costs.

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>PMP- Nias</th>
<th>RUF 1-Nias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peanuts</td>
<td>0.55 – 0.57</td>
<td>0.46</td>
</tr>
<tr>
<td>Wheat flour</td>
<td>0.40</td>
<td>0.40</td>
</tr>
<tr>
<td>Soybean/mungbean</td>
<td>0.11</td>
<td>0.11</td>
</tr>
<tr>
<td>Palm oil</td>
<td>0.39</td>
<td>0.20 – 0.30</td>
</tr>
<tr>
<td>Sugar</td>
<td>0.27</td>
<td>0.18</td>
</tr>
<tr>
<td>Egg</td>
<td></td>
<td>0.13</td>
</tr>
<tr>
<td>Whole-, skim milk powder</td>
<td>1.44 - 2.99</td>
<td></td>
</tr>
<tr>
<td>Vitamin/mineral premix</td>
<td>0.04</td>
<td>0.04</td>
</tr>
<tr>
<td>Total</td>
<td>2.69 – 4.26</td>
<td>1.52 – 1.62</td>
</tr>
</tbody>
</table>

Table 3: Cost of ingredients per kg of PMP-Nias and RUF-1 (in euros)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.22 – 0.30</td>
<td>0.27 – 0.43</td>
<td>0.15 – 0.16</td>
</tr>
</tbody>
</table>

Table 4: Price comparison (Note: the calculation does not include costs of equipment and salaries for NGO staff responsible for production, distribution and monitoring)
The World Health Organization (WHO) revised its guidelines for the management of severe malnutrition in 1999 and introduced therapeutic milk for severely malnourished children with medical complications – a treatment that has been successfully implemented in hospitals worldwide. However, therapeutic milk powder requires clean water for reconstitution as well as close supervision because, if left unrefrigerated in hot climates, milk serves as a favorable medium for bacterial growth. In much of the world, caretakers are required to stay for multiple weeks in clinics with their malnourished child, which causes considerable inconvenience for other family members too.

To reach more children at an earlier stage and to bring the services directly to communities, a food spread called Plumpy’nut™ was developed for severely malnourished children without clinical complications. This product can be given as part of a home-based treatment under a system of weekly supervision. Plumpy’nut™, the first Ready-to-Use Therapeutic Food (RUTF) developed, is nutritionally comparable to therapeutic milk, and is made of peanut butter, milk powder, vegetable oil, sugar, and a vitamin-mineral mix. Packed in air-tight sachets, Plumpy’nut™ has a relatively long shelf life and can be immediately consumed without further preparation. In several studies, Plumpy’nut™ (whether imported or locally produced) enabled similar weight gain in severely malnourished children as therapeutic milk under hospital-based care. RUTFs have thus been successfully used in Community-based Therapeutic Care programs, reducing the constraints posed by lack of access to clean water and caretaker separation from families.

For efficiency, the blanket distribution of an RUTF is recommended. Plumpy’nut™, however, which is mainly produced in industrialized countries, can be too expensive for blanket distribution on a large scale. In order to reduce costs, increase coverage, supplement local diets, and support local economies, experts are advocating the production of RUTFs from locally available ingredients in countries with a high prevalence of malnutrition.

A successful approach in treating and preventing mild-to-moderate malnutrition prevents conditions from worsening to severe forms of malnutrition. Recently, several products for treating and preventing different forms of malnutrition have been proposed by the UN World Food Programme (WFP), under its partnership with DSM.

References for Box 1

h. World Food Programme/DSM. Ten minutes to learn about nutrition programming. SIGHT AND LIFE Magazine 2008, Supplement.

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**Box 1: Ready-to-Use Therapeutic Food (RUTF)**

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| The cost calculation was based on the average price of the ingredients used in Nias in 2007 (1 euro was approximately Rp 12,000). The cost of 100 g of PMP-Nias was between 27 and 43 euro cents, depending on the type of milk powder (whole or skimmed milk), while the cost of the vitamin-mineral premix to produce 100 g of RUF biscuits or PMP-Nias was 0.4 euro cents. This price does not include the cost of transportation from DSM Singapore to Jakarta, which was borne by DSM. |

| Preliminary results |

| Of the 230 moderately/mildly wasted (<3 to < -1.5 WHZ) children |
admitted into the ongoing RUF-Nias intervention study (Part I), 152 recovered successfully (discharged at > -1.5 WHZ).

Despite the higher cost of the PMP-Nias, the RUF-Nias biscuits resulted in better weight gain. The best weight gain (5.5 g per kg body weight per day) was achieved through the use of the biscuits combined with participatory nutrition education, followed by the use of the biscuits alone (3.7 g per kg body weight per day), and finally by the use of the PMP-Nias (3.5 g per kg body weight per day) in daily intervention programs. Data from weekly programs indicate similar results but somewhat lower weight gains.

The average length of participation in the program was approximately 3–5 weeks. In the Part II study, of the 210 mildly wasted (< -1.5 to < -1 WHZ) children admitted into the ongoing Home-Based Foods with Micronutrient Powder intervention, admitted into the ongoing RUF-Nias intervention study (Part I), 152 recovered successfully (discharged at > -1.5 WHZ).

### Box 2: Energy and macronutrient content (per 100 g)

<table>
<thead>
<tr>
<th>Plumpy’nut™</th>
<th>PMP-Nias*</th>
<th>Average of 9 RUF recipes</th>
</tr>
</thead>
<tbody>
<tr>
<td>520–550 kcal</td>
<td>569–590 kcal</td>
<td>500–536 kcal</td>
</tr>
<tr>
<td>10–12 % protein</td>
<td>7–10 % protein</td>
<td>8–14 % protein</td>
</tr>
<tr>
<td>45–60 % fat</td>
<td>63–67 % fat</td>
<td>31–58 % fat</td>
</tr>
<tr>
<td>28–45 % carbohydrate</td>
<td>26–27 % carbohydrate</td>
<td>31–44 % carbohydrate</td>
</tr>
<tr>
<td>Nutriseta (*whole/skim milk)</td>
<td>Shapiro, 2007b</td>
<td></td>
</tr>
</tbody>
</table>

The amount of RUF1-Nias biscuits needed each day was calculated as follows:
- 100g of biscuit dough contains 536 kcal;
- 8 individual biscuits are made from about 100 g dough;
- 1 individual biscuit weighs about 13 g and contains about 67 kcal.

### References for Box 2


**Figure A:** Proposed feeding programs according to nutritional status

**Table:**

- **TFP:** Inpatient Therapeutic Feeding Programs
- **OTP:** Outpatient Therapeutic Feeding Program
- **SFP:** Supplementary Feeding Program
- **CFS:** Complementary Food Supplements e.g. Suppl. Plumpy, RUF biscuits
- **FBF:** Fortified Blended Food
- **MNP:** Micronutrient Powder e.g. Sprinkles, MixMe

TFP: - Milk formula: F-75, F-100
OTP: - RUTF e.g. PlumpyNut, BP-100
SFP: -
101 children were discharged successfully (≥ -1 WHZ). Accompanying participatory nutrition education also improved weight gain in this study.

**Recommendations**

Given the efficacy of locally produced RUF-Nias biscuits (without milk powder) in improving weight gain among moderately/mildly wasted children, the biscuits should next be tested and compared with PMP-Nias for use in treating severely wasted children. RUF-Nias biscuits with milk powder (providing high quality protein and essential fatty acids) should also be tested for an impact on weight gain among severely and moderately wasted children; if successful, RUF-Nias biscuits would be appropriate for a wider range of malnutrition problems.

Given the improved weight gain among wasted children who received RUF in combination with nutritional training for their caretakers, the results further suggest that participatory nutrition education should accompany nutrition interventions.

**Acknowledgements**

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**References**


**Reader Survey on-going**

**Questionnaire available at:** www.sightandlife.org

As a platform for the exchange of programmatic and scientific information, we would like the SIGHT AND LIFE Magazine to remain ever-evolving and adaptive to the new realities of the micronutrient field. We are, therefore, currently conducting a survey to gather our readers’ opinions.

We would very much appreciate it if you could participate in our survey, and share with us your views on the Magazine and your suggestions for ways to improve it through a short online questionnaire. This should only take 5 to 10 minutes of your time and would be a great help to us in making the Magazine better suited to meet your information and knowledge needs.

Readers who dedicate some of their time to answering this survey will be included in a lucky draw after the survey period to receive rewarding prizes.
An innovative and timely gathering was convened on the campus of McGill University in Montreal, Canada, over two days and six working sessions on September 25–26, 2008, with developing country participants from Haiti and Guatemala in the Western Hemisphere; Uzbekistan, India and China in Asia; and Ethiopia, Nigeria, Morocco and Kenya in Africa.

The nation’s tradition of international concern and its major agricultural potential accounted for the timing and location of the meeting. In fact, the momentum for this conference emanated from the University’s Faculty of Agriculture, under the leadership of its dean, Dr Chandra Mandramootoo.

Speakers in the first working session, entitled ‘Voices from the Field,’ highlighted key topics, including the status of food and agricultural production, food insecurity, and the issues and possible solutions for diverse nations and regions of the world. Current data on production and prices of food, risk of hunger, and the contributing factors for both were brought to the forum by residents of the various countries from different disciplinary backgrounds.

Among the factors mentioned as determinants of local food availability were climate change, soil erosion, dependency on natural rainfall, and post-harvest losses. In some settings, food safety standards can be a hindrance to the abundance of foodstuffs. Although food prices have risen acutely in the past months, the fraction of family income spent for food had been falling over the past three decades. Controversy raged regarding the degree to which liberalization of food trade has acted as an aide or an obstacle to maintaining food. This is true for Haiti, which has no option but to import food from the world market, and China, which is debating the option of integration with – or isolation from – world food trade and international price norms. In fact, 84% of the total rate of inflation in China is attributable to the increase in the cost of food.

The second session, which covered the ‘World Food Situation,’ synthesized national case studies into more comprehensive and integrated descriptions and analyses. Representatives from a potpourri of organizations and institutions related to agriculture, either in its production or distribution sense, contributed to the discussions.
Among the entities represented on the program were McGill University, the International Rice Research Institute, the International Food Policy Research Institute (IFPRI), the Farm Foundation, and the Inter-American Institute for Cooperation on Agriculture.

The discussion began by framing the recent World Health Organization analysis of the world food situation in terms of recent changes that have brought on the crisis. The adaptive measures in the face of food shortage include reducing the number, size and diversity of foods in meals. Grains used for biofuels compete for land and water, and IFPRI has called for a moratorium on using grains for biofuels. The underlying contributors to food inflation are export bans on cereals and edible oils and price speculation. With the intimate linkage of food to human survival, aggressive regulation of speculation can be advocated. IFPRI has written a major policy paper on the crisis that summarizes a four-point package (see Box 1).

Rice became the centerpiece of discussion, as it is the most widely consumed of the staple grains. Technical advances were highlighted, including a hybrid variety of rice that can produce substantial yields even when totally submerged, as during the monsoon season in Bangladesh. There is a need, however, for rebuilding human resources for the research endeavor to create a new ‘green revolution’ for this important crop. Responses came from a panel of three discussants representing the Canadian Faculties of Agriculture and Veterinary Medicine, the Organization for Economic Cooperation and Development (OECD), and the Canadian Federation of Independent Grocers.

The third session pursued ‘The Underlying Factors for the Food Crisis,’ with speakers from five entities: the International Federation of Agricultural Producers, the George Morris Centre, the Carnegie Endowment for International Peace, the Canadian Centre for Policy Alternatives, and the African Rice Centers. Climatic factors led the discussion: Droughts in Australia disrupted the world wheat trade, with ripple effects throughout the globe. In Bangladesh, severe effects from flooding were felt. However, it is more productive to examine factors on a local or regional basis, as impacts are variable depending on geography. The fallacy in a one-size-fits-all approach to solutions was decried, and the necessity for nuance in resolving the problems was highlighted.

The response panel included representatives from Pulse Canada, the Canadian Agro-Food Policy Institute and McGill University. Much was made of the differential impact on incomes from increasing food prices, depending on whether households or nations are net producers or net consumers of food. In settings where farmers are net producers of food, increased family incomes and improved wellbeing arises when food prices rise. Assuring better incomes across all sectors would be a strategy by which farmers could benefit while other groups still have purchasing power to face higher food costs.

The ‘International Response to the Crisis’ was the topic of the fourth session. Its task was to integrate the facts and insights of the first three blocks. United Nations, and international and bilateral agencies were represented, including the World Food Programme (WFP), the Food and Nutrition Organization, the International Federation of the Red Cross and Red Crescent, OECD, and the International Commission on Irrigation and Drainage (ICRD). It was clear that WFP and the Red Cross/Red Crescent are primed to humanitarian assistance in response to the negative consequences of food scarcity, with targeting and focusing being key to strategies. Within Africa, there is an acknowledgement that the areas with the highest endemicity for HIV merit special attention. No mention was made of micronutrients, fortification or the nutritional quality of the diet. The rational use of water for irrigation is key to the support of food agriculture.

Panelists from the International Crop Research Institute for the Semi-Arid Tropics, McGill University, and the Carnegie Endowment for International Peace led the discussion, which highlighted the potential for using non-conventional crops suited to arid lands, such as sorghum and cow peas. At least 1.6 billion people live in semi-arid climes. An important point, however, was the delineation between short-term measures to mitigate the suffering and long-term strategies for development.

The fifth session, entitled ‘Getting Food to the People: Success Stories,’ accommodated speakers from the Canadian Foodgrain Bank, the Nanking Agricultural

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**Box 1: Four point response package of the International Food Policy Research Institute**

- Expand emergency and humanitarian assistance
- Eliminate export restrictions on food
- Promote crop production programs with short-term impact
- Change policies for directing grain and oil seed to biofuels
University in China, the Ministry of Agriculture of Guyana, the Biotechnology for Sustainable Development in Africa Foundation, and ICRD. An important strategic point came up in this session: the need for a twin track. The first is to meet the immediate needs of the hungry. The second is for action to strengthen livelihoods, as the impact is most serious for those who were hungry before the crisis. Interesting contrasts were drawn between the two Asian countries whose combined populations make up over one-third of humanity, China and India. China has one-fifth of the world's population, with 10% of the arable land but only one-fourth of the world average per capita water availability. China has a mixed strategy of domestic production and trade to fill its food needs. India has one-sixth of the world’s population, balanced with one-sixth of the arable land. Forty percent of the crop land is irrigated, but 60% is monsoon-rainfall dependent. While up to 70% of the Indian laborforce is dedicated to agriculture, the sector contributes only 25% of gross domestic product (GDP). India is currently self-sufficient in food.

For sub-Saharan Africa, the situation is distinct. Most of the processing and profits for materials from Africa are generated outside of Africa. When it comes to food for human consumption, there is a widespread skepticism about quality control standards in Africa. A case-study of the plant, Moringa (Moringa oleifera), an African food plant used in a food supplement was cited. Its successful production for local and for international markets is an example to be followed, and allows for the optimism for the motto ‘trade not aid’ to become the standard for Africa, as well.

The topics of Food Security in China, with respect to rising prices and the search for policy solutions, were analyzed by Dr Jing Zhu, agricultural economist at the Nanjing University in the People's Republic of China.

The economics of agriculture in Canada are a threat to food security. It is unprofitable to be a farmer. Higher price for food is inevitable, and it needs to be framed within popular expectation.

A prestigious panel for this last session included the High Commissioners to Canada from Kenya and Nigeria, the Minister of Agriculture of Guyana, the Moroccan General Council of Agricultural Development, a pastor who leads a faith-based relief agency, the Deputy Minister of the Nova Scotian Department of Agriculture, and a representative of the Food and Agricultural Policy Group constituted the discussant panel. The points made included that the problems of getting food to people will eventually affect everyone, political will and collaboration will be needed to meet the challenges, and one cannot expect a unique solution to multifaceted problems.

The topic of the sixth and last segment of the program was ‘The Way Forward: Elements of a Framework for Managing the Crisis and Concluding Remarks.’ The Honorable Michael Chong, Member of the Canadian Parliament for Wellington-Halton Hills District, was the keynote speaker for the final session. He drew some considerations of Canada in the world at large, including features on Canadian soil and features overseas. The key points of MP Chong’s discourse are included in Box 2.

Box 2: Key Points raised by the Honorable MP Michael Chong

- Urban sprawl is a major factor in reduction of arable land devoted to cultivation. The growth of cities around the Great Lake Basin has environmental consequences, including damaging the aquifers of the region. Water levels in the Great Lakes are at low or record low levels.

- Climate change is a reality, and Canada should sign on to the efforts to cap carbon emissions into the environment.

- Increased cost of crude oil is a threat to the model of food trade, growing in one location and consuming in another. Canada must continue to avoid the practice of ‘dumping’ excess agricultural production into countries in which it will suppress the price and adversely affect local production.

- Biotechnology is not the whole solution to the food security problem, but it is part of the solution.

- The economics of agriculture in Canada are a threat to food security. It is unprofitable to be a farmer. Higher price for food is inevitable, and it needs to be framed within popular expectation.
Organization (FAO), and a former Canadian prime minister, Joe Clark, who is currently a Professor at the McGill Centre for Developing-Area Studies. The speakers tried to impart some notes of wisdom on the overall themes to carry the effort forward. It was emphasized that the farmer needs to be at the center of food policy considerations, and that women are often the farmers in developing countries. Technologies to improve the income of farmers must be applied. Beyond the small farm sector, general civil society is a principal stakeholder, along with the private sector and academia.

The most inspirational words came from Rev. Jim Cornelius and Prof. Clark. The former is a church pastor who runs the faith-based Canadian Foodgrains Bank. He urged a strategy to decide on one thing to do differently to make a difference for hungry people, build collaborative networks, turn the food crisis to the advantage, and give surplus to those who do not have. The latter urged the attendees to build on the momentum of the conference, starting with the simple “doable” actions. He further urged a triple alliance of public, private, and people partnership. With this alliance, moreover, corporate responsibility should come from beyond the agro- and food-industry sectors, including the international mining sector in the case of Canada.

In summary, the two-day meeting allowed a variety of speakers from diverse geographical experiences and professional backgrounds to share their reflections on the world food crisis. It was evident that it was easier to find instances of grave consequences of food insecurity than to cite successful case studies of successful responses. Policy makers are grappling with multiple options, and it is timely to have all of the ideas aired and discussed.

A memorable phrase from the meeting was from Prof. Clark: “Paradigms do not just shift – they get shoved.” This crystallized a consensus that conventional ways of viewing agriculture, food trade and family incomes need to be re-evaluated. Demography, climate and water resources are important constraints, as are the fuel costs to transport grains from producer to consumer nations.

Perhaps it was disappointing that the elements to shove the paradigm even further did not arise. The sense of the meeting seemed to be simply to get things back to the state they were before the crisis, without a real critique of what might have been wrong with nutritional adequacy and health in pre-crisis times. The acuteness and severity of the crisis may have drained the optimism to move the agenda to a third way; this would continue to move thebulk of humanity from a precarious and marginal (albeit calorically adequate) diet to a secure and quality diet.

**Key reflection from the conference**
- *If you have no water, you have no food security.*
- *Hunger is the result of poverty and the cause of poverty.*
- *Preventing the distraction of hunger allows people to work and hopefully receive an income that lifts them out of poverty.*
The 3rd African Nutritional Epidemiological Conference (ANEC III) was held in Cairo, Egypt, from October 13–16, 2008. Prof. Ashraf Shaalan, of Egypt’s National Research Centre (NRC), was the Conference chairman, while Prof. Anna Lartey, of the University of Ghana, chaired the international Scientific Committee. They jointly guided the three days of academic sessions.

Held at the NRC, at the center of Cairo, the Conference saw over 250 attendees gathered on the theme, ‘The Epidemiological and Nutritional Transition in Developing Countries: Accelerating progress for nutrition in Africa.’ A total of 25 countries – including 14 African countries – were represented.

Unique to this conference were special awards ceremonies for two venerable leaders of human and public health nutrition: Prof. Nevin Scrimshaw, from the USA, and Prof. Mohammed Gabr, from Egypt. The career trajectory and contributions of Dr Scrimshaw was narrated and interpreted by two of his former students, Noel Solomons and Ricardo Uauy. The narrative extended from his founding of the Institute of Nutrition of Central America and Panama in Guatemala, to his leadership of the International Nutrition Foundation, with stops as department chair at the Massachusetts Institute of Technology, president of the International Union of Nutritional Science (IUNS), vice-rector at the United Nations University, and World Food Prize Laureate, along the way. A massive birthday cake honored the 90 years of this lion of human and clinical nutrition, whose creative impact has been felt in every region of the globe, including the length of Africa. Although unable to travel to Cairo in person, Prof. Scrimshaw addressed the assembly by way of a video message.

Prof. Gabr, a native of Cairo, distinguished himself through his publications on pediatrics and pediatric nutrition, as the former president of IUNS, and the ex-Minister of Health of Egypt. Prof. Osman Galal, cur-

Key messages from ANEC III

- Malnutrition (undernutrition, obesity, micronutrient deficiencies and associated diseases) are still public health concerns in Africa.
- Research and interventions, capacity building and partnerships (public-private-community) are key actions to contribute to the sustainable improvement of nutrition and food security in communities.
- The dissemination of research results is another way to help communities in raising awareness about their conditions.
- Advocating for better integration of nutrition concerns in government policies will also strongly boost better nutrition among communities.

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rent secretary general of IUNS, recounted the distinguished accomplishments of Dr Gabr in the context of Egyptian society and international projection.

**Box 1: Titles of the keynote addresses in the plenary sessions of the 3rd African Nutritional Epidemiology Conference**

- Global nutritional challenges: Accelerating progress for nutrition in Africa
- The role of nutrition in the attainment of the Millennium Development Goals
- Epidemiological and nutrition transition: Global perspectives and examples of successful approaches
- Epidemiological and nutrition transition: How much progress has been made in addressing the double burden of disease in sub-Saharan Africa
- Facing nutrition transition under the double burden: Challenges and potential programs in Africa
- Training and capacity-building needs for nutrition in Africa
- Cancer trends in Africa: a cause for concern?
- Innovation in the management of malnutrition in developing countries
- Tackling obesity in Africa: Pragmatic approaches
- Scaling up nutrition interventions: Examples of programs to prevent zinc deficiency
- Interventions among school-aged children in developing countries
- Current trends in HIV/AIDS and their implications for human and economic development
- Biodiversity: A tool for addressing nutrition problems in Africa
- The challenge of breaking the cycle of poverty and hunger in an unequal world
- Ensuring community participation and scaling up nutrition through NGO work

**Keynote addresses**

Fifteen keynote addresses were programmed to provide a voice for an equal number of distinguished professionals from Africa and around the world. Their titles are listed in Box 1. On the one hand, they attest to the seriousness with which the double burden of health concerns – implicit in the thematic key term of ‘nutrition transition’ – was brought into the meeting program. On the other hand, although vitamin and mineral topics were treated in many of the keynote discourses, only that by Dr Kenneth Brown, regional advisor for Helen Keller International, based in Dakar, Senegal, was explicitly related to a micronutrient.

Dr Brown spoke on ‘Scaling up Nutrition Interventions: Examples of programs for preventing zinc deficiency.’ He reviewed the evidence for the existence of endemic zinc deficiency in low-income nations, and the impact that zinc supplementation and fortification have had in controlled, efficacy field trials. He then addressed the challenges and, to some extent, frustrations related to an agenda of getting public health interventions onto a scale to cover the needs of all vulnerable segments of the population. Appropriate technology, cost, political will, programmatic integration, and long-term sustainability were among the issues identified.
Plenary sessions

The ANEC III program featured three plenary symposia. The first was sponsored by Unilever and entitled ‘Advancing Nutrition and Health in Africa: The Power of Partnership,’ which included presentations from industry, a private consultancy, academia and the United Nations system. The second in this series was entitled ‘Food Biotechnology and Biodiversity in Africa,’ which included topics such as probiotics, transgenic fish, wild foods, protein quality and iron-fortified whole maize flour. The final symposium, ‘Recent Advances in Amino Acid Research,’ was held to honor Prof. Scrimshaw and the field he pioneered. After a video presentation from the honoree, six presenters covered an array of advances in understanding amino acid requirements and the bioactive functions of specific amino acids.

The two workshops in the program were astutely tailored to the needs of modern nutritional epidemiology. The first was entitled ‘Validation of Dietary Assessment Instruments’ and provided a useful orientation on the nuances of field approaches to assessing dietary intake and exposures. The second was entitled ‘How to Use the New WHO Child Growth Standards’ and provided clarity on the World Health Organization’s new standards and an orientation to the online tools available to analyze survey databases.

Forward-looking themes and projections of Africa’s future characterized the two roundtable panel presentations that closed the proceedings. One roundtable panel was on public-private partnerships and included speakers from GAIN, Unilever, Nestlé, the World Food Programme and UNICEF in an interactive discussion about improving nutritional health in Africa. The other roundtable panel considered research and training needs for the nutrition profession in Africa. It drew together the experiences of the Nutritional Leadership Program in Africa and comparisons with other efforts across the continent as well as in the USA and the UK.

Free-paper program

Interspersed among the invited presentations, the organizers programmed almost 200 free-papers submitted by students, young investigators and seasoned professionals from around the world. Sixteen oral-presentation sessions on free-papers were presented, which numbered a total of 87 papers. Of these, 15 were explicitly related to micronutrients of interest to the readership of the Magazine (Box 2).

Specifically named in these free-paper titles were multiple micronutrients (four papers), iron (four papers), zinc (two papers), and ascorbic acid, folic acid, and iodine (one paper each).

A total of 98 free-papers were included in the poster sessions (Box 3). Vitamin A is mentioned in four, iron in three, zinc in two, and...
iodine, folic acid, vitamin B_{12} and vitamin C in one each among the titles. A multiple micronutrient context was explicit in one title and implicit in another.

Conclusions

The shores of the Nile and the shadow of the Pyramids of Giza represent a splendid setting for any event. This meeting in Africa was made all the more impressive by the diversity of geographical representation, superb organization, and broad development of the program. The ANEC III program gave a serious and contemporary treatment to relevant nutritional and public health problems affecting Africa with rigorous and scholarly evidence. The organizers took a big-tent approach in two important and favorable respects. Although the meeting was dedicated, in name, to nutritional epidemiology, all aspects of nutrition from biochemical to clinical to population were included. Moreover, the participation of private and corporate entities, both in final sponsorship and plenary presentations, advanced the reality of private-academic-public partnership.

Authors’ acknowledgements

We are grateful to SIGHT AND LIFE, INF, IUNS, Unilever and all other sponsors for granting fellowships to many of the participants to attend ANEC III, which gave us the opportunity to meet, share knowledge and create networks with stakeholders from around the world.

Box 3: Free-paper themes explicitly related to micronutrients in the poster presentation program

- Contribution of food-based interventions to the consumption of vitamin A-rich foods among children 6–36 months of age in Salelugu-Nanton District of Northern Ghana
- Provitamin A carotenoids content of dried fermented cassava roots: Influence of food fortification
- Effect of steam-drying on the content of β-carotene, vitamin C and total lipids in squashes (*Cicurita spp.*) from Cameroon
- A study on iodine stability under different storage conditions
- Wild leafy vegetable consumption in the Buhera District of Zimbabwe: A potential means of improving micronutrient nutrition in resource-poor communities in developing countries
- The impact of consumption of traditional Food Multi-Mix (FMM) recipe on serum ferritin and iron nutritional status among low-income pregnant women in Gauteng, South Africa
- Production and acceptability of Edam cheese fortified with zinc
- Homocysteine: Vitamin B_{12} and folic acid plasma levels in relation to cognitive function in Egyptian elderly group
- A study of anemia among pregnant women in Ouagadougou: Links with diet and consequences for fetal growth
- Iron and zinc nutritional status of women in their reproductive age in urban Africa
- Maternal vitamin A deficiency during pregnancy: A disaster waiting to happen
- Infant and follow-up milk-based formula and iron fortification in relation to iron deficiency in Egypt
Dietitians and nutritionists from around the world convened, shared research findings, and discussed issues, policies and education relating to nutrition and the activities of dietitians at the 15th International Congress of Dietetics (ICD), held in Yokohama, Japan, on September 8–11, 2008.

On the theme, ‘Global Dietetic Linkage and Cooperation for Human Health,’ the congress explored approaches to new solutions to global food and nutrition issues. A particular focus was the double burden of malnutrition, where both over- and undernutrition affects the same population. Lifestyle-related chronic diseases are no longer only a problem among developed country populations, they are also increasingly affecting rapidly urbanizing developing country populations. The globalization of diets, both healthy and harmful, requires global cooperation to ensure adequate nutrition and health among all populations.

Programs on various topics in dietetics were organized during the congress. Program sessions consisted of lectures by high-profile speakers from around the world on the latest topics in nutrition and food, clinical nutrition, food service management, public health nutrition, education, and dietetics skills. The congress created opportunities for participants to present on and share their activities and experiences, and to discuss topics with experts from various sectors.

The International Congress of Dietetics is an international conference held every four years by the International Confederation of Dietetic Associations (ICDA). ICDA is comprised of national dietetic association members from around the world, representing about 150,000 dietetics professionals. The first International Congress of the ICDA was held in 1952 in the Netherlands; successive Congresses have continued to serve as a way for members to meet and receive support from beyond national and regional boundaries.
Introduction
The food and nutrition situation among populations in sub-Saharan Africa remains of concern and is aggravated by the dual action of demographic growth and degradation of the ecological bases of food production.

To deal with this situation, it is increasingly being recommended that food and nutrition considerations be integrated into all sustainable development programs. Training in nutrition and food science for the different participants contributing directly or indirectly to this development represents one certain way of achieving this integration and, in turn, reducing the effects of malnutrition in Africa. To this end, the Department of Nutrition and Food Science, at the Faculty of Agronomic Sciences at Abomey-Calavi University in Benin, has been running a program of International Training in Nutrition and Food Science (known under its French acronym, FINSA) since 1992.

The implementation of this training program resulted from recommendations made at a regional seminar to introduce education on human nutrition in agricultural training. This seminar was organized jointly by the United Nations Food and Agriculture Organization (FAO), the International Course in Food Science and Nutrition at the International Agricultural Centre (ICFSN/IAC, Wageningen, the Netherlands), and the Faculty of Agronomic Sciences (FSA) in Cotonou, and held on 11–13 November 1987.

FINSA 2008 took place at the FSA from 18–30 August 2008 and included three courses:
- Food and Nutrition Security and Development: the Impact of the HIV/AIDS Pandemic;
- Infant Nutrition, Care of Children of Mothers Affected by HIV/AIDS, and Production of Supplementary Foods; and
- Planning of Community Nutrition Programs (CNPs)

Context of the training
The food crisis in Africa is a major concern of governments, NGOs and development partners. To reduce the effects of food and nutrition insecurity due to the ever-increasing rate of infection and death, and low productivity, institutions and public authorities have started implementing various programs of action in various fields, including nutrition, public health, environment, and livelihoods. The aims of such programs are to

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achieve poverty reduction based on strong community participation. Toward this, UN agencies and other institutions have put into place CNPs in several African countries. Following comparative evaluation studies of these programs, shortfalls were revealed in terms of planning, implementation, and monitoring and evaluation. These shortfalls may be corrected, in part, by training CNP managers.

Through short regional training courses on the planning of CNPs, FINSA equips participants with the necessary tools so they can subsequently undertake effective interventions to guarantee food and nutrition security at the local level, within a context of sustainable development.

**Objectives**

FINSA’s objectives are to:

- provide participants with knowledge of the methods used in identifying food and nutrition security problems;
- enable participants to empower the community;
- enable participants to design and plan a food and nutrition security program;
- provide participants with a global understanding of CNP implementation; and
- increase participants’ capacities in CNP monitoring and evaluation.

**Participants**

A total of 16 participants from Niger, Cameroon, Burkina Faso, Guinea, Mali, Senegal, Cote d’Ivoire, and Morocco attended this course. Participants came from different backgrounds and affiliations, including doctors in public health, nutritionists, and managers of NGOs for development and international affairs. This diversity resulted in extraordinary exchanges during discussions in the different course sessions. The additional expertise of different members aided the development of the intervention strategy for a CNP.

**Overview of training**

The training was participative and gave priority to field work. It comprised sessions that clarified and provided knowledge, case studies and group work. Training took place over a two-week period, characterized by an impressive amount of information and knowledge. Highly qualified trainers facilitated the different sessions, favoring a participative approach involving exchange and communication between participants. The course was organized around two modules:

**Module 1: Process of planning CNPs**

The module contained theoretical sessions on the monitoring of food and nutrition security programs, advocacy in nutrition, nutrition in emergency situations, and the impact of HIV/AIDS on food security in urban households. During this module, the experience of the NGO, PLAN Benin, regarding community nutrition in the country was presented. The focus was on the CNP, which is a set of activities aimed at resolving nutritional problems within a community with its full participation and cooperation. These programs can improve the nutritional situation in many countries, provided they are community-based.

The key factors for a successful CNP include responding to the community’s dominant problems, involving other development sectors, and using local resources. Home visits are essential in terms of monitoring the implementation of the CNP within the community. A participatory approach is essential and a determining element in the success of any CNP because program implementation will be easier with the support of the community, which must be involved from the initial conceptualization of the CNP and consideration of:
• making optimum use of local knowledge;
• limiting dependence on external resources;
• promoting leadership within the community;
• adapting programs to the socioeconomic and cultural context and conditions;
• enhancing service access for vulnerable people; and
• incorporating the CNP in the global development plan.

The planning of nutritional interventions at the village level is carried out in accordance with the 3A cycle (Assessment, Analysis and Action). The CNP planning process identifies and analyzes the problem, defines different strategies and feasibility criteria, and then develops a plan of implementation.

Module 2: Implementation, monitoring and evaluation of a CNP

This module gave participants the opportunity to familiarize themselves with different techniques, methods, and participative approaches to implement a CNP at the local level. Participants went through the whole process of planning a CNP, starting from the identification of the problem to the development of a full intervention strategy, with the complete participation of the concerned community. Participants were asked to develop a CNP in the village of Houékèhonou.

The process of developing a CNP follows a sequence of activities that starts with a preparatory phase during which the teams contact the representatives of the village and provide information on its activities. Questionnaires to identify potential food security problems facing the community are prepared based on a detailed study of the village. Data collection follows, with teams carrying out the surveys and collecting complementary information. Analysis of the results helped to determine the intervention required and ways to involve the villagers in the strategy to be developed; this was followed by community consultations that led to the finalization of the strategy and the program.

Certification

At the closing ceremony of the training program, certificates of participation were awarded to participants by the former dean of FSA and founder of FINSA, the vice dean of FSA, and the director of FINSA.

Conclusion

My participation in FINSA contributed considerably to my advancement and benefited me on different levels. On a professional level, it has helped me to gain knowledge in the planning of CNPs, which complements my training in nutrition. The course improved my understanding of the importance of community involvement during the whole planning process. Their input largely facilitated the development of the intervention strategy. Moroccan delegates attended this FINSA course for the first time in 2008. The established contacts will ensure closer cooperation and sharing of experiences between countries in North Africa and sub-Saharan Africa.

On a personal level, visiting the village and communicating with the villagers was a wonderful experience which motivates me to further commit myself in contributing to the nutrition agenda in Africa.

Acknowledgements

Special thanks to SIGHT AND LIFE and Nestlé Foundation for the financial support, to Mrs Najat Sarhani (AMSED) for the institutional support, and Prof. Hassan Aguenau (Ibn Tofail University) for the academic and scientific supervision.

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Norman Irving Krinsky, a scientist who led the field of carotenoid research to unexplored places, passed away on November 28, 2008, after more than a half century of dedication to research with these plant pigments. Dr Krinsky gave his gift of looking at nature’s yellows, oranges and reds, and discovering the secrets to their importance in our lives. Few research publications on carotenoids will not include a reference to Dr Krinsky’s work.

Born in Michigan’s Upper Peninsula, Dr Krinsky (or Norman, as he was known to both impressionable graduate students and professors alike) grew up in Chicago and began his college education at the age of 16 years at the University of Illinois at Urbana-Champaign. At the time, he was not particularly sure of where he wanted to focus his studies. His interests were many and varied. He was not a particularly scholarly student, receiving his first ‘A’ in psychology. However, this changed with his parents’ move to California. Norman’s search for direction found him moving to the West Coast in his junior year. The intersection between Norman and biochemistry began at the University of Southern California, where he received a BSc and MSc in this field. During his master’s degree, in his collaborations with Harry J. Deuel, a noted lipid biochemist, he learned a standard that carried him through his career: “If something’s worth doing, it’s worth doing right.”

To our fortune, he found a lot of “somethings” to do with carotenoids. This began in 1952, when he was awarded a PhD in biochemistry with a dissertation entitled ‘Studies of Carotenoid and Vitamin A Complexes with Protein in Plasma and Tissues.’ In this work, Norman explored the transport of vitamin A and carotenoids in plasma of several species. It was novel work at the time as the biological importance of carotenoids to

“The real voyage of discovery consists not in seeking new landscapes but in having new eyes.”

Marcel Proust

health, beyond a vitamin A role, was not well recognized.

This interest in the biochemistry of carotenoids was an ideal platform for the next phase of his illustrious career. In 1953, an opportunity brought Norman across the country to Harvard University. As a US Public Health Service Postdoctoral Fellow, he worked with George Wald, who received a Nobel Prize in Medicine for his work with vitamin A and vision. Norman continued his work with Wald with a postdoctoral fellowship from the National Council to Combat Blindness. In their work together, they investigated vision in a variety of species, including the frog (from which Norman enjoyed a nice repas of legs after the experiments were completed).

The experience at Harvard was one that Norman truly cherished. He easily settled into the intellectual environment of the University. Cambridge fed into his broad interests, which included both the sciences and non-sciences. He was at Harvard for seven years, during the latter part of which he discovered his love of teaching while serving as an instructor and lecturer in the Department of Biology.

In 1960, Norman became an assistant professor at the Tufts University School of Medicine, where he remained for the rest of his career. Norman realized in these early days that the importance of carotenoids spanned across many forms of life. His studies in algae and bacteria laid down some of the ground work for the biochemical conversions and function of various carotenoids in these organisms. Sprinkled throughout these decades were studies employing the conventional laboratory rat, evaluating β-carotene metabolism. His work with rabbits looked at the conversion of carotenoids to vitamin A and retinoic acid. The monkey model allowed for exploration into the biological control of carotenoids in the primate retina.

However, it was his collaborations using the ferret model that were particularly interesting. This work spawned from the epidemiological studies had shown that dietary and plasma levels of carotenoids were related to decreased risk of lung cancer. Contrary to these observations, intervention studies using pharmacological doses of β-carotene showed that smokers were at a greater risk of lung cancer. Norman and his longtime collaborators, Robert M. Russell and Xiang-Dong Wang, proposed that large doses of β-carotene, in an oxidatively stressed environment, e.g. smokers’ lungs, were oxidized to compounds that were harmful.

This was the beginning of the realization that, while dietary intakes of carotenoids were probably protective against disease, pharmaceutical doses of β-carotene could have adverse effects due to diminished retinoic acid receptor-β gene expression and overexpression of tumor promoting genes. In fact, when it came to dietary carotenoids, Norman was known to say “Get it from your food.” There was no magic bullet in his mind. Norman continued with his collaborations with Russell and Wang with work on a second pathway by which carotenoids are broken down and the biological significance of this. Following the molecular identification of excentric carotene cleavage enzyme by von Lintig’s group in Germany, they cloned and characterized this enzyme from ferrets and demonstrated that the enzyme effectively cleaved an excentric bond of cis isomers of lycopene, which are the predominant forms of lycopene in mammalian tissues. This work provided valuable insights into the mechanisms underlying the actions of carotenoids via their metabolites.

An additional significant contribution that Norman made to the field of carotenoids was his support of the studies that evaluated the bioconversion of carotenoids in various food vehicles to vitamin A. Norman, Rob Russell, and Guangwen Tang at Tufts (as well as other groups) showed that the bioavailability of vitamin A from β-carotene varied considerably from one food source to another. Prior to this work it was believed that three molecules of β-carotene were equivalent to one molecule of vitamin A (6 to 1 by weight). Through their studies in human subjects they found that the ratio was actually much higher and varied, depending on the food. For example, in spinach, the ratio was 20:1. This led to the realization that not only was the amount of carotenoid contained in a food of importance, but also the amount that was available for absorption from the gut into the body. These findings were of such importance that Norman was invited to chair the panel that set the recommended daily allowance of antioxidants. The World Health Organization changed its recommendations to 12:1 in light of this work.

The significance of this work cannot be underestimated given that vitamin A deficiency is a major public health issue in developing countries, where the dietary source of vitamin A is primarily through carotenoid food sources.

In collaboration with Giancarlo Aldini at the University of Milan and Kyung-Jin Yeum at Tufts, Norman developed a unique assay to measure antioxidant capacity in both the aqueous and lipid compartments of plasma. Unlike other assays, this assay captures the antioxidant activities of fat-soluble antioxi-
dant nutrients (such as carotenoids) as well as water-soluble antioxidant nutrients in vivo. Furthermore, Norman and his colleagues demonstrated that the activities of antioxidant nutrients in human plasma depend on the localization of attacking radical species, providing information for practical applications to optimize antioxidant defenses in the human body.\textsuperscript{13}

Norman did not limit himself to the study of a few carotenoids. He covered many, from astaxanthin\textsuperscript{14} to zeaxanthin.\textsuperscript{15} Work with astaxanthin and canthaxanthin found these carotenoids to be potent antioxidant in membranes.\textsuperscript{14} His work with the macular pigments, lutein and zeaxanthin\textsuperscript{16,17} helped in our understanding of factors related to the uptake of these carotenoids into the eye, which is believed to be important to eye health. Studies using supplemental lycopene found this to reduce lymphocyte DNA damage in postmenopausal women.\textsuperscript{18} Over the years, he collected the spectrum of over 70 carotenoids, which are now available at Dr Krinsky’s Notebook (http://hnrc.tufts.edu/1192109 687036/HNRC-A-PAGEHNRCAS_1192109687099.html). This website contains a treasure trove of Norman’s handwritten notes and data needed to produce these spectra.

Apart from his work in the field of carotenoids and antioxidants, Norman was deeply interested in the recent advances of others. This was reflected in the many conferences and committees that he helped organize. In 1981, the increasing interest in the field of free radicals and related oxidants in relation to health and disease initiated a Gordon conference on ‘Oxy-Radicals in Biology and Medicine.’ Norman was a part of this initiative and was the first chair of a conference that continues today. By the early 1990s, the nutritional science community realized that there were carotenoids of interest beyond the major ones found in diet and human tissues. This led to the initiation of another conference. In 1992, he chaired the first Gordon Research Conference on the ‘Chemistry and Biology of Carotenoids,’ which also continues to this day. Norman attended every one of these conferences except the last, in 2007, to which he attempted to go, but fell ill. His absence was felt, as at these meetings he would be at the front, intent on the topic at hand, ready with comments and questions, often accompanied with tact and good humor.

From his early years at Harvard and throughout his rich and colorful career at Tufts, Norman was continually involved with students and teaching. He loved the research, but was passionate about the teaching and he wanted others to carry on that passion. When he retired from Tufts in 2001, he and his wife established the Norman & Susan Krinsky Excellence in Teaching Award for students in the Sackler School of Graduate Biomedical Sciences and the Medical School at Tufts. This award honors Norman’s 40 years of service in the Sackler School and is meant to recognize individuals who have shown sustained teaching excellence. To date, this award has been presented to 15 PhD and MD students, in fields ranging from biochemistry to genetics to immunology to microbiology and pharmacology.

Retirement came easily to Norman. His varied interests found him involved in a number of intellectual and communal activities, such as serving as a docent at the Harvard Semitic Museum and as an active member of the Wellness Community’s Men’s Cancer Support Group. He continued to be an engaged participant in research at Tufts, sharing his insights on the projects at hand. All of this is a testament to his commitment to being a responsible member of the communities to which he belonged.

Dr Krinsky continued his sincere, dedicated interest in and communication of carotenoids with publications up until the year of his death.\textsuperscript{19,20} These works were reminiscent of those that began his career, with publications that contained several co-authors – a testimony to his giving and sharing of his gift of bringing new eyes to view and study these special colors that surround us.

Norman passed away the day after Thanksgiving in 2008, an occasion he celebrated with his loving family. He leaves his wife, a daughter and son, their spouses, and two grandchildren. His wit, wisdom, and wonder will be missed by all.

**Norman ‘by numbers’**

- 80 years of age → 137 peer-reviewed publications
- 56 years in carotenoid research → 123 co-authors
- 49 years at Tufts → 112 times as an invited speaker
- 47 journals published in → 66 book chapters/invited reviews
- > 30 carotenoids researched → 33 professional honors
- 13 professional society memberships → 1st chair of Gordon Research Conference on Carotenoids
- Contributions to carotenoid research: unlimited
References


For more on tributes to Norman Krinsky, see:


“Norman Krinsky, A Pioneering Biochemist” Tufts Medicine, Tufts Medical Alumni Association and Tufts University Office of Publications vol 68 (1), p 34 (2009)
In Memoriam:
John Lawrence Beard
October 30, 1947 – February 13, 2009

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John was considered to be one of the most influential and well-respect-
ed experts in the world today on iron in the brain and neurobehavioral
function. His research has been instrumental in changing the way sci-
entists think about how the brain uses iron, it has influenced approaches to
dietary supplementation in developing countries, and has offered new
perspectives for the treatment of clinical disorders. In addition to under-
standing the correlation between iron and brain function, John was most
interested in translating these findings into ‘real world’ applications, in
order to help those most in need. Some of his recent research on studies
assessing the usefulness of iron fortification in staple foods such as rice
and beans has had profound public health implications. He has also
recently demonstrated the importance of iron status in postpartum
depression and the impact of iron in Restless Legs Syndrome.

John was known to conduct studies of the highest quality and findings
from his studies were often cited and used when setting public policy.
Additionally, his knowledge of iron biology and the impact of iron defi-
ciency on human health were highly sought after as evidenced by the
constant invitations that he received to speak at national and internation-
al meetings. He was known for ‘thinking outside the box’ and providing
a rational, objective viewpoint. His findings have been published in
more than 150 peer-reviewed manuscripts – including more than 60 arti-
cles in the past five years alone. As he was in the midst of conducting
and writing up findings from multiple other studies, his name will
undoubtedly appear on many more research articles to come.

In addition to outstanding teaching and research contributions, John was
generous with his service to the field. He was President-elect of the
American Society for Nutrition, a member of the American Journal of
Nutrition and the Journal of Nutrition editorial boards, an associate edi-
tor of the Journal of Nutrition for the past nine years, and chaired sever-

John Beard, one of the world’s
most renowned iron researchers,
died February 13, 2009. He
received his MS in biochemistry
from the University of California
and his PhD in nutrition from
Cornell University. He served as a
Penn State faculty member for the
past 25 years and was recently
named ‘Distinguished Professor’
in the Nutritional Sciences depart-
ment this past December. John
was a well-respected colleague
with a genuine desire to provide
the highest quality teaching and
research opportunities to both
graduate and undergraduate stu-
dents. He had an unparalleled
commitment to science, his col-
leagues, and his students.
In Memoriam

Al committees. Additionally, he served on committees of many other national as well as international public health organizations.

While his professional accomplishments are remarkable, those of us privileged to have called him our mentor recognize that it was the everyday manner in which he conducted himself which is his greatest legacy. Among the students at Penn State, Dr. Beard had the reputation of being intimidating as a result of his deep knowledge of the field and his uncanny ability to formulate questions that required a great amount of thinking in order to provide an adequate answer. Because his reputation preceded him, most of his graduate students were rather anxious the first time they met him. I remember well the nervousness that I felt the first time I walked into his office to discuss his research and the possibility of becoming his graduate student. I quickly learned that his reputation as an incredibly intelligent and articulate scientist was well deserved. However, what also came across was his passion for the field and his desire to impart his knowledge to others. While I was still rather intimidated, I started to sense that underneath it all, he cared deeply. That was 13 years ago, and in the ensuing years, John became one of my favorite people.

Over the last 13 years, I have worked closely with John on many projects, including studies of iron and cognition in the USA and South Africa, and studies on iron biofortification in the Philippines. As such, I’ve had many opportunities to witness John’s character, firsthand. I learned that despite his many accolades, John was a humble person, eager to impart his knowledge to others, and always kind to everyone. He was excited to watch my own knowledge grow and pushed me to my limit, constantly encouraging me to improve, and always believing that I could reach that next level.

One of John’s greatest gifts to his students was the gift of time. He had an ‘open door’ policy with his students. During my seven years as his graduate student, John never once told me that he didn’t have time for me. As a result, I have spent many, many hours in his office, discussing issues, wrestling with problems, and agonizing over decisions, during which time he patiently listened and guided me. I learned so very much from him during those times.

Even after graduating and moving on, John kept in close touch. It became very evident to me that John was eager to see his students succeed and was so proud of their accomplishments. He continued to offer advice and encouragement and act as a sounding board. But, John went above and beyond, caring about our personal lives in addition to our professional lives. During every conversation, he would ask me how my husband was doing and he called multiple times the week after my son was born to make sure that mom and baby were doing fine. Since then, he was eager to hear about every ‘milestone’ that my son reached. John was a phenomenal and tough mentor to his students who taught us as much about life as he did about science. I have no doubt that my professional successes are a direct result of the time that he invested in me and I will be forever grateful for that.

John’s direct legacy on this earth ended much too soon for our liking. But, each of us who knew and learned from him has the opportunity to ensure that his indirect legacy continues. This will occur every time we patiently guide our students, enthusiastically impart our knowledge to others, passionately conduct our research, labor over the wording of a grant until it is just right, or publish our research findings – as John always reminded us, “It’s not really research until it’s published!”

Although John gave tirelessly of himself in order to advance the nutrition field, his first passion was his family. John is survived by his wife, Diane Brannon, and sons, Zachary and Matthew Beard. His love for them was evident by the proud manner in which he constantly spoke of them and the gentle way in which he interacted with them. John was truly a remarkable husband, father, scientist, colleague, mentor, and friend. He will be sorely missed.
My responsibilities in my new job fall into two main areas. Within the framework of the DSM-WFP partnership, my role is to provide technical expertise concerning the studies and programs which are conducted. I am therefore responsible for ensuring that such studies and programs are properly designed, implemented and evaluated.

I also have to ensure that the data provided is analyzed using appropriate and accurate methodologies, so that well-founded conclusions may be drawn from the information collected. The dissemination of information is also an important part of my role, which means that I do a lot of writing and also liaise closely with the relevant institutions and publications.

**Simple messages**

I also have a separate role within SIGHT AND LIFE. I am responsible for developing information, communication and education materials on a range of nutritional topics including nutritional anemia, hidden hunger and micronutrient powders. A lot of these subjects are highly complex, so my job is to translate the advanced scientific concepts into easily accessible terms. We need simple messages for the beneficiaries of programs in developing countries, and so I have to make this material easy to understand. I also help with the editing of SIGHT AND LIFE magazine and will be working closely with the summer intern who will be coming from Johns Hopkins University to evaluate grant applications. So both my roles are very interesting and offer me a great deal of variety.

My background is in international nutrition. My Bachelor’s degree was in Food and Nutrition from Ewha Women’s University in Seoul, Korea. My Masters was in Food Science and Human Nutrition from the University of Illinois at Urbana-Champaign, and my Ph.D. was in International Nutrition from Johns Hopkins Bloomberg School of Public Health in Baltimore, Maryland. I did an internship with SIGHT AND LIFE last year, spending much of my time evaluating grant proposals, and I enjoyed this very much. I was therefore extremely interested in the opportunity of coming back to Switzerland to work in this newly created role.

**Improving the WFP’s food basket**

Much of my time at the moment is spent on supporting the efficacy trial for NutriRice™ which we will be conducted in India. Our object is to demonstrate the efficacy and effectiveness of this specially fortified form of rice: this is a prerequisite for the inclusion of such product in the WFP’s food basket, which helps to provide nutrition to approximately 90 million of the world’s most impoverished people. I therefore work very closely...
with Klaus Kraemer, Anne-Catherine Frey and Svenia Sayer-Ruehmann. I also have close contact with numerous colleagues from DSM and with the people running the NutriRice™ trials in India.

Working for SIGHT AND LIFE means a great deal to me. Despite its small size as an organization, SIGHT AND LIFE plays an enormously influential role in international nutrition and has terrific potential for doing good in the world. Scientists and other academics are continually developing new insights into the relationship between nutritional intake and health, and these insights need to be communicated in clearly intelligible form to the people who are running programs in the field. I enjoy reading SIGHT AND LIFE magazine and am particularly looking forward to helping with the editing of it. It is a great source of new knowledge in the field of international nutrition, but I think it could do even more to bridge the gap between academia on the one hand and programs in the field on the other.

And another thing dear to my heart…
I very much enjoy living in Switzerland, but the rest of my family is in South Korea, where I grew up. I therefore spend a lot of my free time staying in touch with them. Before dedicating myself very intensely to the study of international nutrition, I used to be a jazz pianist. With my PhD behind me now, I am looking forward to the opportunity to play jazz piano once more, which is very dear to my heart.

Anne-Catherine Frey and Svenia Sayer-Ruehmann, assistants

To have a real influence in the world, SIGHT AND LIFE has to operate very efficiently and make the maximum use of its resources. This would be unthink-

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**Helping to Build Stronger Societies**

**DSM’s partnership with the United Nations World Food Programme**

*‘We cannot be successful, nor can we call ourselves successful, in a society that fails’*

Feike Sijbesma, CEO DSM

DSM’s belief in the importance of building successful societies is the inspiration for our partnership with the United Nations World Food Programme (WFP). Hunger is the number one cause of death in the world, killing more people than AIDS, malaria and tuberculosis combined. A related global scourge is a type of under-nutrition referred to as hidden hunger, whereby people have enough food to survive, but have access only to a diet which lacks key (micro)nutrients. ‘Hidden hunger’ is associated with a wide range of chronic diseases as well as physical and cognitive underdevelopment. As the world’s largest manufacturer of micronutrients and vitamins, DSM is strongly committed to help in the fight against global hunger.

The largest humanitarian agency in the world, WFP provides food aid to an average of 90 million people, including 58 million hungry and malnourished children, in 80 of the world’s poorest countries. By supporting WFP in defining a (micro)nutrient strategy, we support the building of stronger societies that can make a positive contribution to the world economy in years to come. This requires creating a global alliance comprising a wide variety of stakeholders such as UNHCR, UNICEF, WHO and GAIN (Global Alliance for Improved Nutrition) who are dedicated to helping meet the needs of the ultra-poor.

In 2008 WFP and DSM received recognition for their role in these efforts in the form of an ICIS (International Chemical Information Services) Innovation Award. This was given for the development of MixMe™ micronutrient sachets.

Initiated in 2007, our partnership with WFP led to activities on many fronts during 2008. Drawing on the expertise in micronutrient science of SIGHT AND LIFE as well as the support of our commercial Nutrition Improvement Program (NIP), we provided much-needed assistance in Bangladesh, Kenya, Nepal and Zambia, as well as supporting WFP at its headquarters in Rome. DSM employees and senior managers made their professional skills and experience available in a range of projects run by WFP, reporting back on their experiences in widely read web logs.

Source: The DSM Triple P Report 2008
Anne-Catherine has been with SIGHT AND LIFE since 1999 and Svenia since 2006. Anne-Catherine works four days a week and Svenia two, dividing between them the many tasks necessary for the smooth operation of our organization.

“A lot of our work involves the basic administration which you would expect to be necessary within any comparable organization,” says Anne-Catherine. “We support Klaus Kraemer in many ways – organizing his diary, for instance, and making his travel arrangements for him. Klaus travels extensively in his role as Secretary General of SIGHT AND LIFE, and his work would not be possible without extensive support from the office here.

“We help to arrange meetings and conferences, to develop presentations, to update the SIGHT AND LIFE website, to maintain the SIGHT AND LIFE archive, and also, of course, to put together SIGHT AND LIFE Magazine. This involves liaising with contributors as well as with our graphic design agency and printer. We are also responsible for organizing shipments of educational material and micronutrient sachets and paying the grants without which the beneficiaries of our programs would not be able to do their work in the field.

Mission-critical

“This element of our work is mission-critical: when we make a shipment, we know that there are people waiting eagerly for the goods to arrive and when we make a grant payment we know that there are people equally eagerly awaiting the arrival of the funds, without which they cannot deliver their programs. It can be difficult and time-consuming to deal with the customs authorities, but this is something we have to accept as part and parcel of our work.”

Making a positive difference

“I think it’s very important to both of us to have a job which is not only interesting and varied but which also gives us the opportunity to make a positive difference in the world. If there was one thing I could change about my job, I would increase the budget available to SIGHT AND LIFE and expand the staff. We are a very small team but I believe that we are a real force for good.”
Monitoring Anemia-Control

Programs

David I. Thurnham

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Background

Iron deficiency, with or without iron-deficiency anemia, affects all populations of the world irrespective of race, culture or ethnic background. Children, adolescent women and women of child-bearing age are especially prone to developing iron-deficiency anemia (IDA), and this is despite iron being the fourth most common element on earth.1

Early estimates suggested iron deficiency was responsible for anemia in approximately 15% of the world’s population and its overall prevalence was quoted to be around 50% in developing and 10% in developed countries.2 This situation has not improved and recent estimates put the worldwide prevalence of anemia for the period 1993–2005 at 24.8% and, in each age and gender group studied, the highest prevalence rates occurred in Africa. Anemia is particularly common in infants and preschool-age children, with a global prevalence of 47% but this reaches almost 65% in Africa.3 Anemia leads to impaired physical work performance, cognitive impairment, adverse pregnancy outcomes and developmental delays in toddlers.4

There is evidence that iron is needed for lymphocyte activation and proliferation as part of the acute phase response,5 but there is also evidence that iron deficiency may be protective against infectious disease1 or that excess iron is harmful6. Routine prophylactic supplementation with oral iron and folic acid or placebo to preschool children in areas with high malaria transmission was associated with a 12% increase in morbidity and 15% more deaths in the iron recipients.7 In view of the conflicting factors affecting iron metabolism, it is important that iron status is correctly monitored and the effects of iron treatment correctly interpreted.

Causes of anemia

While iron deficiency is the principal cause of anemia there are many other factors that contribute.8 Several micronutrients have been shown to be directly involved in hemoglobin synthesis, such as folate, vitamin B12, and copper, but vitamin A deficiency (VAD) is the micronutrient deficiency most frequently associated with iron deficiency. In a recent study on anemia-associated micronutrient deficiencies in Mexican preschool children, only 30% of those with iron deficiency did not have a deficiency of retinol, folate or vitamin C but VAD was most strongly associated with iron deficiency in children both with and without anemia (Table 1).9

Table 1: Anemia-associated micronutrient deficiencies in Mexican preschool children

<table>
<thead>
<tr>
<th></th>
<th>Percentage with low plasma retinol concentration</th>
<th>No iron deficiency (N = 50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia</td>
<td>40.6 (%)</td>
<td>16.0 (%)</td>
</tr>
<tr>
<td>No anemia</td>
<td>27.7 (%)</td>
<td>11.9 (%)</td>
</tr>
</tbody>
</table>

1 Plasma retinol concentration < 0.7 µmol/L.
2 Iron deficiency when % transferrin saturation < 16% and hemoglobin < 110 g/L.
3 Significantly higher prevalence of low plasma retinol concentration in both anemic and non-anemic children. From Villapedo et al9
Numerous reports have highlighted the strong association between the two deficiency states and that supplementation with vitamin A not only restores vitamin A status but often also synergistically improves hemoglobin when administered with iron. However, there is no known metabolic role of vitamin A in hemoglobin synthesis, which therefore suggests that vitamin A stimulates hemopoiesis by other mechanisms. Vitamin A is well known for its anti-infection properties and vitamin A supplements significantly depress morbidity and mortality in children. In the following pages, I describe how such effects reduce the level of inflammation and promote the mobilization of iron from the liver for hemopoiesis.

It is well known that both plasma retinol and iron concentrations are depressed by infection or trauma. In volunteers given endotoxin to induce therapeutic fever or others given live attenuated virus vaccine, depression of serum iron values of up to 50% began within several hours, maximized at 24 hours, and was greatest in those developing severe fever. Likewise, plasma retinol concentrations of South African women who underwent minor operations fell by 25% in two to four hours and to 50% in 48 hours, and many studies show that where there is inflammation, plasma retinol concentrations are depressed.

These changes in iron and vitamin A occur following the inflammatory response that is initiated by trauma and infection. The response is accompanied by the induction of the inflammatory cytokines, interleukins 1 (IL-1) and 6 (IL-6) and tumor necrosis factor alpha (TNF-α) from a range of immune cells. These cellular messengers target hepatocytes and other tissues in the body to stimulate alterations in metabolism to meet the threat of the infection. Therefore, the low plasma iron (hypoferrremia) and low retinol concentrations (hyporetinolemia) of inflammation are not genuine (i.e. nutritional) deficiencies, but there is no way of distinguishing them from real dietary deficiencies unless evidence of accompanying inflammation can be ascertained.

In many developing countries, the prevalence of infections is high and with each new infection a new inflammatory response occurs, each time depressing iron and vitamin A. Constant exposure to chronic inflammation is well known clinically to influence iron metabolism and result in anemia of chronic inflammation (ACI). ACI is usually mild, that is, red cells are usually normal in color (normochromic) and size (normocytic), and with a normal reticulocyte count (very few or no young red cells). Red cells can occasionally be macrocytic but there is little evidence of iron deficiency. The administration of iron to such patients by oral or parenteral routes can have little effect on serum iron or other indices of iron status, probably because iron absorption is inhibited by the inflammatory process.

Hepcidin is a 25 amino-acid, peptide hormone that has, in the last few years, dramatically advanced our understanding of iron metabolism. The hormone is produced primarily by the liver and secreted into the circulation. Its synthesis is increased in response to iron and inflammation, and reduced in response to erythropoiesis, anemia and hypoxia (Figure 1). IL-6 is the most important cytokine regulating hepcidin. Hepcidin regulates systemic iron metabolism by interacting with its receptor ferroportin, a

![Figure 1](image-url): Factors influencing hepcidin production in the liver. Hepcidin blocks iron release by duodenal enterocytes and reticulo-endothelial macrophages. Therefore, factors inducing hepcidin production block the absorption of iron from the diet and the reutilization of iron from senescent red cells. Modified from Collins et al.
trans-membrane iron-exporter protein. Ferroportin is abundantly expressed on the cell surface membrane of reticulo-endothelial (RE) macrophages, i.e., resident macrophages in the liver, spleen and bone marrow, and on the basolateral membrane of the duodenal enterocytes. Hepcidin inhibits iron release at these sites by binding to ferroportin and the complex is internalized and degraded. RE macrophages are especially important for the re-use of 20–25 mg iron daily from senescent red cells and duodenal enterocytes release 1–2 mg dietary iron into the circulation each day. RE iron normally undergoes rapid turnover, thus iron retention in this cell population acutely lowers circulating iron concentrations.  

As indicated earlier, anemia is very common in the developing world from an early age and a recent study in Gambian infants provided persuasive evidence that the constant pressure of morbidity was a principal cause in the development of anemia over the first 12 months of life. Infants are rarely anemic when born as the oxygen concentration in utero is relatively low (hypoxic) and results in high hemoglobin concentrations at birth. However, as the oxygenation of the blood improves, erythropoiesis ceases and hemoglobin concentrations drop over the first two months of life, mainly due to hemodilution and natural red cell senescence (Table 2).

The information in Table 2 was obtained from the placebo-controlled vitamin A supplementation study in Gambian infants. As there were no differences attributable to the supplement, the data were combined. In the study, morbidity data were collected by field workers every two weeks, and blood was collected for hemoglobin and plasma acute phase protein measurements from apparently healthy infants at birth, 2 months, 5 months, 9 months and 12 months, in a study lasting approximately 2.5 years. Morbidity was high throughout the first 12 months of life (Table 3) but the constant exposure of these infants to sickness appeared to stimulate strikingly similar rates of increase in C-reactive protein (CRP), α1-acid glycoprotein (AGP), and, three months later, anemia.

It is very tempting to conclude from the development of these changes in the infants that inflammation was the major cause of anemia in the Gambian infants. Figure 2 shows that overall morbidity affected 30% of children in the first three months of life when there was very little anemia and lit-

### Table 2: Hemoglobin concentrations and anemia prevalence in Gambian infants during the first year of life

<table>
<thead>
<tr>
<th>Age (months)</th>
<th>Hemoglobin g/L</th>
<th>% &lt; 90 g/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cord</td>
<td>135</td>
<td>10</td>
</tr>
<tr>
<td>2</td>
<td>110</td>
<td>15</td>
</tr>
<tr>
<td>5</td>
<td>109</td>
<td>15</td>
</tr>
<tr>
<td>9</td>
<td>98</td>
<td>45</td>
</tr>
<tr>
<td>12</td>
<td>90</td>
<td>75</td>
</tr>
</tbody>
</table>

1 Hemoglobin concentrations are means  
2 From Darboe et al

### Table 3: Morbidity rates in Gambian infants during first 12 months of life

<table>
<thead>
<tr>
<th>Age (months)</th>
<th>Diarrhea</th>
<th>Vomiting</th>
<th>Fever</th>
<th>Cough</th>
<th>Other</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 to 3</td>
<td>4.0¹</td>
<td>1.6</td>
<td>5.6</td>
<td>10.3</td>
<td>9.1</td>
<td>31</td>
</tr>
<tr>
<td>4 to 6</td>
<td>3.0</td>
<td>1.5</td>
<td>7.2</td>
<td>12.3</td>
<td>8.7</td>
<td>33</td>
</tr>
<tr>
<td>7 to 9</td>
<td>4.2</td>
<td>1.6</td>
<td>9.5</td>
<td>14.1</td>
<td>10.3</td>
<td>40</td>
</tr>
<tr>
<td>10 to 12</td>
<td>2.0</td>
<td>1.0</td>
<td>6.3</td>
<td>10.9</td>
<td>8.7</td>
<td>29</td>
</tr>
</tbody>
</table>

1 220 infants recruited over approximately 2.5 years and followed for 12 months. Morbidity data were collected during community visits twice a week.  
2 From Darboe et al
3 Average number of days during which infants had symptoms, over a period of 90 days
tle inflammation. At five months, morbidity and the prevalence of anemia had not changed but at least 50% of the infants now displayed evidence of inflammation. Inflammation inhibits dietary iron absorption and iron release from RE macrophages, hence, at nine months, the prevalence of anemia had trebled (15–45%) and continued to rise to 75% at 12 months. It thus appears that inflammation may be the precipitating cause of anemia in the Gambian infants.

Most anemia in the world is mild anemia and this was also the case in the Gambian infants, supporting the view that much of the anemia was ACI. Of course, the infants continue to grow and the hemopoietic system expands. If iron absorption continues to be inhibited, then any stored iron will eventually be depleted and the anemia will become iron-deficient anemia. Fortunately, children are not sick all the time and, if the frequency of morbidity falls, inflammation will decrease and iron absorption will be restored.

Unfortunately, in the Gambia and in many other developing countries, unhygienic conditions provide a constant source of infections and seasonal weather patterns often increase exposure to infection, e.g., seasonal diarrhea. The important message, however, is that by monitoring the acute phase proteins CRP and AGP, these measurements provide direct information on the ‘sub-clinical’ state of health of persons, and their risk of anemia and iron deficiency.

**Plasma ferritin concentrations**

A recent WHO consultative group recommended that the best measurement of iron status was a plasma ferritin concentration, but that one or more acute phase proteins should also be measured to inform on inflammatory status. The plasma ferritin concentration has been shown to be a direct measure of the iron stored in the liver. However, ferritin is also influenced by inflammation, and the concentration rises rapidly in parallel with CRP at the onset of trauma and appears to remain elevated during the convalescent or chronic phase of illness, marked by elevated AGP concentrations. What can be done with ferritin values where inflammation is present? Where the numbers are small, the data are often excluded or arbitrarily higher cut-off values such as 30 µg/L may be used to define iron deficiency. However the former action is not practical if inflammation is extensive, and there are now ways of making better use of these data.

The two acute phase proteins, CRP and AGP, can give a lot of information on the nature of infection in a community and its impact on the individual. CRP concentrations rise rapidly following the onset of a trauma to reach a maximum between 24–48 hours, remain high during the clinical phase of disease, and then decline quickly as the clinical phase subsides. In contrast, AGP concentrations rise more slowly and may take four or more days to reach the maximum. They then remain high during the clinical phase and continue to be elevated for a variable period during convalescence.

In most studies on apparently healthy persons, the number with an elevated AGP concentration usually exceeds the number with a raised CRP. However, where disease transmission is high – e.g., where there is active malaria transmission – then the number of raised CRP values usually exceeds those with raised AGP. In apparently healthy persons, the use of these two acute phase proteins enables people to be grouped according to their most recent infection expo-
sure. Those with no raised proteins are the reference group or people who have had no recent infection. Those people with only a raised CRP are recently infected but still incubating disease. Those people where both CRP and AGP are raised have recently had disease and are in early convalescence, and those in whom only AGP is raised are in late convalescence. By using these groups to categorize biochemical data from an apparently healthy population, the effect of the ‘inflammation cycle’ on nutritional indices can be determined.

Plasma ferritin concentrations of apparently healthy HIV-1 positive Kenyan women are shown in Figure 3. Median values for each group of subjects with inflammation indicate the elevation in plasma ferritin at that stage in the inflammation cycle, and the ratios of the respective medians of the reference and inflammatory groups give correction factors that can be used to adjust the ferritin values in the respective groups to remove the influence of inflammation. See elsewhere for fuller information on removing the influence of inflammation from biochemical data.

A scenario where the correction is useful is in analyzing data following a supplementation study. Potentially in supplementation studies, inflammation can influence data differently both at the start and end of a study. Therefore, the influence of inflammation must be removed from both data sets before the data can be analyzed for the effect of the supplement. The method described above was used recently to correct ferritin and hemoglobin data to determine whether an iron supplement had improved iron status in apparently healthy, HIV-1 positive Kenyan men and women.

Figure 3: Plasma ferritin concentrations in apparently healthy HIV-1 positive Kenyan women by inflammation group. Inflammation groups are defined in the text. Cut point for deficient iron stores is 15 µg/L. Heavy horizontal lines indicate median ferritin concentrations in respective groups. Data from Thurnham et al

Figure 4: Bars show median changes in ferritin concentrations of apparently healthy HIV-1 positive men and women following 3 months supplementation. All subjects received a food supplement but those in the iron group received a multi-micronutrient capsule containing 30 mg iron/day. Significant difference in ferritin concentrations between men receiving iron (a) and those receiving the placebo (b) (P < 0.05 independent ‘t’ test). Data from Mburu et al
Median plasma ferritin concentrations for the women at baseline are shown in Figure 3 for the four inflammation categories. Ferritin concentrations in the men were similarly distributed, except the concentrations were much higher. There were no overall changes in hemoglobin in men or women in response to the supplements, whether the data were corrected or not. In contrast, there were positive effects on ferritin in men and women who received additional iron, whether corrected or not. Correction did, however, lessen the apparent negative effects of the placebo treatment on ferritin (Figure 4).

More importantly, knowledge of the inflammation status of the subjects at baseline and three months revealed that the response to the iron supplement by those with inflammation at both time-points was different to that in those who never showed evidence of inflammation. Iron status improved in response to iron in both those with inflammation and without. However, in those with no inflammation, there was a significant increase in hemoglobin and a non-significant improvement in ferritin, but in those with inflammation, only ferritin improved (Figure 5).

These data clearly indicate that where there is evidence of inflammation, even mild inflammation in apparently healthy persons, that inflammation influences the distribution of iron. Where there is inflammation, iron mobilization is suppressed and any iron absorbed is retained as ferritin. In contrast, those with no inflammation were able to absorb iron and mobilize it for the synthesis of hemoglobin, so less was available for storage as ferritin (Figure 5).

What to measure to monitor iron status?

As indicated earlier, hepcidin is an important regulator of iron metabolism in both health and disease.21,22,34,35 In chronic inflammatory conditions, increased hepcidin levels correlate with increased ferritin levels,36 suggesting that hepcidin production remains high during inflammation, and it would be tempting to suggest that hepcidin might provide a single biomarker to replace both CRP and AGP. However, recent human evidence suggests that hepcidin increased before ferritin35 in the early stages of inflammation, whereas ferritin correlated very closely with CRP concentrations at that time in other human experiments.27 Therefore, from the point of view of interpreting the influence of inflammation on ferritin, CRP may be a better biomarker of acute inflammatory effects on ferritin than hepcidin.

Other biomarkers of inflammation include the cytokines but most have relatively short life-spans. Cytokines like IL-1 and IL-6, TNF-α, interferons like IFN-γ, and others are increased by inflammation but their life-span is often short as anti-inflammatory cytokines (e.g., IL-10) are also stimulated to counteract or restrict the inflammatory response. The biological effects of cytokines are also determined by the receptor concentration in target tissues, thus cytokine concentration in blood may not correlate with biological activity. Cytokines are also more likely to be elevated when symptoms of disease are present. Thus cytokines are not likely to be useful for studies on apparently healthy persons.

Since most studies obtain cross-sectional data with which to assess iron status, it is important to be able to relate the life span of the inflam-
monitoring biomarkers to that of the iron biomarkers of interest. In the case of ferritin, both ferritin and CRP increase at a similar rate following inflammation. However, plasma ferritin concentrations remain elevated for a longer period of time than CRP but the acute phase proteins have longer half-lives than the cytokines and, AGP together with CRP appear to be elevated over a similar time period to that of ferritin as explained above. It may also be possible to use a similar approach to quantify the effects of disease on ferritin during the clinical phase to quantify iron stores but such information is not currently available.

Hemoglobin provides information on whether a person is anemic. Hemoglobin synthesis takes place in the bone marrow and is sensitive to iron availability and to inflammation. However, the red cell has a mean half-life of 120 days so the concentration of hemoglobin in the blood reflects iron availability and inflammation over that period. The hemoglobin concentration in the blood is therefore cushioned from the effects of inflammation, and it is only when inflammation is prolonged that hemoglobin concentrations will fall as in the anemia of inflammation. Therefore, the presence of anemia only tells you that there has been a shortage of iron for some period of time but it cannot tell you whether this is due to a dietary deficiency or chronic inflammation. Other biomarkers are needed to provide that information.

Lastly, plasma transferrin receptor (sTfR) concentrations are sensitive markers of iron deficiency. The concentration of sTfR on cell membranes increases when iron is lacking in the cytosol and the amount in serum is proportional to the amount on cell membranes. There is a much smaller effect of inflammation on sTfR than ferritin but, currently, there is no universally accepted standard or gold standard method for sTfR.

It is therefore suggested that hemoglobin, ferritin, CRP and AGP should be used to provide the minimum amount of information in any survey to assess iron status. Hemoglobin can be easily measured in the field using the HemoCue® hemoglobinometer. The machine is readily standardized and easy to use. Hemoglobin has other advantages in that it is a well accepted biomarker of iron status and the ease of obtaining results in field studies is often well received by mothers. Plasma ferritin and sTfR concentrations are recommended as the best indices of iron status, but ferritin is preferred for the reasons outlined above. Where possible, these measurements should be done on venous or capillary blood as serum suitably stored (< -20°C) as quickly as possible after collection and centrifugation. A number of methods are available and additional micro-techniques are being developed to assess ferritin, sTfr, retinol-binding protein and CRP measurements using as little as 30 µL of serum in total. Others have extended this to include AGP.

ELISA techniques on dried blood spot (DBS) material are also being developed to enable the collection of materials in field circumstances where electricity may not be available. Once DBS are properly dried, they can be stored at -20°C for up to 15 months. However, collection and storage of DBS under humid tropical conditions where there is no electricity does present problems and CRP is particularly sensitive to damage if stored at ambient temperatures, although others report no effect of storage for three days at very warm ambient temperatures. Nevertheless, for safest results, DBS should be dried quickly, stored with a desiccant and rapidly transferred to -20°C. Collection of capillary blood whether for plasma or DBS has other problems because the finger- stick used is often painful, and squeezing the finger to restrain the child or obtain the blood alters the composition.

In conclusion, venous blood is always to be preferred for the most accurate measurements. Capillary blood for either plasma or DBS can now be processed to provide information on both iron and inflammation biomarkers. Transport of plasma or serum samples requires electricity to provide refrigeration for sample stability. Long-term storage of DBS also requires refrigeration but DBS provide a stable and convenient medium for transport. The biggest problem seems to be the drying of the blood spot before storage, particularly in areas where there is no electricity to increase the speed of drying. The use of suitable racking for the blood spot papers and a hot box with desiccant exposed to tropical sunshine may be a ‘low-tech’ solution but experiments still need to be done to test and refine the process.

References


*It has recently come to my attention that PATH has initiated development activities for a multiplex micronutrient assessment tool that will assay ferritin, AGP, CRP and in addition, transferrin receptors and retinol binding protein in one dilution. This will be very welcome news for nutritionists wanting to interpret nutritional biomarkers in the presence of inflammation.
44. Personal communication. Christine Clewes, February 2009.
News

The World Food Crisis: A Wake-Up Call to Save a Generation of Children

Calling for “a wake-up call to save this generation of children,” a group of eminent scientists met early this year to map out more effective responses to the global financial and food crises that would not only protect jobs and infrastructure, but also the lives and future productivity of the world’s poorest people.

“Without immediate action, we are exposing ourselves and our children to greater shocks than those we face today,” declared the group in a statement. “We know what to do – we call upon the world’s leaders to do it.”

The seriousness of the message was underscored by the credentials of the 14 scientists, who hail from an ivy league of international development institutions and academia, including the World Bank, the United Nations World Food Programme (WFP), the Johns Hopkins Bloomberg School of Public Health, the United Nations Children’s Fund (UNICEF), SIGHT AND LIFE, the International Food Policy Research Institute (IFPRI), Harvard Medical School and School of Public Health, Stanford University, and the Friedman School of Nutrition Science and Policy, Tufts University.

Meeting at Castel Gandolfo, Italy, on 25 January 2009 in their personal (not organizational) capacities, they were united in their conviction on the need to place nutrition back at the centre of actions to mitigate the worst effects of high food prices, job losses and the general economic downturn. Compelling evidence shows that improving nutrition protects health, prevents disability, boosts economic productivity and saves lives. The billions lost by the world’s financial markets pale in significance compared to the economic losses due to growing hunger and its effects on human capital, according to the group.

Pulling together current best practice and science, the group concluded that not enough of what is known to work is being done. Some of the most cost-effective interventions include tackling deficiencies in vitamins and minerals, including the distribution of vitamin A capsules to prevent blindness and reduce mortality, the use of zinc tablets in the treatment of diarrhea, and the fortification of salt with iodine to protect mental capacity. These and other essential nutrients should also be ensured in the food supply through fortification and dietary diversification supported by agricultural growth. But it is not just about more food, the group insists; it is about reinforcing the nurture of mother and child. Exclusive breastfeeding practice for the first six months of life is still insufficiently supported and practiced, effective antenatal care is inaccessible to far too many pregnant women and appropriate low cost, quality foods for infants and toddlers remains an unmet need.

Additionally, short-term actions are crucial to buffering the most vulnerable to economic or climatic shocks. For example, in West Africa, severe malnutrition has been reduced over the past year in countries such as Niger and Burkina Faso by a combination of targeted food distribution, increased vaccination coverage, bed nets to ward off malaria, and education of mothers in the best ways to ensure the future growth and development of their surviving children. Therefore, immediate investments to improve the nutritional wellbeing of mothers as well as their children generate short-term rewards but even greater long-term returns.

The workshop was made possible through an educational grant from SIGHT AND LIFE. It is planned to publish the proceedings of the meeting as a supplement to The Journal of Nutrition.
In February 2009 SIGHT AND LIFE and its partners in India launched a Marathi-language version of the widely popular Healthy Eyes Activity Book, commonly referred to by its acronym, HEAB, in Aurangabad, Maharashtra.

The Marathi translation of the HEAB was undertaken by volunteers committed to the education of children in Maharashtra in their local language for eye care, with support from the Nutrition Improvement Program of India. SIGHT AND LIFE provided financial support to print 5,000 copies of the Marathi HEAB for distribution to schools in Maharashtra.

The HEAB, which was first developed by the International Center for Eye Health (ICEH) and Sight Savers International, then adopted and supported by SIGHT AND LIFE for wide distribution, was published to meet the need for eye health communication specifically targeted to and accessible by children. It has been published in more than 10 languages, with the addition of Marathi.

In 2007, SIGHT AND LIFE and ICEH produced the second edition of the HEAB. The HEAB has proven to be a unique and effective tool for educating children in eye health. SIGHT AND LIFE has supported...
Canada’s Micronutrient Initiative Celebrates 5 Billionth Vitamin A Capsule

Canada’s Micronutrient Initiative (MI) celebrated its role in saving over two million children’s lives worldwide with the manufacture of its five billionth vitamin A capsule in November 2008.

“It only takes two doses of vitamin A every year, from age six months to five years – that’s about nine capsules – to help save a child’s life,” explained MI President Venkatesh Mannar. “Vitamin A is a simple, cost-effective way to boost children’s immune systems so that their bodies can fight off deadly infections, such as measles, and get the best start in life.

MI’s vitamin A child survival program reaches children in over 70 countries around the world. Since 1997, the organization has provided for more than 75% of the developing world’s need for vitamin A.

Supported by the Canadian International Development Agency (CIDA), MI’s vitamin A program is one of Canada’s most successful international development stories. Each capsule costs only about two cents to manufacture; the manufacture of five billion capsules highlights Canada’s commitment to saving children’s lives. The vitamin A capsules manufactured in Canada are donated primarily to UNICEF, which then distributes them through national child health programs.

MI is an Ottawa-based international nonprofit organization dedicated to ensuring that the world’s most vulnerable – especially women and children – in developing countries get the vitamins and minerals they need to survive and thrive, through supplementation and food fortification programs. Its mission is to develop, implement and monitor innovative, cost effective and sustainable solutions for hidden hunger, in partnership with others.

Communicated by:
Email: amorris@micronutrient.org
Web: www.micronutrient.org
Dear Sir,

We would like to report an observation, which was made during a screening of around 2,900 children and adolescents from slums of Kolkata, Howrah, and 24 Parganas South districts in India for ocular signs of vitamin A deficiency (VAD). These children and adolescents attended the free medical dispensaries of our NGO in 2008 for various medical reasons.

Bitot’s spots were found to be more frequent among the school-age children and adolescents than in the age group of the preschoolers. We found 52 children and adolescents with Bitot’s spots; the Figure shows their age distribution.

We recorded a history of consumption of a vitamin A supplement in the previous six months for each of the screened children and adolescents, and searched in their available medical documents for such a supplementation. The Figure summarizes the occurrence of Bitot’s spots in all screened children, whether they had received a vitamin A supplement during the previous six months or not.

The following observations are restricted to those children and adolescents, who did not receive such a supplement:

- The frequency of Bitot’s spots in the different age groups was found to be 2.7% for the children in the age group of 1–5 years, and to be 4.9% for those in the age group of 6–16 years. As these figures relate only to children without a history of vitamin A supplementation, we are sure that vitamin A supplementation of the preschoolers was not the reason for the observed lower frequency of Bitot’s spots in this age group.
- The frequency of night blindness was 1.4% among the preschoolers, while it was not determined among the older children and adolescents. However, several of the children and adolescents between 6 and 16 years of age who were found with Bitot’s spots were also night-blind.
- Keratomalacia was observed with a frequency of 0.14% among preschoolers, while it was not observed among children of school age and adolescence.

Of note, maternal night blindness varied between 1.5% and 10.6% among the screened mothers from different slums of the said districts. Bitot’s spots were rarely seen also in pregnant women and mothers up to six months after delivery, with and without concomitant night blindness in the same patient.

These observations were made in children and adolescents from high-risk slums in Kolkata, Howrah and 24 Parganas South districts, which our NGO selected for its medical work due to the obvious poverty of the area. The mentioned data can therefore not be generalized to the entire child or adolescent population of the said districts. We screened children and adolescents who attended free medical dispensaries for various health reasons, mostly due to minor illnesses. Their vitamin A status may therefore not even be generalized to the healthy child and adolescent population of the same high-risk slums. However, even for the highly localized setting of a busy medical OPD in a slum, it is useful to know the frequency of xerophthalmia among its pediatric patients.
Singh and West recently estimated, from the available data, that 2.8% of the school-age children (5–15 years) in India have mild xerophthalmia (night blindness or Bitot's spots), and mild xerophthalmia thus concerns 6.8 million Indian school-age children in absolute numbers.1 Singh and West pointed also to the gaps in knowledge about the health consequences of VAD for school-age children and adolescents, and about the prevention of this condition in this age group. For those working in the field, the question remains whether, if an assessment has shown a high prevalence of mild xerophthalmia among school-age children in a certain setting, all children of this age group should get a vitamin A supplement periodically.

In our local setting, the frequency of mild xerophthalmia varies significantly between dispensaries in slums that are only a few miles away from each other. This makes it difficult to formulate a policy even for a highly localized setting like ours.

Sir, thank you for your continuous support in the provision of vitamin A capsules and advice to our NGO.

Communicated by:
Tobias Vogt, St Thomas Home,
158 Bellilious Road, Howrah 711 101, West Bengal, India
Email: drtvogt@web.de

Reference

The Healthy Eyes Activity Book (HEAB) 2nd Edition
This is a Health Teaching Book for Primary Schools, which helps the children to know what is the best thing to do if someone has a problem with his eyes.

The second edition of the HEAB is now available in 6 languages (English, French, Spanish, Hindi, Telugu, and Marathi).
Dear Sir,

The administration of Bijilo Lower Basis School in the Gambia – on behalf of the teachers, students and parents – are very glad to inform you that we have received your wonderful donation of 500 copies of the Healthy Eyes Activity Book and a lot of color pencils. The parent-teacher committee and the Regional Education Directorate are all aware of these donations. Personnel from the eye care unit of our department have been invited to see the books and were similarly very amazed.

We have thought it wise to organize a school-based training workshop for teachers on the use of the books. It will involve all the 31 teachers in our school, two from each of the four neighboring schools, representatives from the Regional Education Directorate, four resource persons and four school management committee members (parents). The training will be a whole day program on a Saturday, and will involve about 51 participants.

We would also like to highlight some constraints facing our school, at which over 1,000 children are enrolled, most of whom come from poor families:

- Our school feeding program has been phased out for almost six years now; however, we believe that poor parents normally send their kids to school just to ease the number of cups of rice they must cook at home.
- Due to the lack of staff quarters for teachers to stay in the school, all our staff members must travel to the school each day; having staff quarters at the school would add to the security of the school and ensure teachers are there on time.
- Our school field is not fenced, and sometimes teachers and pupils face problems when having their physical education lessons or games in such an open area.
- We have started working on the school garden but there is lack of gardening materials, which are expensive to buy and we do not have the funds to buy them.
- Learning materials, like exercise books, pencils, erasers, are a big problem too; 80% of our students come from poor families, who are generally unable to buy stationery for their children.

On behalf of the teachers, pupils and parents of Bijilo School, we most profoundly thank SIGHT AND LIFE for the wonderful gesture of your donation. We assure you that the books will be put to good use. We further hope you can assist further and add to the development of education in our school, in particular, and the Gambia, in general.

Communicated by:
Kebba Fatty, Headmaster, and Isatou Joof, Deputy Head Mistress, Bijilo Lower Basis School, the Gambia
Dear Sir,

With this letter, I would like to inform you about the effects of the MixMe™ and the biscuits that SIGHT AND LIFE has donated to the children of the Sedimosang Day Care Center in Ivory Park, South Africa.

Ivory Park is a very poor township where lots of elderly people, orphans and child-headed families survive below the poverty line. Because of HIV and AIDS, many children depend on the care of their grandparents, aunts or the oldest child in the family. A lot of problems arise because of their poverty and lack of access to food. In the areas directly surrounding Sedimosang are three poor schools that receive a government grant to provide children with one meal a day. Such meals consist of ‘maispap’ – a cornflour-based dish – which is usually the only thing the children receive.

The kids of Sedimosang are very happy with the MixMe™ and biscuits! In the beginning, we were learning how to get the best results with MixMe™ and we were monitoring the kids. By the end of last year, we got our first evaluation. The most important progress is that the kids are much more aware and have better concentration. We followed some of the children who where always very tired and apathetic. We slowly saw them changing; they started being active and were more attentive to others. With them, we even see a healthy form of naughtiness. Great results!

In January of this year, when the new school year started, new kids came in. Normally, we have about 84 kids, but this year, 104 kids were enrolled. Sedimosang is now fully packed. We have to ‘fight’ with parents, grannies and others who take care of these children – all because the news about MixMe™ spread around and now everyone wants to have their kids admitted to Sedimosang! Also, we have been monitoring the new children and, again, we see noticeable results. One child, who always had a cold and had never been interested in playing at all, is now doing much better. He really enjoys coloring and painting.

We would also like to thank DSM’s Nutrition Improvement Program for the beautiful MixMe™ T-shirts. The kids wear them proudly as a school uniform!

One of our other projects is the Ke A Bona Eye Clinic. Clinic Director Henny Stege and his staff expressed their concerns about the large number of children with eye problems they meet every day in the various schools in Ivory Park. One of the main causes seems to be malnutrition. It would be very interesting to see if the clinic will also see changes as soon as we start with MixMe™ and biscuits at the primary schools.

In addition to the kids, the poorest elderly people who visit our soup kitchen, Supa di Mama, now receive the biscuits. They are very grateful as well and the biscuits mean a lot to them. Many of these elderly people live off a small grant, from which they not only have to feed and support themselves but also their grandchildren. They come to Supa di Mama twice a week and they spend the whole day there. Not only do they enjoy a meal with the biscuits, they make a social happening out of it: helping each other, talking with each other, and they even started their own exercise program, including playing soccer! This activity program started after a discussion about the biscuits and they are now ‘showing off’ how fit they have become. It is amazing to see how much power your contribution gives to these people!

On behalf of all people involved in South Africa: Baie dankie en baie groete!

Communicated by:
Trees Stege, Sedimosang Day Care Center, PO Box 39207, Moreleta -park 0044, South Africa
Email: stege@mweb.co.za
Adequate nutrition is of utmost importance during infancy and childhood, due to the rapid growth and development that characterizes this phase of life. As many studies have shown, ensuring an appropriate amount and composition of nutrients for infants and young children are critical for growth, functional outcomes (such as cognition and immune response), and long-term well-being.

Paediatric Nutrition in Practice provides concise information to readers who seek quick guidance on practical relevant issues in the nutrition of infants, children and adolescents. Its editors have distilled this information into a compact reference book for busy physicians and other healthcare professionals who often find it difficult to devote sufficient time to study elaborate and extensive books on just one aspect of their practice.

Key topics covered in the book include general aspects of childhood nutrition; nutrition of healthy infants, children and adolescents; and nutritional challenges in special conditions and diseases. It also includes WHO Growth Standards Charts, the CDC and Euro Growth Charts, and Reference Nutrient Intakes for Infants, Children and Nutrition.

A global editorial board provides the book with an international perspective, confronting challenges both in affluent and poorer populations, and contributes further to the unique worth of this book.

For more information, please visit http://www.karger.com/Ped-Nutrition-Practice.

Entrepreneurship in the Social Sector


The emerging field of social entrepreneurship has led the way to a remarkable revolution in which entrepreneurs are transforming the social sector through the application of business know-how. Entrepreneurship in the Social Sector introduces and develops the concept of social enterprise organizations, which are characterized, first and foremost, by their social mission as well as by their innovative combinations of social and commercial approaches.

Building on the flagship Social Enterprise MBA elective course at Harvard Business School, the book focuses on developing the knowledge and skills for creating, leading, or supporting social purpose organizations through the application of entrepreneurial and managerial skills. Social entrepreneurship is defined as
an innovative, social value-creating activity that can occur within or across the nonprofit, business, or government sector. Creating and building sustainable social entrepreneurial initiatives not only requires the application and adaptation of business skills to the social enterprise context, but also the development of new conceptual frameworks and strategies tailored specifically to them.

Among its key features, the book provides clear examples of social enterprise activity from a range the nonprofit, business, and government contexts. Not least of such examples are the Harvard Business School case studies included, which address critical components of social entrepreneurship, including start-up, funding, growth, alliances and collaboration, and performance measurement. The case studies include not only US cases but also a number in international settings. The further inclusion of the latest social enterprise research provides readers with detailed analyses and frameworks on the key themes and ideas illustrated throughout the book.

This book will not only deepen interest and understanding of the practice of social entrepreneurship among students, instructors, and practitioners alike but will also enable social entrepreneurs to achieve mission impact as effectively, efficiently, and sustainably as possible, and enable them to pursue social or non-profit entrepreneurship more strategically in the areas of business, management, marketing, and public policy.

For more information, please visit http://www.sagepub.com/booksProdDesc.nav?level1=W00&currTree=Subjects&prodId=Book230730.

**Nutrition Manual for Humanitarian Action**


Written by a nutrition advisor to the ICRC for 24 years, this publication contains the distillation of Alain Mourey’s unique insights on nutrition issues in humanitarian contexts from his experience of the world’s worst conflicts and resulting nutritional crises.

While nutritional action has, for decades, remained largely confined to directly responding to cases of malnutrition, Mourey considers nutrition in its broadest sense and derives practical recommendations for humanitarian action. The manual provides the scientific basis for action through an in-depth understanding of nutrition, which includes the social dimensions of food. It further demonstrates the interrelations between nutrition and other relevant sectors, notably the economy, placing nutrition within the legal framework set by international humanitarian law, reminding readers that nutritional actions are not simply technical, but also pertain to the protection of victims’ rights in times of conflict.

Mourey links his analysis of the impact of armed conflict and vulnerability with the need for integrated approaches in recommended responses. This overall approach is defined in chapters devoted to ‘classical’ nutritional interventions, such as general food distributions and nutritional rehabilitation, with an emphasis on planning. He goes further in encouraging the examination of their relevance in terms of context and alternative forms of response, based on a multidisciplinary analysis.

The book delivers on many fronts, not least of which is the coherent linking of scientific theory with practice, providing the basis for a professional standard for nutrition responses in humanitarian action. It is available in English and French, and can be downloaded online at http://www.icrc.org/Web/eng/siteeng0.nsf/html/p0820.