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As I write of the risk of doing nothing, *Sight and Life* is devastated by the tragedy unfolding in the Horn of Africa – a humanitarian crisis on a scale we have never seen before. There is daily loss of life and untold long-term effects as children are starved of both calories and vital nutrients, leaving them stunted forever if they survive. *Sight and Life* and DSM have responded by donating to the World Food Programme ready-to-use food to feed a significant number of children until the end of the year. We urge all our readers to take action and to make a difference. At times like this donations to the World Food Programme are urgently required and ensure the immediate provision of ready-to-use foods for those in dire need. Visit [www.wfp.org](http://www.wfp.org) and let us as the world’s nutrition community show our support for those doing something to save the lives of thousands.
Welcome

The risk of doing nothing ...

As Sight and Life commemorates 25 years of service to science and humanity, it is appropriate that we ask ourselves if our existence has made at least some difference to the way in which micronutrient malnutrition is addressed or has helped ensure that this issue receives greater attention within the ever noisier global public health and nutrition space.

For us the answer is yes. We believe we have made a contribution. Now we would like to reflect more closely on the specifics and magnitude of this contribution, a question which is more difficult to answer and quantify. Over the years, we have gathered many letters from grateful beneficiaries, in addition to numerous case studies on how Sight and Life’s direct contribution to vitamin A supplementation and, more recently, the way in which it has addressed multiple micronutrient deficiencies has improved lives; and on how our partnerships, capacity building initiatives and sponsorship of individuals to attend meetings and programs have given people an opportunity for personal and professional development that they would never otherwise have had. We are certainly “building bridges for better nutrition,” as our by-line states. Yet the very word “building” implies and was carefully selected to mean that the process is still happening – it is ongoing, and needed now more than ever. We only need to look at the current global nutrition statistics, and the real concern about reaching the Millennium Development Goal (MDG) targets that are linked to nutrition, to know that we still have a long way to go before we can truly say that we have done our work and achieved our mission of “ensuring a sustainable and significant improvement in human nutrition, health and well-being.” The challenges are enormous and frequently the obstacles seem insurmountable.

We have to act

So, what is the risk that those involved, from all sectors of society, do nothing? The dictionary has a number of definitions for risk, but the one that strikes me as being relevant to the field of humanitarian work is to “act in such a way as to bring about the possibility of an unpleasant or unwelcome event.” Add to that the definition of nothing, “not anything; no single thing,” and it becomes clear that if we, the global public health nutrition community, do nothing, we must ask ourselves if this will result in an unpleasant or unwelcome event? I am sure that most of us would agree that inaction would have negative consequences. The prevalence of malnutrition in all its forms would increase, the quality of life of millions of individuals would decrease, and the negative impact on the growth of economies would continue. Thus, indeed, we have to act – defined as “the process of doing”; however, it is perhaps time to act and do differently.

“The world we’ve made, as a result of the level of thinking we have done thus far, creates problems we cannot solve at the same level of thinking”

Albert Einstein

In the words of Albert Einstein, “the world we’ve made, as a result of the level of thinking we have done thus far, creates problems we cannot solve at the same level of thinking.” In other words, “insanity is when you keep doing the same things expecting different results.” However, challenging the way in which we have done things can be uncomfortable. It means we need to be prepared to shift, to move out of our comfort zone or even to consider that what we have done has not yielded the results we had hoped for.

The need for political will

In her thought-provoking book Dead Aid, Dambisa Moyo challenges the aid culture and writes, “Has more than US$1 trillion in development assistance over the last several decades made
African people better off? No ... Aid has helped make the poor poorer, and growth slower.” She follows the aid culture from the 1960s, which she defines as the decade of industrialization, through the 1970s (“the shift to poverty”), to the 1980s (“the lost age of development”) and the 1990s (“a question of governance”), and into the 2000s, which she refers to as “the rise of glamour aid.” Moyo ascertains that we need to abandon our obsession with aid and, instead, focus on proven financial solutions and models – which, she says, should not be on a one-size-fits-all basis. Above all, she states that what is needed, but what is lacking, is political will.

We can and must advocate for the political will component and are grateful that the Scaling Up Nutrition (SUN) movement recognizes, in the words of Special Representative on Food Security and Nutrition to the UN Secretary General, David Nabarro, that the main investors in SUN are national governments themselves. However, those of us involved in humanitarian work also need to look at how we have done things in the past and reassess and be open to change! We cannot simply be do-gooders which, as the dictionary states, is a disparaging term for a well-intentioned, naive idealist who supports philanthropic or humanitarian causes or reforms.

Research and programs at scale in parallel
The challenge we face going forward, however, is the need to balance the evidence, which is critical to forming and growing knowledge, and to continue monitoring, evaluating and fine tuning the policies that guide public health nutrition, with turning the evidence into scaled-up programs at the community level where there is a real urgency for delivery. The dilemma is to decide whether more research is still needed to sharpen our knowledge of what to do and how to do it, or whether we should turn immediately to the scaling up of interventions at a country level to achieve the MDGs. Perhaps this is a case of ensuring that both research and programs at scale run in parallel and both receive adequate attention and funding. If we neglect one for the other, we could find in future that we have missed an important piece of the puzzle.

We also need to tread carefully between the triumphalism – the attitude or belief that a particular doctrine, religion, culture, or social system is superior to and should triumph over all others – necessary for advocacy, and the realism relative to the potential risks and benefits and nutrition programming’s limitations. The time has come to break down the silos in which we have traditionally functioned and to build meaningful partnerships across multiple cross-cutting disciplines: the need for direct nutrition interventions, together with nutrition sensitive investments. Ultimately, none of our individual actions directly result in reaching the goal of the improved nutritional status of the world’s population. It is the compounded effects of all our actions that lead to a world where this goal becomes possible.

We cannot “do nothing”
In a world where so many families still live in poverty, where some billion people go to bed hungry each night, and hundreds of millions of children will never reach their full potential because of micronutrient deficiencies and inadequate care, doing nothing is not an option. We must not become paralyzed by the enormity of the challenges we face. What is so insidious about the absence of action is that no single decision to delay ever appears monumental at the time. Because the cost of inaction takes time to be fully revealed, it does not necessarily impact the world today, but may well severely affect the world of tomorrow.

By and large, policy makers are risk averse, which perpetuates the cycle of inaction: They would rather do nothing today than run the greater risk of taking the wrong decision. This confers an ethical dimension on the risk of doing nothing, but this is a discussion on its own. Ultimately, I strongly believe that, despite the risk involved, doing something outweighs doing nothing – but I also believe that it is time to reassess what we do and how we do it ...
The *Sight and Life* editorial board are pleased to announce the incorporation into *Sight and Life* Magazine of *Nutriview*, the newsletter previously published by the DSM Nutrition Improvement Program (NIP). This follows in the footsteps of the very successful incorporation of the Xerophthalmia Club Bulletin into *Sight and Life* Magazine in the year 2000 under the editorship of late Secretary General Dr Martin Frigg.

*Nutriview* and *Sight and Life* have already overlapped extensively, particularly as *Sight and Life’s* focus shifted from vitamin A alone to covering all micronutrients and nutrition in general. Indeed, both publications address similar stakeholders and have followed similar objectives for some time. Such objectives include contributing towards a better understanding of the importance of micronutrients for good health; encouraging efforts aimed at improving human nutrition; and communicating relevant aspects of nutrition research to show how the public and private sectors can interact to improve human health.

We are also pleased that *Nutriview* editor Anthony Bowley, who has headed the newsletter for the past 18 years, will continue to contribute his perspectives on nutrition research developments around the world to *Sight and Life* Magazine.

Given the close overlap between both organs, the merger is a welcome next step in the development of *Sight and Life*, as well as a logical progression in the organization’s 25th anniversary year.
The “Sight and Life in My Life” Essay Competition

The **Sight and Life** in My Life essay competition was set up with the goal of finding out how **Sight and Life** has influenced its readers over the years, as part of the organization’s 25th anniversary.

In the final issue for 2010, therefore, we asked our readers to submit stories to us by mid-March 2011. Entrants were asked to address their personal experiences, provide an assessment of the relevant community’s experience, and give a definition of **Sight and Life**.

We received many fascinating stories, as well as some beautiful photographs and original artwork, from many countries, from Ghana to Sri Lanka, and our **Sight and Life** team of judges in Basel, Switzerland was delighted with every entry. As promised, we are sharing the winning entries with you in this issue. However, we will also share highlights of other entries with you in the next issue of our magazine.

A heartfelt thank you again to everyone who entered the competition, for the time you spent on your wonderful entries and, last but not least, the great work you do in your communities.

With warmest wishes.

The **Sight and Life** Team
I am a refugee who lives in Kenya, and have spent many years in Kakuma refugee camp. I was forced to leave my land and my country and had to flee to Burundi, Rwanda, Uganda, and Kenya after the outbreak of civil war. I have been separated from my family since 2003, which was the beginning of my long and unending journey as a refugee. I am in Kakuma refugee camp. This camp is located in the Turkana district of the northwestern region of Kenya, 120 km from Lodwar district headquarters and 95 km from Lokichoggio and the Kenya-Sudan border.

Life in the semi-arid desert environment of Kakuma is rather challenging. The area has always been full of problems: dust storms, high temperatures, poisonous spiders, snakes and scorpions, outbreaks of malaria and cholera and other hardships.

The camp is a small city of thatched-roof huts, tents and mud abodes. Living in here is like living in a prison. Life in a refugee camp is life without hope; it’s about living like a blind person, who only knows where he or she comes from, but does not know where he or she is heading. This was my way of life in Kakuma camp. Living in a camp is not an easy task, nor is life easy without employment or any means to generate income. I did find it difficult to survive the day, and mostly relied on the limited food supplies distributed twice a month by the World Food Programme (WFP).

However, being in the camp taught me more about life. I decided to volunteer and start helping others; first of all, I worked for the Lutheran World Services (LWF) as a food clerk at the distribution centers. Secondly, I joined the International Rescue Committee (IRC) which deals with health issues in the camp – after being trained as a nurse aid and nutritionist. After that, I was retrained by the Jesuit Refugee Services (JRS) as a counselor, inspired by the situation people are living in. Many people commit suicide and this is what pushed me to become a community counselor ...

As my aim is to help people who cannot do things on their own, I did not stop there. I continued to help the most vulnerable, in a different field. As the camp was also full of different types of violence, I was also trained as an ambassador for women in Gender Based Violence. The camp is multicultural and there used to be conflicts. In this instance, I also decided to do “Peace and Reconciliation” in order to become a peacekeeper in the community. All of these projects were to the end of assisting my people who cannot do things on their own.

In Kakuma refugee camp, the most challenging issue is food. It’s what I call the source of everything – if people don’t get food, this can lead to disease and fighting, among many other things. This is why I decided to join WFP. After being selected by the community to represent them on the Food Advisory Committee (FAC), my work involved attending meetings on the food basket and food pipeline situation, and the distribution plan through working with WFP.
I started to have *Sight and Life* in my life. That is to say, I started seeing ahead, because it was through WFP meetings that I met different WFP donors and held discussions and also interactions with them. Everything was about food-related issues. The beginning of my new journey also started when I first met the new WFP donor – DSM. We held a meeting with Madam Milka when she first visited the camp in 2008. She told us about a new micronutrient product called MixMe™. She also told us that she was working hand in hand with *Sight and Life*, DSM’s humanitarian initiative. That was the first I had ever heard about this; later on, we met the DSM team and *Sight and Life* when they visited the camp.

Later, I had the opportunity to meet Dr Klaus Kraemer, the Director. This was a special day and something I had never experienced as a refugee, or indeed since I had started volunteering as an FAC. Working with WFP and *Sight and Life* on MixMe™ at Kakuma was a great opportunity. I was able to take part in every activity and every survey in the camp; I had the chance to transform myself and overcome my own limitations. I also developed the skills to help my people and unfortunate Rwandese and Burundians who did not know about MixMe™, as well as other refugees from other countries.

“Thanks to *Sight and Life*, I got the chance to see far and to regain hope”

Thanks to *Sight and Life*, I got the chance to see far and to regain hope. It has helped me find myself again, re-think and also restore my dreams. *Sight and Life* gave me the chance to go back to school. As I write, I am in Nairobi, the Kenyan capital – a place that I could not have imagined visiting as a refugee. But I am here now, pursuing my degree in Arts & Social Sciences at the Catholic University of Eastern Africa.

In my life, *Sight and Life* is more than everything to me. It has rebuilt my life and has given it sight. Today, I am a person who can speak out and to whom people listen, who can share ideas and change other people. I will become a social scientist tomorrow and all of this is thanks to *Sight and Life*. I am so grateful to you. It is my hope and belief that this companionship will remain for many years to come, not only for me but also for those who are in greater need than me. With your help, I know who I am. I promise to work hard and do more to help those who cannot help themselves. Assisting and helping will be my personal battle, so that I can help the vulnerable without expecting any rewards in return.

I hope one day to develop my own non-profit entity to attempt to help solve some of the issues of poverty in Africa, by providing people with the skills to reduce poverty in their countries.

I would like to acknowledge the efforts of the *Sight and Life* team for their charity, stimulation, love and support, which has given me success in my life. Thank you very much and may God bless you all.

Correspondence: Abubakar Bulako, Catholic University of Eastern Africa, Department of Social Science, Faculty of Arts and Social Sciences, PO BOX 863-00600, Nairobi, Kenya

E-mail: aboubadiobg@yahoo.fr

“I entered the competition because, after reading *Sight and Life* Magazine, I felt that I had something to be proud about. I wanted to share this with people who might have lost hope in their lives.”

Abubakar Bulako
Nairobi, Kenya

“I would like to send my thanks to all the team members who selected me. I don’t know how to express my feelings because I am so happy and feel as if I am flying without wings!”
Until recently, PPHC did not have a comprehensive nutrition module for children and adolescents, especially those in school. This was because we did not have much information to deal with on improving their nutritional status. I am, however, grateful to Sight and Life because I was put in charge of developing a module for school children on nutrition, which I was able to do with the help of the books and other materials we received from you. I also developed a small book called Youth Nutrition, to enable me undertake a program known as “School Health”, which educates young people in our catchment areas – the northern and upper east regions of Ghana. It teaches better ways to improve their nutrition and health status, and educates them on how they can help their illiterate parents and siblings at home.

This program has received the necessary support from the school authorities and from the students themselves. They have sent appreciative messages to me, thanking me for helping them learn how to improve their nutritional status, and their general health status. I have also been given the green light from the office to continue with the program in 2011 at various schools, thanks to the wealth of information I have received.

I first learned about Sight and Life in August 2009, when I joined Presbyterian Primary Health Care (PPHC) – Bolgatanga, Ghana after school. I completed my University for Development Studies (UDS) in Ghana and now have a bachelor of science in Community Nutrition.

One day, I was at the office and came across an old magazine with the inscription Sight and Life, and began to look through it. It was a 2008 edition and I was so happy about the wealth of information it contained. I fell in love with the magazine; it led me to its website, where I learned more about the organization and its work on improving the health of the masses. There, I came across a “call for proposals”, asking organizations to submit proposals for the funding of nutrition programs in their communities.

I told my immediate boss, who was a senior nutritionist, about the proposal and he said we should give it a try. After reading through the procedures and requirements, we sent our application to Sight and Life for consideration. Although we were not selected for the maximum $15,000 grant, we were asked if we would like to receive materials on nutrition and other equipment on a periodic basis. Our answer was a resounding yes; since then, we have received hard and soft copies of relevant information that equips us for better health delivery in the nutrition department.

“\"We receive relevant information to equip us for better health delivery in the nutrition department\"”
Personally, I have improved my level of knowledge in the field of nutrition and I have had a lot of project topics from one of the CDs you gave me. This will help me as I prepare to pursue my master’s degree in September. It has enabled me to present a research proposal to the University of Ghana for consideration for a master’s program in public health. I presented a project proposal on how to improve the nutritional status of pregnant women and lactating mothers in rural areas. I have had most of my references and other information from the materials I receive from you, and will hopefully be in school in September.

I am also very grateful to you because, during our proposal submission, we came across a document on how to write proposals. The title was Tips for Proposal Writing which was prepared by Muzi Na, a graduate student from Johns Hopkins School of Public Health. We printed it out and have since been using it as a guide to write proposals to various organizations, churches and other partners to fund our nutritional and other health programs. I am happy to inform you that these materials are more important to us than money. We are receiving favorable responses from our partners, as well as a lot of help from our partners from Switzerland (the parish of Horn) and others from the Netherlands. Your materials have also helped me in my work during reporting, after conducting various programs or projects such as school health, and other reports for PPHC.

Thank you for your materials and the help they have given me. Thank you for all the relevant information I receive from you. The Bible says, “For lack of knowledge my people perish.” Thank God that I have knowledge relating to my field of work. Continue with the good work you are doing, for you impact many more lives than you can imagine. Thank you.

Correspondence: Abugri Prince, Presbyterian Primary Health Care (PPHC), PO BOX 42, Bolgatanga, Ghana
E-mail: princekebo@yahoo.com

“Thank you for selecting me to be the joint winner of this prestigious award. I feel so honored to have won an award from such a great organization. This is a wonderful moment for me, because it is the first time I have won an award from an international organization such as Sight and Life.

“I did not enter for the sake of winning an award, because I did not know what prize I was going to win. I joined the competition to let the world know that there is a group of people out there in an organization that is changing the lives of many around the world, and that it is good to be associated with them in order to help improve the health standards of people in vulnerable communities. This group is Sight and Life.”

Prince Abugri
Bolgatanga, Ghana

“I also wanted to let the staff of Sight and Life know that they are doing great work and that I appreciate everything they are doing”
“Non-Communicable Diseases (NCDs) are the leading causes of death globally, killing more people each year than all other causes combined. Despite their rapid growth and inequitable distribution, much of the human and social impact caused each year by NCD-related death could be averted through well-understood, cost-effective and feasible interventions.” WHO 2010

**Infant and young child overweight trends from 1990 to 2015 (by World Bank income group)**

- High-income
- Upper-middle-income
- Lower-middle-income
- Low-income

**Associations between poverty, non-communicable diseases and Millennium Development Goals**

- **Globalization**
  - Urbanization
  - Population ageing

- **Increased exposure to risk factors**
  - Tobacco use and exposure
  - Poor nutrition
  - Physical inactivity
  - Alcohol misuse
  - Decreased access to health care
  - Air pollution

- **NCDs**
  - Heart disease
  - Stroke
  - Cancer
  - Diabetes
  - Chronic respiratory disease

- **Limited ability to reach Development Goals**
  - MDG 1: Poverty reduction
  - MDG 4: Reduce child mortality
  - MDG 5: Improve maternal health
  - MDG 6: Combat HIV/AIDS, malaria, and tuberculosis

- **Social and economic determinants of health**
  - Poverty
  - Trade agreements
  - Agriculture and transportation policies
  - Capital flows
  - Activities of multinational companies

- **Health effects**
  - Premature deaths & disability
  - Household effects
  - Low productivity
  - High household costs
  - Health care effects
  - Limited access to effective and equitable health-care services
  - Macroeconomic effects
  - Losses in economic growth

- **Loss of household income from**
  - High health-care costs
  - Poor physical status & premature death
  - Agriculture and transportation policies
  - Unhealthy behaviours
PREVALENCE OF OVERWEIGHT* MALES | AGES 20 +

*BMI ≥ 25kg/m²

Percentage of overweight

- <20%
- 20 – 39.9%
- 40 – 59.9%
- ≥60%
- No data

DEATH RATES FROM NCDs PER 100,000 ADULTS AGED 15 – 69 YEARS IN 23 HIGH-BURDEN COUNTRIES

Death rate per 1,000 adults aged 15 – 69 years

- Other chronic diseases
- Chronic respiratory diseases
- Cancers
- Cardiovascular diseases and diabetes

SOURCE: WHO Global Status Report on Noncommunicable Diseases 2010 / Lancet Series on Chronic Diseases 2010: Chronic Diseases and Development
Introduction
Two thirds of all deaths in the world are due to non-communicable diseases (NCDs), and 80% of NCD deaths occur in low- and middle-income countries. Cardiovascular diseases, obesity and type 2 diabetes (T2D) are the major contributors to the global burden of NCDs. Studies in the life course evolution of these chronic diseases have highlighted an etiological role for factors which govern intrauterine and post-natal growth. Research in this field could offer a novel solution to the “primordial” prevention of conditions which are the most prominent killers in today’s world.

These novel ideas arose from a series of studies by David Barker and his colleagues in the UK. They proposed that intrauterine undernutrition initiated a number of adaptations in the fetus which increased disease susceptibility in later life, especially when post-natal nutrition tended to be “excessive”. A developing fetus has the ability to grow in different ways depending on the surrounding (intrauterine) environment; this ability is called the “plasticity”. An unfavorable environment restricts the ability of the fetus to grow “wildly” and causes a permanent structural or functional change, known as “programming”. India is the world’s capital of low birth weight (LBW) babies, while at the same time it is evolving into one of the economic powers of the world. It was clear that research in India would shed important light on these new and exciting ideas.

Fetal nutrition, growth, birth size and programming
The original ideas in this field were based on birth weight, for which there is a large database. However, it was clear from the beginning that birth size was only a proxy for factors which affect fetal growth. These include genetic factors, maternal size, and intrauterine environment. Birth weight is not a sensitive indicator of intrauterine nutrition, nor is it specific for nutrition. Animal experiments show that a brief nutritional disturbance in early pregnancy permanently alters fetal physiology without any effect on birth size. Thus, birth weight studies helped focus attention on intrauterine life as an important determinant of future health, but the excitement will focus on defining the environmental factors which are the “true exposures” in this association. This is where the current research is being directed.

Possible mechanisms of programming
Fetal growth and development are influenced by an interaction between genetic factors and the intrauterine environment. This was beautifully shown with reference to the interaction between the glucokinase gene and maternal hyperglycemia. The birth size of the newborn is influenced not only by inheritance of the gene, but also by maternal glycemia.

Fetal programming can be manifested in various ways. It might affect size, body composition, systems, organs and cells. It also affects physiology, sometimes without affecting size. Changes include altered setting of different enzyme systems and resetting of the endocrine axes. Endocrine mechanisms are major contributors to programming. Insulin-IGF (insulin-like growth factor) and the hypothalamic-pituitary-adrenal axis have been shown to be prominently affected.

It is increasingly being appreciated that epigenetic changes are at the center of programming. These changes may be mediated by methylation of DNA, acetylation of histones and through the role of micro RNAs, all of which modify gene expression.
“Epigenetic changes are at the center of programming”
The role of DNA methylation in influencing the phenotype of a growing fetus has been well demonstrated in animal models. Feeding pregnant Agouti mice with a methylating cocktail (vitamin B₁₂ + folate + betaine + choline) changes the coat color and reduces obesity, despite inheritance of the mutation. The change in phenotype is linked to methylation in the promoter region of the Agouti gene, which silences it.

Evidence from Pune studies
Research at the Diabetes Unit, King Edward Memorial Hospital, Pune has made important contributions to programming research. Our original observation was that diabetes occurred in Indians at a much lower body mass index (BMI), as compared to Europeans, and that this could in part be due to their higher central obesity and higher body fat percent, or adiposity. This led to the “thin-fat” Indian concept. Many suggested that this was “genetically” determined, but we have not found any major differences in genetic associations of T2D in Indians compared to Europeans.

In 1991, we joined David Barker and Caroline Fall in their “fetal origins” research. The first collaborative research (Pune Children Study) confirmed that low birth weight was associated with insulin resistance as early as four years of age, and that children who were born small but grew big in childhood had the highest level of risk factors for diabetes and cardiovascular disease. We assessed maternal nutrition via anthropometric measurements, nutrient intake and physical activity, and by measurement of circulating nutrient levels.

Predictors of fetal growth and birth size
Fetal growth and size are influenced by genes, parental body size, maternal nutrition and the mother’s metabolic and vascular competence during pregnancy. Our measurements were guided by McCance’s writings of over 50 years ago: “The size attained in utero depends on the services which the mother is able to provide; these are mainly food and accommodation.” We assessed maternal nutrition via anthropometric measurements, nutrient intake and physical activity, and by measurement of circulating nutrient levels.

Maternal body size, body composition and weight gain during pregnancy
The average mother in the PMNS was 21 years old, weighed 42 kg (BMI 18.1 kg/m²), and ate ≈1,700 kcal and 45 g proteins per day during pregnancy. The newborns weighed on average 2,700 g with a ponderal index (PI) of 24.1 kg/cm³; 28% were LBW (<2,500 g).

Babies of heavier mothers were larger in all aspects, and babies of taller mothers were longer. Maternal fat measurements influenced the baby’s weight and skin folds. It is interesting that

FIGURE 1: Thin-Fat Indian Baby. A schematic diagram to compare the body composition of Indian and white Caucasian babies. Indian babies were ≈800 g lighter, muscle thin but more adipose compared to the white babies.

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The PMNS was established between 1993 and 1996 in six villages near Pune, to investigate the influence of maternal body size and nutrition during pregnancy on fetal growth and its future metabolic risks. We also investigated the fathers’ contributions. Over 800 pregnancies were studied. Children were visited every six months for anthropometric measurements, and parents and children were investigated every six years for a detailed assessment of body composition, cardio-metabolic risk factors and neurocognitive development.
paternal size predominantly influenced skeletal measurements, while the baby’s adiposity was predominantly determined by maternal factors. Short and fat mothers gave birth to the most adipose babies, suggesting an intergenerational influence of maternal early life “growth retardation” and the mother’s subsequent weight gain on body composition of the growing fetus. One more interesting finding was that babies born to multiparous women had higher skin folds and a higher abdominal circumference than those born to primiparous women.

“A gain in maternal tissue during early weeks is an important determinant of fetal growth”

Maternal weight gain during the first 18 weeks influenced all neonatal measurements, indicating that a gain in maternal tissue during early weeks is an important determinant of fetal growth. Placental volume measurement at 18 weeks’ gestation was also an independent determinant of fetal growth, highlighting the role for this important organ.

The “thin-fat” Indian baby

We compared the birth measurements of Indian babies with those of white Caucasian babies born in Southampton, UK. Indian babies were lighter (2.7 vs. 3.5 kg, z score -1.74), shorter (47.3 vs. 50.2 cm, z score -1.01) and thinner (PI 24.5 vs. 28.2 kg/cm³, z score -1.62), but their sub-scapular skin fold measurements were relatively well preserved (4.2 vs. 4.6 mm, z score -0.53). At any sub-scapular skin fold thickness, Indian babies had a lower PI than that of the white Caucasian babies.

In a subsequent study, we used whole body MRI to calculate body fat and its regional distribution in neonates. Compared to the larger white Caucasian babies, the Indian babies had similar whole body adipose tissue content (“thin-fat”) and significantly higher absolute adiposity in all three abdominal compartments, viz internal (visceral), deep subcutaneous and superficial subcutaneous. Non-abdominal superficial subcutaneous adipose tissue was, however, lower. Thus, Indian babies are more adipose and have a fat distribution that is suggestive of a higher risk of diabetes, as compared to white Caucasian babies. (Figures 1 and 2)

**FIGURE 2: Thin-Fat Indian Baby.** Anthropometry and MRI comparison of Indian and white Caucasian babies. Despite their anthropometric smallness, Indian babies had a higher amount of fat in subcutaneous and visceral abdominal compartments. White Caucasian babies are used as reference, and z scores for Indian babies are plotted. This figure is not to scale. The figure highlights relative adiposity of Indian newborns.
Maternal nutrition during pregnancy

In the PMNS, we measured maternal macronutrient and micronutrient nutrition, with special attention to one-carbon (1-C, methyl) metabolism, which is crucial for cell growth, differentiation and development. Maternal energy and protein intake was not associated with birth size; fat intake was weakly associated. On the other hand, the intake of micronutrient-rich foods (green leafy vegetables, milk and fruits) had a substantial effect on fetal growth. Maternal erythrocyte folate concentrations and vitamin C concentrations predicted larger neonatal size; vitamin B₁₂ was not predictive. Maternal plasma homocysteine concentrations predicted smaller birth weight. Our results suggested an important role for micronutrients, especially for maternal 1-C metabolism in fetal growth and its body composition. (Figure 3)

“The intake of micronutrient-rich foods had a substantial effect on fetal growth”

Adipocytes – more than a bag of fat: the role of adipocytokines

It is remarkable that the human newborn has the highest body fat percentage (~15%) of all mammals, including pigs (~2%) and sea lions (~5%). The significance of this fact is yet to be established, but it suggests that neonatal adipose tissue must have a significant role in survival. Until recently, adipose tissue was considered only to be a storehouse for triglycerides, to provide energy and mechanical and thermal insulation. We now know that it is the biggest “endocrine organ” in the body. The amount and distribution of adipose tissue influence a wide variety of physiological functions and also predispose to a variety of clinical disorders. Adipocytes secrete a number of molecules called “adipocytokines”. These influence food intake and energy metabolism, the insulin sensitivity of tissues, vascular reactivity, blood clotting mechanisms and, importantly, regulate “innate inflammation”. A growing number of adipocytokines are being discovered and ascribed crucial physiological roles. This represents a novel link between diet, physical activity and susceptibility to a number of non-communicable disorders.

We studied one such adipocytokine, leptin, in newborn Indian and white Caucasian babies. Cord leptin concentrations (median: 6.2 ng/mL, Pune; 6.4 ng/mL, London) were comparable in the two groups, but higher in Indian babies when adjusted for the difference in birth weight. Thus, the excess adiposity of the Indian babies was reflected in functional disturbances indicative of an increased risk of diabetes and related disorders.

Recently, there has been interest in other adipocytokines which influence insulin resistance and, therefore, the risk of diabetes. These include adiponectin and retinol-binding protein 4 (RBP4). Adiponectin has the highest circulating concentration of all the adipocytokines and influences insulin resistance, inflammation and other cardiovascular risk factors. Low adiponectin is an important risk factor for diabetes. RBP4 transports circulating retinol and is synthesized in liver and adipose tissue. It reduces insulin sensitivity and affects glucose metabolism. There is scant information on adiponectin and RBP4 concentrations in cord blood.

We measured adiponectin and RBP4 concentrations in stored cord blood samples, and investigated their associations with maternal size, nutrition and metabolic parameters and newborn size. Adiponectin and RBP4 concentrations in cord blood were lower compared to the published data on western newborns. Maternal calorie, fat and protein intake and the mother’s body size were not related to cord adiponectin and RBP4 concentrations. Both adipocytokines were positively associated with the baby’s body composition (adiponectin with neonatal length, and RBP4 with sum of skin folds). Cord RBP4 was positively associated with maternal intake of vitamin A rich foods, suggesting that maternal vitamin A status may influence fetal adipocyte functioning. Longitudinal follow-up of these associations is ex-
Intrauterine Programming of NCD

INTRAUTERINE PROGRAMMING OF NCD

Recent developments in the field of DOHaD have thrown an interesting light on the life-course evolution of many of the chronic NCDs. It is becoming increasingly obvious that a substantial proportion of adult health is programmed in utero. The health of young girls in a community is of paramount importance and is a major influence on the health of the next generation. Maternal micronutrient nutrition contributes to the fetal programming of NCDs. Current ideas on preventing NCDs in the middle-aged and the elderly via difficult-to-perform lifestyle adjustments are very ineffective models. Future research should target the more promising option of intervening in the young to influence the intergenerational transmission of health. Balanced micronutrient nutrition of young mothers may be the key.

Acknowledgements

We are funded by the Wellcome Trust (London, UK); the Nestlé Foundation (Lausanne, Switzerland); The International Atomic Energy Agency (Vienna, Austria); the Department of Biotechnology (DBT), Government of India (New Delhi, India); and Sight and Life, Basel, Switzerland. Thanks are due to colleagues, collaborators, field workers, and parents and children who participated in the studies mentioned in this article.

Correspondence: Prof. Chittaranjan S Yajnik, Diabetes Unit, 6th floor, Banoo Coyaji Building, KEM Hospital, Rasta Peth, Pune 411011, Maharashtra, India E-mail: diabetes@vsnl.com

Follow-up of the PMNS children

The Developmental Origins of Health and Disease (DOHaD) theory suggests that structural and functional changes in the fetus consequent upon maternal nutritional, metabolic and other influences persist in later life. There are not many human studies linking maternal nutrients with offspring body composition and risk factors for NCD. Design of the PMNS allows us to follow up the children and study the effects of fetal programming.

We found that a child’s adiposity (DXA) and insulin resistance, the two major risk factors for future diabetes, were significantly related to maternal micronutrient nutrition, especially those nutrients which regulate 1-C metabolism. Maternal folate concentrations were directly related to the adiposity of the child at six years of age, and also to insulin resistance. On the other hand, low maternal vitamin B₁₂ status predicted higher insulin resistance. The most insulin resistant children were born to mothers who had the lowest vitamin B₁₂ but highest folate status.

In addition, we found that maternal vitamin B₁₂ and folate predicted a child’s neurocognitive function, suggesting that the 1-C metabolism of the mother also programs the child’s brain development and function.

“Our research suggests that an imbalance in vitamin B₁₂ and folate nutrition and consequent disturbances in maternal 1-C metabolism may contribute to the epidemic of adiposity and T2D in India”

In the PMNS, two-thirds of mothers had low vitamin B₁₂ (<150 pmol/L) status during pregnancy, and a third had raised tHcy concentrations (>10 μmol/L). Folate deficiency was rare.29 This nutrient pattern is at least partly ascribable to vegetarian food habits and partly to the prescription of folic acid by obstetricians. Our research suggests that an imbalance in vitamin B₁₂ and folate nutrition and consequent disturbances in maternal 1-C metabolism may contribute to the epidemic of adiposity and T2D in India.

Folate and vitamin B₁₂ are the major methyl donors in diet, and methylation of DNA is one of the major mechanisms of regulation of gene expression (epigenetics). Methylation silences the genes and affects the phenotype. It will be important to study how an improvement in the maternal nutrition of these nutrients influences the growth of a fetus and its future health and susceptibility to disease. This will be a step forward in the “primordial prevention” of diabetes and other NCDs.

“Future research should target the option of intervening in the young to influence the intergenerational transmission of health”

Summary

Recent developments in the field of DOHaD have thrown an interesting light on the life-course evolution of many of the chronic NCDs. It is becoming increasingly obvious that a substantial proportion of adult health is programmed in utero. The health of young girls in a community is of paramount importance and is a major influence on the health of the next generation. Maternal micronutrient nutrition contributes to the fetal programming of NCDs. Current ideas on preventing NCDs in the middle-aged and the elderly via difficult-to-perform lifestyle adjustments are very ineffective models. Future research should target the more promising option of intervening in the young to influence the intergenerational transmission of health. Balanced micronutrient nutrition of young mothers may be the key.
References


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Isotope Dilution Assessment of Vitamin A Status

Harold C Furr
University of Wisconsin, Department of Nutritional Sciences, Madison, Wisconsin 53706 USA

Methods for estimation of vitamin A status
Vitamin A deficiency is still a major public health problem in many parts of the world. The clinical, social, and economic consequences of vitamin A deficiency are well known, and will not be discussed here. But this problem creates a need for appropriate methods for estimating human vitamin A status. Hence a number of methods exist for assessing vitamin A status, each of which is useful in only certain ranges of vitamin A status. Therefore, it is worth keeping in mind that, whenever there are so many different methods for doing something, not one of those methods is fully satisfactory – each of these methods has disadvantages.

It is generally accepted (and numerous studies have agreed) that most of the body’s vitamin A is in the liver, especially in the well-nourished subject (animal or human). Therefore determining vitamin A concentration in the liver is unequivocally the best method of assessing vitamin A status. From considerations of the estimated length of time for protection from vitamin A deficiency, liver concentration at which plasma RBP is saturated with retinol and catabolism of vitamin A, Olson defined vitamin A status in terms of liver vitamin A concentration, and suggested that liver vitamin A \(>0.07 \text{ μmol/g (20 μg/g)}\) is adequate, 0.035 to 0.07 μmol/g (10 to 20 μg/g) is considered marginal, and \(<0.035 \text{ μmol/g (10 μg/g)}\) is considered deficient. But, in practice, obtaining liver samples from human subjects is difficult and can be readily achieved only by biopsy of subjects undergoing abdominal surgery or by autopsy after death.

Isotope dilution should provide a quantitative measure of vitamin A status with minimal invasiveness. This article summarizes some of the principles and applications of isotope dilution. The principle of isotope dilution is quite simple: addition of a known quantity of tracer (which has some distinguishable marker) to the unknown pool, followed by removal of a sample and measurement of the concentration of tracer; simple calculation should provide the mass of the initial pool:

\[
\text{Concentration}_1 \times \text{Volume}_1 = \text{Concentration}_2 \times \text{Volume}_2
\]

It is assumed that plasma retinol mixes thoroughly with other body pools of vitamin A (or at least with liver vitamin A pools), so that measuring the ratio of tracer to tracee in plasma allows estimation of liver vitamin A pool size. (Figure 2)

Terminology and techniques in isotope dilution
Tracer: Molecules of the substance of interest (vitamin A), which incorporate a distinguishable characteristic but which should be (if possible) biochemically indistinguishable from the unlabeled mass. Ideally, the mass of tracer should be very low, so that it does not perturb vitamin A metabolism. Isotopic labels are most used, but Burri and Jacobs used chlorinated analogs of vitamin A. The modified relative dose response (MRDR) can be thought of as an isotope-dilution technique using the vitamin A analog 3,4-didehydroretinol, and the MRDR response shows the hyperbolic relationship characteristic of dilution.
“Determining vitamin A concentration in the liver is unequivocally the best method of assessing vitamin A status”
Radioactive tracers use $^3$H or $^{14}$C incorporated into the vitamin A molecule. Each has been used in animal models and in early human studies and usually employs liquid scintillation counting for quantitation. Accelerator mass spectrometry allows the use of minute amounts of $^{14}$C which pose no discernable risk to human subjects, but is expensive to implement. Non-radioactive tracers use $^2$H or $^{13}$C labels and mass spectrometry to determine the ratio of labeled to non-labeled vitamin A.

Quadrupole mass spectrometers have been used to measure $^2$H retinol; they are relatively inexpensive and rugged instruments, but do not have as much sensitivity as other techniques. Isotope-ratio combustion mass spectrometers provide high sensitivity for measuring $^{13}$C/$^{12}$C ratios, thus allowing lower doses of tracer; but sample preparation is more demanding.

**Tracee:** The molecule of interest (vitamin A) which is to be quantitated. Concentrations of vitamin A in plasma and liver can be measured by conventional techniques (HPLC or fluorescence).

**Mixing (“equilibration”):** In early writings on isotope dilution as a means of quantitating vitamin A pools, it was assumed that the tracer would completely equilibrate with the tracee, and that a certain period of time would be necessary for equilibration. However, kinetic considerations show that true equilibration of tracer with tracee can occur only if there is no dietary input of vitamin A after the administration of the tracer, and this is usually not realistic in practice. Dietary input of vitamin A continuously dilutes the tracer, as both tracer and tracee are catabolized and lost.

**Pools (compartments):** Vitamin A in the body (animal or human) is present in a number of discrete compartments, distinguishable by tissue and even by cell type. It is difficult to distinguish all the compartments by kinetic models, however. In the well-nourished individual, some 80 to 90% of total body vitamin A is in the liver, so the usual validation of isotope dilution estimates is by comparison with the vitamin A content of the liver.

**Introduction of isotope dilution for estimating vitamin A status**

The first publication on the use of isotope dilution to assess vitamin A status was by Rietz et al at Hoffmann-La Roche, describing the use of radioactive vitamin A to estimate vitamin A stores in rats. Subsequent publications expanded on the initial experiments, and a paper by Bausch and Rietz summarized a number of experiments, using both radioactive and stable isotope-labeled tracers, in both humans and animals. Good correlation was obtained with direct analysis of vitamin A in liver in the animal studies; in the human studies, a single subject, there

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**FIGURE 1:** The relationship of vitamin A status indicators to liver reserves of vitamin A. (CIC, conjunctival impression cytology; RAG, retinoyl β-glucuronide; RBP:TTR, retinol binding protein to transthyretin molar ratio; RDR, relative dose response; MRDR, modified relative dose response.) From Tanumihardjo.

<table>
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<tr>
<th>INDICATOR</th>
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was good agreement with total vitamin A as estimated by the use of both radioactive and stable isotope labels.

Their equation contained an “experimental factor” ("0.5" in the equations) for loss of tracer, attributed to inefficiency of absorption or catabolic loss; this experimental factor was not examined for dependence on time nor on vitamin A status, but was taken to be a constant for either radioactive or stable isotope tracer studies.12

For radioactive tracer:
Vitamin A liver stores = \( \frac{0.5 \times \text{test dose (dpm)}}{\text{Specific activity of vitamin A in plasma}} \)

For stable isotope tracer, the vitamin A liver stores were calculated by use of the ratio of tracer-to-tracee in plasma retinol (as determined by mass spectrometry); their calculation included a correction (“+ 1”) for the mass of tracer dose administered.

For stable isotope tracer:
Vitamin A liver stores = 0.5* test dose* \([(H\text{-retinol}/D\text{-retinol}) + 1]\)

→ A similar relationship was observed in rat studies by Huque13,14 and by Cullum et al.15

The first study in human subjects to directly compare measured liver vitamin A content with the predictions of isotope dilution was performed in the laboratory of Prof James Olson at Iowa State University.16,17 Robert Bergen synthesized the labeled vitamin A; Andrew Clifford and Daniel Jones performed the mass spectrometric analyses of D/H ratio at the University of California; Olivier Amedee-Manesme, a visiting pediatrician from France, was the liaison with the local hospital where the study was performed; and Dale Anderson was a surgeon in the local hospital in Ames, Iowa, who obtained the liver biopsies. We used a rather substantial oral dose of \(^2\text{H}\)-vitamin A, 45 mg for each subject, to ensure that there would be sufficient tracer label to measure with confidence. When we had the resulting data in hand, I spent weeks trying to make sense of them; they did not fit the Bausch and Rietz equation well. One Friday afternoon, Dr Olson and I discussed the problem; he offered to take the data home over the weekend. On Monday morning, he came in with the “Olson equation”, which provided a good fit for almost all the data: (Figure 3)

Total liver reserves = \( F \times \text{dose} \times [S \times a \times [(H:D) - 1]] \)

where

- \( F \) is a factor to express efficiency of storage (taken to be 0.5 from the work of Rietz)
- \( H:D \) is the isotope ratio of non-deuterated (tracee) to deuterated (tracer) retinol in plasma
- \( S \) is the ratio of specific activity of retinol in plasma to that in liver (taken as 0.65 from rat studies)
- \( a = e^{-kt} \) is the fraction of absorbed tracer dose remaining in liver at time \( t \) after dosing, using the estimated rate of catabolism of vitamin A obtained by Sauberlich et al18 (\( k = (\ln 2) / 140 \text{ days} = 0.00495 \text{ per d} \)); this was assumed to be constant, independent of the size of vitamin A stores.

→ This relationship was subsequently corroborated by Haskell et al19 in Bangladeshi subjects; a linear relationship between measured liver vitamin A content and total body vitamin A stores as calculated by the Olson equation was found. Haskell et al found the ratio of plasma to liver specific activities to be 0.80, and they estimated mean recovery of tracer in liver to be 0.378; multiplied together in the Olson equation, the product of these factors is 0.30, which was statistically not different from the product of \( F \times S \) (0.5 \times 0.65 = 0.325) used originally by Olson.

![Figure 2: Simple dilution calculation, for one unit of tracer added to a tracee pool of varying size. Note that the tracer/tracee ratio gives highest precision at low tracee pool size (most important for detecting deficient and marginal vitamin A status).](image-url)
Applications of isotope dilution assessment

Ribaya-Mercado et al.\textsuperscript{20} showed that the isotope dilution technique could indeed detect changes in total body stores of vitamin A in elderly subjects in Guatemala. Haskell et al.\textsuperscript{21} found that the isotope dilution technique could detect changes in total vitamin A body stores in male adult subjects in Bangladesh, subsequent to long-term consumption of different amounts of vitamin A. These two studies provided early corroboration of the technique. The improvement in vitamin A status in Nicaraguan schoolchildren after a sugar fortification program was evaluated by Ribaya-Mercado et al.\textsuperscript{22}

The kinetics of an oral dose of tracer vitamin A was examined in preschool children in Peru.\textsuperscript{23} There was also an apparent correlation between serum tracer/tracee ratio at three days after dosing with the total body stores, as estimated from the ratio at longer times of mixing.

Conversion of carotenoids to vitamin A and estimates of bioequivalency

Tang et al.\textsuperscript{24,25} were the first to use isotope dilution to demonstrate that carotenoids from green and yellow vegetables can maintain liver vitamin A stores, from a study in Chinese children. Lin et al.\textsuperscript{26} used double-label techniques (tracer retinol labeled with \(\text{H}_6\), and \(\text{H}_6-\beta\)-carotene which yielded \(\text{H}_3\)-retinol on cleavage) to verify that the extent of conversion of \(\beta\)-carotene to vitamin A is quite variable among human subjects, a finding corroborated by Wang et al.\textsuperscript{27} Ribaya-Mercado et al.\textsuperscript{28} subsequently found that the extent of conversion of provitamin A-carotenoids to vitamin A varies inversely with vitamin A stores as determined by isotope-dilution, but is independent of serum retinol concentration. Tang et al.\textsuperscript{29} used the double-label approach to show that \(\beta\)-carotene can be cleaved to vitamin A in tissues after absorption. And Ribaya-Mercado et al.\textsuperscript{30} showed an increase in vitamin A pools in Filipino children after dietary consumption of carotene-rich foods.

Haskell et al.\textsuperscript{31} determined the bioequivalence of \(\beta\)-carotene from sweet potato (13:1) and Indian spinach (10:1), compared with that from isolated \(\beta\)-carotene in capsules (6:1). You et al.\textsuperscript{32} did not estimate vitamin A status, but did use labeled retinol to estimate the intestinal absorption and conversion of an oral dose of carotenoids from red palm oil. Wang et al.\textsuperscript{33} measured a conversion factor of 4.5 for spirulina \(\beta\)-carotene in Chinese adults. The vitamin A equivalency of labeled \(\beta\)-carotene in capsules was determined to be approximately 3.36, whether administered in an oil matrix or a vegetable diet, but the absorption efficiency of \(\beta\)-carotene was much greater from the oil than from the vegetables.\textsuperscript{34}

Estimation of human dietary requirements of vitamin A

The dietary intake of vitamin A (preformed plus provitamin A-carotenoids) was correlated with vitamin A stores by Ribaya-Mercado et al.\textsuperscript{35} in an elderly Filipino population. They calculated that a daily intake of 400 μg RAE for women, or 500 μg RAE for men, is sufficient to maintain adequate vitamin A stores. (This may be compared with estimates of 567 μg RAE for women, 707 μg RAE for men, calculated by Olson from other considerations).\textsuperscript{36} Recently, Haskell et al.\textsuperscript{37} used isotope-dilution estimates of vitamin A pool size to calculate an estimated average requirement of approximately 350 μg RAE per day to maintain a liver pool of 0.047 μmol/g for Bangladeshi men of small stature; maintaining a higher vitamin A pool would, of course, require a greater intake. Clearly, this approach is useful for estimating Recommended Dietary Intakes for vitamin A.

\begin{figure}[h]
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\caption{Relationship between calculated and measured amounts of vitamin A (μmol/g wet weight) in the livers of 11 generally healthy human adults. The solid line is the line of identity (1:1 correspondence). From Furr et al.\textsuperscript{16}}
\end{figure}
Alternative isotope dilution calculations

A practical problem with the Olson equation is the implied need for a lengthy mixing period between administration of tracer and collection of a blood sample for determination of isotope ratio. From the human studies by Bausch and Rietz and Sauberlich et al., it was concluded that 21 days were necessary for complete mixing. However, tracer:tracee ratios at three and six days after dosing were shown by Ribaya-Mercado et al. to correlate well to those at 21 days. Three-day predictive equations were determined by Tang et al., Haskell et al. and Ribaya-Mercado et al. Although these equations differ in form, they give similar results.

Duncan et al. developed empirical two-component exponential regression equations to correlate rat liver vitamin A stores with plasma isotope dilution data for 4, 4.4, 5 and 5.4 days for rats given tracer intravenously. Similarly, Adams and Green developed empirical biexponential regression equations to correlate rat liver vitamin A stores with plasma isotope dilution data at 3 days, 4, 4.4, 5, 5.4, and 6 days after oral administration of tracer dose. An extension of this approach for application to humans has been developed (Duca and Green, personal communication).

Further research needs for application of isotope dilution to assess human vitamin A status

The kinetics of vitamin A metabolism in children has been examined in only one study, among 12–24 month children. So far, the Olson equation as determined for adults has been used without verification. Although such studies pose ethical concerns, further data on vitamin A metabolism in young humans are essential for developing suitable prediction equations to allow the extension of this technique to children.

Further development of short-term prediction equations will facilitate the use of the isotope-dilution procedure. Mathematical models of human vitamin A kinetics show promise for the development of general prediction equations which are applicable to a wide range of sampling times (Green MH and Furr HC, unpublished work).

Reviews

Among the generally available reviews of isotope dilution for assessment of vitamin A status are those of Wasantwisut, Tanumihardjo et al., Furr et al., Haskell et al. and Furr et al.

Acknowledgments

The author happily acknowledges the support of Prof James Olson in helping understand and implement the application of isotope dilution for assessment of human vitamin A status, and is also grateful for collaborations with many colleagues.

Correspondence: Harold C Furr, 115 West Rainbow Drive, Bridgewater, VA 22812-1735 USA E-mail: hfurr581@yahoo.com

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“Further data on vitamin A metabolism in young humans are essential for developing suitable prediction equations to allow the extension of this technique to children”


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We face a harsh health reality in the developing world. Nutritional deficiencies, predominantly in the form of micronutrient malnutrition, increase the susceptibility to communicable diseases and non-communicable diseases (NCDs) such as heart disease, diabetes and cancer. Many economically developing regions are now suffering a double burden of obesity, diabetes and other related NCDs, on top of nutritional deficiencies and infectious diseases.

These all have a significant and negative impact on the lives of individuals that flows over to affect communities and ultimately harms national economies. Low- and middle-income countries are at the center of both longstanding and new public health challenges. Much is now being spoken about nutritional deficiencies in the context of undernutrition; while important, we also need to focus attention on addressing the NCDs that will cause over three quarters of all deaths in 2030 and will pose additional challenges for already stretched health care budgets. A key link between undernutrition and NCDs is micronutrients (vitamins and minerals), which yet again mostly affects the world’s poor women and children – further increasing the disparities between the affluent and the poor. The fact remains that women make up little over half of the world’s population, but they account for 60% of the world’s hungry. They also produce between 60 and 80% of the food in most developing countries, where they have less access to land and credit than men do.

The powerful consequences of nutrition transition

Human diet and nutritional status have undergone a number of major shifts over the last three centuries. The concept of the nutrition transition can be defined as a stepwise sequence of characteristic changes in dietary patterns and nutrient intakes associated with societal, economic and cultural changes during the demographic transition of populations. It focuses on shifts in diet, especially its structure and overall composition, is reflected in outcomes such as changes in body stature and body composition, and is paralleled by major changes in health status. A clear example is how changes in European and American diets have caused fluctuations in the average height of men and women throughout time.

Now, more than ever, we need to not only understand the dietary and health changes taking place and their consequences, but we also need to define and implement program and policy changes that will positively improve the total nutritional and health status of people in developing economies.

The prevalence of overweight and obesity exceeded that of undernutrition in the majority of 37 developing countries studied as far back as 2005. Recent trends show the rising prevalence has spread and the incidence of obesity has further accelerated not only amongst adults but also adolescents and even children in the emerging middle class. It is not obesity alone but also diabetes, hypertension, dyslipidemia and artherosclerosis that appear to be on the increase. The reality is that four out of five NCD deaths are in low- and middle-income countries. (Figure 1) This indicates a negative nutrition transition that has serious implications for physical and mental development and performance.
“Nutrition has to be the basis of judging national development”

The double burden of malnutrition occurs in a single family, as seen with this mother and child in Micronesia.
"Research shows that stunting at two years of age is possibly the best predictor of human capital"

Disease susceptibility determined in first 1,000 days of our lives

Some 20 years ago, Dr David Barker’s ground-breaking research showed that low birth weight babies had a greater lifetime risk for coronary heart disease. Subsequently numerous studies have extended the association to an increased risk of hypertension, stroke and type 2 diabetes. This phenomenon is now recognized as the “Barker Hypothesis” or “Fetal Origins Hypothesis.” The theory proposes that coronary heart disease, and the diseases related to it, originates through responses to undernutrition during fetal life and infancy. These responses permanently change the body’s structure, physiology and metabolism.

Recent findings have shown that a woman’s body composition and diet at the time of conception and during pregnancy have important effects on the subsequent health of her offspring. Malnourished mothers often give birth to underweight babies who are 20% more likely to die before the age of five; around 17 million babies are born underweight every year. The risk of later chronic disease is further increased if a baby has not only a low weight at birth but also a low weight gain after birth, resulting in the child being underweight or stunted at the age of two. In addition, rapid post-natal weight gain – especially during childhood and adolescence – further increases the risk of later NCDs. Research shows that stunting (low height-for-age) at two years of age is possibly the best predictor of human capital and that undernutrition is associated with lower human cognition and lower lifetime income potential. The damage suffered in early life leads to permanent impairment, and may also affect future generations. Its prevention can bring about important health, educational and economic benefits.

In 2008 the *Lancet* issued a five-part series on nutrition that reviewed the evidence for the impact of undernutrition on infant and child mortality and its almost irreversible long term effects on health and on cognitive and physical development. Optimal nutrition is now recognized as being especially critical in the first 1,000 days – from conception (in fact from even before pregnancy) to two years of age. Thus this research adds an important dimension to maternal and child health by spotlighting the critical role nutrition plays in health and development.

**NCDs and the Millennium Development Goals**

Some believe that human development initiatives, such as the Millennium Development Goals (MDGs), will not fulfill their goals until they include strong international and country actions against NCDs, especially in low- and middle-income countries. A recent WHO publication on health and the MDGs has recognized this and noted that there is scope for them being considered within Goal 6 (Combat HIV/AIDS, malaria and other diseases). It is now well documented that antiretroviral therapy itself in-
creases the risk of cardiovascular complications, thus having a direct impact on NCDs. In addition, health more broadly, including NCD prevention, contributes to poverty reduction and so anti-NCD strategies could also be part of Goal 1 (Eradicate extreme poverty and hunger). The MDGs have to address the notion of human development having quality of life, not only the extension of life, as a central value.

A recent Lancet paper on NCDs highlights that there are two reasons why the poorest are the most likely to develop and die prematurely from NCDs. First, they have less access to comprehensive health services and secondly, they live in environments where policies to tackle NCDs are either non-existent or inadequate. Furthermore, they are more likely to be exposed to risks including a poor nutritional status. Thus it cannot be neglected that NCDs can also be causal in poverty. (Figure 2)

Addressing NCDs among women and children

Governments and development and donor agencies need to be proactive with regard to NCDs. The approach needs complex, multifaceted, and intersectoral interventions based on long time periods to tackle the wide range of social determinants of health; a decisive move in this direction is a prerequisite for the reduction of poverty and health inequities.

The conditions in which women and children are born, grow up, live and work have a major impact on their health. Thus the Global Strategy for Women’s and Children’s Health states: “Efforts to improve health must be closely linked to those intended to tackle poverty and malnutrition, improve access to education, ensure gender equity and empowerment, tackle major diseases, and improve access to safe drinking water, adequate sanitation and a clean, safe environment. Integrating the care of women and children with other services is an efficient and cost-effective route to success.” The reality is that, despite the billions of dollars given and spent on aid and development each year, we simply do not allocate enough resources to solve all of the world’s biggest problems. It thus becomes necessary to direct additional resources where they can achieve the most good.

Nutrition’s role in human health and development

Over and above food security (sufficient food to provide the required energy), nutrition security (the nutritional quality of the food and care) is thus not only the cornerstone to preventing undernutrition but also contributes to reducing and, in many cases, preventing NCDs. Nutrition has to be the basis of judging national development. Without good nutrition, neither nutritional deficiencies nor NCDs can be controlled. The 2008 Copenhagen Consensus saw the world’s most distinguished economists compare ways to spend US$75 billion on more than 30 interventions aimed at addressing the world’s top 10 biggest challenges. Their basis was costs versus benefits, analyzing interventions that with relatively small amounts of money could generate significant returns in terms of health, prosperity, and community advantages. Among these interventions, five in the top 10 featured nutrition programs, supplementation and fortification with micronutrients.

**FIGURE 2:** Inter-relation between poverty, chronic disease, and development

- **Key risk factors influencing the onset and course of chronic diseases**
  - Tobacco use and exposure
  - Poor nutrition
  - Physical inactivity
  - Alcohol misuse
  - Indoor air pollution
  - Decreased access to health care services

- **Chronic diseases and their risk factors limit the ability to reach development goals**

- **Millennium Development Goals**
  - Poverty reduction (MDG 1)
  - Reduce child mortality (MDG 4)
  - Improve maternal health (MDG 5)
  - Combat HIV/AIDS, malaria, and tuberculosis (MDG 6)

- **Effect of chronic diseases and their risk factors on individuals and families**
  - Low productivity
  - Increased risk of disabilities
  - High household expenditures, which include health care
  - Increased risk of premature death

- **Poverty and social determinants of health**
For example, every US$1 spent on vitamin A supplements was calculated to achieve more than US$17 of benefits in health and long-term prosperity. In the words of the Scaling Up Nutrition (SUN) Framework: “Undernutrition is one of the world’s most serious but least addressed health problems.” Nutrition is often an afterthought in terms of development priorities and has largely been neglected.

Preventing NCD through adequate nutrition

The Lancet series also demonstrated that there are proven and highly cost-effective interventions that could address the problem and save millions of lives. Supplementation, fortified staples, the promotion of exclusive breastfeeding for the first six months and appropriate complementary foods after six months of age, together with continued breastfeeding, are some of the interventions available to help break the cycle of malnutrition that will also see a reduction in NCDs in the future. Just one example of such an effective intervention are the research findings that show that supplementation of pregnant women with just one recommended daily allowance (RDA) of multiple micronutrients not only improves the health status of the mother but also increases birth weight and substantially reduces the rates of low birth weight and small-for-gestational-age births in children. This has a potentially important impact on reducing chronic disease in later life amongst these children.

Saving lives, improving futures

The Global Strategy for Women’s and Children’s Health states that addressing undernutrition in pregnant women and children leads to an increase of up to 10% in an individual’s lifetime earnings and an estimated 2–3% growth in the economic wealth of developing countries. This is as a result of the fact that women are the sole breadwinners in one out of three households around the world, so improving their nutrition is crucial. The SUN road map identifies investments that have been shown to work if implemented in the context of nutrition-focused development policies. Comprehensive and integrated actions at the country level are what will ultimately lead to real change. The SUN Road Map is expected, if fully implemented, to avert the deaths of one million children per year; mitigate against disease and reduce the burden on healthcare systems; increase school attendance and educational attainment; and improve economic prosperity and the ability of all citizens to realize their full potential.

Failure to respond is now a political, rather than a technical issue. We need political will and resource commitment to turn knowledge and talk into action. Action that will save lives now and into the future.

Correspondence: Klaus Kraemer, Sight and Life, PO Box 2116, 4002 Basel, Switzerland E-mail: info@sightandlife.org

This article originally appeared in The Commonwealth Health Ministers Update 2011

Resources:
> For details on the work of Sight and Life visit: www.sightandlife.org
> For details on the Copenhagen Consensus 2008 visit: www.copenhagenconsensus.com/Home.aspx
> For details on the 1000 Day movement visit: www.thousanddays.org
> For the Scaling Up Nutrition (SUN) documents search on www.unscn.org
> For the Lancet series on Chronic Disease: The Lancet, Volume 376, Issue 9753, 13 November 2010
Building bridges for better nutrition.
Plasma 25-Hydroxy-Cholecalciferol (Vitamin D) is Depressed by Inflammation: Implications and Parallels with Other Micronutrients

David I Thurnham
Northern Ireland Centre for Diet and Health, University of Ulster, Coleraine, BT52 1SA, UK

It was recently shown that serum concentrations of 25-hydroxycholecalciferol (25-hydroxyvitamin D; 25(OH)D) fell by more than 40% within 24 hours of elective joint replacement surgery and were still 20% lower than pre-operative values three months after the operation. Quantification of serum 25(OH)D concentrations has provided us with a measure of vitamin D status for more than 40 years. The pioneering work of David Frazer, Eric Lawson, Egan Kodicek, Michael Holick and Hector DeLuca in the 1970s identified 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D; they showed us that 25(OH)D and 1,25 dihydroxy-cholecalciferol (1,25(OH)₂D) were the two major metabolites of vitamin D in our blood controlling calcium and phosphate metabolism. Subsequent work showed that the plasma concentration of 25(OH)D was an accurate indication of vitamin D stores, whether obtained from ultraviolet irradiation or dietary intake over long periods.

Since that time, vitamin D has been found to be an important modulator of immune function with anti-inflammatory and anti-proliferative properties. In recent years, low concentrations of serum 25(OH)D, ie poor vitamin D status, have been associated with an increased risk of a number of chronic diseases, including cancer, diabetes, rheumatoid arthritis, cardiovascular disease and mortality. However, the rapid and long-lasting effect of trauma on circulating 25(OH)D concentrations should make us pause to consider whether the low concentrations of serum 25(OH)D associated with chronic disease are a metabolic consequence of those diseases and not a true reflection of vitamin D status.

Endogenous vitamin D synthesis

Endogenous vitamin D synthesis is summarized in Figure 1. The action of sunlight on human skin converts 7-dehydrocholesterol into cholecalciferol, otherwise known as vitamin D₃. The knowl-
I speculate that the surgery also activated many components of the immune system.

Therefore, the fall in plasma 25(OH)D concentrations may be associated with a rapid uptake of 25-OHD by immune cells, priming innate immune defences in the body.

I speculate that the 25(OH)D results obtained following surgery may also be obtained following any infection or inflammatory trauma.

Therefore, the many epidemiological studies showing low 25(OH)D concentrations associated with chronic diseases may be a consequence of those diseases and not the cause.

A worrying feature of the surgical study was the persistent depression in plasma 25(OH)D concentration by 20-25% for 3 months following surgery.

We also do not know what implications these results have for children’s vitamin D status, especially where they may be exposed to frequent infections.

Interpretation of plasma 25-hydroxy-cholecalciferol concentrations

In my previous commentary on vitamin D,5 a major concern was the reproducibility of plasma 25(OH)D measurements, inter-assay variation and appropriate cut-offs to assess those at risk of vitamin D deficiency. The methodological issues were under study at that time by the UK Food Standards Agency; the subsequent report indicates the most reliable methods. The report also points out the newly available Reference Material from the National Institutes of Standards and Technology, which should improve inter-laboratory comparisons.6 Newer studies will therefore be better able to assure accuracy; however, the problem of interpretation may, if anything, have worsened if plasma concentrations of 25(OH)D are influenced by inflammation.1 Appropriate cut-offs to assess the risk of vitamin D deficiency are still not resolved. Deficiency is generally regarded as <30 nmol/L (12–ng/mL), but sufficiency is variously stated as >50, >807 or even >1508 nmol/L.

In terms of functional vitamin D concentration, some workers consider it is best to assess the free (ie unbound) concentration in plasma,9 although this is probably not necessary in most clinical settings.7 Most plasma 25(OH)D circulates bound to vitamin D-binding protein (VDBP; 80–90%) and most of the remainder is bound to albumin (10–20%). Very little 25(OH)D remains free, ie biologically active in plasma (0.02–0.05%).10,11 VDBP also binds to 1,25(OH)2D but the relative affinity is 10-fold less than for 25(OH)D, so the proportion of free plasma 1,25(OH)2D concentrations is 10-fold higher compared with 25(OH)D (0.2–0.6%). The concentration of VDBP in plasma is 20-fold higher than the total amount of vitamin D metabolites and the physiological consequence is therefore that all circulating vitamin D compounds are protein bound and will have limited access to target cells. Thus, concentrations of free rather than total forms of 25(OH)D and 1,25(OH)2D may provide a better assessment of functional vitamin D status.12

“Workers suggest that the molar ratio of 25(OH)D:VDBP or free 25(OH)D may be more useful indices of biological activity in the plasma than the total 25(OH)D concentration alone”

The influence of variations in the concentration of VDBP on the availability of the free vitamin D metabolites was clearly shown in a comparative study of patients with idiopathic...
There was no difference between the groups in plasma 25(OH)D concentrations but plasma VDBP concentrations were significantly higher in the patients with the result that unbound concentrations of 25(OH)D and 1,25(OH)₂D were significantly lower in the patients with osteoporosis (Table 1). The converse can also be true, since plasma VDBP concentration can decrease with cellular damage and tissue loss and this would have the effect of increasing vitamin D accessibility to tissues. Thus, workers suggest that the molar ratio of 25(OH)D:VDBP or free 25(OH)D may be more useful indices of biological activity in the plasma than the total 25(OH)D concentration alone.

Influence of elective joint-replacement surgery on plasma DBP and “free” 25(OH)D concentrations

The study of Reid et al provided an opportunity to examine the influence of an altered inflammatory state on vitamin D status without the complication of accompanying disease. In fact, similar observations to those of Reid et al were first reported by Louw et al almost 20 years ago. Louw et al showed that a transient depression in plasma 25(OH)D concentrations of ~16% followed uncomplicated orthopedic surgery in 25 volunteers of both sexes. The fall in 25(OH)D was accompanied by similar rapid falls in plasma retinol, retinol-binding protein (RBP), leukocyte vitamin C, α-tocopherol, total lipid, albumin and pyridoxal-5-phosphate over the first three days post-operatively. In almost all cases, concentrations had normalized by day 6, when C-reactive protein had also almost returned to normal. The authors pointed out that the nutritional status of the group prior to surgery was good and no patient fasted more than 12 hours post-operatively. The authors also monitored hydration and concluded that the patients had a normal fluid intake; this made hemodilution very unlikely. The authors concluded that the self-correcting nature of the decreased values in the study argued against the low values representing true nutritional status.

In contrast to the study by Louw et al, Reid and colleagues focused their efforts entirely on vitamin D. They measured the effects of inflammation on plasma 25(OH)D, 25(OH)D:VDBP ratio and free 25(OH)D concentrations in the immediate post-operative period. The depression in concentrations was large (~40%) (Table 2) but consistent with the previously observed effects of inflammation on plasma retinol, ferritin and many other nutrients. Not only concentrations of 25(OH)D were depressed, but also the 25(OH)D:VDBP ratio and free 25(OH)D. Furthermore, in blood samples taken at three months, the three markers of vitamin D status were no different to those observed in the samples collected on day 5 post-operatively, but CRP concentrations had returned to the pre-operative value.

Thus, the behavior of the 25(OH)D concentrations in the surgical studies of Louw (South Africa) and Reid and colleagues...
VITAMIN D AND INFLAMMATION

Table 1: Influence of idiopathic osteoporosis on “free” vitamin D metabolites

<table>
<thead>
<tr>
<th>Vitamin D metabolite</th>
<th>Osteoporosis n=56</th>
<th>Controls n=114</th>
<th>P&lt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td></td>
</tr>
<tr>
<td>Vitamin D-binding protein mg/L</td>
<td>224 ± 62</td>
<td>143 ± 34</td>
<td>0.001</td>
</tr>
<tr>
<td>25(OH)D nmol/L</td>
<td>44.7 ± 21</td>
<td>43.3 ± 17</td>
<td>NS</td>
</tr>
<tr>
<td>1,25(OH)₂D pmol/L</td>
<td>90 ± 37</td>
<td>103 ± 39</td>
<td>NS</td>
</tr>
<tr>
<td>Free 25(OH)D pmol/L</td>
<td>6.1 ± 31</td>
<td>9.1 ± 4.4</td>
<td>0.001</td>
</tr>
<tr>
<td>Free 1,25(OH)₂D fmoL/L</td>
<td>77 ± 37</td>
<td>142 ± 58</td>
<td>0.001</td>
</tr>
</tbody>
</table>

The study shows how a significantly higher concentration of the vitamin D-binding protein in patients with idiopathic osteoporosis depresses concentrations of both free 25-hydroxy-cholecalciferol (25(OH)D) and free 1,25-dihydroxy-cholecalciferol (1,25(OH)₂D) in the plasma.

(Scotland) was similar except that in the more recent study baseline 25(OH)D values were not restored by Day 5. Mean plasma 25(OH)D values remained approximately 25% lower than pre-operative values at day 5 and were still depressed by this amount at three months post-op. It is probable that the depression of 25(OH)D concentrations at three months may have been due to the nature of the surgery. For patients undergoing replacement of a knee joint, it is conceivable that mobility remained a problem, whereas the CRP response of the subjects in the South African study suggested that the severity of the surgery was less. Furthermore, the latitude of the surgical unit in Scotland (55ºN) and the high rainfall in that area will not have helped the patients to obtain much useful solar radiation throughout much of the year.

Reid and colleagues would appear to dismiss the idea that turnover and cellular uptake of 25(OH)D could explain the large decrease in plasma concentrations, but the increase in CRP in the patients (Table 3) was similar except that in the more recent study baseline 25(OH)D values were not restored by Day 5. Mean plasma 25(OH)D values remained approximately 25% lower than pre-operative values at day 5 and were still depressed by this amount at three months post-op. It is probable that the depression of 25(OH)D concentrations at three months may have been due to the nature of the surgery. For patients undergoing replacement of a knee joint, it is conceivable that mobility remained a problem, whereas the CRP response of the subjects in the South African study suggested that the severity of the surgery was less. Furthermore, the latitude of the surgical unit in Scotland (55ºN) and the high rainfall in that area will not have helped the patients to obtain much useful solar radiation throughout much of the year.

Reid and colleagues considered what might have contributed to the loss of 25(OH)D from the blood. The possibility that the fall in the binding protein and albumin concentrations may have contributed to the loss of 25(OH)D was considered, but the fall in protein concentrations was only ~20% while 25(OH)D concentrations fell by 40%. However, it is interesting to compare the behavior of 25(OH)D with that of plasma retinol, about which more is known. (Table 3) Early changes in epithelial permeability and vasodilatation may well facilitate the movement of plasma retinol into the extracellular fluid compartment, contributing to an initial decline in plasma retinol concentrations. Furthermore, losses of the retinol:RBP complex into the urine during fever have been shown and there is inhibition of the liver RBP synthesis from 12 hours following experimental infection in rats.

Movements between the blood and extracellular fluid in the 25(OH)D:VDBP complex similar to those of retinol may also follow the onset of trauma. Inflammation may also depress VDBP synthesis since a fall in VDBP concentrations is associated with multiple trauma, organ dysfunction and sepsis. However, I can find no direct evidence for an effect of inflammation on VDBP synthesis and the fall in serum concentration may be associated more with its intrinsic immunological activity.

There is evidence that the 25(OH)D:VDBP complex can be found in urine. Patients with uremia can excrete considerable amounts (Table 3), but glomerular filtration in the arthroplasty patients was unaltered throughout the five post-operative days. Reid and colleagues would appear to dismiss the idea that turnover and cellular uptake of 25(OH)D could explain the large decrease in plasma concentrations, but the increase in CRP in the patients

Table 2: Peri-operative measurements of vitamin D metabolites in patients following elective knee surgery

<table>
<thead>
<tr>
<th></th>
<th>Pre-operative</th>
<th>6 – 12 hr</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
<th>P&lt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP mg/L</td>
<td>2.8</td>
<td>—</td>
<td>56</td>
<td>164</td>
<td>189</td>
<td>136</td>
<td>113</td>
<td>0.001</td>
</tr>
<tr>
<td>25(OH)D nmol/L</td>
<td>40</td>
<td>26</td>
<td>23</td>
<td>23</td>
<td>25</td>
<td>28</td>
<td>29</td>
<td>0.001</td>
</tr>
<tr>
<td>Albumin g/L</td>
<td>39</td>
<td>—</td>
<td>33</td>
<td>32</td>
<td>31</td>
<td>30</td>
<td>31</td>
<td>0.001</td>
</tr>
<tr>
<td>VDBP μmol/L</td>
<td>7.5</td>
<td>6.6</td>
<td>6.9</td>
<td>7.1</td>
<td>—</td>
<td>7.9</td>
<td>—</td>
<td>0.001</td>
</tr>
<tr>
<td>Molar ratio</td>
<td>6.9</td>
<td>5.4</td>
<td>4.2</td>
<td>4.8</td>
<td>—</td>
<td>4.0</td>
<td>—</td>
<td>0.001</td>
</tr>
<tr>
<td>Free 25(OH)D pmol/L</td>
<td>9.04</td>
<td>—</td>
<td>5.41</td>
<td>6.40</td>
<td>—</td>
<td>6.09</td>
<td>—</td>
<td>0.001</td>
</tr>
</tbody>
</table>

All values are medians. Data taken from the report by Reid and colleagues.

1.
## Table 3: Factors influencing vitamins D and A in serum in health and disease

<table>
<thead>
<tr>
<th>Factors of interest</th>
<th>Vitamin D</th>
<th>Vitamin A</th>
</tr>
</thead>
</table>
| **Predominant form in serum** | 25-hydroxy-cholecalciferol (25(OH)D)
Gc-globulin or vitamin D binding protein (VDBP, 80–90%); albumin (10–20%)
| Retinol 1:1 molar association with retinol-binding protein and transthyretin (95%); retinol:RBP (∼4.5%) |
| **Transported by** | Gc-globulin or vitamin D binding protein (VDBP, 80–90%); albumin (10–20%)
|  |
| **Unbound vitamin in serum** | 0.02 – 0.5%
| <0.5%
| **Effect of acute inflammation on total vitamin in blood** | Fall in serum 25(OH)D ∼40% in 24 – 48 hours
Fall in concentration of VDBP of <20% over 24 hours and falls observed in other diseases
| Fall in serum retinol ∼40% in 24 – 48 hours |
| **Effect of acute inflammation on binding proteins** | \(|\) |
| **Effect of inflammation on binding protein synthesis** | No evidence of a direct effect of inflammation on protein synthesis
| Evidence of inhibition of hepatic RBP synthesis from 12 hours
| **Excretion of vitamin: binding-protein complex** | In health – <0.17 nmol/day;
In uremia – 0.27–10 nmol/day and increased amounts in patients with albuminuria
| In health – trace;
In pneumonia and sepsis 0.78 μmol/day;
In fever 1.67 μmol/day
| **Potential benefits associated with depression of vitamin concentration in serum during inflammation** | Inflammation activates macrophages which take up 25(OH)D and use it to synthesize the anti-microbial protein cathelicidin
Low VDBP may potentially increase free 1.25(OH)2D in blood. This may have anti-inflammatory functions by suppressing TNFα and promoting IL-10 release
| Inhibition of RBP synthesis and depression of s. retinol may conserve vitamin A by preventing urinary losses
Retinol is generally anti-inflammatory and promotes Th2-CD4 thymocyte development. Low concentrations may promote a more pro-inflammatory action
| **Potential benefits from vitamin supplements** | No survival benefits from vitamin D (+calcium) given to ICU patients on admission or from long-term administration to patients with congestive heart failure
Prevents rickets and osteomalacia and has potential other benefits
| Large vitamin A doses to children with measles reduced symptoms and accelerated recovery
Vitamin A supplements prevent morbidity and mortality in community studies |
indicated a considerable inflammatory response. This inflammation will have also increased the activity of macrophages in body tissues and the uptake of 25(OH)D by stimulated macrophages can be considerable.

“Innate immunity is the body’s first line of defense against microbial attack”

Innate immunity is the body’s first line of defense against microbial attack. 25(OH)D taken up by stimulated macrophages and epithelial cells is rapidly converted to 1,25(OH)₂D, which induces production of cathelicidin, a potent anti-microbial peptide.

“Innate immunity is also especially important in protecting the gut, and vitamin D modulates anti-inflammatory Treg cells and interleukin-10 production.”

Experimental work has shown that 1,25(OH)₂D inhibits the development of inflammatory bowel disease in IL-10, knock-out (KO) mice and that vitamin D-receptor-KO mice were hypersensitive to exogenous injections of bacterial lipo-polysaccharide (LPS), while others have shown that if such mice are infected with Salmonella there is greater bacterial burden and mortality than in wild-type mice. Further research is needed, however, to determine to what extent an up-regulation of macrophage activity could explain the changes in plasma 25(OH)D concentrations.

It was interesting that the reduction in free 25(OH)D concentrations slightly increased plasma calcium during the post-operative period, but did not disturb parathyroid hormone (PTH) concentrations. PTH would normally be sensitive to changes in plasma calcium, so the absence of any movement was a reflection of the minimal changes in calcium as a result of the inflammation. Alterations in fluid balance could also explain the concentration changes in vitamin D, but the authors assured the reader that any fluids given were to maintain fluid balance and not expand volumes. Furthermore, they were given over several hours and therefore would have equilibrated with the entire extravascular fluid volume of ~14 L in an adult. This large volume would not have significantly altered during the post-operative period and would not, therefore, explain the 40% decrease in 25(OH)D concentration.

There was no association between plasma 25(OH)D and CRP concentrations. This is not surprising, since we have observed similar effects with other nutrients influenced by inflammation. No doubt there would be a close correlation between 25(OH)D and CRP if multiple samples were taken over the first 24 hours post-operatively. However, CRP concentrations will start to fall as soon as the clinical symptoms of the trauma recede. In contrast, 25(OH)D concentrations and biomarkers such as retinol, ferritin and many other nutrients remain affected by the inflammation into the convalescent period.

“The potential benefit of large changes in 25(OH)D”

What the potential benefit of the large changes in 25(OH)D concentrations brought about by trauma is for the patient, is an interesting question. The data suggest that not only did total 25(OH)D concentrations fall but there were also similar large reductions in the biologically active “free” 25(OH)D. It has to be remembered, however, that the concentration of 25(OH)D in plasma is 1,000-fold higher than 1,25(OH)₂D in plasma and the authors did not measure this important vitamin D metabolite in the patients. Furthermore, a fall in the concentration of the VDBP may have the effect of increasing the concentration of “free” vitamin D in the plasma are likely to be part of the innate immune response.”

**TABLE 4: Free (unbound) concentrations of 25-hydroxy-cholecalciferol (25(OH)D) in maternal and cord serum**

<table>
<thead>
<tr>
<th>Vitamin D binding-protein mg/L</th>
<th>25(OH)D μg/L</th>
<th>Free 25(OH)D ng/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mothers n =30</td>
<td>574</td>
<td>14</td>
</tr>
<tr>
<td>Infants n =30</td>
<td>268</td>
<td>8</td>
</tr>
</tbody>
</table>

Data shown are means taken from Bouillon et al.

*Free 25(OH)D concentrations were significantly higher in cord than maternal serum.*
1,25(OH)₂D in target tissues. An example of a low concentration of VDBP increasing the relative amount of “free” 25(OH)D was observed in a study of the VDBP in maternal and cord serum. Table 4 shows lower 25(OH)D and VDBP concentrations in the cord compared with maternal blood, although these were associated with a substantially higher concentration of “free” 25(OH)D.

Free 25(OH)D did not increase in the study by Reid, but we do not know what effect the low VDBP concentrations had on 1,25(OH)₂D concentrations in the tissues. Alterations in the 1,25(OH)₂D concentration would modify the immune and anti-inflammatory functions of vitamin D in spite of, or in partnership with, the fall in total 25(OH)D. As discussed above, vitamin D is important for innate immunity and the rapid changes in vitamin D metabolites in the plasma are likely to be part of the innate immune response. However, caution should be used before speculating on changes in free vitamin D metabolites. Such molecules are small and easily lost in the urine, even though no significant changes were reported in glomerular filtration in the study of Reid et al.  The reason for the depression in plasma 25(OH)D concentrations associated with inflammation is currently not known. We have suggested above that a fall in VDBP may increase the concentration of “free” 1,25(OH)₂D in target tissues, but this has not yet been shown and more research is needed. Most early features in the acute phase response are generally regarded as beneficial activities to protect the host metabolism from the cause or consequences of infection or trauma. Likewise, comparative evidence with several other micronutrients similarly affected by inflammation would suggest that the depression in plasma 25(OH)D concentrations may be associated with a protective function, but this remains to be elucidated.

Can the effects of acute inflammation on 25(OH)D be extrapolated to chronic inflammation?

Reid et al argue that it would not be reasonable to extrapolate the data from their study to the relation between the systemic inflammatory response and plasma 25(OH)D concentrations in chronic disease. They argue that changes in CRP in chronic inflammatory conditions are likely to be of a lesser magnitude than those seen after arthroplasty. However, the changes in 25(OH)D were not correlated with CRP in their study and the concentrations of 25(OH)D remained depressed when CRP was already falling. That is, we cannot assume that a lesser increase in CRP would necessarily not be associated with a fall in 25(OH)D concentrations. Earlier work with plasma retinol showed that acute inflammation was associated with a 40–50% fall in concentration. Where the cause of the fall in retinol was acute stress and recovery was quick, retinol concentrations tended to return to the pre-existing conditions. However, we have shown in apparently healthy persons living in the community that plasma retinol can be depressed by 32% (95% CI, 12-55%) in persons having both a moderately raised CRP (>5mg/L) and a raised chronic acute phase protein, namely α₁-acid glycoprotein (AGP; >1g/L). These are the conditions associated with early convalescence. Inflammation is a universal response to trauma. In the initial inflammatory response, the body does not distinguish between knee arthroplasty and severe pneumonia or any other severe illness. It responds to the magnitude of the pro-inflammatory cytokine stimulus. It is therefore quite probable that the initial depression in 25(OH)D is a universal response to inflammation; however, the magnitude and duration of that response will vary in relation to the severity of the stimulus. “It is quite probable that the initial depression in 25(OH)D is a universal response to inflammation; however, the magnitude and duration of that response will vary in relation to the severity of the stimulus.”

The measurement of plasma 25(OH)D concentrations to provide an assessment of vitamin D status is widely used and low concentrations of 25(OH)D have been shown to be associated with a number of chronic diseases, including cancer, diabetes, rheumatoid arthritis, cardiovascular disease and mortality. In fact, other workers may have suspected that sickness predisposed to vitamin D deficiency. Lee and colleagues in Australia reported a high prevalence of hypovitaminosis D in 1,100 patients admitted to the intensive care unit and supplementation with either calcium or vitamin D or both before admission was not protective. The authors accepted that limited exposure to sunlight during chronic illness was probably an important factor causing low 25(OH)D concentrations, but also did not rule out altered parathyroid metabolism. Acute and chronic disease is accompanied by an activated acute phase response; thus, the observation of Reid and colleagues could well suggest that the low concentrations of 25(OH)D accompanying chronic disease are both a product of disease and poor vitamin D status.

In considering any chronic disease, it is always very likely that people with the poorest health will be the ones at risk of least exposure to sunlight. Hence, observations that people with the lowest 25(OH)D concentrations have the greatest risk of cardiovascular disease (CVD) or diabetes, etc are not surprising and do not necessarily point to any direct effect of inflammation on vitamin D status. However, there is evidence of inflam-
matory activity in people who subsequently develop cancer or cardiovascular disease, five or more years before the disease is clinically evident. In the British Regional Heart Study, blood was taken from 7,735 healthy middle-aged men and there were 660 deaths during an average follow-up period of 9.2 years. The authors reported that low plasma albumin concentrations (a negative acute phase protein) was the principle factor associated with mortality from cardiovascular disease and cancer, even when deaths in the first five years were excluded.\(^{34}\) Similar data was obtained in the Multiple Risk Factor Intervention Trial, when low albumin was associated with cardiovascular deaths 6–10.5 years after the serum was measured.\(^{35}\) Similar results were also obtained from the National Health and Nutrition Examination Survey Epidemiologic Follow-up Study, although they were expressed differently. In subjects followed up for a median of 15 years, high albumin (>45 g/L) was associated with a lower risk of death from all causes and CVD.

**The use of albumin versus CRP**

These days, the use of albumin to indicate inflammation has been replaced by CRP but, nevertheless, all three studies point to evidence of inflammation being present in people who were apparently healthy at the time the blood was taken, but we do not know how or whether that inflammation will have influenced plasma 25(OH)D concentrations. However, in a very recent study of vitamin D and mortality risk in the general population, albumin (positively) and CRP (negatively) were both correlated with plasma 25(OH)D concentrations.\(^{2}\) In addition, there is another group of subjects who displayed evidence of mild inflammation as raised CRP concentrations\(^{36,37}\) and have been reported to have poor vitamin D status.\(^{38}\) Brot and colleagues\(^{38}\) listed a number of studies that showed smokers had poor vitamin D status and concluded that the effects of smoking on vitamin D metabolism was not likely to be explained by other confounding lifestyle variables. Five hundred and ten healthy peri-menopausal women, of whom 50% were smokers, were found to have similar dietary intakes. If anything, the smokers sunbathed more often than the non-smokers, but serum 25(OH)D levels in the smokers were 10% less than in the non-smokers. There was a significant negative association between smoking and serum concentrations of 25(OH)D and 1,25(OH)\(_2\)D. Unfortunately, Brot and colleagues did not include indices of inflammation in their investigations, but it would be important to measure both acute and chronic markers of inflammation as CRP alone only measures acute inflammation.

In fact, a study to examine the possibility that serum 25(OH)D concentrations were correlated with CRP or other biomarkers of sub-clinical vascular injury was reported by Michos and colleagues.\(^ {39}\) The authors were investigating whether serum 25(OH)D was causally linked to subclinical vascular disease. Serum CRP levels are associated with cardiovascular risk; therefore, the authors speculated that 25(OH)D and CRP would be correlated. They found no correlation between 25(OH)D and CRP or any other marker of vascular disease and concluded that there is no causal relationship between 25(OH)D and CVD risk or, if there is, it may be mediated through mechanisms other than subclinical vascular disease severity. However, if low 25(OH)D concentrations are a product of inflammation with a protective function in the inflammatory cascade, the concentrations of 25(OH)D seen in a cross-sectional study will be both a product of that clinical condition, the pre-sickness concentration of 25(OH)D and the length of time being ill. We should not necessarily expect to see any relationship with markers of vascular disease as there are too many variables potentially influencing the 25(OH)D concentration and this will be a general feature of many diseases.

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**If the depression of plasma 25(OH)D is a general response to inflammation, what are the consequences for vitamin D status in children?**

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A final point to consider is that, if the effects on plasma 25(OH)D are a general response to inflammation, what are the consequences for vitamin D status in children? The acute depression in plasma 25(OH)D did not appear to affect concentrations of PTH in the adults, but would this be the same in the growing child? The continued depression in plasma 25(OH)D concentrations in the Scottish study is also a point of concern. It is important to determine if the depression was due to mobility and environmental factors directly influencing the patients or to something more insidious associated with the inflammation. These points cannot be answered without further studies.

**Harmful effects of low plasma 25(OH)D concentrations**

Although I have argued that the fall in plasma 25(OH)D concentrations associated with acute inflammation may be a physiological response by the body to increase “free” plasma 1,25(OH)\(_2\)D and benefit or modulate immune function, it is possible that the concentration of 25(OH)D may be too low at the outset to produce any benefit from the response. Plasma 25(OH)D concentrations in critically ill patients admitted to an intensive care unit in Sydney, Australia were found to be inversely correlated with their disease severity as assessed by the Simplified Acute Physiology Score (SAPS; high scores indicating severe organ dysfunction). Plasma 25(OH)D and age were the only two independent predictors of SAPS (\(\beta=0.59, P<0.001; \beta=0.33, P<0.02\) resp). In 42 of the patients on admission, mean (SD) 25(OH)D concentrations...
were 41 (22) nmol/L with 38% <30 nmol/L and another 17% <15 nmol/L. Limited exposure to sunlight during chronic illness prior to admission was probably an important factor explaining the low 25(OH)D concentrations. The authors commented that vitamin D deficient or insufficient states may worsen metabolic and immune functions leading to worse outcomes.  

Again, parallels between plasma retinol and 25(OH)D concentrations can be drawn. In places where plasma retinol concentrations are low, such as places in Africa and Asia, severe disease can produce dangerously low plasma retinol concentrations. For example, in a study by Mitra and colleagues in Bangladesh, children admitted with Shigella dysentery had a mean (SD) retinol of 0.36 (0.22) μmol/L.  In similar situations, severe meases was frequently associated with blindness — to such an extent that measles was believed to be the cause of the blindness. Severe meases is, however, associated with very low plasma retinol concentrations  and it is more likely that the low retinol concentrations were the important etiological factor responsible for the blindness. Several groups of workers in Africa showed that giving vitamin A to children on admission considerably reduced the severity of the meases illness. Unfortunately, no apparent benefits were obtained after giving vitamin D, with or without calcium, on admission to the intensive care unit or on the survival of patients with congestive heart failure who were given vitamin D for 9 months. (Table 3)  

Conclusions
This is obviously an area where more research is needed. Two surgical studies reported a large fall in the concentration of plasma 25(OH)D in patients who underwent orthopedic or prosthetic surgery but had no underlying disease.  Although the changes were part of the acute phase response, there were no obvious advantages for the patients. However, in neither study did the authors measure the concentrations of the metabolically-active, “free” 1,25(OH)₂D. The more recent study did measure concentrations of both the vitamin D binding protein and “free” 25(OH)D and these also significantly fell for reasons which were not apparent.
It seems probable that the fall in 25(OH)D concentrations seen in the two surgical studies is a general response to inflammation. There is evidence in the literature that vitamin D plays an important role in innate immunity and it is possible that an acute fall in 25(OH)D concentrations following surgery may be associated with the up-regulation of immune cells throughout the body by the inflammatory response. The physiological advantage of the fall in 25(OH)D concentration may be a more “alert” innate immunity. The failure to restore 25(OH)D levels in the Scottish study may indicate the inadequacy of solar radiation and a need for vitamin D supplementation in the convalescent period. The failure by workers to demonstrate any benefits from vitamin D and/or calcium supplements given to intensive care patients prior to admission, or to patients with congestive heart disease, cannot currently be explained but may indicate that vitamin D is primarily needed for disease prevention and not repair.

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Research in vitamin D has increased dramatically, mainly due to the discovery that vitamin D is important not just for bone health, but also for a range of body functions, and in terms of the risk of chronic and infectious diseases. While some of the research is basic science, much is based on observational epidemiology, linking low serum concentrations of 25-hydroxyvitamin D (25(OH)D) to various diseases. Since the validity of most markers of micronutrient status is affected by an acute phase response, the review of the validity of 25(OH)D by Dr. Thurnham in this issue is timely.

The main source of vitamin D is sunlight, yet deficiency seems to be a problem in Asia and Africa, and even in equatorial countries. The burden of infectious diseases is high in low income populations, even among apparently healthy individuals. If, indeed, an acute phase response reduces 25(OH)D independent of vitamin D status, this will lead to an overestimation of the prevalence of deficiency, and probably confound the estimates of association between 25(OH)D and the various outcomes.

Vitamin D and tuberculosis
An area of research that illustrates the implications of poor validity of 25(OH)D in the presence of an acute phase response is the role of vitamin D for the risk of pulmonary tuberculosis (TB). It is biologically plausible that vitamin D – given its importance for the immune system – is a determinant of TB. However, most research has been based on case-control studies, in which 25(OH)D is determined, as a measure of vitamin D status, in new cases with TB and in controls. Since TB patients have a huge acute phase response, any negative effect on 25(OH)D will, hence, either lead to overestimation of a true or create a false negative association.

Not surprisingly, a review of seven studies found that low 25(OH)D was associated with the risk of TB. The authors rightly conclude that there is a need for prospective studies, but argue that, given the evidence for the role of vitamin D in immunity, the association is likely to be due to an effect of vitamin D deficiency on risk of TB. But what is the evidence for the opposite? Well, other protein-bound vitamins are affected during the acute phase response, since most proteins behave as negative acute phase proteins. And, as Dr. Thurnham points out, not only the recent paper by Reid but also an older study suggest that the acute phase response affects the validity of 25(OH)D as a vitamin D marker. However, several other studies failed to demonstrate such an effect. Yet the absence of evidence is not evidence of absence, and the issue should have been much better researched.

So, what is the way forward? Intervention trials are important but expensive, and research funding is scarce. Thus, observational studies are needed to justify and prioritize trials, and to guide the design. There is a need for a better understanding of vitamin D metabolism, better markers of vitamin D status, and ways to adjust for the acute phase response, as has been suggested for other nutrients. Finally, when vitamin D trials are conducted, this provides an opportunity to study the effects on various metabolites that should not be missed.

Correspondence: Henrik Friis, Department of Human Nutrition, University of Copenhagen, Rolighedsvej 30, 1958 Frederiksberg C, Denmark E-mail: hfr@life.ku.dk

References


Opinion 2: The D-Cline may be Due to Drug-SXR Interaction

Michael F Holick
Department of Medicine, Section of Endocrinology, Nutrition, and Diabetes, Vitamin D, Skin and Bone Research Laboratory, Boston University Medical Center, Boston, MA, USA

The dramatic 40% decline in serum 25-hydroxy-vitamin D (25(OH)D) levels recently reported by Reid et al1 within 24 hours of elective joint replacement surgery has important short- and long-term consequences, especially during post-operative healing after surgery. It has been suggested that this 40% decline is, in part, due to the uptake of 25(OH)D by the inflammatory cells. It has been known for more than 100 years that vitamin D deficiency was associated with increased risk for upper respiratory tract infections, and that sun exposure was effective in helping to treat patients with tuberculosis.2

The connection between vitamin D and the immune system is nicely documented by Dr Thurnham. Activated macrophages after ingesting an infective agent like a tuberculous bacterium immediately begin preparation for its destruction by increasing transcriptional activity to produce 1,25-dihydroxy-vitamin D (1,25(OH)₂D), and to enhance its responsiveness to this hormone by increasing the number of vitamin D receptors (VDR).3 Once 1,25(OH)₂D is bound to the VDR and retinoic acid X receptor, this complex interacts with the gene that produces the defensen protein, cathelicidin, which in turn binds to the tubercle, resulting in its demise. Therefore, one explanation for the observation of the marked decrease in circulating levels of 25(OH)D can be attributable to this mechanism.

“Another mechanism could also have a dramatic influence on vitamin D status during and after surgical intervention”

The role of steroid and xenobiotic receptor (SXR)

However, what is not appreciated is another mechanism that could also have a dramatic influence on vitamin D status during and after surgical intervention. The steroid and xenobiotic receptor (SXR) is responsible for destroying foreign substances that enter the body. It accomplishes this by increasing the expression of cytochrome P450 enzymes such as CYP 3A4 and CYP 2C8. It is believed that the association of taking a wide
variety of medications, including antiseizure medications, glucocorticoids and some antibiotics, such as rifampicin, with increased risk for developing vitamin D deficiency osteomalacia is due to enhancing the destruction of 25(OH)D and 1,25(OH)₂D. These drugs activate SXR, which enhances the expression of the CYP3A4 enzyme in the liver and small intestine that hydroxylates both 25(OH)D and 1,25(OH)₂D on carbons 23 and 24, leading to the formation of water soluble inactive metabolites.¹

Thus, another explanation for the observation that is often overlooked is that the variety of medications that these patients received prior to, during and after surgery may have activated the SXR-CYP3A4 pathway, causing increased catabolism of 25(OH)D which, in turn, resulted in the dramatic decrease in the serum 25(OH)D levels that persisted for several months after the surgery. The message is clear; the serum 25(OH)D is a true reflection of vitamin D status. These patients should receive vitamin D before any surgical intervention and should then be maintained on an adequate amount of vitamin D for at least three months after surgery. You can treat vitamin D deficiency with 50,000 IU of vitamin D₂ or vitamin D₃ (the equivalent to taking 6,000 IU of vitamin D a day). To prevent the recurrence of vitamin D deficiency, patients can receive 50,000 IU of vitamin D₂ or vitamin D₃ once every two weeks (the equivalent to taking 3,000 IU of vitamin D a day). This is an effective method for treating and preventing vitamin D deficiency under most circumstances.⁵

Correspondence: Michael F. Holick, Boston University School of Medicine, 85 East Newton Street, M-1013, Boston MA 02118, USA. E-mail: mholick@bu.edu

Sources of support
This work was supported in part by the UV Foundation.

References

Erratum: Diversification from Agriculture to Nutritionally and Environmentally Promotive Horticulture in a Dry-Land Area

In the article Diversification from Agriculture to Nutritionally and Environmentally Promotive Horticulture in a Dry-Land Area in Sight and Life Magazine 25 (1) | 2011, the technical support of N Venaktesham was not acknowledged. We would like to take this opportunity to acknowledge Mr Venaktesham’s technical support with this project, and apologize for any confusion this error may have caused.
Systematic Data Analysis in Qualitative Health Research: Building Credible and Clear Findings

Stephen Kodish, Joel Gittelsohn
Johns Hopkins Bloomberg School of Public Health, Department of International Health, Social & Behavioral Interventions Program & Center for Human Nutrition, Baltimore, MD, USA

Overview
Textual data sets can be intimidating to public health researchers and practitioners who are unfamiliar with qualitative research. The amount of textual data collected from in-depth interviews (IDI), focus group discussions (FGD), and direct observations – three common methods in qualitative research – can be extensive and can prove challenging to systematically analyze.

This article outlines one primary approach to qualitative data analysis (QDA) in health research and discusses the analysis process and interpretation, leading to the development of a credible product. It also briefly describes how computer software can assist in both the analysis and display of findings through data graphs, tables, and conceptual models.

A dynamic aspect of qualitative inquiry is the variety of approaches that one can take. The disparate approaches include, but are not limited to, phenomenology, ethnography, or grounded theory, each of which might utilize a different analytic approach to data. Although there is no one-size-fits-all approach to data analysis in qualitative health research, commonalities across methodological approaches do exist and can be represented by an illustrative schemata (Figure 1) developed by Creswell.

Analysis starts at the bottom of the figure (i.e., during data collection) and proceeds upward through various stages until a written account is developed that presents the findings. The spiral image highlights the non-linear, iterative nature of QDA and offers both procedures and examples throughout each stage of the process, from initial data management to representation of findings. The remainder of this paper will highlight the three procedural stages at the top of Creswell’s spiral: “Reading, Memoing”, “Describing, Classifying, Interpreting”, and “Representing, Visualizing”.

Reading, memoing
An important analytic strategy in QDA is memo writing, or “memoing”, which assists a researcher in making a conceptual bridge from raw textual data to abstractions used to explain the phenomena of interest. It is the process of writing down thoughts and questions in relation to the text in which the researcher is immersed. Writing memos is often an intermediate step between data collection and coding and, as Charmaz explains, the process of memoing helps to, “catch your thoughts, capture the comparisons and connections you make, and crystallize questions and directions you want to pursue.”

Describing, classifying, interpreting
After textual data have been collected, read, and reviewed, a researcher may begin coding the data in order to reduce them into meaningful segments for interpretation. Any kind of textual data can be coded, including memos, field notes, or direct observation notes. This article focuses on in-depth interview and focus group discussion data due to their popularity as methods in the field. Coding is a process of identifying themes – that is, analytic categories – in text and is one of the key elements in QDA. Codes, identifiers of themes in the coding process, are the building blocks for theory or model building and the foundation on which project findings most often rest. One might develop 100 codes for a data set or perhaps just 10. For ease of interpretation and clarity, however, Creswell recommends utilizing no more than 25–30 categories of information regardless of the size of the database. Coding can be inductive or deductive.

Inductive coding
An inductive coding approach is commonly utilized in an early, exploratory stage of a research project, when the researcher has
not formulated hypotheses, and is based on few (if any) preconceived notions of the final results. Plans for additional data collection are frequently the outcome of early coding with this exploratory approach.

Consider, for instance, a qualitative acceptability study of a specialized food commodity, such as a lipid-based nutrient supplement (LNS), perhaps Nutributter™ (Nutriset SAS, Malaunay, France). LNS containing energy, protein, essential fatty acids, and micronutrients have been developed to overcome nutrient shortfalls in existing diets of young children 6–24 months. Although Nutributter™ has been accepted by target populations in some settings, a researcher examining acceptability in a new setting using a qualitative approach might analyze initial qualitative data using open coding; that is, he or she explores the textual data line-by-line for conceptualization of “emergent” themes related to beneficiary perceptions of the unfamiliar commodity. Themes from the data might emerge that are unexpected to the researcher, for example, unique cultural characteristics that directly relate to acceptability. In such a scenario, analysis using inductive coding would be concurrent with data collection to shape future stages of the research project. New questions could be asked or additional methods added based on those emergent themes.

**Deductive coding**

Deductive coding is oriented towards confirming or testing the investigator’s preconceived terms and relationships. It is often based on a researcher’s *a priori* (a Latin term that refers to prior knowledge about a population) hypotheses and might utilize “prefigured” codes derived from a theoretical model or existing literature on the topic of interest. Using pre-determined codes is popular in the health sciences – a field that utilizes many models to explain health-seeking behavior.

As an example, consider the Theory of Planned Behavior (TPB) (Figure 2), which seeks to explain why people perform certain actions – for example adhering to daily consumption of Nutributter™. A researcher deductively analyzing a textual data set would apply codes based on the TPB in relation to the major constructs of the theory: perceived behavioral control (PBC),
attitude (ATT), subjective norm (SN), and intention (INT). While examining texts, he or she would specifically look for themes in relation to those constructs and, perhaps, ignore other topics unrelated to the theory. Creswell suggests, however, that researchers who employ this approach to analysis be open to additional codes emerging during the analytic process, because using this type of coding scheme may limit the analysis to the “prefigured” codes rather than open up the codes to reflect the views of participants from an emic perspective and, consequently, may limit findings.

Using a codebook

In both deductive and inductive coding, researchers usually develop a codebook to assist with the process. The standardized structure of a codebook provides a stable frame for the analysis of textual data and can help to establish more stability and guidance when coding. Put simply, a codebook is a reference tool that tells a researcher when to apply what code to a chunk of text in a transcript. Both the codes themselves and their respective definitional parameters should be included in a codebook. (Table 1) In general, during inductive analysis a researcher develops the codebook as part of the coding process, whereas during deductive analysis the researcher develops the codebook before the textual analysis.

Representing, visualizing

Following memoing and coding, researchers present what was found during analysis, often in the form of a table, matrix, or chart. A visual representation of findings can be helpful for summarizing and highlighting key findings. For example, a simple 2 x 2 table that compares individuals by gender or ethnic group in terms of one of the themes or categories in the study might be useful and informative. In public health research, conceptual

<table>
<thead>
<tr>
<th>Mnemonic or numeric “Brief” Code</th>
<th>Full Description of Code</th>
<th>When to use/not to use the code</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.0 Life in Kakuma</td>
<td>Refugee experiences residing in KRC</td>
<td>Use this family of codes when the CL or MNP beneficiary discusses his or her life as a refugee at KRC.</td>
</tr>
<tr>
<td>2.1 Hardship</td>
<td>Hardships faced while living in Kakuma, related to security, violence, tribalism, etc</td>
<td>Use this code for the array of hardships refugees discuss at KRC unrelated to illness experiences.</td>
</tr>
<tr>
<td>2.2 Illness</td>
<td>Illness experiences of the individual or of his or her family and/or community</td>
<td>Illness is mentioned a lot but use 2.2.</td>
</tr>
<tr>
<td>2.2.1 Ill. Anemia</td>
<td>Experiences with anemia or malnutrition, specifically</td>
<td>Use this umbrella code for any health-related experience related to life in KRC. It can be related to anemia or another illness. Codes 2.2.1 and 2.2.2 will be used to distinguish between the types of illness discussed.</td>
</tr>
</tbody>
</table>

Source: Adapted from one of the authors’ projects

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Provides an organized storage file system, especially large data sets</td>
<td>1. Requires the researcher to learn how to use the software program, which can be very time consuming</td>
</tr>
<tr>
<td>2. Helps a researcher locate textual material quickly</td>
<td>2. Better programs may be cost prohibitive</td>
</tr>
<tr>
<td>3. Creates visually informative schemata to illustrate findings</td>
<td>3. Distances the researcher from the data</td>
</tr>
<tr>
<td>4. Provides time-saving functions (eg, quickly can determine frequencies of codes)</td>
<td>4. Makes analysis as a team challenging due to logistics behind sharing files</td>
</tr>
<tr>
<td>5. Allows for coding of not only text, but also images and video files</td>
<td>5. Nascent compared to quantitative software programs can be frustrating to work with</td>
</tr>
</tbody>
</table>

Content adapted from and the authors’ experiences

Table 2: Advantages and disadvantages of using computer software.
models are commonly used to illustrate relationships between themes, with the purpose of showing how different factors relate to a health-seeking behavior or outcome. Figure 3 is offered as an example. When choosing the most appropriate display of findings, one should consider not only what visual representation most clearly and completely answers the research question(s), but also the audience for whom the graphics are intended.

**Using computer software**

Computer software programs are available to help with the analysis and presentation of textual data. Such programs help a researcher code and retrieve text, create data matrices, and build models of how the themes in a data set are associated with each other. As the process used for textual analysis is the same for hand coding or using a computer, this type of software may be most useful while working with large data sets (eg, more than 500 pages of text) and an unnecessary burden while working with those smaller. Two popular commercial programs available include NVivo (Nvivo (Version 9.0). [Computer Software]. Victoria, AU: QSR International Pty Ltd) and Atlas.ti (Atlas.ti (Version 6.1) [Computer Software]. Berlin: Scientific Software Development), both of which can only be used with Windows-based operating systems.

**Credibility of qualitative research findings**

Computer software can help with coding, but it cannot help ensure high-quality data or findings. Strategies exist to enhance the quality in qualitative research, some during data collection and others during analysis. Creswell points to eight major strategies that can be utilized to help ensure the “trustworthiness” of a study and recommends that at least two be used in any given qualitative study. (Table 3) Member checking, peer debriefing, and investigator triangulation, described in Table 3, are particularly useful tools for enhancing the credibility of qualitative findings.

**Conclusions**

Creswell’s data analysis spiral offers a good representation of the dynamic process that QDA should undergo. It highlights an iterative and systematic approach to data analysis that can help to ensure credible findings. However, just as is the case while analyzing a quantitative data set, one’s findings are only as good as the process used for textual analysis is applied.
as the data that have been collected. Methodological rigor during data collection can help make analysis easier and findings more credible.

Correspondence: Stephen Kodish, MS, Social & Behavioral Interventions Program, Department of International Health, The Johns Hopkins Bloomberg School of Public Health, 615 N. Wolfe St., Baltimore, MD 21205-2130, USA
Email: skodish@jhsph.edu

References

TABLE 3: Qualitative data validation procedures.

<table>
<thead>
<tr>
<th>Validation Procedure</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Prolonged engagement in the field</td>
<td>Building trust with participants, learning the culture, and checking for misinformation that stems from distortions introduced by the research team</td>
</tr>
<tr>
<td>2. Triangulation</td>
<td>Making use of multiple and different sources, methods, investigators, and theories for data corroboration</td>
</tr>
<tr>
<td>3. Peer review</td>
<td>An external check of the research process</td>
</tr>
<tr>
<td>4. Searching for negative cases</td>
<td>Refinement of a working hypothesis by an active search for disconfirming evidence</td>
</tr>
<tr>
<td>5. Clarifying researcher bias</td>
<td>Critically reflecting on what the researcher, him or herself, brings to the research project (eg, past experiences, prejudices, etc)</td>
</tr>
<tr>
<td>6. Member checking</td>
<td>Soliciting participants’ views of the credibility of the findings and interpretations during analysis</td>
</tr>
<tr>
<td>7. Providing a thick description</td>
<td>Enables the reader to determine which characteristics, if any, of a program can be transferred to other settings through a detailed description of participants and setting</td>
</tr>
<tr>
<td>8. External audits</td>
<td>When an external consultant examines both the process and product for accuracy</td>
</tr>
</tbody>
</table>

Source: Adapted from 3
Promoting partnerships and capacity building.
Feike Sijbesma
A Vision of Life

Feike Sijbesma is the CEO and Chairman of the Managing Board of Royal DSM NV. He talks about his work at DSM, as well as his involvement in Sight and Life and in initiatives such as the United Nations World Food Programme (WFP).

Sight and Life magazine (SAL): DSM has been the sponsor of Sight and Life since 2003. What does this relationship mean to DSM?

Feike Sijbesma (FS): It fits completely with DSM’s activities and competences in the nutrition field, but also with our responsibility towards the world, and so with our values.

SAL: DSM entered into a partnership with the WFP in 2007. What is the significance of this?

FS: We wanted to further leverage our knowledge and competences in the nutrition field, even beyond what we have built with Sight and Life. We believe we can contribute to making food healthier, so that people can grow up healthy and develop their full potential without developing diseases and abnormalities. Micronutrient deficiencies, if occurring over a longer period, or during infancy and childhood, can have very harmful effects for an entire lifetime. We can be of help here! This is why we make available to the United Nations World Food Programme our know-how, technologies, expertise, patents, and so on, all to be used by them for free, to the benefit of people who cannot take care of themselves. Besides that, we are involved in developing new products and product concepts which work for the UN programs (such as MixMe™ – micronutrient powder sachets, corn/soy-blends, vitamin-enriched NutriRice™, datebars, and so forth). Our people are actively involved in all of this. And, finally, we also provide monetary help.

SAL: WFP is celebrating the 50th anniversary of its foundation this year, while Sight and Life is celebrating its 25th anniversary, yet the scourge of hunger is growing steadily worse. What can be done to reverse this terrible trend?

FS: I have difficulties with the word “celebrate”. There isn’t much to celebrate here. We need to conclude that we and the UN and several others have already been committed for a long time to addressing this huge problem. Apparently we aren’t there yet! In the last couple of years, the number of people going to bed hungry every evening has been fluctuating. On top of that another circa 2 billion are suffering from so-called hidden hunger (sufficient carbohydrate intake in combination with a shortage of micronutrients). It should be our concern to reduce that number significantly. DSM’s help has already seen millions of people get a better diet. If more people from the private sector were to become involved, with a good deal of help from the public sector, we could improve the situation. Food security remains an important topic and we are absolutely not yet done with this.

SAL: You have said of DSM that “We cannot be successful, nor can we call ourselves successful, in a society that fails.” How have DSM employees responded to this statement?

FS: We live in a global village, so to speak. And as in your own family: if your direct surroundings aren’t OK, you can’t be OK. The world is no different! All the people in DSM are fully behind the collaboration with the WFP. When the 2008 crisis occurred and we needed to make cost savings, many employees of DSM agreed not to cut any costs on the WFP … and we did not. We cannot let down people who are hungry. We are continuing our efforts. For example, around 25 DSM volunteers a year – including myself, in Bangladesh and Ethiopia – go into the field, get the experience for themselves and return and tell stories internally. Many thousands of DSM people are completely energized by the work we do here.

SAL: You have traveled extensively in connection with DSM’s partnership with the WFP. What are your most memorable impressions?

FS: In both Bangladesh and Ethiopia, I was overwhelmed by the poverty and the food need. What I found very hopeful was visiting the school feeding programs. At school they are learning something, which is very important because they can then develop their country better than their parents were able to. In Ethiopia, I saw the Food for Work program, whereby farmers get
“We live in a global village, so to speak. And as in your own family: if your direct surroundings aren’t OK, you can’t be OK.”

Felke Sijbesma, the CEO and Chairman of the Managing Board of Royal DSM NV.
three years’ free food if they develop the land in the right way and so have better farm yields thereafter! That’s great.

SAL: In 2010 you received the Humanitarian Award of the United Nations Association of New York. What did it mean to you?

FS: I see this award as being given to everyone in DSM and as recognition for the effort we all make. Every DSM employee is helping to change the lives of 200 other people via our partnership with WFP. DSM is a big company but, in the relative setting of the world, we are small – so this shows what companies can do.

SAL: DSM recently launched a new brand with the strap-line Bright Science. Brighter Living™. Why did the company decide to rebrand itself this year, and what does this strap-line mean?

FS: Over the last 10 to 20 years, we have been transforming our company from a bespoke chemical company into a Life Sciences and Materials Sciences company. This is DSM’s second big transformation – the first one, of course, was from being a coal-mining to a chemicals company. Our divestment process is finished, and now we wish to grow the company. We are a company that is based on science and technology. We have Bright Science, making products to make the quality of life better in this world: a brighter living! I think the new strap-line really catches what the company does and stands for.

SAL: Sight and Life also rebranded itself this year. What is the significance of this new style of presentation?

FS: Sight and Life started by providing vitamin A to ward off malnutrition-related blindness to the displaced populations affected by the Ethiopian Civil War in the mid-1980s. Over the years, it has broadened its perspective to cover all kinds of health and nutrition issues. This new style reflects that broadening. It positions itself as being a little bit more modern, but with a scientific basis that is still very strong. It reflects the impact it makes on people’s Brighter Living.

SAL: Besides your responsibilities towards DSM and your support for the DSM-WFP partnership, you are a member of various other influential bodies. How do you cope with the stress that must be associated with so much responsibility?

FS: Sometimes there’s a bit of pressure, but it’s also a gift. Nothing is nicer than working for a company, doing business, providing shareholder value, making a profit and, at the same time, taking care that the company, business and all the employees have a higher purpose in life and contribute to the well-being of the people of this planet and of the planet itself. I think that we make important contributions here, which is great.

SAL: What do you enjoy most about your work?

FS: I’m running a business, a company: and I like doing business very much, but at the same time I’m doing something broader in life, which is a combination I enjoy very much. It’s not only about growing the profits and share price. We perhaps did not inherit this planet in an excellent state from our parents, I agree: we (though not all) live well, but at the same time have the responsibility to improve it in such a way that our children can continue to build on it, too. It’s a kind of stewardship, which I really enjoy.

SAL: What are your interests outside work?

FS: I am a (not so good) golf player, but while the children are young, I am devoting all my time to my wife, my children and my family. I do some exercise at least three times a week to keep myself fit.

SAL: Do you have a hero, or someone who you specially admire?

FS: There are several people whom I admire for several aspects: journalists, governmental leaders and business leaders. But no one in particular is “my hero”. A book that caught my attention recently was something by Parag Khanna, a young US-Indian management guru. He wrote a book entitled How to Run the World, in which he comes to the conclusion that the world’s problems are so complicated that they can only be solved by governments, businesses and NGOs working together. What we do in the framework of the World Economic Forum in Davos, and in the UN with WFP, fits fully into that. I support this philosophy.

SAL: Is there anything else that you would like our readers to know?

FS: Sight and Life and WFP would not have been possible without the support of our shareholders, customers, scientists, university collaborators, NGOs, and all our employees in DSM who give much in this respect and, of course, to the benefit of society at large. I would like to thank everyone who contributes to that.

Interview by Jonathan Steffen
Sharing knowledge for improved nutrition.
The 2011 Carotenoids Research Interaction Group (CARIG) Conference was held as part of Experimental Biology in the Washington Convention Center, Washington, DC, on 8 April 2011. The meeting was chaired by Sherry Tanumihardjo and co-chaired by Mario Ferruzzi, with some 70 professionals and students in attendance. The central theme of this year’s conference was Carotenoids in Human Nutrition, focusing on diverse, recent research involving human subjects.

A pioneer in the field
As has been the custom since 2002, the conference began with the James Allen Olson Memorial Perspectives on Carotenoids Lecture, this year delivered by Dr Harold Furr on the topic “Isotope dilution assessment of vitamin A status.” This was a field that he pioneered with James Olson, elaborating the first comprehensive methodology and mathematical calculation for determining the total body vitamin A pool using isotopic tracers of the vitamin A. This was also a precursor to the introduction of isotope-labeled carotenoids into human experimentation. The entire lecture is presented as a feature article elsewhere in this issue of *Sight and Life* (see pp 24 – 31).

The remainder of the program picked up on the theme of human surveillance, experimentation or both. Georg Lietz, of Newcastle University in the UK, spoke on the topic of “Physiological consequences of single nucleotide polymorphisms in the β-carotene 15,15’-monooxygenase gene.” The next two presentations came from researchers at the University of Wisconsin at Madison. First, Julie Mares spoke on “Lutein and eye health” and pondered whether factors affecting uptake of the intact xanthophylls from the intestine could explain the inconsistency in the epidemiological data. This was followed by a presentation from Sara Arscott, a collaborator with Phillip Simon and Sherry Tanumihardjo at Wisconsin, who presented “Colorful carrots: Basic nutrition and functions food.” The final presentation on the program was given by Shellen Goltz of Purdue University on the topic: “Meal triacylglycerol profiles modulates carotenoid postprandial absorption in humans.”

The CARIG-VARIG Reception
At the end of the day, interested students and professionals gathered in the Renaissance Hotel for the traditional Carotenoids Research Interaction Group – Vitamin A Research Interaction Group (CARIG-VARIG) Reception. Graduate students with free papers on carotenoid and retinoid research programmed at Experimental Biology 2011 displayed posters to be judged in the annual contest.

This year, the outstanding poster prizes were awarded to four posters. These included: 1. “A daily dosing regimen of α-retinol supports growth in rats despite its inability to bind to retinol-binding protein” by Napaporn Riangroy of the University of Wisconsin, whose advisor is Sherry Tanumihardjo; 2. “Some
α-apocarotenoids function as antagonists of retinoic acid receptors by directly competing at the ligand site” by Abdulkarim Eroglu of the Ohio State University, with Earl Harrison as his mentor; 3. “Laboratory-scale production of tomato carotenoids using bioengineered *Escherichia coli*” by Chi-Hua (Peter) Lu; and 4. “CMO-II KO mice display altered lipid metabolism compared to CMO-I KO and wild-type mice” by Amy Eisen, both of the University of Illinois and the laboratory of John Erdman.

Next year’s CARIG-related events will be held in San Diego, California at Experimental Biology 2012
Iron deficiency and control: A call to action and consensus

KB Harding

Following the publication of results from the Pemba trial, which showed an increased risk of hospitalization and mortality after iron supplementation among iron-replete children in a malaria-endemic setting, the World Health Organization (WHO) recommended that iron supplementation for young children living in malaria-endemic areas be targeted to only those who are iron-deficient and/or occur in the presence of effective mechanisms to control malaria and other infectious disease. There has since been much debate in the nutrition research community over how best to address iron deficiency (ID) and anemia in this context. Some question the feasibility of screening for ID in resource-poor areas which hold the majority of the ID and malaria burdens.

“Millions of children in malaria-endemic areas are at risk of anemia, iron deficiency and their consequences”
Five years have passed since the initial WHO response to the Pemba trial and, although there are some advances in the understanding of the biology, much debate and little agreement exists among nutrition experts on the way forward. Meanwhile, millions of children in malaria-endemic areas are at risk of anemia, ID and their consequences, and program developers and policy makers are left with little guidance on how to address these problems in their countries. The scientific community plays a critical role in developing policy guidance, and country program developers look to this group to provide advice that is practical, feasible and based on the best available evidence, even when that evidence is not yet perfect. The incomplete understanding of risks and benefits of iron supplementation in malarial areas presents a great challenge to this community.

Researchers as well as agencies such as the Micronutrient Initiative have increasingly received requests for country guidance on iron programming in malaria-affected areas. On a relatively small scale, iron programs using micronutrient powders or lipid-based nutrient supplements are being implemented, for example in Kenya. WHO recommended the same precautions be taken with these home fortification products as with iron supplements because, although the former approach may be safer due to the food base, safety had not been demonstrated.

Although forums on this important issue have been organized at recent international meetings, few have addressed programmatically relevant issues that can assist policy makers to make decisions that maximize the potential benefits and minimize the potential harm of programs that provide young children with iron. A recent symposium at the American Society for Nutrition annual meeting had the objective of exploring options for addressing infant and young child ID and anemia in malaria endemic areas, now, with safe, effective and feasible interventions. This article presents an overview of the proceedings.

The global malaria situation: implications for iron deficiency control strategies

PE Duffy

Malaria transmission levels range from low, or hypoendemic, to very high, or holoendemic (Table 1). The absolute rate of severe malaria is quite stable over a wide range of transmission intensities, i.e. lower transmission rates do not necessarily mean lower rates of progressing to severe disease or death. Although major progress has been made in reducing the disease burden worldwide, malaria remains a major cause of death and claimed an estimated 780,000 lives in 2009. The majority of malarial deaths, approximately 90%, occur in Africa. Populations affected by malaria are also likely affected by anemia and ID, both because malaria is a major cause of anemia and because all these conditions share many underlying and basic causes. It is therefore not surprising that the region with the highest prevalence of anemia among children is Africa, where approximately two-thirds of preschool-age children are anemic.

“The region with the highest prevalence of anemia among children is Africa”

There is evidence to suggest that ID may protect against malaria and death, and that provision of iron may lead to increased risk of malaria and death. In general, however, studies that show no increased risk of malaria with iron supplementation have occurred in the context of intense malaria surveillance and treatment. With regard to the relationship between iron, ID and malaria, there are three important points to consider: 1) iron (status or supplementary iron consumption) may exacerbate malaria, for example by enhancing parasite growth in the liver; 2) both ID and malaria are causes of anemia, making disentangling causal pathways extremely difficult; and 3) there are several other amendable factors that can modify the potential effect of iron status or supplementation on malaria risk, including immune status, malaria surveillance and control, and malaria transmission intensity.

Targeted provision of iron: the evolution of a practical screening option

CC Crowley

Targeting may present the safest option for iron delivery, but there are many theoretical and practical issues to be resolved before effective screening prior to provision of iron can be rolled out in the field. Key theoretical considerations include the selection of indicators (for anemia, iron status or both) and the inherent tradeoffs (eg sensitivity and specificity of the indicators). Ideally, screening should include both iron and anemia status; given the evidence of increased risk of harm, specificity (i.e. correctly identifying and excluding those who are not anemic, not
Iron-deficient or both) should be prioritized in malarial areas. Practical limitations include the application of screening tests in the field in resource-poor settings, and the inherent invasiveness of blood tests.

Experience in Guatemala with four applications of three non-invasive (eg body-surface probe photometry or spectrometry) devices from two manufactures to measure hemoglobin levels has been informative. The major advantage of all these approaches is that they do not require the extraction of even capillary blood samples, improving the chances of universal acceptability in field settings and eliminating the risks of drawing blood. Of the four applications illustrated in Figure 1, three required cumbersome finger-clip sensors, and none of these achieved the requisite diagnostic accuracy. Only the Haemospect® (MBR Optical Systems, Germany), as applied directly to the skin with a pen-like probe, showed a promising sensitivity and specificity profile, although sensitivity was compromised at lower cut-off points for anemia.

Improvements to current non-invasive methods should include: 1) the improvement of diagnostic discrimination at lower cut-off points (particularly important for children and pregnant women); 2) the development of more robust and field-friendly devices; and 3) the adaptation of applications to and testing in children under three years of age, ie those most susceptible to severe malaria. Currently, non-invasive instruments to assess iron status are not available, although efforts are under way to develop this technology using zinc protoporphyrin as an indicator.

Universal iron provision through home fortification of complementary foods

KG Dewey

Since the Pemba trial, a more comprehensive approach to improving nutrition in infants and young children has been recommended as a programmatic priority, for example focusing efforts on improved complementary feeding as a whole, instead of iron supplementation alone. Typical complementary foods in vulnerable populations, however, are low in many micronutrients, including iron. A number of options to improve iron content and bioavailability of complementary foods have been explored. These include home fortification products (eg micronutrient powders or lipid-based nutrient supplements), fortified complementary foods, and traditional food processing techniques to enhance iron absorption.
“Part of the complexity of estimating the risk associated with the provision of iron through different products is our lack of understanding of the mechanisms underlying adverse effects.”

Part of the complexity of estimating the risk associated with the provision of iron through different products is our lack of understanding of the mechanisms underlying adverse effects. There are currently two dominant hypotheses. The first is that a large bolus of iron triggers a spike in plasma non-transferrin-bound iron (NTBI). NTBI may induce cell damage via reactive oxygen radicals, and the entry of NTBI into the liver may also facilitate the penetration of hepatocytes by malaria sporozoites. A second hypothesis is that iron stimulates the growth of enteric pathogenic organisms, which may impair the innate immune response of the gastrointestinal tract and lead to bacterial invasion through the gut into the systemic circulation, causing bacteremia and septicemia. Iron may influence morbidity by either, both, or perhaps neither of these routes.

Home fortification may be the most promising alternative to supplementation for the universal provision of iron. It is likely to be safer than supplements given with food, and adequate amounts of iron can be provided, regardless of the amount of complementary foods consumed. A review of findings, for the purpose of this symposium, from five home fortification studies in malarial areas (some not yet published) showed no increased risk of adverse effects. Most of these studies, however, had relatively small sample sizes, so adverse events cannot be adequately assessed. There is also a lack of information on the potential modifying effect of initial iron status on treatment effects. Although the evidence to date suggests home fortification with iron in malarial areas is safe, more research is needed.

However, it is very challenging, if not impossible, to obtain conclusive evidence on the safety of home fortification in malaria endemic areas. Adverse events associated with iron consumption are likely only to be seen where infectious disease control is lacking, yet it would be unethical in this type of setting to conduct studies without providing any services to monitor and treat infectious disease, including malaria. A huge sample size would be required to rule out a modest increase in severe adverse effects. For the moment, the safest option is to deliver home fortificants within the context of comprehensive malaria control strategies.

Research gaps
AM Prentice

The review of the literature related to malaria, screening for ID and anemia and the potential of home fortification and other alternatives for universal delivery of iron to children, for the purpose of the symposium, has highlighted a number of important research gaps. Some promising developments in field-level screening have been demonstrated, particularly for the non-invasive assessment of hemoglobin concentration, but these are still not diagnostically specific for ID. Alternative indicators of ID and anemia have not been explored. For example, hepcidin, the principal regulator of iron homeostasis, could be assessed to indicate need for additional iron; this would require creative and innovative research and development.

The biggest challenge relates to our lack of a clear understanding of the role of iron and ID in infection. Such interactions have been reported in the literature for decades and some have hypothesized that ID is a phenotypic adaptation to reduce risks among those chronically exposed to infectious disease. At this time, we do not have real evidence to support the hypotheses of the mechanisms underlying iron-malaria interactions. To fully understand the complex relationship between iron status and malaria, we should carefully review the malaria parasite lifecycle and how interactions with iron may vary by developmental stage; we must also carefully review all results from the Pemba and other trials, exploring tendencies across the duration of the intervention and the implications that these may have for the underlying mechanism(s) of effect.

Some new research may also stimulate further discussions related to mechanisms. For example, results from a recent PhD thesis found an increased risk of malaria infection in iron-deficient children consuming a multi-micronutrient supplement with no increased risk among those iron-replete at baseline. Findings from this study cannot be compared directly with the Pemba results because of different interventions and indicators of iron status. This does, however, highlight that multiple contextual factors may influence the associations between micronutrient interventions and adverse outcomes and the risks of altering policy based on single study findings.
The trials addressing the safety of home fortification reviewed in this symposium are somewhat reassuring, but they were not powered to detect group differences in rare adverse events. The types of studies that would provide definitive answers about safety can no longer be conducted for obvious ethical reasons. Particular attention should be paid to the careful and thoughtful design of research and programs in this context, where access to healthcare is also limited. (Figure 2)

Further research is needed to elucidate the mechanisms behind the interactions between iron status, supplementary iron and morbidity, and is vital to advance our thinking about safe and effective programs. Following the revised WHO recommendation, the US National Institutes of Health, with funding from the Bill and Melinda Gates Foundation, promoted research to explore the mechanisms responsible for the adverse impact of iron supplementation. They have formed a technical working group and have funded a number of research projects relevant to this challenge.

BOX 1: Programmatic strategies for addressing iron deficiency and anemia among infants and young children in malaria-endemic areas.

- Adopt a lifecycle, preventative approach to policy and program design that avoids provision of relatively high doses of oral iron to infants and young children
- Target iron interventions to those who are most iron-deficient and likely to benefit (targeting can occur at the individual and/or group level)
- Coordinate closely with malaria control programs

Programmatic strategies

Policy makers often operate with incomplete information, incomplete research and competing priorities and timelines.27 We know that providing iron supplements to some children under some circumstances can increase the risk of severe morbidity, but keeping children iron-deficient as an intervention to decrease malaria risk is unacceptable. The adverse effects of ID for long-term child development are well known.28

“Viable alternatives exist to address ID and three programmatic strategies to identify them should be adopted”

We know little about the biological mechanisms underlying the relationship between iron and malaria, and about which children under what circumstances are most at risk. Despite this uncertainty, viable alternatives exist to address ID and three programmatic strategies to identify them should be adopted. (Box 1)

First, programs should adopt a lifecycle, preventative approach; ID and its consequences begin before infants reach six months of age. Ensuring adequate maternal iron status before and during pregnancy and delayed umbilical cord clamping can promote adequate reserves for this period. Home fortification and other alternatives to traditional iron supplements can avoid exposing children, as of six months of age, to relatively high doses of oral iron. Second, interventions should be targeted to those children who are most iron-deficient and, therefore, most likely to benefit. Although individual indicators of iron status require further development, multiple level targeting (group and/or individual) could be developed. Finally, nutrition programs should coordinate closely with malaria control programs. This could also be considered a form of targeting, to children least likely to suffer adverse effects, and interventions do exist with unprecedented coverage and success.

Stopping all iron interventions in malaria-endemic areas is a policy option, but would leave many children at risk of the adverse effects of deficiency in those regions. Thoughtful and creative applied research to resolve mechanistic and operational programmatic issues must continue hand in hand with moving forward with programmatic strategies. Finally, in the face of uncertainties, deliberations with local stakeholders are essential and will yield a variety of reasonable options for moving forward.
Acknowledgements: Support for the symposium was provided by the American Society for Nutrition and the US Army Military Infectious Disease Research Program. The authors are grateful to Dr Noel Solomons for comments on the draft paper.

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Thika is a low-income, urban town located approximately 40 miles northeast of Nairobi, Kenya. Nearly 50% of households in Thika District are impoverished and HIV/AIDS affects nearly 34% of the population. As a result of infectious disease, undernutrition and poverty, it includes a large orphan population.

Macheo Children’s Centre recognizes the disproportionate burden of disease and poverty in Thika and seeks to meet the needs of its community. Founded in 2005, Macheo is a non-governmental organization whose vision is to “provide the children of today with a brighter future.” It runs several child-centered projects, with core activities centered around a children’s home and an education program.

“Macheo Children’s Centre recognizes the disproportionate burden of disease and poverty in Thika and seeks to meet the needs of its community.”

Activities and outreach
Currently, Macheo operates a children’s home for 56 orphan children where they are provided with regular meals, access to education, and housing. At the children’s home, Macheo is active with infrastructure development. The children have recently transitioned into family-style housing where there is a mix of gender and ages. The office space and number of staff is expanding, and security is being improved.

In 2006, Macheo launched an education program in public primary schools in Thika. Its primary objective is that all children in this impoverished region obtain at least a basic level
The porridge provided by Thika school is a valuable source of nutrition for pupils.
of education by 2015, in line with the second Millennium Development Goal. Macheo sought to meet this objective with a food-based strategy, whereby primary schools are provided with one meal per day. For orphans and the most vulnerable children, the lunchtime meal is supplemented with porridge. The education program now operates in 18 primary schools and feeds over 11,000 students.

Program progress
Macheo continues to cultivate its core programs while fostering new programmatic activities. These include investing resources in income-generating, social business and family empowerment projects in Thika. Macheo will soon be accepting HIV positive children into the children’s home setting. They will be doing a thorough medical history and will work with the district hospital to ensure that the children are getting the necessary care. The nutritional status of the children is also a consideration. During the field visit, anthropometric measurements were used as indicators of their nutritional status. Age, height and weight were used to calculate their BMI-for-age z-score, which were then compared with WHO standards. While many of the children living at Macheo were malnourished upon arrival, only three children at Macheo had a BMI z-scores at or below negative two. As a result of the field visit, Macheo is closely monitoring the weight and individual meal plans of all newly admitted children.

The next steps for Macheo include improved data collection practices and program evaluation. Perhaps most notably, it continues to seek input from its community to identify gaps in social services and health-care and then strives to address those needs. Its strong relationship with the community lends itself to long-term sustainability and success.

Correspondence: Vanessa Oddo, Tufts University School of Medicine, 145 Harrison Avenue Boston, MA 02111, USA
E-mail: vanessa.oddo@tufts.edu

For more information on the Macheo Children’s Centre please contact: Simon Wachieni, Program Manager at Macheo Children’s Centre operations@macheo@gmail.com
Report from Nairobi

Programmatic Qualitative Research: A New Initiative to Build Capacity for Nutrition Programming Within the DSM-WFP Partnership

Stephen Kodish, Joel Gittelsohn
Johns Hopkins Bloomberg School of Public Health, Baltimore, United States

As part of the continuing efforts by Sight and Life to build capacity in nutrition program implementation within the DSM-WFP partnership, a qualitative research workshop for the introduction of specialized food commodities was held in Nairobi, Kenya from 21–25 March 2011. The workshop was implemented in collaboration with Johns Hopkins Bloomberg School of Public Health (JHSPH).

The World Food Programme (WFP) is increasingly using innovative commodities such as micronutrient powders (MNP) and lipid-based nutrient supplements (LNS) to improve the nutritional status of vulnerable groups such as women and children. These products are new to most populations, as well as to WFP staff. Hence, the carefully designed, culturally appropriate introduction of the product to the target population is critical for successful program implementation and to achieve anticipated benefits. Qualitative research knowledge and skills for exploring contextual factors such as traditional medical systems and local health-seeking behaviours of the target population are instrumental in program design and implementation. Most WFP staff have limited knowledge of how to elicit these types of information using qualitative data collection techniques.

Qualitative research theory, methods and analysis

The workshop was supported by Sight and Life and facilitated by Dr Joel Gittelsohn, a professor at JHSPH in the Center for Human Nutrition, and his doctoral advisee Stephen Kodish. The participants comprised WFP international and local nutrition staff from headquarters, country and regional offices in Africa and Asia, as well as UNHCR staff, and Sight and Life staff. The workshop taught participants qualitative research theory, methods, and analysis, both in seminar format and experientially in the field. One day of the workshop was dedicated to data collection in Thika, a poor slum area roughly 50 kilometers outside of Nairobi, to practice some of the skills learned. One participant commented, “The field visit was a very good training on the use of the methodology presented.”

Rapid assessment procedures

A key component of the workshop featured the testing and refinement of a Rapid Assessment Procedures (RAP) manual, which may be utilized in future DSM-WFP nutrition programming to assist with the culturally appropriate introduction of specialized

“Participants gained theoretical and practical skills, including the introduction of qualitative methods in the context of the RAP manual and an emphasis on qualitative data management and interpretive data analysis in nutrition programming”
food commodities. The RAP is a tool that aims to quickly gain sufficient understanding of a cultural setting from the community’s perspective, in order to make key decisions regarding the design and implementation of effective nutrition programming, using a mixed methods approach. Because various data collection methods, such as in-depth interviews, focus group discussions, and direct observations, are critical to systematic, qualitative work using the RAP manual, WFP staff were introduced to these methods and given opportunities to practice both in the classroom and the field. The sentiment after the qualitative training was positive; one participant reflected that the RAP manual was a “very good method that fits well with the work of WFP.”

“...I would really like such workshops to be conducted at least twice annually to better prepare WFP staff to introduce new products...”

Overall, the workshop was a successful capacity-building experience. Participants gained both theoretical and practical skills, including not only an introduction to qualitative methods in the context of the RAP manual, but also an emphasis on qualitative data management and interpretive data analysis in nutrition programming. As one attendee noted, “I would really like such workshops to be conducted at least twice annually to better prepare WFP staff to introduce new products.” Plans are being made to continue with similar workshops on different continents.

Correspondence: Stephen Kodish, MS, Social & Behavioral Interventions Program, Department of International Health, The Johns Hopkins Bloomberg School of Public Health, 615 N. Wolfe St., Baltimore, MD 21205-2130, USA
Email: skodish@jhsph.edu

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The new “Manual on Vitamin A Deficiency Disorders (VADD)” by Sight and Life Press
Growing the evidence base for micronutrients.
Remembering
Michael C Latham
(1928–2011)

William Grimes
The New York Times, 13 April 2011 (abridged)

Professor Michael C Latham, an expert on international nutrition and tropical health who waged a long campaign against the use of infant formula and for the practice of breastfeeding in developing countries, died on 1 April 2011 in Boston at the age of 82.

Michael Latham was born on 6 May 1928, in Kilosa, Tanganyika (now Tanzania). After earning a medical degree from Trinity College, Dublin, in 1952, he worked in hospitals in Britain and the United States before returning to Tanganyika to practice medicine in rural areas. During intermittent leaves, he earned a diploma in tropical public health from the London School of Hygiene and Tropical Medicine in 1958.

After leaving Tanzania in 1964, he taught nutrition at Harvard, where he received a degree in public health in 1965. In 1968 he was recruited by Cornell as a Professor of International Nutrition. He turned the university’s small Program in International Nutrition into one of the world’s largest training centers for nutritionists, many of whom went on to work in international agencies and public health departments around the world. His research led to improved programs on infant nutrition, the control of parasitic diseases in humans, and the supply of micronutrients to poor populations.

Dr Latham often did consulting work in Africa, Asia and South America for organizations such as the World Health Organization, the United Nations Food and Agriculture Organization, UNICEF and the World Bank. He was the author of two important books on international nutrition, Human Nutrition in Tropical Africa (1965) and Human Nutrition in the Developing World (1997), as well as a family memoir, Kilimanjaro Tales: The Saga of a Medical Family in Africa (1995).

Recollections by Bruce Cogill
Former Chief of Nutrition, USAID, Washington DC, USA

When asked to write about Michael Latham’s recent passing, I did not want to recall him as a chronology of significant events that amounts to a life lived. No doubt, he had a singular, impressive life. The obituaries in the New York Times and the Washington Post eloquently covered his life. What we thought would be better is a reflection on the man and his impact on our lives.

My first contact with Michael was in the highlands of Papua New Guinea, in the late 1970s. He, together with the late Professor John Waterlow, took the time to write and help me in my work in nutrition, and to encourage me to pursue nutrition at the graduate level. Michael’s generosity, wisdom, grace and intelligence existed long before that time, and were born of his family and a life that began in Tanganyika.

“One of Michael’s greatest qualities was his ability to listen”

One of Michael’s greatest qualities was his ability to listen. He engaged you when so many would speak at you. He had this quality of being able to empathize and being willing to speak on behalf of those who could not speak. So many prominent people in our work often have forgotten to listen. Their cause dominates as they do. Michael consistently humbled himself to the topic and the audience.

He was not without controversy. Michael was critical of the role of the food and pharmaceutical industry, and was a champion for sensible solutions to malnutrition. His tireless efforts remind me of the words of William Blake in Auguries of Innocence:

“To see a world in a grain of sand,  
And a heaven in a wild flower,  
Hold infinity in the palm of your hand,  
And eternity in an hour.”
“Michael consistently served the international health and nutrition community, often exceeding expectations, for close to six decades”
Michael consistently served the international health and nutrition community, often exceeding expectations, for close to six decades. In his capacity as physician, public health worker, nutritionist, author and academic, Michael contributed to the achievement of the many ambitious goals in technical fields, policy, programs, information sharing and capacity building in the USA and internationally. He was one of the pioneers in moving a global public health agenda to one that embraces public health nutrition; nowhere is this needed more than in low- and middle-income countries where malnutrition continues to affect millions of women and children. Michael established a technical and policy foundation that continues to serve us well as we face a future of challenges embodied by financial uncertainty, climate change, diminishing natural resources and insecurity.

**Lives saved and enriched**

For countless people throughout the world, his life, his work and his passion lives on. Not only have lives been saved as a result of his work, but also all of our lives have been enriched by his grace and kindness. His love of and dedication to his family, place, students and mission was a constant part of his life.

One of the last times we spoke was about the promise of a new US President. Michael’s enthusiasm and optimism for another Washington politician was truly impressive. He was someone who had witnessed 10 administrations and was willing to stand on the threshold of another, embracing much needed hope. Here was a son of Africa, sharing dreams with another son of Africa. There is an Afghan proverb that states: “There is a path to the top of even the highest mountain.” Michael C Latham took that path and I am grateful that he touched us on the way.

**Recollections from Victoria Quinn**

*Senior Vice President, Programs, Helen Keller International, New York, USA*

The nutrition community across the world has lost a good friend and colleague in Professor Michael Latham. I learned about Michael’s death the day it happened, whilst in Dakar this past April, working on my laptop looking out the window across the water and waves. Unexpectedly, an e-mail with this stunningly sad news arrived in my inbox, just like that. In a millisecond, I was trying to process what it truly meant, as it seemed so surreal. I spent some time reconstructing the last time I saw Michael, which was in Bangkok at the 2009 International Congress of Nutrition – where he was in full fighting form, energetically challenging the room of people to think beyond the typically safe boundaries.

We can all admire, and thank, Michael for pushing us to question the accepted “norm” and strive to do better as nutritional professionals. Michael was never complacent, and may have shaken some of our community up in recent years with his thinking. But, when all is said and done, we must thank Michael for making us think, reflect, reassess and do things better to improve the nutrition and social conditions of those most in need. I can say with all sincerity that I owe my attending Cornell’s Program in International Nutrition to the lure of Michael and his work. I will never forget the first department party I went to at his and Lani’s house in Danby, over 30 years ago in 1979, which was bursting with people and music from many different countries, along with many other interesting offerings. It remains firmly imprinted on my memory forever.

On a personal level, Michael’s support to me was especially kind, as he provided handwritten letters of reference that he posted from his research station in Kwale, Kenya. It was a miracle that they all arrived safely in my mailbox in Ithaca NY. In such a way, Michael provided unflagging support to “his” students. He always had the time to talk, and took care of the next generation of nutrition professionals. In time, we all became members of his huge extended family across the globe. Michael was a gracious and warm-hearted man, and I am honored to have had him as my friend, professor and colleague.

**Recollections by Peter Heywood**

*Honorary Professor of International Health at the University of Sydney, Australia*

I arrived at Savage Hall in the spring of 1969 with the aim of studying International Nutrition and was soon sitting in Michael’s office for the first of many meetings over the course of the next five years. I have many abiding memories of Michael, of which three illustrate the man and his concerns. At that time, the Biafra war was an important concern to many – especially to Michael. Eventually, he was involved in assessing the health and nutrition situation of the region and reporting to senior leaders in the USA. Given Michael’s deep commitment to Africa, this was obviously of great importance to him and he devoted much time and effort to it, something that made a great impression on me at the time.

My second memory is much more personal. With Michael’s encouragement, I had run for election to the newly created Cornell Senate. In the second year of the Senate, I was elected Chairman of the Senate Executive Committee, a position which demanded a lot of time. Several days after my election, I received a note from Michael asking that I come to see him to discuss my courses for the next semester. At the meeting, I presented a full course load for his approval. In a very “Michael” sort of way, he suggested that a full course load and discharging my Senate responsibilities required more time than I had available. After considerable discussion, he suggested that I halve the course load to make sure that I had enough time for the Senate. In many ways, this single meeting characterizes Michael for me – he believed in commitment to a cause and that required engaging with the world. At
that time, the Senate embodied the response of the whole Cornell community to the extraordinary events of the Spring of 1969, and if my participation in the Executive Committee required rearranging my academic program for that period, he would, as my supervisor, encourage me to do so.

**Passionate commitment to nutrition**

My third memory is about Colombia, where Michael was, at the time, a major collaborator in a large study of the effect of malnutrition on the behavioral development of children. With strong support from Michael, I was lucky enough to do my Master’s fieldwork as part of that project. This illustrated his passionate commitment to understanding and alleviating the broader developmental effects of malnutrition.

For me, these three memories illustrate the essence of Michael – his great concern for people and the need to engage with the world in pursuit of a better life for all; his consistent and enthusiastic encouragement to students; and the sweeping breadth of his view about the scope and importance of nutrition.

I remember him very fondly and benefited greatly from his guidance and friendship.

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*Correspondence: Bruce Cogill, E-mail: bcogill@gmail.com*

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“We must thank Michael for making us think, reflect, reassess and do things better to improve the nutrition and social conditions of those most in need”
Remembering
Philip Musgrove (1941–2011)

Abridged from article by Chris Fleming, Health Affairs blog, March 22, 2011

Health Affairs journal Deputy Editor Philip A Musgrove, 70, an economist and leading expert in global health, and a cherished colleague, died in a tragic boating accident at Iguazu Falls in Argentina on March 21, 2011.

“Words can’t express our shock and grief at the loss of Phil,” said Health Affairs editor-in-chief Susan Dentzer. “His expertise in the economics of global health and development was profound. He was a generous and caring colleague, who always had a moment to help anyone on our team grapple with any economic or statistical issue. We were all the beneficiaries of his talents, wisdom, and friendship, and will miss him utterly.”

Health Affairs’ executive editor, Don Metz, added, “Phil’s passing is a terrible loss to his family, the journal, and the health policy community. Phil had deep knowledge of many subjects, but what I’ll remember most is his generous nature and his deep commitment to improving the lives of others through his work as an economist and editor.”

Phil, who lived in Rockville, MD, USA, joined Health Affairs in 2005 as a deputy editor in charge of global health coverage. From 2002 to 2005, he worked as an editor at the Fogarty International Center of the National Institutes of Health on the Disease Control Priorities Project. Prior to that, he was a principal economist at the World Bank, from which he retired in 2002. He was especially expert in health systems in Latin America, serving from 1990 – 92 in the bank’s Technical Department, Latin America and Caribbean Region, and in 1992 – 93 on its World Development Report. From early 1996 to mid-1998 he worked in its Resident Mission in Brasilia, Brazil. In 1999 – 2001 he was seconded by the Bank to the World Health Organization, where he worked as editor on the World Health Report 2000 – Health Systems: Improving Performance.

From 1982 to 1990 Musgrove was Advisor in Health Economics at the Pan American Health Organization (PAHO). Before joining PAHO, he was a consultant to the World Bank’s Living Standards Measurement Study, and before that, from 1966 – 68 and again from 1971 – 80, technical coordinator in the ECIEL Program of Joint Studies of Latin American Economic Integration and a member of the staff of the Brookings Institution. In 1977 – 78, he was a Research Associate with Resources for the Future. He taught full time (as visiting professor) at the University of Florida, and part time at Johns Hopkins University’s School of Advanced International Studies, George Washington University, and American University.

Phil also lectured at numerous Latin American universities and research institutions. His many publications range from Consumer Behavior in Latin America; The General Theory of Gerrymandering to Public and Private Roles in Health: Theory and Financing Patterns, in addition to more than 50 articles in economics and health journals and chapters in 20 books. He also edited and co-authored numerous publications.

Phil received a PhD in economics from Massachusetts Institute of Technology in 1974, following studies at Haverford College (BA, mathematics, 1962) and Princeton University (MPA, public affairs, 1964).

“Phil had deep knowledge of many subjects, but what I’ll remember most is his generous nature and his deep commitment to improving the lives of others through his work as an economist and editor”
“Phil’s passing is a terrible loss to his family, the journal, and the health policy community”
Great Famine of 2011: Tragedy Looms in the Horn

This was the headline of the on-line edition of The East African on 10 July 2011. The picture was, once again, one that we have come to know – a desperately thin woman cradling an even more desperately thin and lifeless-looking child. The images of famine always stir up emotions of shock and horror, as did the warning from the USAID-funded Famine Early Warning Systems Network (Fews Net), which described this famine as one of the world’s most severe food security emergencies. As drought, high food and fuel prices and conflict take their toll, the lives of at least 10 million people in the Horn of Africa are threatened. There will be a growing need for special fortified food products to help protect children against malnutrition.

The worst affected country appears to be Somalia, where estimates are that 2.85 million people (a third of the population) are now in humanitarian crisis and in need of urgent assistance. This is an increase of 42.5% on the figure given some six months ago. The World Food Programme (WFP) estimates that around US$ 477 million is needed to address hunger needs in the region through to the end of the year. Currently, it has a 40% shortfall in funding, with about US$ 190 million still needed.

You can visit www.wfp.org or become a Facebook friend of the WFP to keep up to date with the latest developments.

United Nations Standing Committee on Nutrition (UNSCN) Quarterly Newsletter: Nutrition Information in Crisis Situations (NICS)

Just before the new crisis hit, the UNSCN Newsletter on Nutrition Information in Crisis Situations (available at www.unscn.org) was released. This quarterly publication provides updates on the current situation and who is being affected in crisis situations across Africa (the most vulnerable continent), Asia and the Caribbean, as well as giving information on public nutrition and mortality rates. It notes that Africa’s major economic sectors are particularly at risk of climate change and that the existing developmental challenges are exacerbating its vulnerability. In Asia, future climate change is likely to affect agriculture, increase the risk of hunger, and increase the scarcity of water, with enhanced climate variability and more rapid melting of glaciers. In the Caribbean, Haiti has the highest vulnerability index to cyclones and is particularly sensitive to the adverse effects associated with climate change.

The information highlights just how fragile the global food and nutrition security situation is in already challenged regions and countries – and how quickly it can change. This is a must read for anyone working in Africa, Asia and the Caribbean; you can also join the UNSCN e-group on Nutrition and Climate Change.

Did you know?
According to the global assessment report on Disaster Risk Reduction, the number of reported natural disasters has more than doubled in the last decade, from approximately 200 to over 400 a year (UN International Strategy for Disaster Reduction 2009).
Delivering Improved Nutrition – USAID’s Food Aid Quality Review Report

For almost two centuries, the United States has been delivering food aid to vulnerable people in dire need. However, food aid is now at a crossroads. USAID recently undertook a review of both the formulations and specifications of food aid products, together with the nature of programming and the processes from procurement through to delivery, as part of an effort to improve their quality as priorities and needs evolve. The report found that, although remarkable achievements have been made in terms of impact in often challenging emergency settings, there is scope for improvement along the entire food aid chain. One lesson that everyone now accepts is that the needs of food aid beneficiaries are not homogeneous; there is no one food product that can meet every kind of programming goal, nor is there one programming approach that fits all needs. A salient point that nutritionists often forget is that “Combinations of foods are always more appropriate to the needs of beneficiaries than are combinations of nutrients in a single food.”

The report includes a number of valuable decision trees in the annexure and highlights seven specific recommendations:

1. Improve the formulation of existing Fortified Blended Food (FBF) products. This includes improving sources of protein by adding whey protein; the development of new forms of products; exploring ways to reduce phytates and research new packaging to support more effective targeting and shelf life.
2. Upgrade the vitamin and mineral mixes that are used, and diversify approaches to addressing micronutrient needs, such as developing micronutrient powders and other point-of-use fortification options.
3. Develop or adopt non-cereal-based (e.g., lipid-based) products for the management of nutritional deficiencies offering varying quantities and types of nutrients for different programmatic contexts.
4. Provide clearer programming guidance to enable implementers to match products to specific consumption and nutrition goals; address specific issues such as HIV/AIDS and home preparation of new products; and invest more in behavior change communication and programming that supports global infant and young child feeding principles.
5. Establish an inter-agency committee to oversee all government interests in the food aid agenda.
6. Enhance processes along the product value chain. This acknowledges the need for effective interaction with the private sector to bring industry best practice to bear on food aid supply, food safety and quality assurance, and the need for public-private partnerships to promote product innovations.
7. Strengthen the evidence base for innovations in products, programming approaches, and institutional processes.

All of these recommendations should be taken to heart not only by USAID, but by any organization or government working in providing not only food aid but also nutrition interventions, especially as scaling up nutrition interventions is being encouraged towards the single goal of increasing food and nutrition security around the world and finally conquering hunger.

The MDG Countdown – 2011 Report Available

It seems that, in the foreword to the MDG 2011 report, the annual mantra of UN Secretary-General Ban Ki-moon is that, despite the progress that has been made, we still have a long way to go. This year, the report highlights how much still has to be done in terms of empowering women and girls; promoting sustainable development; and protecting the most vulnerable from the devastating effects of multiple crises, whether conflicts, natural disasters or volatility in prices of food and energy. Ban Ki-moon states, “Progress tends to bypass those who are lowest on the economic ladder or are otherwise disadvantaged because of their sex, age, disability or ethnicity.”

The good news centers around the fact that:
> Many of the poorest countries have made the greatest strides in education, with sub-Saharan Africa being the region with the best record of improvement.
> Investments in preventing and treating HIV, TB and malaria are yielding results. New HIV infections are declining steadily (again led by sub-Saharan Africa) and worldwide deaths attributed to TB have fallen by more than one third since 1990 and those caused by malaria have been reduced by 20%.
> Every region has made progress in improving access to clean drinking water.

There is also good news when it comes to the MDGs that resonate most directly within the nutrition community – poverty and child mortality. The world is still on track to reach the poverty reduction target. In fact, by 2015 it is expected that the global poverty rate will have fallen below 15%, which is well under the 23% target. Moreover, targeted interventions have succeeded in reducing child mortality, with nearly 12,000 fewer children dying each day. Successful immunization-against-measles programs are leading the way and represent one quarter of the decline in mortality from all causes among children under the age of five.

Sadly, nutrition lags behind. Despite some decreases, underweight remains a major problem, especially in Southern Asia. Children living in rural areas of developing regions are twice as likely to be underweight as their urban counterparts. The report lists four factors that still play a key role in underweight: the lack of quality food; suboptimal feeding practices; repeated attacks of infectious diseases; and pervasive undernutrition. The nutrition lag is recognized, and the report states: “Nutrition must be given higher priority in national development if the MDGs are to be achieved. A number of simple, cost-effective measures delivered at key stages of the life cycle, particularly from conception to two years after birth, could greatly reduce undernutrition.” This is in direct support of the Scaling Up Nutrition (SUN) and 1,000 Days movements, and should spur the nutrition community not only to continue to raise its voice but also, more importantly, to get involved in the scaling up of the interventions that are known to have the greatest impact: improved maternal nutrition and care; breastfeeding within one hour of birth; exclusive breastfeeding for the first six months of life; and timely, adequate, safe, and appropriate complementary feeding and micronutrient intake between six and 24 months of age.

It is concerning to note that the proportion of people in the developing world who went hungry in 2005 – 2007 remained stable, at 16%, despite significant reductions in extreme poverty. This makes it unlikely that we will meet the hunger reduction target in many regions of the developing world. The disconnect between poverty reduction and the persistence of hunger has brought renewed attention to the mechanisms governing access to food in the developing world, and will undoubtedly be one of the main focuses of attention in the coming year.

Did you know?

At the close of the World Health Assembly (WHA) 2011 in May, 16 countries announced new commitments to dramatically reduce maternal, newborn and child mortality, as part of the Global Strategy for Women’s and Children’s Health. New commitments were announced by Burundi, Chad, the Central African Republic, Comoros, Guinea, Kyrgyzstan, the Lao People’s Democratic Republic, Madagascar, Mongolia, Myanmar, Papua New Guinea, Sao Tome and Principe, Senegal, Tajikistan, Togo and Vietnam.

Leveraging Agriculture for Improving Nutrition and Health – IFPRI February 2011

New Delhi, India saw some 1,000 delegates from across the agriculture, nutrition and health world in 65 countries come together at a two-day forum. The forum was designed to encourage thinking through interactions between agriculture, nutrition and health, and to consider ways to exploit them to improve human nutrition and health. The meeting allowed for networking, brainstorming and collaboration across sectors, and also offered opportunities for a number of additional side meetings.

What makes this event exciting is that we are seeing the beginning of the breaking down of the silos in which the three sectors have traditionally worked, and where they have only rarely worked together to reach their common goal of improving human well-being. In her broadcast speech, US Secretary of State Hilary Clinton said, “I urge you to use your time together to find ways for all of us to do even more: more to improve agricultural productivity, more to connect farmers to markets, more to increase access to nutritious crops and health-care, and more to support the women who are growing food and caring for children around the world."

Although the challenges ahead for each sector are enormous, individually and jointly, the gains to be made in facing them, creatively addressing them and ensuring ongoing interaction, far outweigh the risks. Just as direct nutrition interventions are the key to addressing global nutrition and health problems, in the long term the best way to conquer malnutrition is to also promote a nutrition sensitive growth strategy. Such a strategy could, among other factors, increase demand for and access to nutritious foods all along the value chain; mitigate the health and nutrition risks associated with agriculture; breed more nutritious varieties of the staple food crops that are consumed by poor people; and promote the diversification of agriculture into nutritious and high value products, such as dairy, the products of horticulture, and fish.

The words of Dr David Nabarro, Special Representative of the UN Secretary-General on Food Security and Nutrition and the Chair of the SUN movement, were sobering, and should drive us to do things differently: “We’ve got nearly a billion hungry people now, and we’ve got to prepare for feeding 9 billion by 2050 ...”

For more information
IFPRI have made available the complete video coverage, conference papers and briefs, and slide presentations of the meeting at http://2020conference.ifpri.info
Cash transfers have become a talking point. Can they offer a possible strategy that benefits food and nutrition security amongst the poorest and most vulnerable? The UK Department for International Development (DFID) has released a comprehensive paper that looks at the multiple forms of the impact of cash transfers, based on the current global experience.

The concept was pioneered in Latin America and is increasingly gaining popularity as an instrument for social protection, where resources are transferred directly to poor people rather than through the state, in order to reduce poverty and increase resilience. These “transfers” may take the form of cash transfers, in kind transfers (eg food), vouchers, or free or subsidized access to goods or services (eg exemption from health service user fees).

While the evidence base for cash transfers is better than for many other policy areas, it is also uneven and less is known about some instruments (public works) and outcomes in certain regions (such as sub-Saharan Africa). The good news is that there is convincing evidence from a number of countries that cash transfers can reduce inequality and the depth or severity of poverty. In Brazil, for example, a combination of cash transfer programs accounted for 28% of the total fall in the Gini index (a summary measure of inequality) between 1995 and 2004. There is also robust evidence that cash transfers have leveraged sizeable gains in access to health and education services, as measured by increases in school enrolment (particularly for girls) and the use of health services (particularly preventative health, and health monitoring for children and pregnant women). They also have a proven role in terms of supporting specific vulnerable groups, such as people living with HIV and AIDS, or orphans and vulnerable children. Effects are typically larger in lower income countries with lower baseline levels.

All this points in the right direction, yet transfers have had less success in improving final outcomes in health or education. Cash transfers can help the poor overcome demand-side (cost) barriers to schooling or healthcare, but they cannot resolve supply-side problems with service delivery (eg teacher performance, or the training of public health professionals). Cash transfers therefore need to be complemented by strategies to improve service quality. Nutrition may be an exception: Households receiving transfers spend more on food, resulting in significant gains in children’s weight and height in several countries. Where the main recipients are women, as in Mexico’s Oportunidades, cash transfers have often helped to increase their role in household spending decisions and promote more balanced gender relations. Cash transfers can

Did you know?
In 2007, one third of the world’s workers were employed in agriculture; however, despite the size of its workforce, agricultural production accounts for less than 5% of the gross world product (an aggregate of all gross domestic products).
support girls’ education and their access to health-care and other basic social services.

As with any intervention, there are numerous factors that influence the success or failure of a cash transfer system. Thus, long term sustainability, monitoring and evaluation, together with ascertaining if they offer value for money, is crucial.

UNICEF Launches Infant and Young Child Feeding Resource

Given the significant focus on the importance of the first 1,000 Days in reaching the MDGs, UNICEF recently launched a timely document, entitled “Infant and Young Child Feeding (IYCF) Programming Guide.” Evidence is growing that supports improved feeding practices for infants and young children as a key component of child survival, growth and development programs. In the Executive Summary, UNICEF notes that: “The importance of breastfeeding as the preventive intervention with potentially the single largest impact on reducing child mortality has been highlighted. In addition, of the available nutrition interventions, improvement of complementary feeding has been shown to be most effective to improve child growth, and thereby, together with maternal nutrition interventions, to contribute to reducing stunting.” This document has therefore been prepared in response to requests from countries to assist with designing appropriate strategies to accelerate progress towards improving the nutrition status of young children, by increasing breastfeeding rates and improving complementary feeding.

The guide is based on the latest scientific evidence, lessons learned, reviews and best practices, and presents the “hows” of programming at all levels. It also pulls together all the important documents and guidelines that have been issued on the topic. Sections include advocacy, partnerships and coordination; situation assessment; developing a national and comprehensive IYCF policy and strategies; costing strategies; prioritizing interventions and mobilizing resources. It clearly defines the regulatory actions required, together with broader health service requirements, community level actions and specific needs in special circumstances, such as HIV and emergencies. A highlight of the document is the excellent annexure, which details the resources, tools and useful websites available.

The conclusion is clear. Success in increasing optimal infant and young child feeding practices is based on commitment to implementing comprehensive, evidence-based, at-scale programming, tailored to the local context. So, for those who are committed to an evidence-based approach, the new guide is without doubt the most comprehensive single reference on IYCF programming to date. The good news is that UNICEF intends periodically to review and update the guide, in the hope that this resource will remain the seminal reference when planning programs or interventions at a time when IYCF is clearly under the spotlight.

For more information on DFID
The full paper is available through the DFID website, www.dfid.gov.uk

The document is not yet on the UNICEF website, but is available for downloading at:
With infant and young child nutrition under the global spotlight, this working paper by a sub-group of the “Maternal, Infant and Young Child Nutrition Working Group of the 10 Year Strategy to Reduce Vitamin and Mineral Deficiencies” is important. The WHO Global Strategy on IYCF recognizes that the complementary feeding period is critical, and that infants are particularly vulnerable during this transition period. It also recognizes the need for “adequate complementary foods that provide sufficient energy, protein and micronutrients to meet a growing child’s nutritional needs.”

Consequently, and in line with the 1,000 Days window of opportunity and call for partnership – bringing together governments, the private sector and civil society organizations to promote targeted action and investment to improve nutrition for mothers and children during this crucial time – commercialized complementary foods and supplements have gained attention and investment. The working group felt that some guidance was needed, even if it was preliminary and incomplete, in order to determine how the International Code of Marketing of Breast-milk Substitutes applies to the marketing of commercialized complementary foods and supplements to ensure that optimal breastfeeding practices are protected and promoted. The document is extensive and practical (giving do’s and don’ts and best practice advice). It is valuable at a time when no official guidance is available to private sector companies which are already moving ahead to develop and market complementary foods and supplements.

A copy of the working paper is included as a supplement to this edition of *Sight and Life* magazine; it is also available electronically from the GAIN website – www.gainhealth.org – under Reports and Publications, a subsection of Media and Resources.

It is important to note that, subsequent to the development of this working paper, the World Health Assembly (WHA) passed Resolution 63.23 in May 2010. This urges member states “To end inappropriate promotion of food for infants and young children and to ensure that nutrition and health claims shall not be permitted for foods for infants and young children, except where specifically provided for, in relevant Codex Alimentarius standards or national legislation.” This means that the issue of the prohibition of nutrition and health claims has not been dealt with in the paper but it is hoped that the WHO will give guidance as to what constitutes “appropriate” and “inappropriate” marketing of complementary foods and supplements at the WHA meeting in May 2012.

You can visit http://www.gainhealth.org/sites/default/files/working%20paper%203LR_with_insert.pdf to download the full report.
A one-day meeting hosted by the International Union of Nutritional Sciences (IUNS), The Home Fortification Technical Advisory Group, GAIN and Unilever was held in Washington DC in early April. Speakers from Bolivia, Ghana, Malawi, Mexico, South Africa, India, Europe and the US addressed the importance of essential polyunsaturated fatty acids (PUFAs), nutrients that are often neglected, for optimal growth, enhanced immunity and neurobehavioral development.

Optimal omega-3 (n-3) PUFAs intake is associated with reductions in prematurity; improvements in gestational age; birth weight; birth length; and, in some groups, enhanced post-natal growth and development. The n-3 fatty acid supplementation of lactating mothers of preterm infants improves infant neurodevelopmental performance, as does supplementation of infant formula with docosahexaenoic acid, n-3 (DHA) and arachidonic acid, n-6 (ARA) for sub-groups of preterm infants. The impact of DHA and ARA on the neurodevelopment of full term infants has been less studied, particularly in developing countries.

Although few studies have assessed PUFAs intake and its status in developing countries, the available data suggest that many women and children are at risk of insufficient intake. Both n-3 and n-6 fatty acids are important, and adequate intakes of both these classes of fatty acids need to be ensured. Even when total fat intakes are adequate, intake of essential PUFAs α-linolenic acid (ALA, n-3) and linoleic acid (LA, n-3) and, particularly, of long-chain polyunsaturated fatty acids (LC-PUFAs) derived from ALA, eicosapentaenoic acid (EPA, n-3) and DHA may be inadequate in some populations. In particular, this may be an issue for n-3 PUFAs intake, given the fact that commonly consumed vegetable oils are good sources of n-6 PUFAs in many developing and emerging countries. However, in situations where total fat intake is low, interventions should aim to increase the intake of both n-6 and n-3 PUFAs in a ratio of 5 to 15. Food availability and intake data in many developing countries suggest that diets are often limited in n-3 PUFAs. Increasing intake is possible through foods that are rich in n-3 PUFAs: animal products (especially fatty saltwater fish, breast milk and eggs), soy, canola oil, some nuts/seeds (chia seeds, walnuts and soy beans) and pastes and spreads made with soy oil or full fat soy flour. It is important to note that supplementation with ALA alone is unlikely to be the solution, as the research shows that the conversion of ALA to DHA is poor and certain micronutrients are important. Turning the science into programs, interventions which resulted in improved n-3 intake (including the fortification of products for consumption by pregnant women or infants and young children) have been successful.

Some examples include:

- Lipid-based nutrient supplements (LNS), which have been shown to have a high acceptance among infants and young children as well as their caregivers and positive growth outcomes have been observed in children consuming LNS;
- LNS given to pregnant women in Burkina Faso has been associated with increases in birth length and placental weight in malnourished women;
- Supplemental DHA given to lactating women increased breast-milk DHA concentration and, subsequently, intake by infants;
- Fortified full-fat soy flour developed by the China Center for Disease Control and Prevention and DSM has had positive impacts on anemia, growth and IQ.

The meeting also looked at the role that can be played by agriculture in increasing the availability of n-3 PUFAs; how health programs need to encourage an increased intake; and what the private sector can do to develop new products, improve shelf life, expand the distribution of products containing n-3 PUFAs and use their marketing expertise in developing behavior change communications that address not only the needs but also the wants of consumer beneficiaries.

There is no doubt that the role of essential PUFAs has been neglected and needs more consideration as new innovations come to the fore, in order to address the spectrum of nutrient deficiencies impacting on low- and middle-income countries.

Did you know? The 1,000 Days movement has a website, www.thousanddays.org, where you can sign up to receive updates on activities and events.
Keeping the Momentum – Stakeholders Unite to Continue Support of Scaling-Up Nutrition (SUN)

At the 1,000 Days to Change a Life event, which was organized by the US and Irish governments in September 2010, CEO of Concern Worldwide Tom Arnold and President of Bread for the World David Beckmann committed to a follow-up meeting in June 2011.

Over 150 government officials (including 35 from developing countries), donors, and representatives from civil society, academia and the private sector who are dedicated to ending child and maternal undernutrition took part in a meeting in Washington DC on 13 June 2011. This unique gathering of key stakeholders and drivers of the SUN movement made a united call for action, and conveyed the urgency and passion for sustained commitment to scaling up nutrition efforts. This served as a voice for civil society’s efforts to maintain and build on the political momentum behind 1,000 Days, and to ensure action going forward. It is expected that a Civil Society Statement endorsing its commitment to SUN will soon be released. The high level of international and developed country commitment to SUN and 1,000 Days was clearly illustrated through the active participation of the keynote speakers, including Maria Otero, US Under Secretary of State for Democracy and Global Affairs; Kevin Farrell, Irish Hunger Envoy; David Nabarro, Special Representative of the UN Secretary-General for Food Security and Nutrition; and a conversation style session between David Beckmann and Robert B Zoellick, President of the World Bank. In addition, Hillary Rodham Clinton, US Secretary of State; Andrew Mitchell, UK Secretary of State for International Development; and Melinda French, Co-Chair of the Bill & Melinda Gates Foundation, prepared video addresses for the meeting.

The morning session included a moderated panel discussion featuring representatives from partner nations and civil society groups. The afternoon session consisted of four concurrent working groups. These focused on advocacy and communications; capacity-building; implementation of SUN at a country level; and linkages with other sectors, such as health, agriculture and education. The working groups were a central and fundamental part of the meeting since they set aside time for participants to share their experiences and convey their perspectives on a variety of issues as SUN progresses.

All presentations from the meeting are available at www.bread.org/meeting

Questions and answers on SUN

As the SUN movement continues to grow and gain momentum, the six Task Teams under the Transition Team led by Dr David Nabarro, as the UN Secretary-General’s Special Advisor on Food Security and Nutrition, are hard at work ensuring not only that the SUN shines, but also that it shines brightly around the world and leads to scaled-up actions and interventions in countries that change the lives of the poorest and most vulnerable.

What is Scaling Up Nutrition?
Scaling Up Nutrition (SUN) is a global movement to improve maternal and child nutrition during the critical window of opportunity between pregnancy and age two. SUN is not a new institution, initiative or financial mechanism. Instead, the movement brings organizations across sectors together to support national plans to scale up nutrition, by helping to ensure that financial and technical resources are accessible, coordinated, predictable and ready to go to scale. The SUN movement focuses on promoting the implementation of evidenced-based nutrition interventions, as well as integrating nutrition goals into broader efforts in critical sectors such as health, social protection, development and agriculture.

Who are the main investors in SUN?
The main investors in SUN are national governments themselves. Successful, sustainable efforts to improve nutrition...
must be anchored at a national level, with national level officials owning and leading tailored efforts to address malnutrition. The SUN movement is built through the engagement of nations that are affected by undernutrition. At the center of the movement is national level leadership that coordinates both national and international efforts, with the SUN movement committed to aligning financial and technical support with these country plans.

What are the SUN Framework and Roadmap?
The foundation for the SUN movement is the SUN Framework, which outlines core priorities, elements and actions necessary to address malnutrition. The SUN Framework is not a prescriptive plan; rather, it is a foundational structure from which national plans can be built and tailored. The SUN Roadmap serves to move the Framework into action, providing the principles and direction for increased support for countries as they scale up nutrition efforts across a range of sectors. The SUN Roadmap encourages a coherent approach amongst national leaders and stakeholders to promoting coordinated actions and increasing the effectiveness of efforts.

Who supports SUN?
SUN is a global movement that brings together broad constituencies of stakeholders in a partnership with shared vision, goals and the priority of initiating action to address malnutrition. The movement’s strategic direction is currently provided by a Transition Team of cross-sector, multi-partner leaders from developing and developed countries, CSOs, NGOs, the business sector, academia and the United Nations System.

A Transition Team, informed by an interim Country Partner Reference Group of focal points from countries scaling up nutrition, along with a UN Reference Group, provides the technical expertise and tools to support efforts at a national level. The Transition Team is organized into six task forces, each focusing on specific key elements of SUN in order to establish a foundation for the movement by mobilizing the support of relevant stakeholders, developing useful resources and ensuring SUN sustainability. The task forces are working to develop in-country capabilities; strengthen the engagement of civil society, development partners and the private sector; monitor progress; and support effective communications and advocacy activities.

2011 Commonwealth Health Ministers Meeting:
Sight and Life Co-Hosts Round Table on Preventing Non-Communicable Diseases in Children and Young People

The theme for the 2011 Commonwealth Health Ministers meeting in Geneva in May was “NCDs – A priority for the Commonwealth.” It is well recognized that the developing world faces a harsh reality where nutritional deficiencies, mainly in the form of micronutrient deficiency, are now also being associated with increased vulnerability to non-communicable diseases (NCD) such as heart disease, diabetes and cancer later in life. This has led to many economically developing regions suffering from a double burden of disease. Together with the Commonwealth Health Professions Alliance, Sight and Life co-hosted a half-day meeting on the day before the Commonwealth Health Ministers Meeting. In the first session, the meeting looked at healthy living and NCDs, including topics such as the role of physical activity, tobacco and alcohol use and dental health, while the second session focused on the role of nutrition.

The nutrition session opened with an address by Dr Anna Lartey, Associate Professor in the Department of Nutrition and Food Science at the University of Ghana.
Women and children are particularly important targets for nutrition interventions, as more than a third of child deaths have been attributed to maternal and child undernutrition. Effective and safe interventions aimed at addressing maternal and child undernutrition and survival need to be scaled-up in many countries.

Under the leadership of Dr Francesco Branca, Director of the Department of Nutrition for Health and Development, in collaboration with internal departments in the World Health Organization (WHO) with a vested interest in nutrition, nutrition guidelines are being developed and updated to help member states and partners in their efforts to make informed decisions on the appropriate nutrition actions to improve nutrition of their population and achieve the Millennium Development Goals (MDGs) – in particular, the eradication of poverty and hunger (MDG 1), the reduction of child mortality (MDG 4) and the improvement of maternal health (MDG 5).

Nutrition-related guidelines and recommendations
The WHO electronic Library of Nutrition Actions (eLENA) aims to compile and display WHO guidelines and recommendations related to nutrition, along with complementary documents such as Cochrane systematic reviews and other evidence that informed the guidelines, biological and behavioral rationales, invited commentaries on recent systematic reviews and their applicability prepared by public health experts, and additional resources produced by member states and global partners. The eLENA will, therefore, serve as an easily accessible web-based tool for policy makers, health workers, international organizations, bilateral agencies, non-governmental organizations, academicians and other interested actors to access the most up-to-date WHO guidance on nutrition, as well as the information that has led to the development of these recommendations.

The content of potential nutrition interventions profiled within eLENA includes not only the most current WHO nutrition guidelines, but also the scientific evidence on which the guidelines were developed and based. This includes links to the Cochrane Library through a collaboration agreement with John Wiley and Sons Inc. The Cochrane Library is a collection of databases that contain high-quality, independent evidence to inform healthcare decision making. Cochrane Reviews represent the highest level of evidence on which to base clinical treatment decisions.

Did you know?
The Commonwealth is a voluntary association of 54 countries that support each other and work together towards shared goals in democracy and development. The world’s largest and smallest, richest and poorest countries make up the Commonwealth. Member countries span six continents and oceans, from Africa (19) to Asia (8), the Americas (2), the Caribbean (12), Europe (3) and the South Pacific (10). The Commonwealth is home to two billion of the world’s citizens.
The six WHO languages
Translation into the six official WHO languages (Arabic, Chinese, English, French, Russian and Spanish) will also begin in 2012, to facilitate the use of the information contained within eLENA and reach the maximum number of potential users. Access to information on the implementation of nutrition actions, allowing programmers and project managers to contribute and retrieve information about different delivery options, is also in the planning stages as a complementary web tool. This feature will be implemented in 2013.

eLENA is now available on the WHO website:
http://www.who.int/elena

This project receives financial support from Micronutrient Initiative, the International Micronutrient Malnutrition Prevention and Control Program at the Centers for Disease Control and Prevention (CDC), the Government of Luxembourg, and The Bill and Melinda Gates Foundation. Technical support is being received from international experts, partners and collaborators.

The World Food Prize 2011:
Two Men – One from Africa and One from Latin America – are Honored

Former President John Agyekum Kufuor of Ghana and former President Luiz Inácio Lula da Silva of Brazil are the recipients of the 2011 World Food Prize. Both men are being honored for implementing highly successful national policies to improve food security, as well as for serving as leaders in the international discussion on hunger alleviation. The awards will be handed over at the 2011 Borlaug Dialogue in Des Moines, Iowa on 13 October 2011.

Advocate for improved agriculture
Former President Kufuor has been a vocal supporter of anti-hunger initiatives both within his home country of Ghana and internationally. Although 60% of Ghana’s population was involved in agriculture when President Kufuor entered office, many rural Ghanaians were food insecure, and Ghana was heavily dependent on imports to meet the domestic demand for food. During former President Kufuor’s two terms in office, the policies that his administration enacted helped to reduce hunger levels from approximately 34% of the population to 9%, making Ghana the first sub-Saharan African nation to achieve MDG 1.

Former President Kufuor implemented a nationwide school feeding program, and helped pass a number of policies to modernize the Ghanaian agricultural sector; create incentives for the private sector to invest in agriculture; provide subsidized inputs, such as pesticides and fertilizers; and ensure that farmers received higher returns for their crops. These initiatives boosted agricultural yields in Ghana and greatly improved domestic food security. As Chairperson of the African Union and Global Ambassador against Hunger for the UN World Food Programme, former President Kufuor advocated for long-term agricultural investments and child nutrition initiatives on an international level.

Defender of the right to food
Former President Lula made food security a priority in his administration by enacting a series of laws and policies that ensured that all Brazilians had access to sufficient, nutritious food. When President Lula was elected in 2002, nearly half of all Brazilians lived in extreme poverty. Just five years after his term began, Brazil announced that they had achieved MDG 1 and had successfully halved the number of hungry through the right-to-food approach.

The central program of former President Lula’s campaign against malnutrition was Fome Zero (Zero Hunger), an initiative that sought to reduce hunger levels through a variety of programs, such as subsidized produce markets; low-cost restaurants that served subsidized meals; and conditional cash transfers for families that vaccinated their children and sent them to school. The government also expanded the school lunch program; created incentives for companies to
provide meals for low-income employees; and re-formed the
National Council of Food and Nutritional Security (CONSEA).
CONSEA is an advisory body that monitors hunger and malnu-
trition, and reports its findings to the President and the Brazil-
ian government. Brazil is also one of several countries to have
legally established the right to food for all of its citizens.

This news is taken from
“The Hunger and Undernutrition Blog” at http://www.hunger-
undernutrition.org/blog/, which aims to promote an informed
dialogue, serve as a resource for those in the field, and empower
people at all levels to do what they can to make undernutrition-
and nutrition-related deaths and diseases things of the past.

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Call for Nominations: The Second Rainer Gross Prize
for Recent Innovations in Nutrition and Health

At a point in global nutrition where innovative thinking and
innovation is a vital component of addressing the pressing
problems of food and nutrition security, the recognition of the
merits of those who generate innovative ideas and projects
in nutrition and health in developing countries is to be
applauded. The Rainer Gross Prize of the Hildegard Grunow
Foundation is awarded for accomplishment in international
nutrition, in the spirit and memory of Dr Rainer Gross,
former director of the Division of Nutrition of UNICEF.

The awardee will be selected from applicants who
describe the merits of their recent work (within the last five
years) making needy communities at nutritional risk and
fellow professionals aware of problems that were previously
unrecognized, while beginning to open pathways to their
practical solution. The award includes US$2,500 in cash, a
trip to the World Public Health Nutrition Congress for a lec-
ture and awards ceremony, and the publication of their talk as
a brief communication in the Food and Nutrition Bulletin.

Did you know?

Blog 4 Global Health http://blog4globalhealth.wordpress.com/ is an interactive blog from the Global Health
Council’s Policy, Research and Advocacy team. It covers
blogs on 19 different health topics, including climate
change, maternal and child health and HIV/AIDS.

The first ever award of this biannual prize went to Aaron Lech-tig of Peru and Angela Cespedes of Panama at the II WCPHN
in Oporto in September 2010.

Detailed information on both rules and instructions for
applications for the award can be found at
http://www.hgrunowfoundation.org/rainer-gross-award
Ukraine has 55 orphanages for 7,000 disabled children and adolescents aged 4 to 35 years which come under the umbrella of the Ministry of Social Affairs. In level 3 – 4 orphanages for children with moderate and severe disabilities, a number of children suffer from severe malnutrition. Ukraine also lacks knowledge and expertise in the field of malnutrition.

The first ever workshop on malnutrition took place in Kyiv (Kiev) on 22 – 24 March, entitled “Malnutrition in children with disabilities in level 3 – 4 internats: clinical signs and symptoms, treatment and prevention” and “Paediatric Nutrition Update.”

**Distinguished speakers**

Jointly organized by the Ministry of Social Affairs of Ukraine, **Sight and Life** and the National Assembly of the Disabled of Ukraine and co-sponsored by the Early Nutrition Academy, the workshop was attended by 32 representatives, including doctors and nurses from 25 regions of Ukraine who work in level 3 – 4 orphanages for children with disabilities.

Following a welcome speech by Ihor Lushnikov, the Deputy Minister of Labor and Social Affairs of Ukraine, it featured input from a range of distinguished speakers. These included Hans Biesalski, director of the Institute of Organic Chemistry and Nutrition, Stuttgart, Germany; Berthold Koletzko, director of the Children’s Hospital, Munich, Germany; neurologist and pediatrician Tetyana Mishchuk, from the Children’s Rehabilitation Center Dzherelo, Lviv, Ukraine; Roksolana Tymiak-Lonchina, founder of the “Starving for Color” foundation; Vassyl Lonchina, director, Surgery and Intensive Care Unit, John H Stroger Hospital of Cook County, Chicago, USA; Mark Fishbein, pediatric gastroenterologist at the Children’s Memorial Hospital, Chicago, USA; Klaus Kraemer of **Sight and Life**, Basel, Switzerland; and Lesya Kalandyak, physiotherapist, the Children’s Rehabilitation Center Dzherelo, Lviv, Ukraine.
From One to Many: Scaling Up Health Programs in Low Income Countries

One of the most glaring differences between the commercial and social worlds is the constrained ability of the latter, in relative terms, to go to scale. Markets, supply chains, and incentives enable consumer goods, many of them non-critical for human existence, to be supplied and “demanded” even in the remotest parts of the world. In the same environment, the infrastructure, resources, and will to mount the necessary scale-up of proven and often life-saving technologies and health interventions are often lacking.

Scale-up is, therefore, a central question to most health interventions and is the focus of Richard Cash and colleagues’ excellent From One to Many. The book, a consolidated output of a conference on the subject hosted by the development organization BRAC in Bangladesh, identifies scale-up in horizontal terms – expanding coverage of existing interventions. BRAC and Bangladesh were a perfect setting for the discourse. With its motto of “small is beautiful but big is necessary” and its operations spanning about 40,000 schools, 7 million microfinance borrowers, and responsibility for the rollout of national public health programs, BRAC is the epitome of what the non-state sector can achieve in terms of outreach capability.

The book has done an impressive job of using case studies to draw attention to strategies and factors common to successfully scaled-up programs. The importance of systems, institutions, and organizations with strong delivery capabilities has been reiterated throughout. A powerful policy

take-home message from the book is that concomitance of community acceptability, stake of local and national governments, and buy-in of local politicians and private entities are all key ingredients for success in community interventions. The case studies are a reminder of the importance of effective engagement of stakeholders to maximize their comparative advantage and to locally tailor community interventions.

Reviewed by

For more information, please visit www.uplbooks.com.bd/
Nutrition, Epigenetic Mechanisms and Human Disease

As nutrition research is shifting its focus from epidemiology and physiology to the effects of nutrients at a molecular level, a uniquely tailored diet that corresponds to the demands of our genetic signature is emerging as an indispensable need. Nutritional genomics uses high-throughput genomic tools to unravel the influence of micro- and macronutrients as potent dietary signals regulating metabolic pathways. Nutrigenomics can unmask how susceptible genotypes are predisposed to diet-related diseases. In the last decade, extensive research on nutrigenomics has unveiled numerous epigenetic mechanisms that are influenced by our dietary signature, and are capable of modifying an individual’s susceptibility to diet-related disorders. The primary objective of this volume is to illustrate how nutrition can influence epigenetic inheritance and the mechanisms that underlie modification of the metabolic imprint of an individual. This enriched understanding of nutrigenomics can then be applied to master a tailored diet that can alleviate imprinted metabolic syndromes. Specifically, the focus of the book is on three key areas: discussion of the basics of nutrigenomics; epigenetic regulation types of nutrition influencing the genetic imprinting; and the role of nutrition in modulating an individual’s predisposition to cancer.

The aim of nutrigenomics is to develop dietary intervention strategies to alleviate diet-related diseases and restore the body’s normal metabolic homeostasis. Epigenetic mechanisms such as DNA methylation and transposing insertion have been shown to play at the nexus between nutrition and the genetic signature of an individual. Chromatin remodeling across the genome, mediated via epigenetic mechanisms and transient nutritional stimuli, can wield persistent changes on the genomic profile that are likely to be passed on to subsequent generations. Genomic imprinting refers to a unique type of epigenetic regulation, whereby differential modification of the parental alleles at certain genetic loci in the parental germlines (imprinting control regions) takes place depending on whether the allele is passed on to the offspring through the male or female gamete.

For more information, please visit
www.crcpress.com
www.taylorandfrancis.com
The Fight for the Right to Food: Lessons Learned

Over one billion people are gravely, permanently undernourished but, according to the 2008 report on world food insecurity by the Food and Agriculture Organization of the United Nations (FAO), world agriculture, in its present state, could nourish 12 billion people. At the beginning of my mandate as UN Special Rapporteur on the Right to Food, I identified seven major problems which directly affect or prevent the realization of the right to food: (a) problems linked to developments in world trade; (b) external debt servicing and its impact on food security; (c) developments in biotechnology and their impact on access to food; (d) wars and their destructive impact on food security; (e) corruption; (f) access to land and credit; and (g) discrimination against women and its impact on food security.

“More people than ever before suffer from grave, permanent undernourishment”

Today, one of the key obstacles to the realization of the right to food is the schizophrenia in the United Nations system and in states’ policies, which on the one hand support the promotion of the right to food, yet at the same time act to undermine it. The first aspect of this schizophrenia is the existence of profound internal contradictions within the international community. The second aspect is that many states are not at all coherent as far as their own practices are concerned. Wide disparities in economic power mean that powerful states negotiate trade rules that are neither free nor fair. Such rules severely affect small farmers and threaten food security, especially in developing countries that have been required to liberalize agriculture to a much greater extent than developed countries. Only the normative approach can gradually eliminate hunger and permanent malnutrition in the world. The human right to food has to be implemented by all states, by all intergovernmental organizations and by all non-state actors, including multinational corporations.

Jean Ziegler, Vice President of the UN Human Rights Council Advisory Committee, Former UN Special Rapporteur on the Right to Food [abridged]

For more information, please visit www.palgrave.com
DRI Dietary Reference Intakes for Calcium and Vitamin D

Calcium and vitamin D are essential nutrients long known for their role in bone health. Over the last 10 years, the public has heard conflicting messages about their other benefits – especially those of vitamin D – and also about how much calcium and vitamin D they need to be healthy. To help clarify this, the US and Canadian governments asked the US Institute of Medicine (IOM) to assess current data on health outcomes associated with calcium and vitamin D. A committee of experts reviewed the evidence and updated the nutrient reference values, or Dietary Reference Intakes (DRIs), used by government agencies and health professionals.

The committee provided an exhaustive review of studies on potential health outcomes and found that the evidence supported a role for these nutrients in bone health, but not in other health conditions.

**Health effects of vitamin D and calcium intake**

The new reference values are based on much more information and higher quality studies than were originally available. This thorough review found that the health benefits beyond bone health were not sufficient to be considered for the DRIs. However, a strong body of evidence from rigorous testing substantiates the importance of vitamin D and calcium in promoting bone growth and maintenance.

The science indicates that, for example, on average 500 milligrams of calcium per day meets the requirements of children aged one through three, while on average 800 milligrams daily is appropriate for those aged four through eight. Meanwhile, women aged 19 through 50 and men up to 71 require on average 800 milligrams daily. Determining intake levels for vitamin D is somewhat more complicated. Vitamin D levels in the body may come from not only the diet, but also from synthesis in the skin through sunlight exposure. Therefore, the committee assumed minimal sun exposure when establishing the DRIs for vitamin D, and determined that North Americans need on average 600 International Units (IU) of vitamin D per day (up from 200 IU from the previous DRIs), while people aged 71 and older may require as much as 800 IU per day.

For more information, please visit www.iom.edu/vitamind
Development and Application of Biomarkers

First introduced to biomedical research in 1980, the term biomarker has taken on a life of its own in recent years and has come to mean a number of things. In biomedical science, biomarker has evolved to most commonly mean a characteristic that can be used as either a diagnostic or a prognostic, but most significantly as a screening indicator for pathologies that tend to be somewhat silent prior to overt clinical display.

Applying scientific rigor, as well as a disciplined approach to nomenclature, Roger L Lundblad’s Development and Application of Biomarkers rationalizes the current enthusiasm for biomarkers with the use of well-established clinical laboratory analytes in clinical medicine. Highly respected for his work as both a classical protein scientist and a pioneer in proteomics, Dr Lundblad catalogs various biomarkers recognized in clinical medicine and, where possible, matches the expectations for advances in screening technologies with the realities of statistical analysis. More specifically, this important reference work details an extensive list of biomarkers for various stages of a number of cancer types, including ovarian, pancreatic, prostate, and breast cancer. It also looks at how proteomics is used for the discovery and validation of biomarkers, and explores the use of microarray technology, ultra-high performance liquid chromatography, and computational bioinformatics’ approaches for the discovery and use of biomarkers. In addition, it examines the use of cells and cell fragments as more complex biomarkers, and organizes a host of significant biomarkers and essential research by type and use in a series of readily accessible tables.

Throughout this volume, Dr Lundblad encourages the consideration of biomarkers more as a concept than as laboratory analytes, emphasizing the relationship between the discovery of a biomarker and the biology underlying its production. Ultimately, it is a thorough understanding of the underlying biology that will lead to the development of assays that are robust and reproducible, as well as clinically significant.

For more information, please visit www.crcpress.com
Advocating better nutrition for brighter futures.
Imprint

*Sight and Life Magazine*  
Incorporating the  
Xerophthalmia Club Bulletin  
and the Nutriview Newsletter

**Publisher:** *Sight and Life*  
**Editor:** Klaus Kraemer  
**Editorial team:** Jee Rah, Anne-Catherine Frey, Svenia Sayer-Ruehmann, Jane Badham

**Communication consultancy and text writing:**  
The Corporate Story

**Layout and graphics:**  
S1 Studio for Graphic Design, Augsburg

**Printer:** Burger Druck, Waldkirch

**Language services:** transparent, Berlin

Opinions, compilations and figures contained in the signed articles do not necessarily represent the point of view of *Sight and Life* and are solely the responsibility of the authors.

**Photo credits**  
cover: Mike Bloem Photography  
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page 70, 71, 72: Vanessa M Oddo  
page 77: Cornell University  
page 81: Musgrove Estate

*Sight and Life*  
Dr Klaus Kraemer  
Director  
PO Box 2116  
4002 Basel, Switzerland  
Phone: +41 (0) 61 815 8756  
Fax: +41 (0) 61 815 8190  
Email: info@sightandlife.org  
www.sightandlife.org

**ISBN** 978-3-906412-65-8

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Building bridges for better nutrition.