Emerging Societies - Coexistence of Childhood Malnutrition and Obesity
Emerging Societies – Coexistence of Childhood Malnutrition and Obesity

New Delhi, March 30–April 3, 2008

Editors
Satish C. Kalhan
Andrew M. Prentice
Chittaranjan S. Yajnik
Contents

iv Foreword

1 Global Changes in Diet and Activity Patterns as Drivers of the Nutrition Transition
   Barry M. Popkin

5 Regional Case Studies – India
   K. Srinath Reddy

9 Regional Case Studies – China
   Shi-an Yin

11 Regional Case Studies – Africa
   Andrew M. Prentice

13 Evolutionary Origins and the Impact of a Rapid Nutrition Transition
   Andrew M. Prentice

15 Prenatal Origins of Undernutrition
   Parul Christian

17 Postnatal Origins of Undernutrition
   Marc-André Prost

20 Malnutrition, Long-Term Health and the Effect of Nutritional Recovery
   Ana Lydia Sawaya

23 Epigenetic Inheritance and the Environment
   Suyinn Chong, Alyson Ashe, Nathan Oates, Marnie Blewitt, Nicola Vickaryous and Emma Whitelaw

25 Methionine in Development, Protein Restriction, and in Fatty Liver Disease
   Satish C. Kalhan
27  Adiposity and Comorbidities: Favorable Impact of Caloric Restriction
    Eric Ravussin

29  Obesity, Inflammation, and Macrophages
    Vidya Subramanian and Anthony W. Ferrante, Jr.

33  Obesity, Hepatic Metabolism and Disease
    John M. Edmison, Satish C. Kalhan and Arthur J. McCullough

36  The Imperative of Preventive Measures Addressing Lifecycle
    Chittaranjan S. Yajnik

39  New Approaches to Optimizing Early Diets
    Staffan Polberger

41  Prevention of Low Birthweight
    Dewan S. Alam

44  Community-Based Approaches to Address Childhood Undernutrition and Obesity in Developing Countries
    Prakash Shetty

47  List of Speakers
Foreword

Three Nestlé Nutrition Institute Workshops have addressed the topics of obesity and malnutrition; namely the 49th NNW in 2001 on ‘Obesity in Childhood and Adolescence’, and ‘The Malnourished Child’ and ‘Linear Growth Retardation in Less Developing Countries’ in the 1980s. Since then, the problems of malnutrition and obesity and their associated health issues have worsened. The WHO estimates that 22 million children under 5 years of age are overweight at present. In the USA the number of overweight children has doubled since 1980. Despite an overall decrease in the prevalence of stunting in developing countries since 1980, childhood malnutrition remains at a disturbingly high level and as such a major public health problem. The coexistence of these two major public health concerns lead us to organize the 63rd Nestle Nutrition Institute Workshop entitled ‘Emerging Societies – Coexistence of Childhood Malnutrition and Obesity’.

The coexistence of undernutrition (low birthweight, poor growth) alongside overnutrition (mainly obesity) is a phenomenon afflicting many countries as their economies develop and food availability increases. This phenomenon, otherwise known as the ‘nutrition transition’, is becoming increasingly prevalent in many emerging nations. To date, community-based interventions are the most widely used approaches to counteract malnutrition. However, evidence is growing that interventions targeting the improvement in maternal nutrition and health may deliver the most promising results for improving child nutrition. The nutrition transition now poses the challenge of how to balance short-term benefits versus long-term risks of increased metabolic diseases. India was cited as an example to demonstrate the magnitude of potential long-term consequences, with a 300% increase in the prevalence of diabetes amounting to an estimated 80 million cases by 2025. The contribution not only of nutritional factors, but also genetic background and epigenetic factors, to these outcomes were addressed. In this context, hypotheses such as the thrifty gene hypothesis were discussed as potential mechanisms to explain the increased susceptibility to obesity in emerging nations.
Considerable research still lies ahead in order to address the question of which population segments and at what stage(s) of their lifecycle should be targeted in order to have the most impactful results.

We are deeply indebted to the three chairpersons of this workshop: Prof. Satish Kalhan from the Case Western Reserve University in Cleveland; Prof. Andrew Prentice from the London School of Hygiene, and Prof. Chittaranjan Yajnik from the King Edward Memorial Hospital in Pune, experts recognized worldwide in their respective fields in nutrition research. Our warm thanks go also to Dr. Natalia Wagemans and her team for their excellent logistic support of the workshop and for enabling the participants to enjoy the wonderful Indian culture.

Prof. Ferdinand Haschke, MD, PhD
Chairman
Nestlé Nutrition Institute
Vevey, Switzerland

Dr. Petra Klassen, PhD
Scientific Advisor
Nestlé Nutrition Institute
Vevey, Switzerland
Global Changes in Diet and Activity Patterns as Drivers of the Nutrition Transition

Barry M. Popkin

The Nutrition Transition

The nutrition transition covers the shifts in the way we eat and move and subsequent effects on our body composition over man’s history [1]. In the 20th century, in most poor and all middle and high income countries, the populations were dominated by the emergence of nutrition-related non-communicable diseases (NR-NCDs).

The Dietary Drivers: More Fats, More Added Caloric Sweeteners, More Animal-Source Foods

Edible oil has been a major source of dietary change in the lower and middle income countries in the last several decades. The recent shift in the pattern of the nutrition transition in developing countries typically begins with major increases in the domestic production and imports of oilseeds and vegetable oils, rather than meat and milk. The global availability of soybean, sunflower, rapeseed, and palm oil has approximately tripled between 1961 and 1990 and continued to increase since then, though at a slightly reduced global pace. See table 1 for the dietary and physical activity pattern data for China.

Caloric sweeteners in 2000 were consumed on a daily basis of 306 kcal/capita across the globe. Figures that underestimate the consumption based on much higher quality diet data. The shift to caloric beverages as the source of calories is particularly important because they do not sate us and there is an emerging consensus that calories from beverages are a potential source of energy imbalance globally. This is true whether the calories come from high fat, high protein or high carbohydrate beverages.
**Table 1.** Dietary and physical activity trends of Chinese adults aged 20–45 years

<table>
<thead>
<tr>
<th></th>
<th>1989</th>
<th>2006</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Food consumption</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plant oils, g/day</td>
<td>014.8</td>
<td>030.9</td>
</tr>
<tr>
<td>All calories per capita from edible oil, %</td>
<td>004.9</td>
<td>012.4</td>
</tr>
<tr>
<td>Beef and pork, g/day</td>
<td>052.1</td>
<td>070.6</td>
</tr>
<tr>
<td>Poultry, g/day</td>
<td>004.4</td>
<td>009.3</td>
</tr>
<tr>
<td>Fish + other aquatic products, g/day</td>
<td>014.4</td>
<td>018.3</td>
</tr>
<tr>
<td>Eggs, g/day</td>
<td>009.4</td>
<td>025.1</td>
</tr>
<tr>
<td>Dairy, g/day</td>
<td>001.6</td>
<td>011.6</td>
</tr>
<tr>
<td>Total animal source foods</td>
<td>102.4</td>
<td>140.5</td>
</tr>
<tr>
<td><strong>Physical activity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adults in light level occupations, %</td>
<td>024.7</td>
<td>040.0</td>
</tr>
<tr>
<td>Households with color TV, %</td>
<td>020.5</td>
<td>095.7</td>
</tr>
<tr>
<td>Households with washing machine, %</td>
<td>036.8</td>
<td>072.8</td>
</tr>
<tr>
<td>Households with refrigerator, %</td>
<td>013.3</td>
<td>052.7</td>
</tr>
</tbody>
</table>

Source: China Health and Nutrition Survey.

*Animal source foods (ASF):* The revolution in ASF refers to the increase in demand and production of meat, poultry, fish, and milk in low-income developing countries. Most of the world’s growth in production and consumption of these foods comes from the developing countries.

**Underlying Eating Behaviors**

We have begun to see rapid shifts in the way people eat in terms of location, methods of cooking, and frequency of intake [2]. Frying is rapidly displacing more healthful cooking methods, snacking and away-from-home consumption are up significantly.

**Physical Activity Dynamics: Changes in the Technology of Work and Movement and Leisure**

Declines in physical activity are particularly profound across market work, but significant changes also have been shown in work at home, leisure, and transportation – each affecting significantly increases in obesity.

*Market work:* The proportion of individuals working in energy expenditure-intensive jobs such as farming, mining, and forestry is
way down while manufacturing has increased slightly, but the major shift is toward lower activity service sector jobs. Equally important has been a major shift in the activity of each occupation [3].

Work at home: Time in food preparation has declined over the past half century from about 2 h/day to less than a 0.5 h in the US and variable amounts elsewhere. Time-saving home technologies affect cooking, cleaning, and shopping time [3].

Transport shifts from active to passive: In most countries the proportion of individuals walking to work or shopping and other activities has declined drastically [4].

Leisure is a major global focus for obesity control but is it earned: There is little leisure time in most of our low and middle income developing countries and a key issue will be how to expand this in a healthful manner. For children, studying, computers, TV viewing and gaming are all important. For adults TV viewing is becoming more important, but its impact is poorly documented.

Figure 1 shows shifts in METS of physical activity changes for Chinese men. The changes in urban and rural areas are comparable.

References


Regional Case Studies – India

K. Srinath Reddy

As a proportion of all deaths in India by the year 2020, cardiovascular disease (CVD) will be the largest cause of disability and death [1]. At the present stage of India’s health transition, chronic diseases contribute to an estimated 53% of deaths and 44% of disability-adjusted life-years lost. India also has the highest number of people with diabetes in the world, with an estimated 19.3 million in 1995 and projected 57.2 million in 2025. On the basis of recent surveys, the Indian Council of Medical Research estimates the prevalence of diabetes in adults to be 3.8% in rural areas and 11.8% in urban areas. The prevalence of hypertension has been reported to range between 20 and 40% in urban adults and 12 and 17% among rural adults. The number of people with hypertension is expected to increase from 118.2 million in 2000 to 213.5 million in 2025, with nearly equal numbers of men and women. Over the coming decade, until 2015, CVD and diabetes will contribute to a cumulative loss of USD 237 billion for the Indian economy. Much of this enormous burden is already evident in urban as well as semi-urban and slum dwellings across India, where increasing lifespan and rapid acquisition of adverse lifestyles related to demographic transition are contributing to the rising prevalence of CVDs and its risk factors such as obesity, hypertension, and type 2 diabetes. The underlying determinants lie in socio-behavioral factors such as smoking, physical inactivity, improper diet and stress [2].

Unhealthy diets and physical inactivity are two of the main risk factors for increased blood pressure, increased blood glucose, abnormal blood lipids, overweight/obesity, and for the major chronic diseases such as CVDs, cancer, and diabetes [3]. Globally it is estimated that approximately 2.7 million deaths are attributable to low fruit and vegetable intake while 1.9 million deaths are attributable to physical inactivity. A large majority of these deaths occurs in low and middle income countries. The changes in diet and physical activity have resulted largely from epidemiological transition that is underway in most low income countries including India. The main driving forces of these
epidemiological shifts are a globalized world, rapid and uneven urbanization, demographic shifts and inter- and intra-country migrations – all of which result in alterations in dietary practices (a shift from high fiber, vegetable and fruit-rich diets to diets rich in saturated fats, trans fats and high salt-containing processed foods) and a decrease in physical activity (due to availability of mass transport systems and mechanization of daily activities). While these changes are global, India has several unique features. The transitions in India are uneven with several states in India still battling the ill effects of under nutrition and infectious diseases, while in other states with better indices of development, chronic diseases including diabetes are emerging as major areas of concern. Regional differences and urban-rural differences in the occurrence of CVD is the hallmark. There is marked heterogeneity in total energy intake in both rural and urban areas. Assam, Gujarat, Kerala, Maharashtra and Tamil Nadu have the lowest rural average caloric intake as compared to mean intakes in Punjab or Haryana (tables 1, 2).

Figures 1 and 2 show comparisons between the rural and urban averages per capita fat and protein intakes, respectively.

All these differences result in a differing prevalence of CVD and its risk factors. For example even among industrial workers and their
families who are economically better off than the general community, there are wide-ranging differences in CVD risk factors. In industries located predominantly in urban localities, CVD risk factor levels are high as compared to those in peri-urban locations \[4\]. However local

**Table 2.** Change in average calorie consumption by states – urban (kcal/capita and day)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Andhra Pradesh</td>
<td>2,143</td>
<td>2,009</td>
<td>1,992</td>
<td>2,052</td>
</tr>
<tr>
<td>Assam</td>
<td>2,135</td>
<td>2,043</td>
<td>2,108</td>
<td>2,174</td>
</tr>
<tr>
<td>Bihar</td>
<td>2,157</td>
<td>2,131</td>
<td>2,088</td>
<td>2,171</td>
</tr>
<tr>
<td>Gujarat</td>
<td>2,172</td>
<td>2,000</td>
<td>2,027</td>
<td>2,058</td>
</tr>
<tr>
<td>Haryana</td>
<td>2,404</td>
<td>2,242</td>
<td>2,140</td>
<td>2,172</td>
</tr>
<tr>
<td>Karnataka</td>
<td>1,925</td>
<td>2,124</td>
<td>2,025</td>
<td>2,045</td>
</tr>
<tr>
<td>Kerala</td>
<td>1,723</td>
<td>2,048</td>
<td>1,966</td>
<td>1,995</td>
</tr>
<tr>
<td>Madhya Pradesh</td>
<td>2,229</td>
<td>2,137</td>
<td>2,082</td>
<td>2,132</td>
</tr>
<tr>
<td>Maharashtra</td>
<td>1,971</td>
<td>2,028</td>
<td>1,989</td>
<td>2,039</td>
</tr>
<tr>
<td>Orissa</td>
<td>2,275</td>
<td>2,219</td>
<td>2,251</td>
<td>2,298</td>
</tr>
<tr>
<td>Punjab</td>
<td>2,783</td>
<td>2,100</td>
<td>2,089</td>
<td>2,197</td>
</tr>
<tr>
<td>Rajasthan</td>
<td>2,357</td>
<td>2,255</td>
<td>2,184</td>
<td>2,335</td>
</tr>
<tr>
<td>Tamil Nadu</td>
<td>1,841</td>
<td>2,140</td>
<td>1,922</td>
<td>2,030</td>
</tr>
<tr>
<td>Uttar Pradesh</td>
<td>2,161</td>
<td>2,043</td>
<td>2,114</td>
<td>2,131</td>
</tr>
<tr>
<td>West Bengal</td>
<td>2,080</td>
<td>2,048</td>
<td>2,131</td>
<td>2,134</td>
</tr>
</tbody>
</table>

Source: Chandrashekar and Ghosh \[5\].

![Fig. 1. Average all-India per capita fat consumption (g/day). Source: FAO \[6\].](image)

families who are economically better off than the general community, there are wide-ranging differences in CVD risk factors. In industries located predominantly in urban localities, CVD risk factor levels are high as compared to those in peri-urban locations \[4\]. However local
dietary practices may alter the prevalence. For example, tea garden workers of Assam receive extra salt as compensation for the putative loss of sodium due to their outdoor work. This has resulted in high prevalence of high blood pressure though other CVD risk factors are similar to other industrial populations which are predominantly located in peri-urban areas.

Therefore while studying nutrition and physical activity shifts in India, the marked heterogeneity and secular changes in dietary and physical activity practices should be taken into account. This principle should also apply to strategies, policies and nutrition and physical activity guidelines so that they take regional differences into account.

References

3 WHO 2007
6 FAO 2003.
The status of childhood malnutrition and obesity in China is reviewed according to the 2002 National Nutritional and Health Survey in China [1–3] and data from a national survey on the health and physical fitness of Chinese students in 2005 [4]. Between 1979 and 2008 a rapid change in economic development has been seen in China, and characteristic of this transition period is the significant increase in the prevalence of chronic non-communicable diseases. Compared with the results in 1992, the body weight and height of preschool children in urban and rural areas were significantly improved; the prevalence of malnutrition (underweight and stunting) in urban and rural areas was significantly reduced; the national average prevalence of overweight and obesity for the children under 6 years was 3.4 and 2.0%, respectively, as estimated by the Chinese and WHO standards (fig. 1, 2) [1, 5]; a deficiency in micronutrients, including calcium, zinc, vitamin A, vitamin B₁, and B₂, is rather common in the preschool and school children. The current data show that the growth and development of Chinese

![Fig. 1.](image-url)
children is far from ideal. We are now facing double challenges: malnutrition and the increase in overweight and obesity in children.

References


Africa is the final continent to be affected by the nutrition transition and, like others that have passed through this phase previously, is characterized by the paradoxical coexistence of malnutrition and obesity. This is vividly apparent by a visit to almost any major hospital in urban Africa where children’s wards are struggling to rehabilitate severely malnourished children whilst neighboring adult wards are dealing with amputations of diabetic feet and other consequences of obesity-related comorbidities.

In sub-Saharan Africa, progress towards meeting one of the key indicators of the first Millennium Development Goals – the proportion of underweight children – is slow and in several countries is in reverse. Current projections indicate that Africa will not meet its target by 2015. Africa is still the home of the most acute nutritional emergencies with unacceptably high levels of severe-acute malnutrition in many regions of conflict and in countries failed by their political leaders.

Proportions of the adult population with a body mass index of <18.5 (set as the definition of chronic energy deficiency) are substantial, but less than in many South Asian countries, and are a lesser concern. Adult height is also greater than in many Asian countries. In mothers the larger adult stature than in the Indian sub-continent is accompanied by larger mean birthweights and a lower proportion of low birthweight babies. This may be significant in terms of the rate at which Africa can emerge from the nutrition transition. It is arguable that Africa will suffer a lesser burden of chronic disease than Asia in which the ‘Developmental Origins of Health and Disease’ thesis predicts a major future burden of chronic disease based upon the mismatch between the fetal and adult nutritional environment.

Yet obesity rates in Africa are escalating fast. The increase is especially rapid in urban areas, though the trends are by no means confined to Africa’s cities. There are several features of the obesity epidemic in Africa that mirror those in other emerging nations: it penetrates the richer nations first (in Africa these tend to be in North Africa); it
penetrates urban areas first with a strong urban-rural gradient, but this diminishes with time; initially it affects the wealthy, but later there is a demographic switch and obesity becomes a condition more associated with poverty (as in Western nations), and it shares many of the same drivers related to the increasing affordability of highly refined oils and carbohydrates, and a move away from subsistence farmwork and towards sedentary lifestyles.

Africa also has some characteristics of the obesity epidemic that stand out from other regions as follows. (1) Africa is probably the only region in which obesity (especially among women) is viewed culturally as a positive and desirable trait. This leads to major gender differences in obesity rates in many countries, and fuels a syndrome of intentional weight gain in young women. (2) Most of Africa has very low rates of obesity in children. To date African obesity is mostly an adult syndrome. (3) Africans seem genetically prone to higher rates of diabetes and hypertension in association with obesity than Caucasians, but seem to be relatively protected from dyslipidemias. (4) The case-specific deaths and disabilities from diabetes and hypertension in Africa are very high due to the paucity of health services and the strain that the ‘double burden’ of disease places on health systems. (5) Recent data suggest that some non-African races may have evolved recently to select genetic traits that offer them some protection from obesity and diabetes, but that these traits have not been under positive selection in Africans.
Evolutionary Origins and the Impact of a Rapid Nutrition Transition

Andrew M. Prentice

There are many obvious and plausible reasons (and some less obvious ones) that may account for the rapid increase in obesity rates in developing and emerging nations. Changes in diet and activity patterns brought about by the economic transition have been previously discussed in this symposium by Popkin. In later papers we will explore the possibility that undernutrition in fetal and early life can reset the metabolic phenotype in ways that make people especially vulnerable to the influences of an obesogenic environment if they escape from the frugality of a subsistence living.

This paper seeks to answer whether people from developing countries may have a genetic predisposition to obesity and its most common clinical outcome, type 2 diabetes mellitus (T2DM).

The concept of ‘thrifty genes’, first proposed by Neel [1] in the 1960s, has been prominent amongst the various theories proposed to explain the sudden rise in global obesity levels in the late 20th century. The basic premise of the thrifty gene hypothesis is that an ability to rapidly deposit energy as body fat in times of plenty would have assisted individuals to survive periods of starvation, and hence would have been under positive natural selection. Many of the earlier proponents of the theory used it to explain why certain populations had very high levels of obesity and diabetes. For instance, it was suggested that modern Polynesian Islanders are the product of a small founder group that had survived starvation during the long sea journeys across the Pacific as the islands were first colonized.

Contemporary interpretations of the thrifty gene story [2] propose that: (a) almost all ancient populations have been frequently subjected to selective pressure by famine, especially since the dawn of agriculture, and hence thriftiness is likely to affect all racial groups in some form; (b) that transmission is unlikely to have been strongly selected by mortality within famines (viability selection) and is much more likely to have been due to fertility selection mediated through the
powerful effects of regular annual hungry seasons, or episodic starvation, on female fecundity, and (c) that the concept of thriftiness (which is generally interpreted in relation to saving of energy) should also encompass an element of the ‘greedy gene’ since disregulated appetite control systems are the most common cause of the genetically based human obesity syndromes so far identified.

It must be stressed that the thrifty gene concept lacks any experimental validation to date and that there are no data to suggest that racial and ethnic groups currently undergoing the nutrition transition (e.g. native Africans and Asians) have a particular genetic predisposition to obesity. However the latest findings in relation to the FTO gene (the first of the multigenic contributors to human obesity to be identified with certainty) strongly suggest that the variant that promotes leanness is only carried by Caucasians. This may be in line with Diamond’s [3] suggestion that Caucasians have been selected to have a lower susceptibility to T2DM, though the likely origins of such putative selection remain a mystery.

Exciting times lie ahead with respect to understanding whether or not evolution has endowed any of us with particular susceptibility to obesity. New statistical methods for comparing genome-wide scans between different ethnic/racial groups are starting to pinpoint those genes that show evidence of recent differential selection. These will soon assist in interpreting whether past famines and food scarcity have created specially vulnerable populations.

Whether such knowledge would ever influence the public health messages and government initiatives required to combat obesity remains a moot point. We already have strong evidence that urban populations in developing countries do exhibit high levels of obesity, and this fact alone should drive the public health agenda.

References
Prenatal Origins of Undernutrition

Parul Christian

Childhood undernutrition including stunting and wasting continues to be high in many regions of the developing world. Overall, 178 million children under 5 years of age throughout the developing world are estimated to be stunted and 19 million are severely wasted. Birthweight, a common proxy measure of intrauterine growth, is commonly low in the same regions of the world where childhood undernutrition exists. Low birthweight (<2.5 kg) caused either by preterm birth or intrauterine growth restriction affects immediate survival and function and is a determinant of later life risk of chronic diseases including type 2 diabetes and cardiovascular diseases. Birth size is influenced by numerous prenatal factors including maternal nutritional, environmental and lifestyle exposures during pregnancy and infection. Maternal pre-pregnancy weight and height are independently and directly associated with birthweight and are also known to modify the effects of pregnancy weight gain and interventions during pregnancy on birthweight and perinatal mortality. Few studies have examined nutritional interventions beginning in the pre-periconceptional phase for outcomes such as gestational duration and birthweight. Maternal diet during pregnancy, specifically of micronutrient-rich foods such as milk, and fruits and vegetables, may also enhance birth outcomes. Other prenatal factors commonly known to impact birthweight in developing countries include maternal age, parity, sex, and birth interval. In many settings early marriage and pregnancy are a norm resulting in a substantial proportion of pregnancies occurring during adolescence when competition for nutrients for growth of the mother and the fetus is high, especially in environments where food availability is low. Lifestyle factors such as physical activity and maternal stress, as well as environmental toxicants have variable influences on birth outcomes. Tobacco and other substance use can reduce gestational duration and be deleterious to fetal growth. Infections, specifically ascending reproductive tract infections, malaria and, increasingly, HIV can cause preterm and intrauterine growth restriction (IUGR) in many settings. Few
studies have examined the contribution of birthweight and prenatal maternal nutritional status to childhood stunting and wasting. Studies have generally found adjusted odds ratios for low birthweight ranging between 2 and 5. In other words, after adjusting for determinants of childhood undernutrition including feeding practices and morbidity, being born low birthweight continues to carry a two- to fivefold increased risk of stunting in many developing country settings. Even fewer studies have examined birth length or maternal nutritional status as risk factors. More research is needed to determine the proportion of childhood undernutrition attributable to IUGR in different settings in order to better target interventions to appropriate life stages for combating childhood undernutrition.
Emerging countries are undergoing a rapid nutrition transition. Non-communicable diseases are the leading causes of death, but underweight together with iron, zinc and vitamin A deficiencies are still among the 15 biggest killers. Undernutrition impairs physical growth, increases morbidity and mortality, impairs cognitive development, reduces economic productivity, and, later, increases the risk of chronic diseases and impacts on offspring birthweight. In this chapter I review how inadequate nutrition, infection, and inappropriate mother–child interactions are the main drivers of undernutrition in childhood. Underlying socioeconomic, environmental and genetic factors are also explored. Some perspectives on how urbanization and globalization may affect undernutrition are discussed.

Globally, length starts to falter immediately after birth while weight starts faltering around 3–6 months, suggesting very different etiologies [1]. Breast milk provides enough energy and protein for growth during the first 6 months. In deficient populations, infants’ micronutrient stores at birth and intakes through breast milk may not suffice to cover the needs for optimal linear growth. Among the 2–5 months age group, early introduction of complementary foods affects both weight and length growth by reducing the quality and quantity of the diet, and increasing infection incidence. Beyond 6 months of age, complementary foods fail to provide enough energy and other nutrients to meet the increasing needs for growth and activity. Poor energy intakes are associated with wasting while micronutrient imbalances affect linear growth. Iron and zinc have been consistently identified as ‘problem nutrients’ in the 6–23 months age group worldwide [2].

Infections are strongly associated with growth faltering. Diarrheal diseases show the strongest association with short-term weight deficit. Other acute and chronic infections impact differently on growth. Effects are greater in high prevalence settings as well as in nutritionally compromised children [3]. The severity, duration, frequency, and type of infection are key factors mediating the effect on growth by
increasing nutrient requirements, losses, and impairing intakes and absorption.

Care provided to children, defined by maternal endogenous factors and societal determinants, affects growth [4]. Maternal influences include education, health status, and self-confidence. Between maternal and societal determinants are maternal workload, time availability, and maternal autonomy and control of resources. The level of social support received by mothers also impacts on care quality.

Factors at the national level explain most of the undernutrition variability between countries, including lower energy availability, lower female literacy rates, lower gross domestic product, or lower vaccination coverage [5]. Other factors consistently correlated with undernutrition include access to safe water, healthcare, sanitation, but also parity, birth spacing, birth order, and marital status. Maternal size at birth has been shown to influence birth size in their offspring, suggesting a transgenerational effect of undernutrition [6]. Weight and length show marked seasonal variations in agro-pastoral communities. Weight variations have been correlated with the timing of lowest food availability and periods of highest diarrhea incidence in many countries.

**Fig. 1.** Worldwide timing of growth faltering. Mean anthropometric z scores by age relative to the NCHS reference (0–59 months) in 39 nationally representative surveys conducted in Latin America, Asia, and Africa from 1987 to 1997. Reproduced with permission from Shrimpton et al. [1].
In 2008 the proportion of the urban population will equal the rural population. In developing countries more than 30% of the urbanized live in shanty towns, meaning higher transmission rates of infections due to a lack of water, poor housing conditions, overcrowding, poor hygiene, and environmental pollution. Urbanization also affects behavior. For instance the duration of breastfeeding is lower in urban than rural settings. Although trade globalization has meant greater food availability, it has also increased the vulnerability to global price fluctuations. Nowadays a booming demand for oil and food commodities from emerging countries drives global prices up. How it will affect the poorest countries is unknown, but they surely are ill equipped to face a global competition for dwindling resources.

The burden of child undernutrition remains so great that there is a renewed moral urgency to find integrated solutions to tackle the problem. Over- and undernutrition are now seen as different manifestations of a global phenomenon. Since they are linked, fighting undernutrition should impact positively on both outcomes.

References

Malnutrition, Long-Term Health and the Effect of Nutritional Recovery

Ana Lydia Sawaya

Worldwide malnutrition is responsible for 50% of deaths in childhood. The prevailing type of malnutrition is stunting, which stands out as an indicator not only of malnutrition, but also of poverty. The causes for stunting are: insufficient nutrition of the mother; intrauterine malnutrition; lack of breastfeeding until the child is 6 months old; late introduction of complementary foods; inadequate quantity and quality of complementary foods, and nutrient absorption impaired by infections and intestinal parasitic diseases. The data on malnourished children being treated at a center for recovery from malnutrition in São Paulo, Brazil (CREN), showed that over 70% were born with low or insufficient weight. CREN is a center that offers treatment to slum children with mild to severe malnutrition. Pediatricians, nutritionists, social workers and psychologists participate in the treatment. The pediatrician monitors the clinical status, laboratory findings and anthropometric progress of each child. The nutritionist follows the child’s diet and corrects the problems identified during treatment. Laboratory tests (blood and stools) are done in each semester. The children also receive Fe and vitamin (A, B, C and D) supplements in prophylactic doses. The children are either treated in an outpatient clinic or in a day-hospital. The children treated in the day-hospital are more severely malnourished. Data from CREN showed that, among the moderately malnourished children under treatment, about 80% had at least one infectious episode in the previous month and, among the severely malnourished ones, that prevalence rose to about 90%. The difference in the severity of malnutrition referred mainly to the rate of infections. 60% of these children also had parasites. Another very common occurrence was anemia, which was verified in 62% of them.

It was estimated that 51.7 million people lived in slums in Brazil in 2003. This population is growing faster than the urban one. This condition is associated with poor sanitation, bad food habits, lower birthweight and stunting. Longitudinal and cross-sectional studies in
Stunted adolescents have shown the high susceptibility to gain central fat, lower fat oxidation and lower resting and postprandial energy expenditure. In addition, higher blood pressure, higher plasma uric acid and impaired flow-mediated vascular dilation were all associated with a higher level of hypertension in low birthweight and stunted children. Stunted boys and girls also showed lower insulin production by pancreatic \( \beta \) cells. All these factors are linked with a higher risk of chronic diseases later in life. Among stunted adults alterations in plasma lipids, glucose and insulin were also present.

Combining all these findings we can say that insufficient consumption during growth causes stress in the organism, leading to an increase in the cortisol-to-insulin ratio. As is well known, malnutrition is a powerful stress stimulator and causes an increase in the cortisol levels and its catabolic action, to direct energy as glucose to brain. Besides, food deficiency reduces the anabolic action of tissue synthesis that depends on insulin, causing wasting. That hormonal balance leads to a reduction in the hormone responsible for growth, insulin-like growth factor-1 (IGF-1). The high cortisol-to-insulin ratio and low IGF-1 also reduce muscle mass gain and linear growth, besides increasing the waist-to-hip ratio and reducing body fat oxidation. If a child in that condition starts to ingest a ‘modern’ diet and presents physical inactivity due to urban living conditions, an excessive fat gain will take

---

**Fig. 1.** Association between short stature, obesity, hypertension and diabetes.
place, which can result in an association between stunting, obesity, hypertension and diabetes (fig. 1).

Recent studies in children who had an adequate nutritional recovery with linear catch-up growth, after treatment in the nutritional rehabilitation center, CREN, showed that the alterations in body composition, bone density and insulin production (found in non-treated stunted children) were no longer apparent.
Epigenetic Inheritance and the Environment

Suyinn Chong, Alyson Ashe, Nathan Oates, Marnie Blewitt, Nicola Vickaryous and Emma Whitelaw

Hypothesized as a possible interface between the genetic and environmental factors that give rise to phenotype, the field of epigenetics is being heralded as the explanation for hitherto poorly understood instances of non-Mendelian inheritance. There exists a small group of genes, known as metastable epialleles, which are sensitive to environmental influences, such as diet, and undergo molecular changes that remain for the life of the individual. These modifications are called epigenetic and in some cases they survive across generations, that is, through meiosis. This is termed transgenerational epigenetic inheritance. These findings have led to the temptation to infer similar processes in humans. Although it seems clear that the lifestyle of one generation can significantly influence the health of the next generation in humans, in the absence of supporting molecular data, it is hard to justify the idea that this is the result of transgenerational epigenetic inheritance in the light of other, more plausible explanations. What is required first is to identify genes that are sensitive to the epigenetic state, that is, metastable epialleles, in humans. Methods are emerging by which we can do this. In light of the paucity of evidence, when extrapolating results seen in mice to humans, we should proceed with caution.
Fig. 1. Chromatin proteins and epigenetic modifications attached to the double-stranded DNA.
Methionine in Development, Protein Restriction, and in Fatty Liver Disease

Satish C. Kalhan

The coexistence of intrauterine and neonatal malnutrition, and the development of obesity and type 2 diabetes in adults, has been confirmed in a number of studies in humans and animal models. Although the exact mechanism of such imprinting has not been understood, data from animal studies suggesting hypermethylation of the genomic DNA suggest that epigenetic changes may be responsible for such patterning [1]. Since DNA methylation is affected by the availability of the methyl groups, derangements in one carbon (methyl) metabolism and of methionine induced by nutritional and environmental perturbations can impact the expression of certain genes at vital moments during development.

Methionine, an essential amino acid, plays a critical role in the one-carbon metabolism in vivo. Methionine is metabolized first by the ubiquitous transmethylation (‘methionine’) cycle, wherein the methyl groups from methionine and from folate-dependent one-carbon pool participate in methyltransferase reactions [2]. The catabolic pathway of methionine involves the transsulfuration sequence, resulting in the synthesis of cysteine, which then participates in the formation of glutathione – a major intracellular antioxidant. Metabolism of methionine is regulated by nutrients, folate, cobalamin, pyridoxine, protein intake, and by insulin and glucagon.

Methionine metabolism has not been examined in detail during pregnancy and in the fetus. Data from studies in human pregnancy show a progressive decline in plasma homocysteine concentration during pregnancy and an increase in plasma choline concentration [3]. In addition, the umbilical arteriovenous concentration gradient suggests fetal uptake and utilization of homocysteine. Finally, it is significant to note that hepatic transsulfuration is not active in the human fetus and appears for the first time after birth. Preliminary data from our studies
in the rat, using the commonly employed model of intrauterine growth restriction, show that as a result of dietary protein restriction, major changes in the plasma amino acid pattern are accompanied by down-regulation of the methionine transsulfuration pathway [4]. Gene-array studies showed a marked increase in the pathway of serine synthesis. The impact of these changes on fetal growth and specific epigenetic changes remains to be determined.

In human adults, obesity and fatty liver disease are also accompanied by changes in methionine metabolism, resulting in a lower plasma concentration of glutathione and an increase in the plasma concentration of homocysteine and cysteine. A significant correlation between insulin resistance and plasma glutathione and cysteine was observed. A significant association between MTHFR 677C>T homozygosity, which may impact folate metabolism, and non-alcoholic fatty liver disease was observed [5].

Perturbations in methionine metabolism, as a result of nutrient/environment interactions early in life or as a result of hepatic dysfunction in adult life, may play a key role in metabolic patterning during development and propagation of the disease process in adults.

References

5 Edmison JM, Dasarathy S, Kalhan SC, McCullough AJ: Severity of non-alcoholic fatty liver disease is related to MTHFR 677C>T homozygosity, lower glutathione and insulin resistance. Hepatology 2007;46:749A.
Adiposity and Comorbidities: Favorable Impact of Caloric Restriction

Eric Ravussin

The focus of my presentation will be on research involving long-term calorie restriction (CR) to prevent or delay the incidence of the metabolic syndrome with age. The current societal environment is marked by overabundant accessibility of food coupled with a strong trend to reduced physical activity, both leading to the development of a constellation of disorders including central obesity, insulin resistance, dyslipidemia and hypertension (metabolic syndrome).

Prolonged CR has been shown to extend median and maximal lifespan in a variety of lower species (yeast, worms, fish, rats, and mice). Mechanisms of this lifespan extension by CR are not fully elucidated, but possibly involve alterations in energy metabolism, oxidative damage, insulin sensitivity, and functional changes in neuroendocrine systems. Ongoing studies of CR in humans now makes it possible to identify changes in ‘biomarkers of aging’ to unravel some of the mechanisms of its anti-aging phenomenon.

Analyses from controlled human trials involving long-term CR will allow investigators to link observed alterations from body composition down to changes in molecular pathways and gene expression, with their possible effects on the metabolic syndrome and aging.

A summary of the physiological and psychological/behavioral responses to 6 months of CR in humans from the Pennington CAL-ERIE randomized clinical trial are summarized in table 1.
<table>
<thead>
<tr>
<th>Physiological responses</th>
<th>Psychological/behavioral responses</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Body composition</strong></td>
<td>Development of eating disorder symptoms</td>
</tr>
<tr>
<td>↓ Fat mass</td>
<td>↓ Disinhibition</td>
</tr>
<tr>
<td>↓ Fat-free mass</td>
<td>↓ Binge eating</td>
</tr>
<tr>
<td>↓ Abdominal fat (visceral and subcutaneous)</td>
<td>↓ Concern about body size and shape</td>
</tr>
<tr>
<td>↓ Abdominal fat cell size</td>
<td></td>
</tr>
<tr>
<td>↓ Intra-hepatic lipid content</td>
<td>↔ Fear of fatness</td>
</tr>
<tr>
<td>↔ Intra-myocellular lipid content</td>
<td>↔ Purgative behavior</td>
</tr>
<tr>
<td><strong>Diabetes risk factors</strong></td>
<td>Depressed mood</td>
</tr>
<tr>
<td>↓ Insulin sensitivity (not significant)</td>
<td>↓ MAEDS Depression scale</td>
</tr>
<tr>
<td>↓ Acute insulin response to glucose</td>
<td>↔ Beck Depression Inventory II</td>
</tr>
<tr>
<td><strong>Cardiovascular disease risk</strong></td>
<td>Subjective feelings of hunger</td>
</tr>
<tr>
<td>↓ 10-year risk</td>
<td>↓ Eating Inventory, Perceived Hunger Scale</td>
</tr>
<tr>
<td>↓ Blood pressure</td>
<td></td>
</tr>
<tr>
<td>↑ HDL-C</td>
<td></td>
</tr>
<tr>
<td>↓ Triacylglycerol</td>
<td></td>
</tr>
<tr>
<td>↓ Factor VIIc</td>
<td></td>
</tr>
<tr>
<td>↔ Fibrinogen, homocysteine, endothelial function</td>
<td></td>
</tr>
<tr>
<td><strong>Biomarkers of longevity</strong></td>
<td>Quality of life</td>
</tr>
<tr>
<td>↓ Fasting insulin</td>
<td>↑ Physical functioning</td>
</tr>
<tr>
<td>↓ Core body temperature</td>
<td>↔ Vitality</td>
</tr>
<tr>
<td>↔ DHEA-S</td>
<td></td>
</tr>
<tr>
<td><strong>Energy expenditure</strong></td>
<td>Cognitive performance</td>
</tr>
<tr>
<td>↓ 24-hour sedentary energy expenditure</td>
<td>↔ Verbal memory</td>
</tr>
<tr>
<td>Metabolic adaptation for 24-hour energy expenditure</td>
<td>↔ Short-term memory and retention</td>
</tr>
<tr>
<td>↓ Sleeping metabolic rate (SMR)</td>
<td>↔ Visual perception and memory</td>
</tr>
<tr>
<td>Metabolic adaptation for SMR</td>
<td>↔ Attention/concentration</td>
</tr>
<tr>
<td><strong>Endocrinology</strong></td>
<td></td>
</tr>
<tr>
<td>↓ T3</td>
<td></td>
</tr>
<tr>
<td>↓ T4</td>
<td></td>
</tr>
<tr>
<td>↔ GH</td>
<td></td>
</tr>
<tr>
<td>↔ IGF-1</td>
<td></td>
</tr>
<tr>
<td>↓ Ghrelin</td>
<td></td>
</tr>
<tr>
<td><strong>Physical activity</strong></td>
<td></td>
</tr>
<tr>
<td>↓ Physical activity level (TDEE adjusted for SMR)</td>
<td></td>
</tr>
<tr>
<td>↔ Spontaneous physical activity</td>
<td></td>
</tr>
</tbody>
</table>

Table 1.
The incidence of obesity has dramatically increased worldwide and is associated with numerous clinical pathologies. Particularly concerning is the rapid increase in obesity and associated comorbidities in children. White adipose tissue not only stores excess calories as energy but is an active endocrine organ that regulates metabolic and immunological processes in the body. In recent years it has become clear that obesity is associated with chronic low grade inflammation that involves activation of inflammatory signaling pathways, increased production of cytokines and acute-phase proteins. This state of systemic inflammation is thought to be a common denominator for the development of many metabolic complications of obesity. The inflammatory response in obesity seems to originate predominantly from adipose tissue though other organs like liver may also be involved during progression of the disease. In both obese humans and rodents, adipose tissue expression and secretion of numerous inflammatory cytokines and acute phase proteins including tumor necrosis factor-α (TNF-α), monocyte chemoattractant proteins (MCPs), interleukin-6 (IL-6), and plasminogen activator inhibitor-1 (PAI-1) are significantly increased [1]. Studies show that elevated circulating concentrations of proinflammatory factors predict the development of insulin resistance and other metabolic complications of obesity.

Adipose tissue is a heterogeneous organ consisting of adipocytes and the non-adipocyte stromal vascular cells. Numerous studies have shown an unexpected role for immune cells, particularly macrophages within the stromal vascular fraction of adipose tissue in the development and progression of systemic inflammation. Gene expression analyses revealed that most of the proinflammatory factors secreted by adipose tissue are predominantly expressed by macrophages in the adipose tissue [2]. Furthermore, in obesity not only is the number of macrophages increased but the character of macrophages from adipose tissue of obese subjects is more inflammatory. These macrophages are
Fig. 1. Adipose tissue macrophages in obesity-induced inflammation. 

a In lean animals the macrophage content is low in adipose tissue. These macrophages express low amounts of inflammatory factors including tumor necrosis factor alpha (TNF-α), interleukin 6 (IL-6), and plasminogen activator inhibitor-1 (PAI-1) and high levels of anti-inflammatory factors including interleukin-10 (IL-10). 

b Obesity increases monocyte adhesion and recruitment to adipose tissue consequently increasing macrophage number in adipose tissue. The macrophages in obese adipose tissue express increased amounts of inflammatory factors including TNF-α, IL-6, and PAI-1 and decreased amounts of IL-10. The inflammatory molecules act locally in a paracrine fashion to alter adipocyte function and adipokine production.
bone marrow derived and their number in adipose tissue is strongly correlated with body weight, body mass index and total body fat [3]. Macrophages actively recruited during weight gain are phenotypically different from resident adipose tissue macrophages. Resident macrophages in the adipose tissue of lean individuals produce relatively low levels of inflammatory molecules including TNF-α, PAI-1, and IL-6 (fig. 1a). In contrast, the recruited macrophages in adipose tissue express high levels of inflammatory molecules that contribute to systemic inflammation and insulin resistance (fig. 1b).

The recruitment of bone marrow-derived circulating monocytes to adipose tissue is a complex process under the control of various chemokines, cytokines, and other local factors [2]. In obesity, among the inflammatory molecules whose expression is increased is the MCPs family that binds a common receptor C-C chemokine receptor-2 (CCR2). CCR2 is expressed on circulating monocytes, and is important in many forms of inflammation that involve macrophage accumulation, including bacterial infections, autoimmune diseases and atherosclerosis. In obese rodents, the genetic deletion or pharmacological antagonism of CCR2 decreases macrophage accumulation in adipose tissue and improves obesity induced inflammation and insulin resistance [3]. In obesity, adipocytes also increase secretion of factors that enhance the adhesion and transmigration of monocytes into adipose tissue as well as their survival. Macrophage colony-stimulating factor (CSF-1), a key factor for the proliferation, differentiation, and survival of monocytes and macrophages, is significantly increased in obese adipose tissue. Additionally, obesity-induced increase in adipocyte death secondary to hypertrophy is also thought to play a role in recruiting macrophages [4]. However, further studies are required to identify the exact signals that turn on macrophage recruitment and inflammation in obese adipose tissue.

Macrophage accumulation and adipose tissue inflammation are dynamic process under the control of multiple mechanisms. Interventions aimed at either reducing macrophage numbers or decreasing their inflammatory characteristics improve insulin sensitivity and decrease inflammation. Investigating the role of macrophages in adipose tissue biology and the mechanisms involved in their recruitment and activation in obesity will provide useful insights for developing new therapeutic options to treat obesity-induced complications.

References


Nonalcoholic steatohepatitis (NASH), the most severe form of nonalcoholic fatty liver disease (NAFLD), is emerging as a common and clinically important type of chronic liver disease in industrialized countries. Rates are rapidly increasing in developing countries as well [1]. NAFLD and obesity should be regarded as a global health problem of increasing dimensions (table 1).

The prevalence of NAFLD and its most severe form, NASH, are estimated to be 30 and 7–8%, respectively, in the Western world [2] (table 2).

NASH is a progressive fibrotic disease in which cirrhosis and liver-related death occur in up to 20 and 12%, respectively, over a 10-year period [3]. NASH-associated cirrhosis can also decompensate into subacute liver failure, progress to hepatocellular carcinoma and recur post-transplantation. In contrast, steatosis alone has a more benign course [1, 3].

Table 1. Prevalence of obesity (%) in Asia using WHO criteria for Asians

<table>
<thead>
<tr>
<th>Country</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>China</td>
<td>12</td>
<td>14</td>
</tr>
<tr>
<td>Japan</td>
<td>24</td>
<td>20</td>
</tr>
<tr>
<td>Malaysia</td>
<td>24</td>
<td>18</td>
</tr>
<tr>
<td>Philippines</td>
<td>13</td>
<td>15</td>
</tr>
<tr>
<td>Taiwan</td>
<td>18</td>
<td>16</td>
</tr>
<tr>
<td>Thailand</td>
<td>17</td>
<td>20</td>
</tr>
</tbody>
</table>
Table 2. Unadjusted and age-adjusted prevalence (%) of the metabolic syndrome among US adults aged ≥20 years

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Original NCEP/ATP III definition</th>
<th>Revised NCEP/ATP III definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>6,436</td>
<td>1,677</td>
<td>23.1 (0.9) 26.7 (1.5)</td>
</tr>
<tr>
<td>Age adjusted</td>
<td>6,436</td>
<td>1,677</td>
<td>24.1 (0.8) 27.0 (1.5)</td>
</tr>
<tr>
<td>Men</td>
<td>3,069</td>
<td>841</td>
<td>22.9 (1.4) 24.1 (2.1)</td>
</tr>
<tr>
<td>Unadjusted</td>
<td>3,069</td>
<td>841</td>
<td>24.6 (1.4) 25.2 (2.1)</td>
</tr>
<tr>
<td>Age adjusted</td>
<td>2,188</td>
<td>28.3</td>
<td>10.2 (1.7) 10.7 (1.9)</td>
</tr>
<tr>
<td>20–39 years</td>
<td>841</td>
<td>234</td>
<td>29.3 (2.4) 33.0 (3.8)</td>
</tr>
<tr>
<td>40–59 years</td>
<td>1,010</td>
<td>324</td>
<td>42.6 (2.4) 39.7 (4.3)</td>
</tr>
<tr>
<td>60 years</td>
<td>988</td>
<td>305</td>
<td>43.9 (2.0) 46.1 (3.7)</td>
</tr>
</tbody>
</table>

Data are percent (SE). According to Ford [6].
There is a strong link between NAFLD/NASH and the metabolic syndrome and, in particular, obesity. It should be emphasized that obesity (defined by BMI) differs between Western and Asian societies, being >30 and >25, respectively. Assessment of central adiposity is extremely important in ‘lean’ people. Although there are a number of potential pharmacological therapies being developed, diet and exercise should be the initial options for the management.

Public health initiatives are imperative to halt or reverse the ‘diabesity’ epidemic, which is the underlying cause of NAFLD. A number of important and unresolved issues must be clarified before the true epidemiology and natural history of NAFLD/NASH can be fully understood; this is particularly so in developing countries [4, 5].

References

The Imperative of Preventive Measures Addressing Lifecycle

Chittaranjan S. Yajnik

The epidemiological characteristics of chronic non-communicable diseases (NCDs) are changing fast. The prevalence has risen to unprecedented levels, and the young and the underprivileged are increasingly affected. The classic view of the etiology of NCDs consists of a genetic susceptibility which is precipitated by aging and modern lifestyle. In a virtual absence of any methods to tackle genetic susceptibility, the preventive approach has so far focused on control of lifestyle factors in those at high risk (the elderly and those with a positive family history and elevated risk factors). Thus diet and physical activity modification have been claimed to ‘prevent diabetes’, while some trials have used pharmacological agents. Such an approach might help high risk individuals but is unlikely to curtail the burgeoning epidemic of obesity and diabetes which is rapidly spreading to the young.

Recent research has suggested that susceptibility to NCDs originates in early life through non-genetic mechanisms (fetal programming), and tackling these may offer a unique opportunity to curtail this epidemic. Size at birth and childhood growth characteristics are strong risk factors for NCDs. Both low and high birthweight and rapid childhood growth (including early adiposity rebound) predict adult diabetes and related disorders. Children born small but having grown big have the highest levels of risk factors (fig. 1). This has led to the new paradigm of ‘Developmental Origins of Health and Disease’ (DOHaD), applicable to a number of conditions which make up the modern day NCD epidemic (diabetes, hypertension, coronary artery disease, cancer, etc.). This new paradigm shifts our attention to the intrauterine and childhood environment, in addition to regulating lifestyle factors in adults. This philosophy is part of the ‘life course’ model of NCD (fig. 2). It is easy to appreciate the importance of the intrauterine period in the life cycle if we remember that over three fourths of cell divisions are over before we are born, and that a newborn human is almost a miniature adult.
There has been intense research in humans and animal models of the factors which regulate growth and which might contribute to the DOHaD. The mechanisms involved in fetal programming are only beginning to be understood. Maternal nutrition and metabolism, and placental function are all involved. Periconceptional maternal nutrition (for example, vitamin B₁₂ and folate) is an important determinant of not only neural tube growth but also of body composition and the metabolic characteristics of the offspring. Thus, there are windows of opportunity in the early life to improve the health of the individual. Research has also pointed towards genetic factors which affect growth.

Fig. 1. Insulin resistance. Source: Bavdekar et al. [5].

Fig. 2. The WHO life course model suggests that non-communicable diseases have their origins in early life. The risk progressively accumulates throughout the life course and disease manifests in later life. According to WHO/NMH/NPH 2001.
and disease susceptibility (fetal insulin hypothesis). The focus is likely to be on the environmental regulation of the expression of such genes during crucial phases of development (epigenetics). One such mechanism is methylation of regulatory portions of the genome which may be modified by the availability of methyl groups in the diet (nutritional programming), so elegantly shown in Agouti mice. Intergenerational transmission of such epigenetic changes explains some of the observations on transmission of phenotypes which otherwise could be mistaken for ‘genetic’ effects.

Thus, improving the early life environment offers a new and exciting opportunity to control the NCD epidemic by influencing the susceptibility in a more durable manner than only controlling lifestyle factors in adult life. The imperative is to address the life cycle rather than concentrate on the end stages.

References

New Approaches to Optimizing Early Diets

Staffan Polberger

The increasing number of surviving extremely preterm infants with gestational age of 23 weeks and birthweights from 400 g yields a new challenge to neonatal nutrition. The vast majority of extremely low birthweight (ELBW; <1,000 g) infants will survive if they are born and taken care of at a hospital with a tertiary neonatal intensive care unit. Preterm infants should be given optimal nutrition for brain growth and development. Nutrition during the vulnerable preterm period, preferably based on human milk, leads to adequate growth, at least corresponding to the intrauterine growth rate.

In Sweden, an individualized feeding system has been developed during the last 10–15 years. Most ELBW infants are fed according to the scheme: (1) mother's own milk (preferred); (2) banked milk (if mother's milk is not available); (3) preterm infant formula (if human milk is not available), and (4) supplementary parenteral nutrition (starting at birth).

There is a trend to a more ‘aggressive’ nutrition of preterm infants, i.e. initiating nutrition early after birth including administration of not only intravenous glucose but also amino acids and lipids immediately after birth or during the first day of life. Enteral feeding, preferably with human milk, is also started during the first few hours of life.

There is growing evidence that human milk is superior to infant formula for all newborn infants including the ELBW infants. Human milk confers nutritional and non-nutritional advantages, and there is now a worldwide trend using more human milk for feeding of preterm infants than infant formula. Outcome data support improved neurological development with human milk, even if the human milk intake has been limited to only a few weeks.

Unfortunately, but still in widespread use over the world, is the misconception that human milk has a predictable and uniform composition. However, several studies have underlined the enormous variation in the nutrient composition of human milk, particularly fat and to a less extent protein. There is a variation between mothers during the
course of lactation, during individual meals and also as a consequence of varying pumping techniques.

To account for this fact, a system with routine macronutrient analyses of the milk based on an infrared technique is used once a week, allowing optimal intakes of protein and energy. Analyses are always performed on 24-hour collections as spot samples cannot be used due to the enormous meal-to-meal-variation. Also, all banked milk is analyzed, and the most protein-rich milk is chosen for a newborn ELBW infant.

To further reduce the variation in nutrient intake of ELBW infants, mother’s own milk is given in chronological order, i.e. in the order it was pumped. Also, all milk is mixed in 24-hour collections before being given or frozen. This will substantially reduce the day-to-day and meal-to-meal-variation in nutrient content, which is likely to increase the gut tolerance.

After a few weeks when the volumes cannot be further increased, the milk is fortified when a computerized calculation has shown that the protein and, secondly, energy intakes need to be further increased. Parenteral nutrition is discontinued when the enteral intake constitutes 75–80% of the total volume intake. The goal is to reach daily protein and energy intakes of 3.5–4 g/kg and 110–120 kcal/kg, respectively. To further assess the metabolic capacity to utilize the protein given, markers, e.g. serum urea and transthyretin, are evaluated. Growth is monitored by regular measurements of weight, crown-heel length and head circumference, preferably by the same person each time, and fortification is continued throughout the tube-feeding period until breast-feeding is initiated before discharge.

References

Prevention of Low Birthweight

Dewan S. Alam

Globally an estimated 20 million or 15.5% of babies are born with low birthweight (LBW) defined as less than 2,500 g at birth with wide variations over different geographic locations [1]. However, over 90% of all LBW infants are born in developing countries and a half of the total global burden of LBW infants is distributed in South Central Asian countries. LBW may result from suboptimal fetal growth relative to gestational age, called intrauterine growth retardation (IUGR) or small for gestational age (SGA), or too early delivery called preterm delivery (<37 weeks of gestation). The distinction of these two entities has important programmatic implications as the determinants are different and so are the interventions.

LBW infants are at increased risk of mortality, morbidity, impaired growth and cognitive function, decreased motor and psychomotor development. In the longer term they are at increased risk of type 2 diabetes, hypertension, and cardiovascular disease [2]. These chronic diseases are emerging as epidemic in many developing countries. This high prevalence of non-communicable diseases in developing countries is consistent with the very high prevalence of LBW. The economic cost of LBW is also enormous due to its immediate and long-term consequences on health and economic productivity [3].

Major determinants included low caloric intake during pregnancy or low gestational weight gain, low prepregnancy weight, short stature, morbidity and cigarette smoking with different attributable risks for LBW in developed and developing countries [4]. In some settings, particularly in African countries where HIV and malaria coexist with maternal malnutrition HIV status, malaria and intestinal parasitic infestations are also important determinants. Micronutrient deficiencies are also likely to influence birth outcome.

Major interventions aimed to prevent LBW include balanced energy protein supplementation, micronutrient supplementation, fish oil, treatment of infection, cessation of smoking, and social interventions. The summary result of the systematic review of balanced
protein-energy supplementation show a positive effect of supplement on birthweight (+32 g) and a one-third reduction in LBW but no effect on gestational age [5]. High protein supplementation during pregnancy is reported to be harmful.

Intervention with micronutrient supplementation includes either single or a combination or more recently a mix of 15 micronutrients recommended by UNICEF and WHO. Among single micronutrient supplementation trials only calcium and magnesium supplementation during pregnancy was found to reduce LBW. A recent study in the United States reported that iron supplementation during pregnancy in iron-replete women improved birthweight and reduced the incidence of LBW [6]. Results of multiple micronutrient supplementation on birthweight and the incidence of LBW have been mixed. Some studies showed no additional benefits on birthweight over traditional iron folate supplementation, and some studies reported the superior efficacy of multiple micronutrients on birthweight and lowering the incidence of LBW [7–9]. Noticeably, the positive effect of multiple micronutrients shown in Nepal worked selectively on normal BMI women and female infants. One study reported multiple micronutrients to be associated with increased perinatal mortality [10].

While absolute prevention of LBW is unrealistic, bringing the incidence to a more acceptable level requires a very comprehensive approach based on the need and feasibility of combined interventions, as single interventions often showed either no or very little effect. There is no single strategy that seems to be universally applicable or efficacious. While IUGR seem to respond well to intervention, preterm delivery is more complex and resilient to intervention, and further investigation on the mechanistic aspect of this problem is required to identify effective interventions. The global epidemic of diabetes, cardiovascular diseases and hypertension which is linked to size at birth can only be effectively prevented with a healthy start to life by preventing LBW.

References

Community-based approaches have been the mainstay of interventions to address the problem of child malnutrition in developing societies. The conceptual frameworks that have underpinned community-based approaches to improve child health and nutrition include the food-care-health triad and the triple A process [1] and the life cycle approach to undernutrition [2]. Many programs have been in operation in several countries for decades and originated largely as social welfare, food security and poverty eradication programs, although the evaluation of the evidence of what intervention works and hence should be central to the community-based program is of more recent occurrence [3, 4]. Conceptual frameworks were developed to guide this activity as our understanding of the complex nature of the determinants of undernutrition and its links to the risk of overnutrition and chronic disease emerged. Alongside this evolution is the accumulation of the evidence of the types of interventions in the community that are effective, practical and also sustainable.

Critical evaluation of the evidence base of intervention studies in developing countries provides key insights [3, 4]. Strategies that aim to improve maternal nutrition and health appear to be the most significant interventions that have the best possible pregnancy outcomes. An adequate and diversified diet promotes weight gain in pregnancy and hence food supplements or balanced energy-protein supplementation may be used to target vulnerable groups such as undernourished pregnant women and adolescent mothers. Multivitamin supplements have shown to be effective not only in improving maternal health and birth outcomes but also have an impact on subsequent infant growth and health. Promotion of exclusive breastfeeding for early infancy followed by optimum complementary feeding in the presence of good hygienic practices diminishes risk of infections, promotes infant
growth and prevents child undernutrition. The success, effectiveness and the impact of large scale nutrition interventions, on the other hand, depend both on the contextual success factors, i.e. the macro-environment in which the program operates, and the program success factors, i.e. the components, features and structure of the program itself [4, 5]. In addition the sustainability of the program depends on political will, availability of resources, both monetary and human, community participation and involvement and the level of institutionalization of the program that takes place over time.

The changing environment in developing societies with rapid developmental transition and urbanization is probably determining the changing scenario of child nutrition and is responsible for the emerging problems of obesity and other metabolic disorders in childhood and in later adult life. This dramatic transition in developing societies is contributing to the double burden of malnutrition where the existing unfinished agenda of undernutrition is complicated and overwhelmed by the shift towards the emerging epidemic of obesity and increasing risk of chronic diseases. Community interventions hence need to be integrated and joined up to reduce both aspects of this malnutrition in societies and the interventions have to begin early in life. Because maternal and child undernutrition is the result of many factors, multiple sectors and strategies will have to bear on the objective of eradicating this problem. Community-based approaches can work if established as broad-ranging, multi-sectored and integrated food and nutrition programs. With child undernutrition and obesity and adult chronic disease apparently linked, tackling the double burden of malnutrition is a priority. The evidence that community-based nutrition interventions can have a positive impact on this emerging problem needs to be evaluated to enable programs to prioritize and incorporate those interventions that work in the community. Community-based approaches have to ensure a minimum package which addresses the ‘food-health-care’ triad of child malnutrition recognizing the documented synergies in these approaches. Programs that are operational and successful need to be evaluated and disseminated in order to enable countries to generate their own programs tailored to tackle the changing nutritional problems of the children in their society.

References


List of Speakers

Prof. Dewan Shamsul Alam  
Public Health Sciences Division  
ICDDR,B  
68 Shaheed Tajuddin Ahmed Sharani  
Mohakhali, Dhaka – 1212  
Bangladesh  
E-Mail dsalam@icddrb.org

Prof. Parul Christian  
Department of International Health  
Program in Human Nutrition  
Johns Hopkins Bloomberg School of Public Health  
615 N. Wolfe Street, Rm E2541  
Baltimore, MD 21205  
USA  
E-Mail pchristi@jhsph.edu

Prof. Satish C. Kalhan  
Department of Pathobiology  
Cleveland Clinic Lerner College of Medicine  
Case Western Reserve University  
Cleveland, OH 44195  
USA  
E-Mail sck@case.edu

Prof. Arthur McCullough  
Department of Gastroenterology & Hepatology  
Cleveland Clinic Lerner College of Medicine  
9500 Euclid Avenue, A-30  
Cleveland, OH 44195  
USA  
E-Mail mcculla@ccf.org

Prof. Staffan Polberger  
Neonatal Intensive Care Unit  
Department of Paediatrics  
University Hospital  
SE–221 85 Lund  
Sweden  
E-Mail Staffan.Polberger@skane.se

Prof. B.M. Popkin  
Interdisciplinary Obesity Center  
Department of Nutrition, School of Public Health  
University of North Carolina  
Carolina Population Center  
123 West Franklin Street  
Chapel Hill, NC 27516-3997  
USA  
E-Mail popkin@unc.edu
Prof. Andrew M. Prentice
MRC International Nutrition Group
London School of Hygiene and Tropical Medicine
Keppel Street
London WC1E 7HT, UK
E-Mail andrew.prentice@lshtm.ac.uk

Prof. Marc-André Prost
MRC International Nutrition Group
Nutrition & Public Health Intervention Research Unit
Epidemiology and Population Health Department
London School of Hygiene & Tropical Medicine
Keppel Street
London WC1E 7HT
UK
E-Mail marco@thepep.net

Prof. Eric Ravussin
Pennington Biomedical Research Center
6400 Perkins Road
Baton Rouge, LA 70808
USA
E-Mail ravusse@pbrc.edu

Prof. K. Srinath Reddy
Public Health Foundation of India
PHD House, Second Floor
4/2, Sirifort Institutional Area
August Kranti Marg, New Delhi
India
E-Mail ksrinath.reddy@phfi.org

Prof. Ana Lydia Sawaya
Department of Physiology
Federal University of São Paulo
Rua Botucatu 862, 2o andar
São Paulo, SP
Brazil
E-Mail anafisi@ecb.epm.br/
alsaway@unifesp.br

Prof. Prakash Shetty
Institute of Human Nutrition
University of Southampton
Medical School
Tremona Road
Southampton SO16 6YD
UK
E-Mail prakash.s.shetty@gmail.com

Dr. Vidya Subramanian
Naomi Berrie Diabetes Center
Department of Medicine
Columbia University
1150 St. Nicholas Avenue
New York, NY 10032
USA
E-Mail vs2223@columbia.edu

Prof. Emma Whitelaw
Division of Population Studies and Human Genetics
Queensland Institute of Medical Research
300 Herston Road
Herston, Brisbane 4006
Australia
E-Mail Emma.Whitelaw@qimr.edu.au
**Prof. Chittaranjan S. Yajnik**
King Edward Memorial Hospital
Diabetes Unit
Sardar Moodliar Road
Pune 411011
India
E-Mail diabetes@vsnl.com

**Prof. Shi-an Yin**
National Institute for Nutrition and Food Safety
Chinese Center for Disease Control and Prevention
29 Nan Wei Road, Xuanwu District
Beijing 100050
China
E-Mail shianyin@gmail.com
Emerging Societies -
Coexistence of
Childhood Malnutrition and Obesity