Under- and Overnutrition: 
A Global Perspective

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Introduction

The world is now confronted with a set of medical problems of nutritional origin with which it has never previously had to contend, i.e. both undernutrition of various types and a huge and rapidly escalating burden of diseases crudely classified as relating to overnutrition. The problems of malnutrition, particularly affecting young children, were highlighted in the developing world in the 1950s by a remarkable series of studies emanating from first-class nutrition research centers in Africa, Asia and Latin America, e.g. in Chile, India, Jamaica, the Lebanon, Mexico, Peru, Thailand and Uganda. In nutritional circles, for example, malnutrition was often considered to be a practical problem of improving children's nutrition with multifaceted approaches to improve the maternal and nutritional care of the young child. The promotion of breast-feeding followed by appropriate weaning was vital, together with a recognition of the fundamental human right of poor families to have adequate support. The World Health Organization (WHO) continued to encourage the monitoring of individual children's growth by means of national statistics while other UN agencies such as UNHCR and WFP, as well as non-governmental organizations, coped with the mounting crises of refugees and displaced persons fleeing from a multitude of wars, or attempting to survive the effects of droughts, floods and consequent crop failures. Support for the steady improvement in agricultural production, on which the escalating numbers of the world's poor depend, was universally accepted and was the responsibility of FAO and the CGIARs, funded by Western governments, the World Bank and the IMF.

More recently, in response to the drive by Grant, the former Director General of UNICEF, the world's Presidents and Prime Ministers expressed their commitment to tackling the continuing burden of childhood malnutrition at a Children's Summit [1]. This led to the development of the Millennium Goals [2]
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which highlighted the fundamental issue of poverty in the developing world and specified the need for a reduction in malnutrition, the improvement in maternal care and the need to tackle the scourge of communicable diseases such as malaria, tuberculosis and HIV. The UNDP has constantly highlighted the major deficiencies in current approaches to the world's problems and has helped, for example, the Water Council to focus world attention on the scandalous shortage of clean water and adequate sanitation for billions of people [3].

The Commission Report for the UN on Global Nutrition Problems

When challenged to explain why the rates of childhood malnutrition were not falling rapidly, a commission established by the UN Standing Committee for Nutrition, with access to the heads of the UN agencies came up with unpalatable conclusions [4]. It became clear that the West was convinced that through the ‘trickle down’ theory of free market economics and improving national wealth the problems of poverty and malnutrition would be solved. It is now clear that this theory does not apply in practice and a radically different approach is needed. Alternative approaches are shown by the remarkable success of community involvement in Thailand and Costa Rica, and the projects in Tanzania where governmental and local intervention empowered local communities, especially women, to radically change their circumstances.

The Commission came to a series of major conclusions:

(a) The current approaches by the UN were of little use to the developing world because there is poor coordination and even conflict between different UN and bilateral aid projects.

(b) There was a continuing and selective loss to the UN and NGOs of the most talented developing country nutritionists concerned with childhood malnutrition, so the capacity at the country level of the national nutrition community to drive appropriate action by governments and to question current projects was often negligible.

(c) The problem of childhood malnutrition itself was often wrongly assessed and its impact neglected. We highlighted the fact that there was a greater problem of protein-energy malnutrition in Asia than even in Africa and that the dominant form of protein-energy malnutrition was childhood stunting. This related in part to the high rates of low birth weight (LBW) babies in Asia, e.g. 50% in Bangladesh and >30% in India. This relationship depended on the fact that one would need substantial catch-up growth postnatally to avoid stunting. We noted that the reported exclusive breast-feeding rates were misleading given the remarkably high use of additional ‘teas’ and other herbal drinks. These were of questionable microbial content and were given routinely in many parts of Asia to babies from birth onwards. So it is little wonder that the intestinal mucosa of babies in Asia has been known for
decades to be very abnormal, with a loss of villi and features of chronic intestinal infection from soon after birth, whereas breast-fed European babies have mucosae with villous folds and fronds which provide a huge absorptive area. Clearly the extraordinarily bad sanitation in so many Asian countries and the absence of adequate supplies of clean water contribute greatly to the prevailing rates of intestinal damage and nutritional ill health.

(d) The Commission highlighted the neglect of maternal health with scandalously high rates of maternal anemia and death in Asia and Africa relating to the poor nutrition of girls who often entered pregnancy undernourished and vitamin-deficient. This meant that there were huge problems affecting billions of young girls and women in particular. There was therefore a new concept of intergenerational malnutrition which needed to be recognized (fig. 1a). This has led to a major change in UNICEF policies, particularly in South-East Asia, and a series of newly funded initiatives by the Asian Bank [5, 6].

(e) Pregnancy weights, weight gain and maternal diets were highlighted as inadequate, particularly in Asia where we already had our own analyses of the remarkably high rates of adult undernutrition which we originally termed ‘chronic energy deficiency’ [7–9]. Ferro-Luzzi, Shetty and ourselves still have unpublished data from rural India showing remarkably high levels of not only adult undernutrition, i.e. with BMIs below 18.5, but also vitamin and immune deficiencies (without HIV infection). Given the fact that 50% of Indian women have a BMI of <18.5 before pregnancy, that a high proportion of babies are born to young girls in India before the age of 18 years (the official, but largely ignored, legal age of marriage), that 85% of Indian (and probably many other Asian-country) mothers are frankly anemic in pregnancy, with profound iron and folic acid deficiency, it is perhaps little wonder that children, as well as mothers, suffer the consequences of multiple nutrient deficiencies.

(f) The long-term consequences of undernutrition are only now being unraveled. It has long been clear from the work of Grantham-McGregor et al. [10] in Jamaica that the original findings of slower mental development in malnourished children needed to be taken far more seriously. Longer term follow-up has suggested that these mental handicaps could persist and might be permanent, leading to poor school performance with all its implications for society as well as for the affected individuals. If this reasonable extrapolation from the findings that stunted children were not achieving their full mental potential is applied to the national setting then, with some Asian countries having up to 60% of their children stunted in the preschool years, it is reasonable to conclude that the actual mental capacity of a nation – now well recognized to be of enormous economic significance – is being unnecessarily limited. This is even more important given the findings that the poor mental performance of the children as well as their stunting can be reversed by appropriate feeding and, remarkably, by ensuring that the mothers play with and stimulate their children. This implies that mental stimulus as well as nutrients are needed for the more complex, micro-structural development of the brain.
**Fig. 1.** The intergenerational cycle of undernutrition now exposed to rapid childhood weight gain (**a**) and a generation later where adult diseases predominate (**b**).
Were this not alarming enough, there is now surprising evidence from the Gambia [11] that small babies born in the hungry season are not only at a disadvantage in the short-term, but have a higher death rate in adult life from infections, with the girls having greater death rates associated with reproduction. We must therefore conclude that the extent and range of handicaps associated with childhood malnutrition are huge and continue to be neglected.

**New Evidence of the Importance of Childhood Malnutrition**

As part of the Millennium analysis of the global health burden, Murray and Lopez, who published the first assessment of disease-specific premature death rates and the disability associated with these illnesses, formulated into Disability-Adjusted Life Years (DALYs) lost [12], set about not only reformulating the basis for these analyses, but also the risk factors and reasons underlying these burdens. Table 1 summarizes the DALYs lost from different regions.

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Developed countries(^a) AMR-A, EUR-A, EUR-B, EUR-C &amp; WPR-A</th>
<th>Low mortality developing countries(^b) AMR-B, EMR-B, SEAR-B &amp; WPR-B</th>
<th>High mortality developing countries(^c) AFR-D, AFR-E, AMR-D, EMR-D, SEAR-D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tobacco</td>
<td>12.2 (1)</td>
<td>4 (3)</td>
<td>2 (9)</td>
</tr>
<tr>
<td>High blood pressure</td>
<td>10.9 (2)</td>
<td>5 (2)</td>
<td>2.5 (8)</td>
</tr>
<tr>
<td>Alcohol</td>
<td>9.2 (3)</td>
<td>6.3 (1)</td>
<td>1.6</td>
</tr>
<tr>
<td>High cholesterol</td>
<td>7.6 (4)</td>
<td>2.1 (6)</td>
<td>1.9 (10)</td>
</tr>
<tr>
<td>High BMI</td>
<td>7.4 (5)</td>
<td>2.7 (5)</td>
<td>0.8</td>
</tr>
<tr>
<td>Low fruit and vegetable intake</td>
<td>3.9 (6)</td>
<td>1.9 (7)</td>
<td>1.3</td>
</tr>
<tr>
<td>Physical inactivity</td>
<td>3.3 (7)</td>
<td>1.3</td>
<td>0.8</td>
</tr>
<tr>
<td>Illicit drugs</td>
<td>1.8 (8)</td>
<td>0.8</td>
<td>0.5</td>
</tr>
<tr>
<td>Unsafe sex</td>
<td>0.8 (9)</td>
<td>1.4</td>
<td>10.2 (2)</td>
</tr>
<tr>
<td>Iron deficiency</td>
<td>0.7 (10)</td>
<td>1.8 (9)</td>
<td>3.1 (6)</td>
</tr>
<tr>
<td>Underweight</td>
<td>0.4</td>
<td>3.1 (4)</td>
<td>14.9 (1)</td>
</tr>
<tr>
<td>Indoor smoke from solid fuels</td>
<td>0.3</td>
<td>1.9 (8)</td>
<td>3.6 (4)</td>
</tr>
<tr>
<td>Unsafe water, sanitation and hygiene</td>
<td>0.4</td>
<td>1.8 (10)</td>
<td>5.5 (3)</td>
</tr>
<tr>
<td>Zinc deficiency</td>
<td>&lt;0.1</td>
<td>0.3</td>
<td>12.5 (5)</td>
</tr>
<tr>
<td>Vitamin A deficiency</td>
<td>&lt;0.1</td>
<td>0.4</td>
<td>11.7 (7)</td>
</tr>
</tbody>
</table>

Attributable DALYs by risk factor as percent of regional DALY (ranking within region).

\(^a\)Total DALYs 214 million.

\(^b\)Total DALYs 498 million.

\(^c\)Total DALYs 833 million.
diseases in three groups of countries classified on the basis of being in either the developed or developing world. The latter are divided into those countries with a much lower childhood (<5 years) mortality and longer life expectancy, and the other countries – mostly of African origin – that had high death rates in preschool children with low life expectancies. This third group of countries has particularly high rates of the prevalent communicable diseases.

It became clear that undernutrition remains of remarkable importance, and indeed in the new analyses, is given far greater emphasis. This emerges because in the old version of DALY analyses children who died before school age were discounted in the calculations because they had not yet imposed a real financial burden on society by needing schooling and would not contribute to the economy! Now, however, by virtue of dying so young, all those years between the preschool years and the putative life expectancy of 75 years were included in the new analyses without any selective discounting. Thus childhood undernutrition is now seen as the biggest health burden in the world.

The new analyses went further in highlighting the selective importance of iodine, iron, vitamin A and zinc deficiency as well as the classical children’s prevalences of underweight. Zinc deficiency has now been added to the classic list as a result of new trials showing the value of zinc not only in promoting children’s growth but also in limiting their burden of recurrent and chronic diarrhea and pneumonia [13–15].

### The Global Impact of Overnutrition

Figure 2 illustrates what many still find surprising – that cardiovascular diseases are the biggest killers and disabling conditions in the world, including developing countries, with cancers also making a huge contribution. Indeed WHO has revealed that there are more deaths from coronary heart disease (CHD) and strokes in the developing world than in the more affluent, developed societies. Thus overnutrition is no longer only a concern for the industrialized West but a huge issue for poorer countries which are now having to contend with an escalating demand for medical care – for hypertension, diabetes, disabling heart conditions, strokes and the number of people with cancers. Recently WHO published a new report [16] which assessed the contribution of diet, nutrition and physical inactivity to these major chronic diseases of adult life. It concluded that excess weight gain, as well as an excess of dietary fat, refined sugars and salt, together with a deficient intake of vegetables and fruit and of the n-3 polyunsaturated fatty acids, make a major contribution (table 2). Physical inactivity is also of exceptional importance, the reduced activity reflecting the outcome of major societal changes induced by government policies and the industrial opportunities for marketing cars, computers, mechanical aids for use at work and in the home, television, videos and other forms of entertainment.
The industrialization of food has also led to completely new processed foods with an unhealthy nutritional content and few, if any, consumers are now able to identify the nutritional value of the ever greater proportion of foods eaten outside the home. The marketing of foods and soft drinks to preschool and school children is also a major force which bypasses parental control. The intense marketing of ‘fast foods’ with the added inducement of greater portion sizes being promoted as better value, are all contributing to an escalation of overweight and obesity which is now not only affecting the adults of the developing world but also its children.

The International Obesity TaskForce has been involved for 3 years in detailed analyses of the prevalence and impact of excess weight throughout the world. We find that there are over 1.1 billion adults overweight with a BMI ≥25.0, of whom over 300 million are classified as obese with a BMI ≥30.0. The regional contributions to this global figure are illustrated in table 3, and table 1 shows the new WHO analyses which now place an increase in BMI (in adults of more than 21.0) within the top 7 contributors to the global burden of ill health. Furthermore, we have shown that there is such a close relationship between excess weight gain and the development of diabetes that in Western societies 85–90% of all diabetes can be attributed to excess weight gain. Such is the link that a new term ‘diabesity’ is being coined for the two conditions.

These recent WHO analyses are only a preliminary approach to assessing the impact of nutritional factors on the global health burden. Thus, for example, the importance of weight gain in promoting the epidemic of high blood pressure has not been taken into account in the prominence given to the role of

![Fig. 2. The global burden of disease in 1999 (numbers in thousands). Based on WHO analyses as set out in its annual reports.](image-url)
hypertension in promoting cardiovascular disease. Nor, in broader nutritional terms, is the excessive consumption of fat with excess saturated fats identified as contributing to higher blood pressures despite the DASH trials showing this effect. The additional importance of low intakes of vegetables and fruit is now set out separately but not the impact of higher salt intakes [17]. Then we must also recognize the overwhelming importance of the fatty acid composition of the diet, together with weight gain, in promoting high blood cholesterol levels. So when the nutritional conditions, which now include hypertension

Table 2. Ranges of population nutrient intake and anthropometric goals

<table>
<thead>
<tr>
<th>Dietary factor</th>
<th>Goal, % of total energy, unless otherwise stated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total fat</td>
<td>15–30</td>
</tr>
<tr>
<td>Saturated fatty acids</td>
<td>&lt;10</td>
</tr>
<tr>
<td>Polyunsaturated fatty acids</td>
<td>6–10</td>
</tr>
<tr>
<td>n-6 Polyunsaturated fatty acids</td>
<td>5–8</td>
</tr>
<tr>
<td>n-3 Polyunsaturated fatty acids</td>
<td>1–2</td>
</tr>
<tr>
<td>Trans fatty acids</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Monounsaturated fatty acids</td>
<td>By difference(^a)</td>
</tr>
<tr>
<td>Total Carbohydrate</td>
<td>55–75(^b)</td>
</tr>
<tr>
<td>Free sugars(^c)</td>
<td>&lt;10</td>
</tr>
<tr>
<td>Protein</td>
<td>10–15(^d)</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>&lt;300 mg/day</td>
</tr>
<tr>
<td>Sodium chloride (sodium)(^e)</td>
<td>&lt;5 g/day ( &lt;2 g/day)</td>
</tr>
<tr>
<td>Fruits and vegetables(^f)</td>
<td>≥400 g/day</td>
</tr>
<tr>
<td>Total dietary fiber</td>
<td>From foods(^g)</td>
</tr>
<tr>
<td>Non-starch polysaccharides (NSP)</td>
<td>From foods(^g)</td>
</tr>
<tr>
<td>BMI</td>
<td>21–23 kg/m(^2)</td>
</tr>
</tbody>
</table>

\(^a\)This is calculated as: total fat – (saturated fatty acids + polyunsaturated fatty acids + trans fatty acids).

\(^b\)The percentage of total energy available after taking into account that consumed as protein and fat, hence the wide range.

\(^c\)The term ‘free sugars’ refers to all the monosaccharides and disaccharides added to foods by the manufacturer, cook or consumer, plus sugars naturally present in honey, syrups and fruit juices.

\(^d\)The suggested range should be seen in the light of the Joint WHO/FAO/UNU Expert Consultation on Protein and Amino Acid Requirements in Human Nutrition, held in Geneva April 9–16, 2002 (WHO, in press).

\(^e\)Salt should be iodized appropriately (document WHO/NUT/96.13).

\(^f\)The category of tubers (i.e. potatoes, cassava) should not be included in fruits and vegetables.

\(^g\)Wholegrain cereals, fruit and vegetables are the preferred sources of non-starch polysaccharides (NSP). The recommended intake of fruits and vegetables and consumption of wholegrain foods is likely to provide >20 g/day of NSP (>25 g/day of total dietary fiber).
and hypercholesterolemia, are added to physical inactivity these dietary and activity contributors to global DALYs make a greater impact than even tobacco!

**The Synergistic Link between Under- and Overnutrition**

Doctors and research workers have traditionally considered the causes of undernutrition and overnutrition as fundamentally different. Thus underweight children have a problem because they are in an unfavorable environment where high-quality nutrient-rich foods are usually scarce and intercurrent infections with poor sanitation and contaminated water supplies amplify and highlight the nutritional deficiencies. Overnutrition, e.g. relating to obesity, arises from being physically relatively inactive and eating or drinking too

### Table 3. Percent overweight (BMI 25–29.9) and obese (BMI ≥30) by WHO subregion and sex

<table>
<thead>
<tr>
<th>Region</th>
<th>Sex</th>
<th>% Overweight</th>
<th>% Obese</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa D</td>
<td>Male</td>
<td>4.2</td>
<td>0.1</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>8.8</td>
<td>1.7</td>
</tr>
<tr>
<td>Africa E</td>
<td>Male</td>
<td>0.5</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>6.7</td>
<td>1.5</td>
</tr>
<tr>
<td>America A</td>
<td>Male</td>
<td>39.8</td>
<td>18.8</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>26.2</td>
<td>23.8</td>
</tr>
<tr>
<td>America B</td>
<td>Male</td>
<td>40.4</td>
<td>16.2</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>34.7</td>
<td>25.0</td>
</tr>
<tr>
<td>America D</td>
<td>Male</td>
<td>32.2</td>
<td>8.3</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>35.4</td>
<td>13.5</td>
</tr>
<tr>
<td>Eastern Mediterranean B</td>
<td>Male</td>
<td>26.1</td>
<td>5.7</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>29.3</td>
<td>12.5</td>
</tr>
<tr>
<td>Eastern Mediterranean D</td>
<td>Male</td>
<td>9.2</td>
<td>1.5</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>18.6</td>
<td>9.4</td>
</tr>
<tr>
<td>Europe A</td>
<td>Male</td>
<td>47.0</td>
<td>15.1</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>33.5</td>
<td>19.3</td>
</tr>
<tr>
<td>Europe B</td>
<td>Male</td>
<td>31.9</td>
<td>9.7</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>29.2</td>
<td>23.0</td>
</tr>
<tr>
<td>Europe C</td>
<td>Male</td>
<td>34.6</td>
<td>9.3</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>32.1</td>
<td>24.3</td>
</tr>
<tr>
<td>South-East Asia B</td>
<td>Male</td>
<td>15.0</td>
<td>1.9</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>19.4</td>
<td>3.2</td>
</tr>
<tr>
<td>South-East Asia D</td>
<td>Male</td>
<td>1.1</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>10.1</td>
<td>2.2</td>
</tr>
<tr>
<td>Western Pacific A</td>
<td>Male</td>
<td>24.0</td>
<td>4.7</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>19.6</td>
<td>4.7</td>
</tr>
<tr>
<td>Western Pacific B</td>
<td>Male</td>
<td>22.1</td>
<td>4.1</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>17.1</td>
<td>5.9</td>
</tr>
</tbody>
</table>
many foods rich in fats and sugars. Therefore, there seems to be no connection between the two conditions. Recent (unpublished) evidence, however, now highlights the greater propensity to both type-2 diabetes and CHD in Asians even when the sex, age and weight status of the population is taken into account. The propensity for Asians, particularly Indians, living in different environments to have high rates of CHD and type-2 diabetes has been recognized for years [18] but the basis for this undue sensitivity to CHD and diabetes has been unclear and often assumed to be of genetic origin.

Recently experimental, clinical and epidemiological evidence has shown that there is a profound change in the human body’s metabolic responses depending on the nutritional well-being of the mother during pregnancy. In animal experiments a reduction in the intake of protein during pregnancy reduces the placenta’s 11-hydroxy-dehydrogenase activity thereby allowing higher maternal corticosteroid influx to the fetus which then profoundly alters the setting of the corticosteroid responsive receptors and their functioning in the brain [19]. This in turn probably moves the child to have a higher cortisol responsiveness based on the early fetal/neonatal ‘setting’ for the hypothalamic-pituitary-adrenal axis controlling circulating cortisol levels. So this may explain why overweight Chinese and other Asians display a state of ‘pseudo-Cushing’s’ when excess weight gain occurs. Rosmond et al. [20] have shown the importance of a more responsive corticosteroid axis in those with visceral adiposity so it is little wonder that this is associated with insulin resistance and a propensity to diabetes and the development of the metabolic syndrome. This syndrome seems so prevalent at modest weight gains not only in Asia but also in other nutritionally compromised nations, e.g. in Mexico [21]. These broad national trends mean, as usual, that some individuals within the population are extremely susceptible to the complications of weight gain for genetic as well as behavioral reasons. Thus Rosmond et al. [22–24] have shown that individuals with a particular allotype in neurotransmitter receptors in the brain are far more susceptible to visceral adiposity with all its morbid consequences. How this also relates to alterations in the secretion of adiponectin, the newly discovered insulin sensitizing and cardiovascular protective hormone, secreted by adipose tissue but inhibited by the expanding fat cells’ secretion of tumor necrosis factor [25–27] is as yet unclear.

The unusual interactions between under- and overnutrition now mean that we are now witnessing an extraordinarily complex of nutritional problems (fig. 1b) Fat, short children are now growing up so that young girls and women, when they become pregnant, are not only anemic from iron and folic acid deficiencies but more readily develop glucose intolerance and gestational diabetes. They then in turn produce fatter babies with much higher risks of childhood obesity and early type-2 diabetes which may even become apparent in adolescence. The mothers themselves are also at far greater risk of permanent type-2 diabetes, hypertension and all the other complications of the
metabolic syndrome. This new nutritional combination, displayed in figure 1b, seems now to be applicable to perhaps half the world's population.

In policy-making terms what emerges from this extraordinary new scenario is that the current perceptions by the public, politicians and even doctors and nutritionists of two fundamentally different problems of undernutrition and adult chronic diseases will need to be recast. The problem of undernutrition engages much more sympathy and a willingness to consider political and economic initiatives, whereas overnutrition is immediately designated as reflecting the outcome of consumer choices in an environment of freely available food. Even though the latter is manifestly untrue [28, 29], a new dimension to thinking must be developed with the less affluent countries recognizing that they have to be far more interventionist to counter current commercial and cultural trends if they are not to witness the most alarming double handicap of continuing nutritional deficiencies with a superimposed overwhelming burden of diabetes, cardiovascular diseases and cancers.

With huge changes planned in the conduct of international trade in foods and other commodities temporarily delayed by the breakdown of the WTO Cancun Conference, there will need to be a new emphasis on the rights of nations to intervene in the free market for public health reasons – perhaps in association with the phyto-sanitary criteria for the national control of the free market in foods. Already we have the dumping of huge amounts of animal fat from Australasia on the Pacific Islands and the same, anecdotally, seems to be happening with US excessive fat exported to Mexico. The EU and US subsidies on fats and sugars also mean that the very products that we now recognize as health hazards [16] are being selectively promoted by the principal governments controlling decision making in the G8 group. The challenge for public health policy makers is therefore enormous as WHO in its next World Health Assembly considers how best to develop global and national strategies to combat the non-communicable diseases and thereby tackle the biggest contributors to premature death in the world.

References

Global Under- and Overnutrition

Discussion

Dr. Basu: The phenotype hypothesis has strengthened but then again we also see an increased prevalence of diabetes in second-generation Indians, for example Indians who have been present in Mauritius and Fiji and other parts of the world. What is the influence of Westernization, the influence of the lack of physical activity, etc., on the development of diabetes?

Dr. Allison: Before Dr. James answers that question, I am sure he is aware of the animal work carried out in Belgium on rats in which diabetes was induced by a kind of intrauterine mechanism while feeding the mother at a particular time of pregnancy. It took seven generations for the diabetes to disappear from the rats. In other words, there is a fascinating non-genetic inheritance conveyed by this. Perhaps Dr. James would comment on this. How many generations does it take for this phenomenon to disappear?

Dr. James: It is interesting that in the 1970s Stewart et al. [1] at the London School of Hygiene induced by diet major intergenerational changes in rats. These beautiful data were published in the British Journal of Nutrition. I was there at the time and I just thought he was just wasting his time on this stupid experiment where the animals were put on a modest lowering of protein intake and they just kept going. Ten or 12 generations later they still found exactly what you are saying, Dr. Allison. Then when protein intake reverted to normal, even by the third generation they had not reverted to normal in physical terms. The implications are quite astonishing. In 1970 Thomson [2], of reproduction and nutrition fame, first displayed data from the Aberdeen classic MRC center where they measured the grandmother's birth weight, the mother's birth weight and the new child's birth weight. They could look at the size of the parents and grandparents, and it was very clear that the grandparents' size influences the size of the baby. Although it is very difficult to actually discriminate these things, these data imply that we should be very careful before automatically assuming that big societal differences in disease across the world are automatically a feature of genetic selection because there is a big challenge as to how you discriminate this genetic contribution. The public health implications are enormous because, if it does take several generations to recover from intra-uterine malnutrition, it implies that we are in for extraordinarily trouble for the next 200–300 years. On the basis of evidence about to be published on Mexicans, I am fairly convinced that we will find elsewhere the same features as described in India. The only hope is that if you say that the Western population and Europeans are more resistant, how long is it that the Europeans have been in a comparatively good state? In the 1920s the poor in Britain were on a terrible diet, and they were short and even to this day when you go up to the north and west of England, the size of the people goes down and the number of low birth weights goes up. In the 1840–1850s malaria and typhoid were present in Britain, similar to that in Africa at the moment. So perhaps if it is true that we are more resistant by virtue of early programming and better maternal nutrition, perhaps in humans the intergenerational adaptation is a bit faster than in rats.

Dr. Basu: Have there been any studies looking at siblings, basically with siblings on a low-caloric diet versus other siblings on a high-caloric diet, to see whether there are any alterations in the risk of developing diabetes or a metabolic syndrome in the later age? I don't know of any.

Dr. James: The Scandinavian twin studies.

Dr. Steenhout: This is a question for Dr. James. I was very interested by the data you showed from Yajnik [3] about folate supplementation and/or the folate status of the mother. To prevent neural tube defects, supplementation of the mothers with folate is being recommended more and more, even before pregnancy. Should we
expect some benefit from this in the future? The second important question I have, and I hope you can enlighten me a little bit, is why we didn’t see a similar effect with the Dutch famine? After the Second World War as a result of the Dutch famine the Dutch didn’t become really obese and insulin resistant. It is only now more than 50 years afterwards that they develop this tendency to obesity; even a little bit later than the rest of the European population. Is it also because the children were breast-fed after birth by malnourished mothers that they cannot have caught up this fast? Is that relevant or do you have other explanations?

Dr. James: I didn’t realize I was going to suffer so much!. Let’s go to the neural tube defect and folate. It is quite interesting, if you look at the official meta-analysis of the WHO, they say that it is inconclusive as to whether appropriate folate supplementation actually increases birth weight. But if you go into detail on the studies that they cite, they are taking the usual miserable approach of people involved in the Cochrane analysis. If you go back to the original data, there are some lovely data from South Africa in the 1970s where there were lots of low birth weight babies and mothers that were on an atrocious mostly maize corn porridge only diet. They had appalling anemia, and were offered iron only or iron and folate, and so on. There was an astonishing reduction in the group that in fact received the folate in terms of low birth weight. If you go to the United States and look at their studies, and I think this was based on NHANES analyses so it was pretty objective, then you can see a relationship between the folate intake of the women in United States who generally have a poor vegetable and fruit intake, contrary to popular belief, and the actual size of the baby. So I think that the folate intake quite early on is not only important for neural tube defect prevention, but is actually fundamentally involved in cellular growth which determines the size of the baby. Now when it comes to the Dutch famine, the Dutch data fit the Barker hypothesis but you have to remember something else. If you go into detail on the Dutch famine, it is quite interesting that the children conceived at the time of the worst famine were actually the fattest as adults. However, don’t forget that most of these women became amenorrheic during the famine. Therefore, and this is me speaking, not the official literature, you have to be careful because the fattest women would have been able to sustain ovulation and fertility longer, and therefore you may have a selective fertility with genetic implications as well. So we have got to be careful that we don’t automatically assume that if you are born at a troublesome time you are automatically fat. I think the evidence is suggesting that if a fetally deprived or malnourished baby gets fat afterwards then they tend to selectively put fat on your belly through, possibly, a hormonal pathway. Don’t forget that the Dutch have the best data on walking to school, physical activity, cycle paths, separated from traffic, unlike Bangkok, so that you can actually cycle and walk around. The danger of being killed while cycling in the Netherlands is 19 times lower than in the United States. The United States is a killer country for all sorts of reasons!. But I think that in the Netherlands, the fact that they are only now getting fat is partly due to the fact that they have kept to just 3 meals a day and the structure of the diet in their culture is surprisingly firm; but there is also physical activity. So I think it is a combination of diet and physical activity. We have to be careful: it is not all fetal with nothing happening of relevance postnatally. I think we are now showing that the fetal phase is making individuals more or less sensitive to the subsequent environmental impact of what we do.

Dr. Allison: Can I come in again here because the Dutch famine was a very short one, it was 3 or 4 months. So it was possible for the people who analyzed the effects of that famine to look at the different phases of pregnancy; in other words those who were exposed to famine in the first trimester as opposed to those that were exposed to the later time. I know we are putting you on the spot here and you are not prepared,
but we are relying on your insight and knowledge of what is going on. Would you care
to comment on the most sensitive stage of pregnancy in relation to the subsequent
events. For example the incidence of schizophrenia was affected tremendously by the
stage of pregnancy.

Dr. James: I thought you were going to challenge me with the Stalingrad siege and
the data that do not fit the Dutch famine data. We have to be careful because, as you
pointed out, the Dutch famine in a sense was a beautiful experimental set up from our
point of view in terms of being so acute with conditions otherwise being extremely
satisfactory, whereas the Stalingrad siege was a disaster with a whole society affected
for a very long time. Therefore, try to distinguish the impact of pregnancy malnutri-
tion, as Yudkin has attempted to do is quite difficult. Now the stage of pregnancy is
very interesting. Contrary to popular belief, if you take birth size as a ridiculously crude
index of what is going on in utero, then of course you know that the last third of preg-
nancy is when there is a maximum increase in size. But when looking at the experi-
mental data, with a large research team in my institute, it looks as though the first
3 months of pregnancy are actually setting the trajectory of growth. So the first 3 months
may be terribly important in terms of the longer term capacity for growth, even though
under difficult conditions in the last trimester there may be a fall in birth weight as in
the Dutch famine. There are data on schizophrenia but I can't remember what they
are. I know that the Medical Research Council when we met in the West Indies were
extremely interested in this because the evidence shows that in some societies there
is a surprisingly high rate of schizophrenia. That is why I would highlight the data from
Edinburgh because they show that mental function and the responses to stress can be
conditioned by protein deprivation in pregnancy.

Dr. Kopelman: This is a point related to Dr. Basu's comment earlier on. I think we
are probably seeing a paradigm shift in the late 20th and early 21st century. Where I
work in East London there is a large Bengali population, and the problem we face now
with the women is that we are seeing, 3–4 generations down the line, a very high inci-
dence of impaired glucose tolerance and gestational onset diabetes. These women
were formerly small and are now becoming obese. Their fetuses, which as far as we
know have a normal birth weight, go on to get established diabetes, and the prevalence
of diabetes in East London in the Bengali population is frighteningly high. In the older
people it is about 75% of the population. Almost 100%, of these pregnant women will
become type-2 diabetic, and their children are becoming obese. We have prospective
longitudinal data showing the increasing prevalence of obesity in Bengali children, and
they are the individuals we are now seeing with type-2 diabetes in their teens.

Dr. James: That is very interesting. I have actually shown a scenario where the
development of adiposity is superimposed upon the classic inter-generation cycle. It
is precisely these babies that are getting plumper. The question is, in physiopatholog-
tical terms, are these babies with abnormal high birth weights actually returning to
normal or are they still abnormal? Evidence from the United States shows that if a
mother develops gestational diabetes then the child has an 8-fold increased risk of
severe obesity by adolescence, and with that goes the increased risk, in the genetically
susceptible, of adolescent type-2 diabetes. Adolescent type-2 diabetes, although it
seems to be so rare, is the one issue that I am confronted with as I go around the world
now. Pediatricians in Singapore asked me 5 years ago why I was not talking about the
problem and when I saw them again 3 months ago they indicated that they now find
more of type-2 diabetes than type-1children in their diabetic clinics. The same is true
in Hong Kong; the same is becoming true in Shanghai; you find the same in Santiago
in Chile; you find the same in Mexico; it is quite astonishing. It is very interesting
because if you look at the Hong Kong diabetes data, you can actually genetically
identify the genetic susceptibility that makes them develop diabetes early, but the
grandmother with a seemingly identical genetic abnormality developed diabetes when she was 65, the mother when she was 45, and here is this 15-year-old child with diabetes. Now that means that we are jumping 20–40 years with each generation. So Dr. Allison, back to your story; it does mean that we humans shift more dramatically through the generation cycle than rats. I talked to Dr. Zimmet, Mr. Diabetes as I call him, and he had not realized that it was quite so dramatic. That has huge implications because, just as Dr. Kopelman is saying, that throughout the developing world we are going to find an accelerated diabetes rate in excess of that which we even now predict.

Dr. Shenkin: I was interested in your comments about the benefits of meat protein versus vegetable protein diets. Is this something to do with a fairly limited intake of particular kinds of vegetable protein or is there something special about meat protein? Or is it something else in the diet, perhaps micronutrients which are beneficial to the development of the fetus?

Dr. James: The early studies before the Second World War from the United States showed that a dose-response in children’s growth could be made depending on how much meat was in the diet. The more meat in the diet the faster those children grew. Prof. Michael Golden analysed all our data on the effects of protein supplements in the Third World. Everybody has been convinced that the vegetarian diet is wonderful and, but the data showed that the growth of children was not enhanced by adding vegetable protein. When the data from e.g. Papua New Guinea are looked at, it is the addition of milk or meat that seems to be critical. Now there is no clear explanation, but new data are coming out from beautiful double blind trials in Thailand and elsewhere showing an absolutely clear response to zinc. So there is zinc deficiency in the sense that if a double-blind control trial of zinc supplementation is made with these children, a clearly accelerated growth in height is seen. So if you then look at the availability of zinc as distinct from just absolute zinc intake, then you can put forward the proposition that with isotope experiments showing that zinc is well absorbed from meat then it is a reasonable hypothesis that zinc is the critical factor. But if you are talking about fetal data then there are a lot of experimental data that suggest that it is not just zinc but it is the detailed amino acid composition particularly the essential amino acids that you find in such abundance in animal protein that is particularly conducive in the development in the early fetus. So the children data look as though it is zinc. For example, the classic Mexican diet is a survival diet, but the Mexicans tell you that the reason they are short and squat is that they are genetically different. It is not true at all; it is a complete societal adaptation to the strange zinc-blocking diet in Mexico. Even when zinc is given to breast-feeding mothers so that they put out more zinc in their breast milk the babies fed by zinc supplemented mothers again show accelerated growth. So my guess is that it is zinc for the most part.

Dr. Go: With regard to the Mexican diet showing that it is a zinc-deficiency problem; are we really looking at zinc as the biomarker or is it the total diet that we are probably missing in the discussion?

Dr. James: If you ask me if you should just take zinc or would you be better off with meat, I would certainly go for meat for all sorts of other reasons. You know about the improved iron absorption with meat and the anaemia scandal in India for example. There is a medical crisis in India; but I cannot get the top Indian medical doctors and policy makers to realize what a crisis they are in. As a result of our UN commission, UNICEF completely changed its strategy for Asia when we highlighted the fact that it is not only low birth weight, but 85% of pregnant women are who frankly anemic in India. It really is a scandal.

Dr. Tantibhaedhyangkul: There have been numerous studies in rats on isocaloric diets, high-fat diets compared with low-fat diets. It is known that with a high-fat diet
compared with a high-carbohydrate diet, insulin resistance can always be produced in a high-fat diet. It is also known that the intake of fat in the new generation is increasing tremendously. Does this increase in fat intake have anything to do with increasing type-2 diabetes due to insulin resistance? As I said insulin resistance can always be produced in rats by increasing the percentage of fat intake, even medium-chain triglycerides and the long-chain also give different insulin sensitivity or a different degree of insulin resistance. In an isocaloric diet in the rat, a medium-chain triglyceride diet is given and compared with a long-chain triglyceride diet on an isocaloric basis. Insulin resistance can always be increased in the long-chain fat compared with medium-chain triglyceride. Now our new generations of children are exposed to a diet which is increased in fat, and the question is, does type-2 diabetes have anything to do with the percentage of fat intake?

Dr. James: This is completely fascinating question because when I talk to diabetologists, and I am sure there are several here who know more about it than I, they don't focus on that particularly. Yet when we look at the animal data as you have described they are quite profound, and I think some of the human data are also very intriguing. For example, if insulin resistance is measured by appropriate techniques in somebody who is overweight and has a propensity to diabetes, of course their weight can be reduced by reducing their fat intake and insulin resistance can also be reduced, but if a fat blocker is used, for example Xenical which is a drug used to help weight loss, there is selective blocking of fat and also an amplification of insulin sensitivity in excess of that which would be predicted from the weight loss as such. So it looks as though the human data agree absolutely with the animal experimental work, but I have never seen the fat issue highlighted as a big question in the diabetes world. It implies that we really ought to be taking it much more seriously. Of course fat intake also seems to amplify blood pressure - the evidence for this is very good too.

Dr. Kopelman: I support what Dr. James has just said on the basis that I don't think diabetologists really have focused on fat to the extent that they possibly should.

Dr. Basu: I agree entirely. Certainly fat and free fatty acids have been shown to cause increased hepatic glucose production and reduce insulin secretion on a longterm basis, but apart from glucotoxicity there is lipotoxicity which is a well-known cause of insulin resistance.

References
