Introduction

Marabou 2005: Nutrition and Human Development
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Nutrition is now becoming once more of intense interest to biological and medical scientists working on the control of development and human health. It is also now of ever greater public health interest. Few scientists, however, recognize that the same interest for those involved in fundamental science and public health developed a century ago focusing on the way in which nutrition and specific micronutrients, as well as general energy and protein intakes, were crucial to infant growth and appropriate development. The discovery of vitamins was matched by the proposition that stunted children in poor communities in the Western world were suffering from poverty-related poor diets. The critical role of nutrition was established by feeding studies, which then led to major food and agricultural policy changes during the Second World War, when food supplies were scarce throughout Europe.

The success of these wartime policies led to a revolution in governmental thinking and a cheap food policy, together with a major boost in national agricultural production as an issue of national security. Nutritionists transferred their scientific interest to the study of childhood malnutrition in the developing world. The promotion of intensive agriculture and the food industry led to a revolution in food supplies, with the intense promotion of meat, milk, butter, and sugar production and consumption. The resulting escalation in cardiovascular disease related to the dietary change slowly altered public health policies, but as cardiovascular deaths decreased in the developed world, obesity and diabetes progressively increased. Now the lower- and middle-income countries (i.e., the developing world) have far more cardiovascular disease as Western diets and cultural habits are imported. The remarkable escalation of diabetes and cardiovascular disease, particularly in populations currently and previously subjected to malnutrition, now reveals unusual susceptibility to these diseases.

This susceptibility is increasingly related to the conjunction of fetal malnutrition and later inappropriate diets. The alarming escalation in the health burden suggests that two-thirds of the world’s population is super-sensitive to weight gain, diabetes, cardiovascular disease, and perhaps many cancers. New evidence on epigenetics and the structural changes in the fetus in response to inappropriate maternal diets provides mechanisms to explain this. Unfortunately, a vicious intergenerational cycle of maternal and fetal epigenetic change seems to herald markedly increased future burdens of disease. The nutrition field is therefore challenged not only in terms of science, but also in new dimensions of public health of immense economic significance.

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INTRODUCTION: THE DEBATE A CENTURY AGO

Nutrition is again scientifically fascinating, as well as of great public health importance, so we may once more be on the verge of a great debate with parallels to those of a century ago. At that time, it was proving difficult to recruit physically robust British soldiers to fight the Boer War. Thus, 40% to 60% of recruits from the Scottish Highlands who attended the recruitment center for the Gordon Highlanders’ regiment in Aberdeen, Scotland were unable either to pass the simplest of physical activity tests or carry the heavy backpacks needed in army service. By contrast, the Highlanders in the previous century were renowned for their tall stature and strength. This issue came to me forcefully the week I took over the directorship of the Rowett Research Institute in Aberdeen, when the Commander of the Gordon Highlanders recounted the long tradition for recruiting 1.8-meter tall, magnificent fighters and not the new puny, 1.5-meter weaklings. This dramatic change and the concern about the Boer war led the British government to convene a committee to investigate this deterioration. One view was that these stunted, feeble characters from...
the lower classes were the offspring of an intellectually and physically inferior section of society that was breeding excessively! This problem was being amplified by the fact that the tall, intelligent, and wealthy aristocrats were having far fewer children, so the average intelligence and physical capacity of the nation was threatened and thought to be in decline. This led to the argument that steps were needed to limit the breeding capacity of the lower classes so that Britain could continue to manage and control its empire!

Eugenicists and social Darwinists such as Karl Pearson were particularly concerned because the previous decades of remarkable microbial discoveries and public health analyses had led to a massive campaign for clean water and sanitary regulations, as well as liberal reforms led by Booth, Rowntree, and many others. Public health had so improved that the mortality rate was dropping steadily—but this might mean that the weak and feeble would not be weeded out but survive and multiply. In other words, was the beneficial impact of natural selection being lost?

The UK Committee on Physical Deterioration, convened in 1904, variously described the affected children as “physically degenerate,” “badly nourished,” or “malnourished,” with these terms seemingly being used interchangeably. After much debate, they did, however, eventually buck the rising tide of medical opinion insisting that environmental conditions were crucial. Furthermore, there were novel proposals emerging in 1905 from Gowland Hopkins and others about the importance of “accessory nutritional elements,” and by 1912, Funk had isolated an anti-neuritic chemical and proposed that beri-beri, scurvy, pellagra, and possibly rickets were caused by the inadequate provision of organic bases he called “vitamins.” Hopkins also highlighted the importance of amino acids such as tryptophan for ensuring adequate protein quality, and the nutritional well-being of people became of intense scientific interest. At that stage, there was a great discussion about whether Eicholtz, a member of His Majesty’s Inspectorate of Schools, was right to assert that “the poorest and most ill-nurtured women would bring forth as hale and strong looking children as those in the very best of conditions” or whether Mackenzie was right to cite animal experiments suggesting that the fetus suffered in the competition between mother and fetus for nutrients. Whatever the competitive balance, the Committee on Physical Deterioration concluded that it was the responsibility of the state to ensure the adequate nourishment of children attending school, but the difficulty of targeting the most needy children with extra food was also recognized.

By the 1920s, there were intense debates as to whether Haldane, Paton, and Cathcart were right in championing a “holistic” view of physiology whereby the nutritional processes affecting the body were really issues relating to social and environmental conditions. The distinguished nutritional scientists Walter Fletcher and Edward Mellanby, the successive Medical Research Council Secretaries, also insisted on focusing on the fundamental effects of these new biochemical factors in food and led major campaigns throughout the 1920s and 1930s to provide schoolchildren with milk to improve their vitamin intake and well-being. The value of this approach was backed by Corry Mann’s experimental long-term feeding of underweight orphan boys in Dr. Barnardo’s homes. They grew best on milk, although a more recent reanalysis of his data by Celia Petty shows that only the stunted children benefited.

FOOD SECURITY AND NUTRITION

It was Boyd Orr’s book, Food, Health and Income (deliberately given for publication to the renowned Harold Macmillan, a publisher and right-wing politician who eventually became prime minister in the UK), that transformed political thinking by revealing the close link between the stunting of children, their poverty, and general ill health. These children, assessed in a Carnegie-funded survey, were shown to live in impoverished conditions on extraordinarily limited diets. Corry Mann and other US scientists had already shown that stunted children were not genetically small, but responded to selective foods, particularly milk and meat, with accelerated growth. The thin children also benefited when given butter or sugar, the extra energy inducing weight gain. These reports then led to a very large number of voluntary organizations demanding that children needed good foods to overcome their anemia, susceptibility to infection, and poor growth. It was not, however, until the beginning of the Second World War that there were any coherent changes at the government level. Prime Minister Winston Churchill was told that Britain would be defeated, not in armed conflict, but because the German submarines were proving remarkably effective in sinking so many of the merchant ships that transported the majority of British food from the British colonies.

Boyd Orr’s son-in-law, David Lubbock, told me how he discovered that the British Ministries of Health and Agriculture were about to introduce a rationing system based on providing defined amounts of bread and other cereals but with meat and butter purchased by those who could afford them. Within days, Boyd Orr had not only lobbied the Ministry with his data from the remarkable Carnegie survey of working class families, but had, through David Lubbock’s Asquith family connections, persuaded Lord Wooten to convince Winston Churchill that a far more coherent policy was needed to secure both
the food supply and the well-being and survival of the nation. At that stage, women were being drawn for the first time into factory work and other roles traditionally occupied by men. Winston Churchill then insisted that all pregnant women and children should be provided with orange juice, extra milk, and cod liver oil. In addition, every child should have at school a substantial, high-quality meal to limit the demands on working mothers. So successful was this effort that not only were the Ministries of Health and Agriculture subsequently acclaimed for their foresighted planning, but the whole political approach to food security became transformed. Thus, within an astonishingly short three-year period, UK agricultural production more than doubled, so that about three-quarters of the food supply of Britain was now being locally produced. No longer could the nation be starved into submission.

Food security therefore became fundamentally linked to strategic issues of national security. As the Western allies confronted the Axis forces in Africa, the Far and Middle East, and Europe, it became clear that as Allied forces advanced they were finding millions of semi-starving refugees and other displaced communities in many parts of the new free world. These wartime experiences led most nations to establish after the Second World War new agricultural policies based on the principle that meat, milk, butter, and sugar were essential sources of protein and energy that had to be safeguarded as an issue of national security.

**POST-WAR AGRICULTURAL POLICIES BASED ON NUTRITIONAL PRINCIPLES**

In the post-war years, the dominant nutritional thinking was that the British had conducted a remarkably successful national experiment proving that the principal issues of nutrition were now settled. So the issue now was how to apply this nutritional know-how to the rest of the world. Given this perspective, Boyd Orr persuaded the world’s diplomats to establish the Food and Agricultural Organization (FAO), and he was made its first director general. He soon resigned, however, because the Allies would not agree to form a world food bank; both the Soviet and Western powers realized that safeguarding their agricultural production was a crucial issue of national security. They would have political leverage when other countries had limited stocks of food. The Soviet Union went further and for decades operated a policy that specified remarkably high protein intakes as appropriate. Cereal growing for cattle feed, originally discovered by Preston at the Rowett to markedly promote the growth of ruminants and increase their milk production, was a critical issue. The Soviet Union and the United States spent years monitoring each others’ cereal harvests and bargaining as the Soviet Union bought cereals from the United States to feed their cattle and attempt to meet the very high protein goals established by their Soviet nutritionists. Only in Gorbachev’s time did it become clear that the vast industrial might of the Soviet Union was being handicapped by flawed nutritional and agricultural policies that were demanding huge purchases of North American cereals. I had the privilege of being the accepted arbiter between the World Bank and the Soviet Union during the financial reconstruction crisis, when 36 million pensioners in Soviet Russia were deemed to need more financial support so that they could continue to eat 120 g of animal protein per person per day!

In the post-war era, nutritional science in Western countries became focused on animal nutrition because this, rather than the further study of humans, was the national priority. Cattle, sheep, pig, and poultry production escalated remarkably with new feeding regimens. The Common Agricultural Policy in Europe was then established as an excellent way of stabilizing and then supporting the small farmers of France and Germany. Intense research and pervasive agricultural advisor systems supported new approaches to agricultural production, and this approach dominated national priorities for research and technical development. Therefore, human nutritionists had to transfer most of their interests to the problems of malnutrition in the developing world. During the 1950s and 1960s, it was accepted that all we needed to consider was a “balanced diet” in which sufficient meat, milk, butter, and eggs were made available. These foods, of course, had to be affordable for even the poorest members of society if we were to combat the original problem identified in pre-war years by Boyd Orr. Thus, there emerged the “cheap food” policy, and a fundamental strategy of making agriculture so efficient that the luxury items of meat and butter were sufficiently cheap so that even the poor could afford them.

To this day, these concepts dominate agricultural policies in many parts of the world, with the animal feed industry backed by the promotion of meat and milk consumption with substantial government subsidies sometimes rivaling the funding of armaments and other issues relating to national security. This systematic policy transformed the food chain, which eventually became politically entrenched in a huge global multibillion-dollar market. Furthermore, the linking of affluence and well-being with commercial success and the Western concepts of good living, began to permeate the world, with everyone seemingly accepting that meat, fat, and sugar not only met primate drives in terms of taste, but also provided the intrinsic needs for health. These diets thus became associated with societal success and affluence.
These nutritional changes led to a number of seemingly new diseases such as coronary heart disease. My father-in-law, when training in Leeds medical school in the 1920s, had to rush to witness the unusual cases of “angina” leading on to a surprisingly dangerous new condition termed a “heart attack.” By the 1960s, these seemingly mysterious problems were exceptionally common, particularly in Western countries. Ancel Keys’ remarkable Seven Country studies in the 1950s, together with his and Hegsted’s detailed analyses of the effects of different fats on blood cholesterol, allowed new approaches to nutritional well-being to be developed in the early 1960s. Norway became one of the first countries to recognize that these new disease patterns were linked to the nutritional changes that had followed the post-war agriculture and food policies. In the United States, it was also recognized that smoking, high blood pressure, and a raised cholesterol level were intimately linked with the development of heart disease. This led the American Heart Association to propose new dietary priorities for individuals, but it was Scandinavia that led the world in terms of changes in national strategy. The history of the changes in Norwegian, Finnish, and other European national nutritional policies were analyzed for the World Health Organization (WHO) and revealed, to our surprise, that the development of government policies followed rather than led the population’s understanding of the new concepts of nutrition. This understanding was stimulated by select groups of professional cardiologists and nutritionists who appealed directly to the public to change their diets. They also called for governmental policy changes using a variety of strategies to influence the political process. At that stage, nutritional deficiencies were deemed a thing of the past—now one had to be concerned with the issues of dietary quality, particularly in relation to fat.

By the early 1970s, however, Burkitt and Trowell were extending our concepts of dietary quality by highlighting that in the post-war period of nutritional change we had focused essentially on the issue of fatty acid composition but completely forgotten about the carbohydrate, specifically the non-starch polysaccharide or fiber, components of the diet. Thus, bowel disorders, including colon cancer, were major issues that they linked to dietary fiber deficiency. Over the last 30 years we have therefore become engaged in a re-analysis of the suitable amounts of macronutrients, protein, carbohydrate, and fat in the diet.

The concept of “a balanced diet” with the motto “a little of what you fancy does you good” led to a transformation of the dietary patterns of the Western world. These major dietary changes in the 1940s through the 1970s were paralleled by major changes in agriculture and the development of a powerful food industry. Women were now recognized, on the basis of their remarkable contributions to the war effort, as major assets in the labor market, but this meant that they were again under intense pressure at home. High-quality foods in a simple, convenient form for ready purchase and with a limited need for meal preparation and complex cooking became highly desirable. These universal desires fueled a transformation in the food processing, manufacturing, distribution, and retailing trades and a progressive concentration of industrial power. This then led to an extraordinary increase in the transportation of foods, ingredients, and products across the world, along with the removal of the seasonal cycle in food availability. A plethora of intriguing new foods was brought to millions of consumers. Indeed, this burgeoning cornucopia of culinary delights was fed by the idea of “free choice,” and consumer individualism with rapidly expanding supermarket chains positioning themselves as operating solely for the consumer’s benefit.

Although the “diseases of affluence” such as cardiovascular disease and cancers had been linked for decades to nutritional issues, the medical profession and the public preferred when possible to deal with these problems by technical fixes such as drugs. There emerged, however, a clear understanding that smoking had to be curtailed as a national policy, and later it was agreed in most countries that people should opt for lower salt intakes and modest amounts of fat of an appropriate nutritional quality. What was not so well understood until recently was the crucial role of the food industry in determining the quality of our food. From the 1960s on, the food industry began modifying their choice of ingredients and processing methods so that new products such as yogurts and low-fat foods would appeal to interested consumers and improve their sales.

The development of the food industry is one of the most prominent political and economic features of the post-war years. New techniques of production, processing, and marketing led to the concentration of industrial power in ever fewer hands; These developments are set out in several analyses (e.g., Fast Food Nation). We are therefore now in the strange position where individual companies are valued in multibillion-dollar terms on the basis of making a few products such as soft drinks or hamburgers. These trans-national giants are entering a
new phase in their development, because in capitalist terms they are still fundamentally required to increase their market share and prove annually or even quarterly their increasing profitability for the benefit of shareholders. It is intriguing to see how these normal industrial pressures have led to three approaches that are also evident in the tobacco and alcohol markets: a) using lower prices to improve market share, b) ensuring the pervasive availability of their products, and c) backing these changes in price and availability with intense marketing of individual products. Clearly, the food industry has now grown into a remarkably powerful industrial lobby that is as dominant politically as any other industrial sector—including the defense industry.

The marketing techniques of the food industry and their effects are well documented. Originally, consumers recognized the immediate benefit of being offered extra value for money when purchasing larger portion sizes. The next approach to improving turnover was to focus marketing on the very young, thereby establishing potentially long-lasting brand loyalty. These strategies have been so successful in Europe that they have transformed food purchasing patterns, with the consequent loss of the traditional diet in most, if not all, of the Mediterranean countries.

The market in western Europe is close to saturation, so the next obvious focus for every major food company and retailer is the burgeoning purchasing power of the liberated ex-Soviet Union countries and the developing world. In practice, the biggest investors in central and eastern Europe after the fall of communism were the confectionery, soft drink, and fast food industries. These industries were also at the forefront of investment options in the developing world, where the future opportunities for earnings are enormous as India, China, Latin America, and the Middle East develop. It is little wonder, therefore, that there has been a dramatic transformation in the pattern of disease in these countries as the benefits of immunization, improved water supplies, and sanitation accompanied by increasing affluence have induced a marked fall in childhood mortality. Unfortunately, the Western industrial and cultural invasion of these still poorly organized countries has produced a dramatic change in the food patterns of even poor people as they migrate to urban slums to search for work. Fat, sugar, and meat intakes rise rapidly, with marked increases in body weight amounting in India to a change from an average body-mass index (BMI) of about 18 in the desperately poor villages to an average BMI of 23 in the adjacent cities. Dramatic decreases in physical activity accompany the dietary changes, so it is little wonder that those diseases previously labeled as “Western” diseases or “diseases of affluence” are now the dominant problems in most of the low- and upper-middle income developing countries. Thus, these countries are now confronted by the “double burden” of persisting malnutrition and deficiency diseases together with burgeoning rates of obesity, diabetes, cardiovascular diseases, and cancers (see below).

PERSISTING MALNUTRITION IN AFRICA AND ASIA

When we were asked to reassess the nutritional problems of the world at the turn of this century by the Standing Committee for Nutrition, the biggest issue confronting us was the persisting high rates of malnutrition despite the many declarations by governments that they were now going to tackle this with the Millennium Development Goals set out as an explicit series of priorities. A group of us was asked to examine why so little progress had been made and what might be done about it. This report proved highly controversial because we took a fresh look at the issues and recognized that global policy makers were focused on poverty alleviation, and the nutritional and development community was mainly concerned with the impact of wars and natural disasters in limiting progress. We concluded, however, that there were other major issues. First, we specified the need to consider the nutritional problems across the lifespan and highlighted the linkages by depicting visually the life cycle of deprivation that affected most European communities in Boyd Orr’s time and persists in many parts of the world (Figure 1).

When nutritionists described the problem of malnutrition, we also recognized that they were taking classic WHO criteria for malnutrition by specifying that protein energy malnutrition was only evident when children fell below the minus-two standard deviations limit of the WHO growth curves. We noted that this crude, categorical approach to diagnosing malnutrition had been used to highlight the public health implications of malnutrition because of the enormous numbers of underweight children. Africa was assumed to have the biggest problem, but it immediately became clear that Asia had both proportionately and in absolute numbers far more malnourished children. At that time, in North Africa there were about 10% of children malnourished, in sub-Saharan Africa, 25%, and in Asia, 47% of children were malnourished on the basis of the WHO criteria for underweight. There was also a shift in the whole spectrum of growth rates, with few, if any, children in the upper percentiles of growth. Therefore, there was an enormous potential burden because we had most, if not all, of the population growing below what could be construed as their optimum growth rates.
We then observed that stunting was the dominant problem determining the prevalence of childhood malnutrition, which we had first recognized in our surveys in the Caribbean for the British Foreign Office in 1970, but few nutritionists wanted to confront the issue as to how best to cope with stunting per se rather than wasting. We found a blinkered view in much of the nutrition establishment, where it appeared that simply providing more food was the answer, when we already knew that chronic infection due to poor water supplies and sanitation, together with a remarkably low animal protein intake in Asia, were fundamental issues.

**INTERGENERATIONAL MALNUTRITION**

The high prevalence of stunting in southeast Asia was soon linked in our Millennium Report to the very high prevalence of low birth weights. Thus, it became clear to us that babies born small would have to grow at an accelerated pace after birth so as not to be classified as underweight and stunted. This in turn put a focus on pregnancy and the well-being of women, when traditionally pediatricians had determined national policies on the basis of the need to cope with underweight and infection-susceptible infants. We had already shown in our original publications on low BMIs in adults that the prevalence of low birth weights in India was related to the postpartum BMIs of the mothers, and that half of the babies were of low birth weight when women after delivery had BMIs under 16. Only when mothers ended pregnancy with BMIs over 25 were the prevalence of low birth weights at a minimum (15%). We then realized that very few nutritionists or pediatricians were considering the nutritional needs of pregnancy or the fact that in southeast Asia so many very short women entered pregnancy with a BMI below 18. Indeed, we soon learned that over a quarter of children born in India were delivered by adolescent girls before the age of 18 years, the legal age of marriage. It then became clear that there was a remarkably high maternal mortality rate in southeast Asia, with over 80% of the women becoming anemic during the course of pregnancy. There seemed to be a long-standing intergenerational life cycle of chronic deprivation with multiple micronutrient deficiencies, particularly iron, zinc, folic acid, and vitamin B_{12}.

This led the Millennium Commission to recognize that we had neglected the plight of young women and therefore the importance of the well-being of young girls. It was widely accepted that the education of young women was critical, but we now had to think about the fundamental importance of fetal nutrition. This new perspective led to a change in UNICEF’s policies in southeast Asia, where the emphasis shifted to maternal well-being and the avoidance of low birth weight. Put simply: if very small babies had to grow fast after birth to avoid being classified as stunted and malnourished, then this would clearly require a completely different set of priorities for weaning foods, and the longer-term objective should be to improve maternal and fetal nutrition.

**THE PROBLEMS WITH ASIAN VEGETARIAN DIETS: MULTIPLE NUTRIENT DEFICIENCIES AND MICROBIAL CONTAMINATION**

More detailed inquiries suggested that in the Indian subcontinent, despite the highlighted benefits of the vegetarian diet, there were many in the community who...
were not only \( B_{12} \) deficient but also had vitamin C, riboflavin, and folate deficiencies. They eat fresh green vegetables and fruit in limited quantities, with much of the food being cooked for a long time. This cultural tradition of vegetarian dishes, cooked for long periods in a variety of sauces, was familiar to us because we had already been told by some of the leading microbiologists in India that it was almost impossible to find even processed foods and drinks that were not heavily contaminated with enterobacteria. This explained the heavy daily infective load for most if not all of the population. In fact, it initially proved impossible to obtain any uncontaminated Indian food or drink products to give to NASA when they were putting an Indian astronaut in space! We also discovered to our surprise that exclusive breastfeeding was very uncommon in Asia because there was a tradition of giving teas and other herbal drinks to babies on a routine basis from a few days of age. This may then explain the long-recognized early mucosal damage in the intestines of Indian babies, which was first recognized in the early 1960s.

Evidence of effective national programs to combat malnutrition were evident in the remarkable reduction in protein-energy malnutrition rates in Thailand, and in the effectiveness of national policies in Costa Rica and of community experiments in Tanzania. In all three of these countries, there had been a community-based combination of local village caregivers backed by a governmental system. These were national priorities with increased funding of maternal and infant welfare clinics and with measures to ensure that there was adequate food for the children. Analyses then under way at the International Food Policy Research Institute also showed that if one took the usual United Nations and World Bank approach to development, then the “trickle-down” remedy of much current economic thinking would not allow malnutrition rates to drop substantially. Indeed, progress was so slow that there was no hope of meeting the Millennium Development Goals when our Commission looked at the strategies under way at the beginning of this new Millennium.

THE CURRENT NUTRITIONAL TRANSITION IN GLOBAL ILL-HEALTH

Recently, WHO has transformed its thinking in terms of nutritional priorities by first assessing the prevalence of different diseases across the world and then analyzing the likely effect of each disease on both disability and premature mortality.\(^{22}\) In these analyses it became apparent that even in the developing world, now re-categorized as comprising countries with low, lower, and middle-income status, there is a remarkable prevalence and burden of adult chronic diseases such as cardiovascular diseases, cancers, diabetes, obesity, and mental ill health. Although infectious diseases still exert an extraordinary burden on the poorest countries of the world, with HIV rates escalating in most sub-Saharan African countries and now in India, China, and other Asian societies, the most common cause of death in the world as a whole is cardiovascular disease. In fact, nearly twice as many people die of cardiovascular disease in the developing world as in affluent Western societies! So now the “diseases of affluence” are actually the diseases of the poor. Popkin and others have linked this extraordinary finding to the so-called nutritional transition, with fat, meat, and sugar consumption rising as incomes improve.\(^{23}\) We have also recently shown that as the GNP of a country rises, so do the average body weights and obesity rates of adults. The blood pressure of populations goes up very sharply in the poorest countries, and even in the most rural communities, blood pressure values are surprisingly high and cholesterol levels and obesity rates rise in proportion to national income until the average GNP is 8 to 10 thousand dollars a year.\(^{24}\)

FETAL MALNUTRITION AND ITS LONG-TERM IMPLICATIONS

Having realized that maternal malnutrition was a huge problem in explaining the high prevalence of low birth weight, we then recognized the impact of the nutrition transition and the remarkable rates of development of diabetes already evident, particularly in Asia. Hales had earlier shown\(^{25,26}\) that feeding animals a lower protein intake altered the structure and metabolic capacity of the liver and pancreas, with clear evidence that the pancreatic capacity for producing insulin would be compromised in the offspring of poorly fed mothers. Other experimental studies confirmed the effects of low maternal protein intakes on pancreatic islet cells, and showed that their vulnerability to apoptosis was enhanced if the mothers had been fed a low-protein diet, this susceptibility to apoptosis being remedied by the provision of extra taurine in the mother’s diet during pregnancy.\(^{27}\) Yajnik in India was also finding that children born of low birth weight were, by the age of four, and again at eight years of age, showing evidence of insulin resistance and higher blood pressures, particularly when children were born small and then grew rapidly.\(^{28}\) At that stage, we recognized that most of Asia depended on eating rice, which has one of the lowest protein contents of the world’s cereals, but we really had no evidence that these lower protein intakes were fundamental in explaining the emerging high prevalence rates of the metabolic syndrome and diabetes. The extraordinary susceptibility of Asians to diabetes had been evident from McKeigue’s studies in London,\(^{29}\) and George
Miller in the 1970s\textsuperscript{30} had also highlighted the far greater risk of cardiovascular disease in Indians whether living in the Caribbean, South Africa, or Europe. We therefore now had a new perspective because the current nutrition transition was not simply an issue of going from the problems of undernutrition to the burdens of obesity, diabetes, and cardiovascular disease. The precursor state of nutritional deficiency was amplifying synergistically the subsequent impact of even modest gains in weight. Thus, both undernutrition and the new dietary imbalance with excess energy in late childhood and as adults were increasing the heath burden dramatically. This was not unique to India; Barker\textsuperscript{31} had highlighted the five-fold increasing the heath burden dramatically. This was not unique to India; Barker\textsuperscript{31} had highlighted the five-fold increased risk of developing the metabolic syndrome in late middle age if UK adults had been born small. He later showed, with colleagues, the association between a low early pregnancy BMI in Chinese women and the propensity to insulin resistance in their offspring when studied 45 years later.\textsuperscript{32}

Detailed analyses showed that intrauterine growth retardation could be prevented if small and underweight women (but not normal-weight women) were provided with a protein energy supplement during pregnancy, and there was some evidence that zinc, folic acid, and perhaps magnesium and even n-3 fatty acid deficiencies might contribute to limiting low birth weights.\textsuperscript{33} Some of the earliest studies\textsuperscript{34} involving the folic acid supplementation of South African women subsisting on predominantly maize-based diets had shown a marked reduction in the incidence of low-birth weight babies in the supplemented mothers, and more recent analyses have supported the importance of adequate folic intakes in pregnancy.\textsuperscript{35,36} Yajnik\textsuperscript{37} has highlighted the link between the intake of green leafy vegetables and folate sufficiency in relation to birth weight in Indian women, and more recently emphasized the particular significance of vitamin B\textsubscript{12} in contributing to potentially major changes in fetal development.\textsuperscript{38}

**FETAL IMPRINTING AND EPIGENETIC CHANGES**

Early work by McCance and Widdowson\textsuperscript{39,40} in the post-war years showed how pigs and rodents could be permanently altered in size, shape, organ structure, and metabolic control by manipulating maternal and/or early postnatal feeding. Then Stewart at the London School\textsuperscript{41} showed over 30 years ago that rats fed a low protein intake through 10 generations produced offspring with a completely different body composition, and that it took about three generations to reverse these effects. Later, Lim et al. in Japan\textsuperscript{42} fed rats either 5\% or 40\% fat during pregnancy but with a standard diet after weaning and induced obesity in the offspring of the mothers fed the high-fat diet. This intergenerational effect was not simply a feature of breast-feeding or other changes in rearing, but seemed to be an imprinted phenotype that affected the offspring on a long-term basis. It was now apparent that maternal changes could affect the phenotype, and possibly the genotype, of the next generation and that this phenomenon might be carried through for several more generations, even when the nutritional insult is removed.

The mechanisms involved in these intergenerational effects were unclear and originally were considered to be a response to limited substrate availability, but then Edwards et al.\textsuperscript{43} proposed that the glucocorticoid feedback system involving the hypothalamic-pituitary-adrenal axis might well be reset by the greater inflow of maternal cortisol into the fetus through the placenta, where the 11 beta-dehydrogenase enzyme system for inactivating cortisol was susceptible to a lowering of dietary protein.

In the last five years, remarkable new work on fetal mechanisms has shown that the selective methylation of discrete portions of the DNA, together with histone changes, silence particular genes and therefore alter gene expression, potentially on a permanent basis. As Reich et al.\textsuperscript{44-46} have demonstrated so effectively, the genetic imprinting may not only affect the fetus, but also the regulation of the supply and demand for maternal nutrients by the fetus, with placental control of nutrient flow to the fetus operating through the IGF2 system with altered placental permeability. The epigenetic controls and the setting even of behaviors and endocrinological responses also continue after birth, with potentially profound effects of breast-feeding. Thus, maternal-child interactions may themselves fix the long-term expression of genes controlling not only feeding responses, glucose, and fat metabolism, but also emotional cues.

These remarkable fetal effects, together with the major changes in organ structure and the resetting of the glucocorticoid system should, in time, explain why there seems to be such a remarkable increase in the prevalence of abdominal obesity associated with diabetes, hypertension, and heart disease in the developing world, linked with the earlier prevalence of low birth weight as a crude index of altered maternal malnutrition. We could, indeed, describe the world’s population as being dominated by societies in which the nutritional experience, with fetal imprinting, makes most communities far more susceptible to chronic disease than the post-war western European and American generations of Caucasians. For too long, we have thought of these differences as racial and dependent on fundamental differences in our inherited range of gene alleles.

We must now be careful not to ascribe big differences in susceptibility to disease to evolutionary and
major genetic selection pressures. The new evidence suggests that not only should we be highlighting the importance of nutrition before and during pregnancy, but that the response of babies in the first two years of life also seems to be crucial. Sally McGregor\textsuperscript{47} decades ago showed the interactions of good nutrition and mother-child interactions in determining the future ability of babies of these children. Much longer-term follow-up has emphasized the crucial role of early mental stimulation by the mother in determining permanently the mental capacity of the child,\textsuperscript{48} so the old concepts of critical periods for development are now being re-emphasized in a broader context.

The determinants of mental development are many. For example, tests of flavor programming during infancy now show the remarkable effects of exposing babies after birth to flavors that then determine their subsequent liking or distaste for foods.\textsuperscript{49} The acquisition of acceptable tastes may therefore relate to flavors in breast milk and indeed to those in the amniotic fluid before birth.\textsuperscript{50} On a more obvious medical level is the observation of Dutch investigators\textsuperscript{51} that babies fed moderately low salt intakes in infant formulas for their first six months of life showed significantly lower blood pressure when subsequently evaluated at the age of 15 years. Uauy’s studies\textsuperscript{52} on the importance of providing the essential n-3 fatty acids during the first few months of life for optimum mental and visual development also emphasize that we have been too cavalier in simply worrying about energy and protein intakes.

THE NEW PUBLIC HEALTH CHALLENGE

Now that nutritional science has become of extraordinary scientific importance once more, we need to confront huge challenges that are analogous to those confronting Boyd Orr and his colleagues 80 years ago. We are now living in a world where nutritional issues dominate the burden of ill health in most parts of the globe, and where in Africa the capacity to cope with the HIV/AIDS epidemic is affected by the nutritional well-being of the affected individuals. Politically, we are also at a turning point, because we are being presented with diets that are hopelessly out of line with those to which we were exposed during the evolution of mankind. We have also developed an economic and industrial system that in practice means that much of our nutritional well-being depends upon the decisions made by the food and retailing industries, where the marketing of poor-quality foods is now becoming of major concern. Thus, nutritionists are once more at the forefront of major societal issues and the question is whether we can rise to this challenge.

Nutritionists have not been involved by many governments or industrial groups unless they agreed to be experts validating the concept of choice and a balanced diet, which implies that there is little for governments to do. If nutritionists do criticize new food products, then the food industry responds strongly with counterarguments and often pay experts who cast scorn on any idea that the particular nutritional issue was of any real concern. Thus, in our report on the dietary factors linked to cardiovascular disease\textsuperscript{53} for the UK government in 1984, we highlighted the importance of having lower intakes of trans fatty acids, saturated fats, and salt on a societal basis. Within days there was intense lobbying with nutritionists employed to question the claims and dispute the validity of the science. Thus, it is only in the last two years—25 years after the initial expression of concern—that the British government demanded that there should be a systematic reduction in the salt and trans fatty acid content of food products.

This enormous political influence of the international food business has been highlighted by Marion Nestle,\textsuperscript{54} who considers that in both the United States and Europe, the industry has essentially emasculated nutritional opinion by recruiting many, if not most, of the opinion leaders as their consultants and lobbyists. Yet independent WHO analyses of the total global health burden reveal that nutritional problems are even more important than smoking, and, in fact, are the principal cause of the majority of the health burdens in the world. We are therefore challenged in an unprecedented way, because there are now nearly twice as many people dying from cardiovascular disease in the poorer countries of the world, and four Asian countries out of the top five have millions of patients with type 2 diabetes. Obesity is also escalating throughout the globe, particularly among the poor, so we seem to be confronted by a food system that is out of control and dominated by the totally legitimate, immediate-profit-focused demands of the international food business.

It is now clear that children and the developing world have become the focus for the international marketing of food, with devastating results as energy-dense and nutrient-poor foods become globally pervasive. The European Union and the United States continue to damage the well-being of their own citizens by supporting fat, meat, and sugar production rather than that of fruit and vegetables by using absurd incentives traditionally provided through the Common Agriculture Policy in the European Union and by the subsidy system in the United States. Poor farmers in emerging economies are made redundant by huge European and American export subsidies for such commodities as sugar. Furthermore, the World Trade Organization’s attempts to open up the markets of the poorer countries on the basis of free trade.
also flout the experience of the Western countries’ own experience of selective restrictions to protect their own industries.\textsuperscript{35} The benefits that have been evident in China, India, and Malaysia when they maintained their own import restrictions and controls on finance are also clear.

We are therefore once more in a world reminiscent of a century ago, when huge economic forces and even issues of national security and economic well-being depend on governments taking action to nurture the well-being of nutritionally vulnerable people. The highest priority now needs to be given to the welfare, education, and support of young women if we are to avoid the astonishing effects of the new nutritional problems merging on an intergenerational basis. Currently we have a global population, the majority of whom are not fataly programmed to contend with the current pervasive food cultures of the West. The nutritional community is therefore challenged scientifically, medically, in public health terms, and in relation to their capacity once more to speak out and contribute to forcing a change in the current laissez fair policies that allow the escalating burden of ill health affecting the most vulnerable people.

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