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Food and the human condition

Textbook

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Food and the Human Condition

Textbook

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Chapter 1

Malnutrition, growth retardation and stunting

S.J. Ulijaszek, L.H. Allen, A. Prentice, P.C. Dagnelie, M. van Dusseldorp, B. Torun, and M.S. Westerterp-Plantenga

As much as nutrition contributes to growth and development, so does malnutrition to growth retardation and stunting. In this respect, this chapter especially focuses on linear growth in various populations, with an emphasis on linear growth retardation in Third World children. Comparing linear growth in different populations gives insight into the contribution of malnutrition, qualitatively as well as quantitatively, to growth retardation and stunting. Therefore, the first paragraph of this chapter discusses between-population variation in pre-adolescent growth.
Then, attention is paid to the roles of specific nutrients in the general linear growth faltering that occurs in developing countries.
A description of the relationship between dietary mineral supply and bone development in children follows, with a special emphasis on mineral deficiencies and its effects on bone development.
In order to give some idea of the type of research executed in this field attention is paid to the research on effects of macrobiotic diets on linear growth in infants and children.
At last, the influence of exercise on linear growth is discussed, with special attention for lack of exercise and decreased linear growth.

1 Between-population variation in pre-adolescent growth

Between-population differences in rates of physical growth and development and attained body size are well documented, but is difficult to determine the extent to which these differences can be attritbuted to genetic and environmental factors. The greatest differences are to be found between populations in industrialised and non-industrialised nations, and between well-off and poorer groups within countries. Although genetic factors cannot be discounted, such differences can largely be attributed to differences in environmental quality experienced, influencing growth largely through differentials in nutritional well-being and exposure to, and treatment of, infectious disease. Growth patterns of well-off populations and groups of high socio-economic status are less heterogeneous, but differences between major global population groupings may still exist, bringing into question the validity of the concept of an international reference for the growth of young children. It is concluded that the growth patterns of all major population grouping are likely to have similar genetic potential, with the exception of Asiatics. However, there are no data on either secular trends or well-off groups from populations that have until recently been genetically isolated, and it is not known whether they share the same potential for growth as the major populations that

2 the migratory route suggests that variation in any trait is likely to be a continuum across populations, and that any classification is to some extent arbitrary;
3 prior to the onset of agriculture, some 12,000 years ago, humans lived as hunter-gatherers at low population densities often in isolation from each other, leading to the possibility of the development of regional population genetic differences.

Migrations taking place after the onset of agriculture served to create larger, more genetically homogeneous populations across wide areas, with genetically isolated populations left in less-hospitable ecological niches. Genetically isolated populations to be found in the world today include tribal groups of hunter-gatherers in Africa, Latin America, and Asia. Large-scale colonisation of the Pacific Islands took place at this time. Later migrations, during colonial times, include the migrations of

1 Europeans to the Americas, Australasia and parts of Africa;
2 Africans, mostly of Bantu origin, to the Americas and the Caribbean;
3 Asiatics, Chinese in particular, and Indo-Mediterraneans, largely South Asians, to most parts of the tropical world and to parts of the New World.

Migrations in the post-colonial period are largely related to economics and urbanisation. Examples include the migrations of Mexicans and Hispanics to the USA, and of South Asians and Afro-Caribbeans to Britain. In addition, there is the global trend of rural to urban migration in post-colonial times.

In summary, therefore, human populations have great homogeneity for most genetically determined characteristics, between-population variation having taken place in the recent evolutionary past. Migrations and population expansions have created several larger population groupings within which genetically isolated groups may be found.

Different human populations are known to vary from each other in a large and evergrowing list of genetic markers; growth patterns, body size and composition are polygenic in character. It is possible to classify populations around the world in a number of different ways (Table 1.1).

TABLE 1.1
Classification of population types

Classification	*Definition*	*Other terms used*
European and European origin	Living in Europe or elsewhere, of European ancestry	Caucasian, White, Anglo-American, European-American
African and African origin	Living in Africa or elsewhere, of African ancestry	Negro, Black, Black British, Afro-Caribbean, Afro-American, African-American
Asiatic	Living in Asia or elsewhere, of Asian ancestry	Asian, Indian (American)
Indo-Mediterranean	People of the Near East, North Africa, the Indian subcontinent and their descendants	Indian, Asian, Indo-Pakistani, Arab, South Asian
Australian Aborigines and Pacific Island peoples		Melanesian, Polynesian, Micronesian

This typology is rather rigid and simplistic. It does not comfortably include mixed populations such as Spanish-Indians in the Americas, European-Africans in the Caribbean, United States and Britain. Further, it aggregates populations that have been shown to have clear differences in growth pattern. For example, the term "African" includes the majority of Bantu-descended populations of Africa, as well as distinctively short-statured hunter-gatherer groups, such as the Mbuti of Zaire and the !Kung bushmen of Namibia. Furthermore, the term "Australian Aborigines and Pacific Islanders" covers populations with considerable genetic heterogeneity. However clumsy the classification is, it is the best that is currently available, and is used in this chapter in considering broad population growth characteristics.

Population differences in growth patterns

The number of studies of human growth and body size carried out worldwide during the latter part of this century, runs to three figures. However, many of them are of groups and populations living in poor environmental circumstances. Possible differences in growth patterns which might be attributed to genetic factors can be examined in a number of ways, including:

1 considering a body size measure such as height, of children at a given age from industrialised countries, and from the highest socio-economic groups in developing countries;

2 examining evidence for a secular trend in body size in European and non-European populations, and whether it has reached a plateau.

A comparison of mean heights of 7-year-old boys of different population types from industrialised countries and from the highest socio-economic groups in developing countries is given in Figure 1.2.

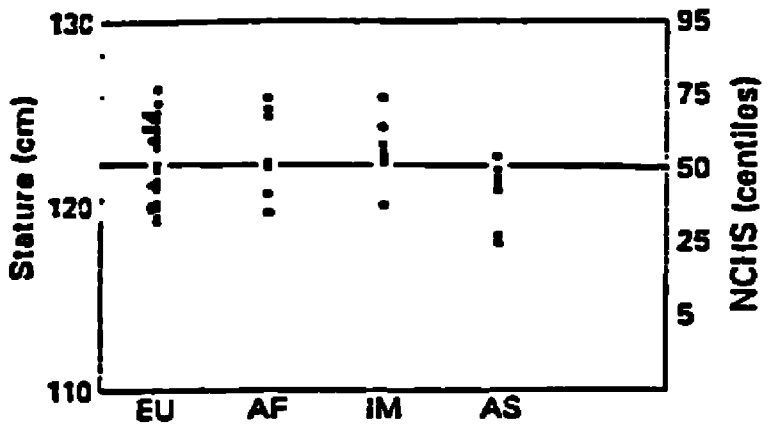


FIGURE 1.2
Mean statures of 7-year-old males from industrialised countries, and from well-off populations in developing countries

The range of means for 28 European and European-origin populations is 119.1 to 126.5 cm, similar to those for African and African-origin populations (119.6 to 126.0 cm), and Indo-Mediterranean populations (120.2 to 126.0 cm), but higher than that for Asiatic populations (118.1 to 122.6 cm). Thus, genetic potential for growth seems to be similar for all groups examined in this way, apart from Asiatic populations.

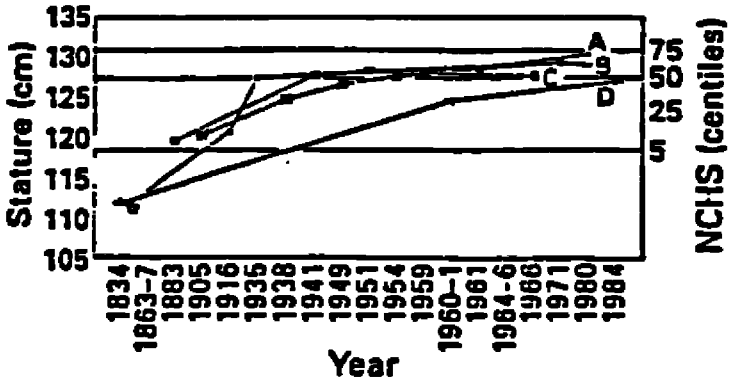


FIGURE 1.3
Secular trend in height of females at eight years of age, European populations

Evidence for secular increases in mean height of European, European-origin, and non-European populations is shown in Figures 1.3, 1.4 and 1.5. Mean heights of 8-year-old girls in the Netherlands, Belgium (Brussels), Britain (London) and Sweden (Figure 1.3) all show a positive secular trend, this having reached a plateau for the Netherlands, Swedish and London girls, with mean heights for all three lying between the 50th and 75th centiles of the National Center for Health Statistics references. For the populations of European origin, all three show a positive secular trend, having reached a plateau between the 25th and 50th centiles of the NCHS reference for Canadian and United States girls respectively, and still continuing for Australian girls. A possible explanation for this difference between Northern Europe and North America is the likelihood that the North American growth patterns represent a mixture of North and South European growth patterns. South Europeans, including

Spanish and Italian, are on average shorter in childhood than their North European counterparts. Thus it appears that North Europeans may have greater genetic potential for growth than North Americans.

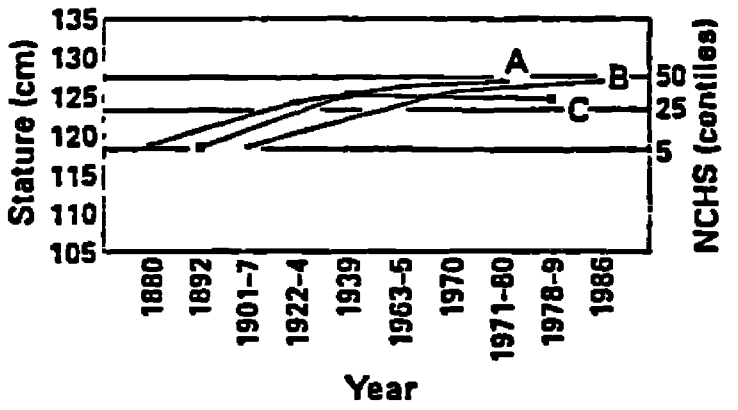


FIGURE 1.4
Secular trend in height of females at 8 years of age, populations of European origin

Evidence for the secular trend in children of non-European origin is sparse. Such as there is, is presented in Figure 1.5. A positive secular trend is shown for:
1 an African origin population (African Americans);
2 an Indo-Mediterranean population (girls in Trivandrum, Kerala, South India);
3 an Asiatic population (Japanese in Japan);
4 a Pacific Islands group (the Bundi, of Papua New Guinea).
However, in no case is there clear evidence that the secular trend has reached a plateau. Therefore, no definitive statement can yet be made about the genetic potential for growth in non-European populations.

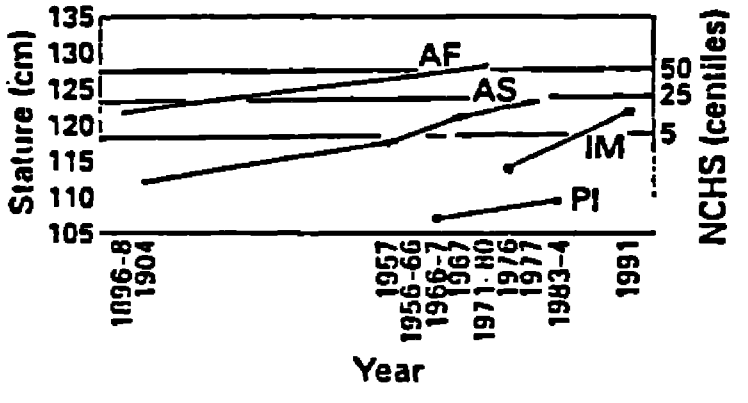


FIGURE 1.5
Secular trend in height of females at 8 years of age, non-European populations

The validity of the concept of an international growth reference
Any use of growth references internationally should acknowledge that they can act, at best, as imperfect yardsticks, since human populations may show similar

growth characteristics, but are unlikely ever to become so homogeneous that they show the same genetic potential for growth. Normal growth can be described as oscillation about a centile, rather that tracking along it. Thus, short-term deviation from a centile cannot be taken as evidence for pathology of any kind.
An international growth reference could be used for European and European origin populations, as well as African, African origin and Indo-Mediterranean populations. Current evidence suggests that they may not apply to Asiatic populations, but in the absence of definitive evidence of a cessation of the secular trend in any well-of Asiatic population, this assumption must remain tentative. It is not clear whether genetically isolated populations in various parts of the world, including Africa, India, Latin America and Asia, are likely to show the same potential for growth when placed in favourable environments. In addition, almost nothing is known about the genetic potential for growth of Aboriginal populations in Australia, or in Pacific Islands populations.

2 Nutritional influences on linear growth

This paragraph reviews what is known about the roles of specific nutrients in the general linear growth faltering that occurs in developing countries. Those reviewed are energy. protein, zinc, iron, copper, iodine and vitamin A. For none of these nutrients was there clear, consistent evidence that supplementation with the nutrient benefited linear growth. Rather, interventions with each specific nutrient had a positive effect on length gain in some studies, while in others these affected only weight gain or had no effect. Reasons for these conflicting results are suggested, including the strong probability that growth is limited by multiple, simultaneous deficiencies in many populations. Most interventions with single nutrients have been tested on children older than the age when linear growth faltering is most rapid, that is, within a few months of birth. Possible reasons why growth stunting begins so early in life are presented, but these are mostly hypothetical because of the paucity of information on this topic.

This discussion of nutritional influences on linear growth begins with a discussion of specific nutrient deficiencies that can cause linear growth retardation. There is a great deal of inconsistency in the reported growth-promoting benefits of supplementation with single nutrients. This may in part be explained by the fact that several nutrient deficiencies probably occur simultaneously in growth-stunted children. Another potential explanation is the fact that growth faltering is most rapid during the first year of life, whereas most supplementation studies have been performed on children older than this. The possible nutritional explanations of this very early growth failure are discussed.

2.1 THE ROLE OF INDIVIDUAL NUTRIENT DEFICIENCIES IN LINEAR GROWTH FALTERING

Energy

In most situations, interpretation of associations between energy (food) intake and linear growth is confounded by the fact that when food intake is low, the intake of many other nutrients will also be inadequate. However, two experimental approaches have shed some light on the question of whether energy deficiency affects linear growth. These include manipulating the energy content of infant formulas, while keeping the content of other nutrients at adequate and/or constant levels, and the provision of supplemental energy alone to stunted children.

Fomon *et al.* (1977) examined the impact on infant growth of manipulating the energy content of infant formulas. Infants were fed either a modified skim milk formula or Similac between 112 and 167 days of age. The low-fat, low-carbohydrate skim milk formula contained 151 kJ/dl, and although the volume consumed was greater than that of Similac, average energy intake was low and ranged from 2173 to 2407 kJ/day. In contrast, Similac contained the recommended energy content of 280 kJ/dl and supported energy intakes between 2550 and 3006 kJ/day. The infants consumed substantially more protein from the low energy formula (which contained 3.56 g/dl protein vs 1.72 g/dl), and more of most minerals and vitamins. In these previously well-nourished infants, low energy intake had a negative impact only on ponderal gain, and did not affect linear growth.

Similar results were obtained when infants were fed a formula providing 226 kJ/dl vs 419 kJ/dl (Fomon *et al.*, 1975). The two formulas contained similar concentrations of protein and micronutrients, and intake of these was substantially higher from the low energy formula, because of the greater volume consumed. Between 8 and 41 days of age, weight gain was 29.8 ± 4.9 g/day vs 41.0 ± 10.4 g/day, with the low vs high energy formulas respectively ($P < 0.01$), while length gain was unaffected (1.23 ± 0.17 mm/day vs 1.26 ± 0.17 mm/day).

In an interesting case study of an obese infant who required intravenous and enteral nutritional support, energy intake was reduced from approximately 293 to 209-230 kJ/day at 12 months of age. The intake of other nutrients was adequate. Her weight and fat (but not lean) tissue mass were markedly reduced while her length gain was unaffected (Peipert *et al.*, 1992).

There are conflicting results concerning whether supplementation with energy alone improves linear growth of stunted children. No effect on linear growth was found in New Guinea, where taro or sweet potato supplied most of the nutrients and children were very stunted, but not wasted (Allen, 1994). Children, age 5.5 to 15.5 years, were provided with supplements of either more of their usual diet by increasing the number of meals from 3 to 5 per day, 30 g margarine/day, or 75 g skim milk/day for 13 weeks. Compared to the unsupplemented control group, height increment was increased 40% by extra food, and 111% by skim milk; based on skinfold thickness, height was gained at the expense of fat stores. The margarine supplement did not increase linear growth. Weight gain was more rapid when either the skim milk or the margarine supplements were provided.

Thus, additional energy did not increase the rate of linear gain in these stunted (but not wasted) children, although it did increase weight gain and fatness.
In contrast, undernourished Indian children, age 1 to 5 years, increased both their height and weight gain when their diet was supplemented daily with a high energy (1298 kJ/day), low protein (3 g/day) cake for 14 months (Allen, 1994). The cake was prepared from wheat flour, sugar and oil, and no micronutrients were added. The supplement was also effective in preventing the loss of height and weight gain which occurred in unsupplemented children affected with measles. These children were certainly malnourished because some of them developed kwashiorkor or marasmus during the study, but actual height and weight data were not provided. Thus, it is unclear whether they were stunted and/or wasted.

Protein
Many investigators have observed an improvement in the linear growth of stunted children after supplementation with protein-rich foods such as milk, either alone or with other foods or nutrients, while others have not (Allen, 1994). However, there is little information on the specific role of protein in linear growth, because low protein intakes are usually accompanied not only by low energy intakes but by inadequate amounts of important micronutrients that are contained in dietary protein sources. These include iron, zinc, copper, calcium and vitamin A.
Linear growth faltering, or subsequent failure to recover, may occur even when intakes of energy and/or protein are adequate. This raises the question of the extent to which micronutrient deficiencies impair linear growth of human populations.

Zinc and linear growth
Zinc supplements improved the linear growth of short, but generally well-nourished children in the United States and Canada. In these children, selected for shortness, zinc did not affect weight gain. In contrast, supplements provided to low weight-for-age infants in the United States, improved only weight. There is no known reason why these children in industrialized countries should be zinc deficient; because the children were selected on the basis of poor growth and evidence of zinc deficiency, they may represent a segment of the population with relatively high zinc requirements. In spite of the generally positive impact of zinc supplements on the growth of small children in wealthier countries, further work is needed to determine whether zinc nutritional status is an important determinant of linear growth retardation in developing countries (see paragraph 3).

Iron
Reports of the benefits of iron supplementation for the linear growth of anemic children have shown mixed results (Allen, 1994).
From the available studies it is quite possible to conclude that linear growth only responds to iron treatment if the child was initially anemic.

Copper
The main risk factors for copper deficiency in children are low birth weight, low copper intake (e.g. due to high intakes of cow's milk), and malabsorption and diarrhea. Children recovering from severe malnutrition have low copper stores and benefit from copper supplementation, especially if fed high-energy, low-copper diets. A beneficial effect on weight gain and weight-for-length of supplementation with 80 µg of copper per kg per day for one month was found in eleven children recovering from malnutrition. Only those with low serum copper and ceruloplasmin initially were found to benefit. Energy intake was also higher after supplementation. Length increase was greater but not significantly so, perhaps because of the short period of study and small number of subjects. Also an improvement in bone-maturation delay in four severely malnourished infants after copper therapy was found (Allen, 1994),

Iodine
Iodine deficiency is endemic in some regions of the world, and when it is severe it can certainly cause substantial linear growth retardation. Marginal deficiency, the occurrence of which has probably been underestimated, is also associated with short height. It is possible that iodine deficiency during fetal life has a persistent impact on later growth. In a region of Ecuador with severe iodine deficiency, interventions with iodinated oil failed to change children's growth. On the other hand, if women are given iodinated oil prior to conception, the birthweight of their infants is increased. Because iodine status is adequate in many of the populations in which growth faltering occurs, it is probably not a major explanatory factor for the global prevalence of stunting. It is also a special case in that its level of intake is relatively independent of the adequacy of the food supply (Allen, 1994).

Vitamin A
The impact of vitamin A intervention on growth is highly variable among studies. During spontaneous recovery from xerophthalmia, weight gain recovery may be more likely than height gain. Length gain was only improved when there was a sustained improvement in the vitamin supply through food fortification. Finally, supplements or food fortification have not benefitted the growth of children under one year of age, when growth failure is most serious.

Summary and conclusions concerning single nutrient deficiencies and linear growth stunting
Interventions with single nutrients, in the case of all of the nutrients reviewed above, have produced conflicting results concerning their ability to reverse growth stunting. For example, zinc supplements have stimulated linear growth in some studies, ponderal growth in others, or have shown no effect. Certainly no single nutrient supplement had a major, consistent effect on linear growth. There are several possible explanations for the lack of consistency among studies. One is that short or underweight children were sometimes selected deliberately by the investigators, while in others all children in a group were studied. Other selection criteria that varied among studies were recent diarrhea, and the exclusion of severely anemic cases. The age of the children differed

across studies and so did the amount and type of supplement used. Nevertheless, the amount of supplement provided in these interventions should have produced an impact on linear growth if that specific nutrient had been growth-limiting. It is therefore plausible that multiple, rather than single, growth-limiting nutrient deficiencies exist in the same children. In the next section this possibility is explored.

2.2 DIETARY QUALITY AND LINEAR GROWTH

Existence of simultaneous multiple micronutrients deficiencies

Except in the case of iodine deficiency, where status is less dependent on the general adequacy of the food supply, there are several reasons to believe that multiple micronutrient deficiencies will exist in most other situations. First, if food is so scarce that energy intake is inadequate, then dietary quality is also likely to be poor. Specifically, a poor quality diet would contain few animal products, fruits and vegetables, and consists primarily of staples such as cereals, legumes or other plants (Allen, 1994). Such poor quality diets are associated with low intakes of several vitamins and minerals and poor mineral bioavailability. Poor dietary quality is a more common situation than actual food shortage in less wealthy countries, population groups and individuals. Also, morbidity is likely to cause depletion of several nutrients simultaneously, through anorexia or malabsorption.

Examples from the Nutrition CRSP

Data from the Nutrition Collaborative Research Support Program (CRSP) support the importance of dietary quality and the existence of multiple micronutrient deficiencies in developing countries. The Nutrition CRSP was a longitudinal study of the impacts of marginal malnutrition on the function of infants, preschoolchildren, schoolchildren and adults in Mexico, Kenya and Egypt. Multiple food intake measures on these individuals made it possible to explore relationships between the intake of specific foods and nutrients, and growth (among other functions).

Similar to the situation in many developing countries, linear growth faltering occurred within a few months of birth and was substantially complete by about 18-22 months of age. The growth pattern was similar in Mexico, Kenya and Egypt. The important question here is the extent to which this linear growth faltering is associated with dietary patterns or nutrient deficiencies. In Mexico and Kenya the staple foods are maize and legumes, while in Egypt wheat and rice provide most of the energy. Dairy products are eaten in very small quantities in all three locations, especially by Mexican and Kenyan schoolchildren. Other animal products, specifically meat and eggs, are eaten in low amounts especially in Kenya. However, among the CRSP preschoolchildren (and other individuals) within each country there was a nutritionally significant range in variation in dietary quality which permitted analysis of the relationship between dietary patterns and growth stunting.

Energy (food) shortage was not a problem in Egypt and Mexico based on evidence such as: energy intakes met recommended levels on average; energy intake of adult women increased substantially in early lactation, showing the

availability of additional food; adult women were relatively fat and body mass index increased with each decade of life. Analysis of data from Mexico showed that household energy intake kept pace with household energy requirements, while the quality of household diets (consumption of animal products), and especially that of preschoolchildren's diets, did not (Allen, 1994). In Kenya, where periods of drought-induced food shortage occurred during the project, diets were low in both quantity and quality.

Beaton, Calloway & Murphy calculated the probability of protein and/or lysine deficiency in the three CRSP locations. In Egypt and Mexico protein and lysine intakes were adequate. There was a very small risk that protein and lysine intakes were inadequate for some Kenyan children, but had energy intake (food supply) been adequate, the prevalence of low intakes would have been negligible. Lysine intakes were about twice as high as the FAO/WHO recommendations, and tryptophan, threonine and sulfur amino acid intakes were even more adequate. It is unlikely, therefore, that protein or essential amino acid deficiencies were limiting the linear growth of these preschoolchildren.

In contrast to the adequacy of energy and protein intakes, none of the diets provided adequate amounts of vitamins or minerals. Also the probability of inadequate vitamin intakes in preschoolchildren, based on approximately two days of food intake per month for one year was calculated. Egyptian preschoolchildren frequently had inadequate intakes of vitamins A, E and riboflavin. Mexico appeared to be the worst situation in that there was a very high prevalence of inadequate intakes of vitamins A and E, riboflavin, B_{12}, and ascorbic acid. In Kenya the main vitamin inadequacies were vitamins E, A and B_{12}. In general, preschoolchildren in the CRSP countries who had low intakes of animal products had the lowest intakes of fat, and vitamins A, B_2, B_{12}, C and E.

Estimation of the adequacy of mineral intakes is complicated by their bioavailability, which is likely to be poorest when diets contain more foods that have a high content of phytate and fiber, and are low in enhancers of absorption such as animal protein and ascorbic acid. It was concluded that between 31% and 65% of the preschoolchildren would not meet their basal requirement for iron, and 12 to 43% would not absorb enough to prevent anemia. Virtually all Kenyan children and most Mexican children are expected to have inadequate intakes of zinc. Copper intake was not inadequate in any of the populations.

The reasonableness of these prevalence estimates is substantiated by biochemical data. Anemia and iron deficiency were highly prevalent in all three countries. At around 30 months of age, the percentages of children with low hemoglobin and low ferritin respectively were: Egypt, 38 and 73; Kenya, 40 and 74; and Mexico, 45 and 62 (Allen, 1994).

In a subsequent study of 220 children, 18-30 months old, in the same region of Mexico, we found that 84% had anemia, 40% had deficient or low serum retinol, 59% had deficient ferritin, and 41% had low or deficient vitamin B_{12}. Although not measured, the presence of other micronutrient deficiencies is highly probable.

Associations between dietary quality and growth of preschoolchildren

The existence of simultaneous deficiencies made it difficult to detect associations between the intake of a single nutrient and growth. For example, in the Mexican preschoolchildren there was no significant relationship between size at 30 months (weight, length or weight-for-length) and each child's average intake of energy, protein, or other nutrients during the previous 12 months (Allen, 1994). Stronger, positive associations were found between the intake of specific foods and linear growth. The usual diet of taller children contained more animal products (especially milk and meat), and fewer maize *tortillas* than that of shorter children. These relationships persisted when socioeconomic status was controlled in analyses. Weight was less strongly related to the intake of specific foods.

These associations raised the question of why animal product intake was associated with the children's linear growth. Several important generalizations emerged from the Mexico data that are likely to apply to many populations with limited resources. One was the appreciation of the importance of considering dietary *patterns* rather than nutrient intakes. Those children who consumed proportionately more maize *tortillas* ate substantially less meat, dairy products, fruit and 'other plant' products (mostly refined cereals). Dairy product intake fell to almost zero when energy intake from *tortillas* exceeded 61%, a situation that occurred in about half of the preschoolchildren. Thus, it is difficult to ascribe growth stunting to lack of a single food group or excess of another, because a lower intake of, for example, dairy products is also associated with a lower intake of meat, fruits and vegetables and a higher intake of high phytate, high fiber *tortillas*. Rahter, it is how the child ranks on this dietary pattern continuum that is important.

Children who ate more *tortillas* actually consumed more iron, thiamin, zinc, energy, calcium and niacin because of the high levels of these nutrients in maize. Because *tortilla* intake was negatively associated with growth, however, it seemed reasonable that the problem might be the poor bioavailability of minerals in this staple food. Indeed, higher intakes of fiber and phytate relative to iron and zinc did predict lower height at 30 months of age.

In addition, those preschoolchildren who consumed the smallest amount of animal products (i.e. the lowest quartile of % energy from animal sources) had an *inverse* relationship between their weight and length gain during the 18-30 month age period (Allen, 1994). In contrast, when more animal products were consumed, weight and length gain showed the expected positive relationship. Similarly, children in the lowest quartile of animal product intake had a negative, rather than the expected positive, relationship between their length at 30 months and the weight of their mother. These relationships indicate that poor dietary quality impairs the growth potential of young children. A similar conclusion was reached in the Egypt and Kenya Nutrition CRSP project (Allen, 1994).

2.3 NUTRITIONAL EXPLANATIONS OF EARLY LINEAR GROWTH FALTERING

Above we have shown that dietary quality is important for the linear growth of preschoolchildren between 18 and 30 months of age. However, it is apparent that the period of greatest growth faltering started very early, at about 3 months after birth, and was essentially complete well before the weaning period. This early growth faltering is common to most developing countries. Between about 22 and 40 months of age, linear growth in the group as a whole is undergoing a slight 'catch-up' relative to rates in well-nourished reference children.

Early growth faltering may be related to suboptimal fetal endowment with nutrients during pregnancy so that stores are low at birth; this may be compounded by low levels of nutrients in breast milk of the same mothers; the peak prevalence of diarrhea and morbidity occurs after growth faltering begins; and in the postweaning period, when most children consume a diet similar to the rest of the household, there is a relatively *faster* rate of growth with some 'catch-up'.

The role of perinatal and maternal nutrition in linear growth faltering therefore deserves more attention; there is almost no information on this topic in human populations. Maternal nutritional status is likely to affect fetal endowment of minerals and vitamins, and to predict the age at which stores of these nutrients become depleted postnatally. The size of the infant at birth is known to be a strong predictor of size at 6-8 months and resistance to growth faltering in the early *postpartum* period, though the reason for this is not understood. In addition, mothers who have suboptimal nutritional status during pregnancy are likely to do so in lactation.

It is now generally accepted that maternal capacity to produce a normal volume of milk is relatively unaffected by moderate maternal malnutrition, so that inadequate milk production is unlikely to be a significant factor in early growth faltering.

There is little available information concerning the important question whether low levels of specific nutrients in breast milk might contribute to infant growth faltering. Zinc and iron concentrations in breast milk seem to be relatively unaffected by maternal intake (including supplements) or status. In contrast, milk vitamin concentrations are relatively strongly associated with maternal intake and stores, especially in the case of water soluble vitamins. Vitamin A in the form of fortified MSG marketed through ordinary channels in Indonesia, increased the concentration of retinol in breast milk by about 16% but had no impact on infant growth (Allen, 1994).

2.4 THE IMPACT OF DIARRHEA, INFECTIONS AND PARASITES ON GROWTH

Although there is clearly an association between infection, especially if accompanied by diarrhea and growth faltering, the extent to which illness is generally responsible for endemic growth faltering is still debatable. Estimates show that perhaps one third of the total amount of linear growth failure can be ascribed to illness.

The problem of linear growth failure must still be regarded as having a nutritional basis, mediated, for example through poor appetite (especially for non-breast milk foods), and malabsorption of nutrients including zinc and copper. It is still important to know which nutrients become growth-limiting in this situation in order to plan effective intervention.

3 Adequacy of dietary mineral supply for human bone growth and mineralisation

The evidence on the relationship between dietary mineral supply and bone development in children is well known. Data from children and primates suggest that overt deficiencies of Ca, P and Zn are likely to produce rickets and growth retardation, while the effects of Mg deficiency on human bone are unknown. The manifestations of marginal deficiencies are little understood. The biological needs for Ca, P, Mg and Zn in childhood have been calculated based on mineral deposition rates, using published values for the mineral content of the human body, and on obligatory endogenous losses. As a rough guide, the estimated biological requirements for the Ca, P, Mg and Zn can be taken as 200, 100, 4 and 1 mg/d respectively. A comparison of measured daily intakes of children in developing countries with biological requirements was made. This revealed that P and Mg intakes were many times higher than estimated needs. Ca intakes at all ages were found to be close to the biological requirement for children in many Third World societies, before any allowance for possible poor absorption. Zn intakes approach estimated needs in breast-fed infants, particularly during weaning, but are 4-5 times higher in older children. Poor absorption from phytate-rich diets could affect Zn supply. Supplementation studies indicate that raising Zn intakes can increase height gains in certain vulnerable groups, such as infant and adolescent boys. In conclusion, the evidence suggests that inadequate dietary intakes of Ca and Zn may contribute to linear growth retardation in children of developing countries but more research is needed.

Considering a possible relationship between dietary mineral supply and bone development in children, the following questions, especially with respect to developing countries, arise:

1 What are the biological requirements of Ca, P, Mg and Zn for normal growth in the human?

2 What are the likely manifestations of an inadequate supply of Ca, P, Mg and Zn in the growing child? Do children in developing countries show signs that could be attributed to mineral deficiencies?

3 Are the mineral intakes of children in developing countries low in relation to the biological requirement or in comparison with well-nourished children in developed countries? Are diet composition and illness likely to affect mineral bioavailability? What is the contribution of breast-milk to mineral intakes in early childhood?

4 What evidence do we have that increasing the intakes of these minerals would improve growth or bone development in Third World children?

3.1 BODY CONTENT, BIOLOGICAL ROLE AND CHILDHOOD ACCRETION RATES

Table 1.2 provides details of the body content of Ca, P, Mg and Zn in a newborn baby at term, a typical man and a typical woman. As can be seen, an adult contains approximately 1 kg of Ca and 0.5 kg of P respectively, while Mg and Zn are present in smaller quantities.

TABLE 1.2
Whole body mineral content and compartments of calcium, phosphorus, magnesium and zinc in the human[a]

		Adult		*Body compartment*	
	Baby[b] (mg)	*Male*[c] (mg)	*Female*[d] (mg)	*Bones* (%)	*Soft tissues* (%)
Calcium	28.2	1344	1008	99	1
Phosphorus	16.2	720	540	80	20
Magnesium	0.76	28.2	21.2	60	40
Zinc	0.053	1.68	1.26	30	70

To convert mg to mmol divide by 40, 31, 24.3, 65.4 for Ca, P, Mg, Zn respectively.

[a] Chemical data from Widdowson & Dickerson (1964).

[b] Based on 3.5 kg full-term infant.

[c] Based on 60 kg fat-free mass (e.g. man 70 kg body weight, 15% fat).

[d] Based on 45 kg fat-free mass (e.g. woman 60 kg body weight, 25% fat).

All four minerals have important functions outside the bone compartment, and are widely distributed throughout the soft tissues and fluids. The remaining 1% of total body Ca is involved in processes such as nerve and muscle function, bloodclotting and intracellular signalling. Non-osseous P is a component of many essential compounds, such as phosphate bonds, like ATP. Non-skeletal Mg is involved in DNA replication, RNA synthesis, and is a cofactor for enzymes requiring ATP. Zn is essential for cell division, nucleic acid and protein synthesis and is a component of many enzymes. Unlike the other three minerals, the major portion of total body Zn occurs not in bone but in the soft tissues, primarily in muscle (Table 1.2), although the concentration of Zn in bone is high.

Considerable quantities of all four minerals are deposited in the body between birth and maturity. The accretion of mineral is greater than the increase in body weight over the same period. Table 1.3 gives estimated values, based largely on the compositional data in Table 1.2 for mineral accretion rates during childhood. The continuous rates have been obtained by assuming that maturity is reached by 18 years of age in both sexes and that the accretion rate is constant throughout childhood.

In addition to the requirements for growth, losses of the four minerals occur in urine, sweat, gastrointestinal fluids, skin, hair and nails.

TABLE 1.3
Estimated mineral accretion rates in childhood

	Continuous[a]		*Infancy*[b]		
	Male	*Female*	*0-4 months*	*4-12 months*	*Peak*[c]
Calcium mg/day	200	149	155	130	400
Phosphorus mg/day	107	80	79	66	214
Magnesium mg/day	4.2	3.1	3.3	2.7	8.4
Zinc mg/day	0.25	0.18	0.5	0.3	0.5

[a] Average accretion rate in childhood, based on assumption of continuous growth and maturity at eighteen years in both sexes (British Nutrition Foundation, 1989).
[b] Accretion in infancy as calculated in Fomon (1974) and Krebs & Hambidge (1986).
[c] Peak rate in adolescence based on calcium calculation of Kanis & Passmore (1989) and assuming proportions of Ca, P, Mg, Zn are the same as during continuous growth.

The figures in Tables 1.2 and 1.3 can only be used to provide an approximate assessment of mineral deposition during childhood. However, these data provide a useful basis on which to discuss the likely adequacy of dietary supply for children in Third World countries. For this purpose, the following figures, based on the continuous accretion rate for boys (Table 1.3) + losses for Zn, are a useful rough guide: Ca 200 mg/day; P 100 mg/day; Mg 4 mg/day; Zn 1 mg/day. These figures will be referred to in the rest of paragraph 3 as the *biological requirement.*

3.2 LIKELY MANIFESTATIONS OF MINERAL DEFICIENCIES IN CHILDREN

Little is known about the manifestations of specific deficiencies of bone-forming minerals in the human. As all the Ca and P needed for building bones must originate from the diet, and as there are no significant extraskeletal reservoirs of these minerals, there must be intakes which cannot support normal growth and bone development.
There is evidence to suggest that very low Ca intakes in children may induce rickets and osteomalacia and that phosphorus deficiency also precipitates rickets in children: the rickets-like metabolic bone disease of premature babies is currently believed to be primarily a problem of phosphorus supply (Prentice and Bates, 1994).
It is possible that the effects of Ca and P deficiencies may arise from an imbalance of the two bone-forming minerals in the diet.
Severe magnesium deficiency in man is characterised by muscle weakness, neuromuscular dysfunction and cardiac disturbances, normally in association with debilitating diseases, such as diabetes and alcoholism. Failure to thrive, growth retardation, bone abnormalities and disturbances of Ca metabolism have been described in Mg-depleted animals. The Mg content in bone of growing Mg-deficient animals can be 80% below normal, although calcium contents are often increased.
In contrast to Ca, P and Mg, the consequences of human Zn deficiency have been well documented due to problems arising from acrodermatitis

enteropathica (an inherited disorder affecting Zn absorption), sickle-cell anemia, chronic renal disease and other conditions. Moderate-severe Zn deficiency in children depresses growth, appetite, skeletal maturation and gonad development, which can be reversed with Zn treatment. Zn deficiency is associated with metabolic disturbances of a wide range of hormones, cytokines and enzymes, involved in growth and bone development. In addition, Zn deficiency affects the immune system, the structure of the skin and intestinal mucosa, taste perception, wound healing, and dark adaptation. Children with severe malnutrition show clinical signs and immunological deficits, which are correctable by Zn. Whether the effects of Zn deficiency on growth and bone development are a direct consequence of inadequate Zn supply for bone formation, or are secondary to the effects of Zn on appetite, the action of growth-promoting factors or cell division is not known.

There have been a number of observations that suggest that Zn deprivation may be implicated in human growth retardation. Adolescent nutritional dwarfism in Middle-Eastern countries, characterised by poor growth and delayed sexual maturity, has been related to Zn deficiency in association with deficiencies of other nutrients. In addition, poor Zn status, as suggested by low Zn levels in blood or hair, has been described in growth-retarded Chinese, Mexican, Thai and Papua New Guinean children among others (Prentice and Bates, 1994).

3.3 DIETARY INTAKES OF CHILDREN IN DEVELOPING COUNTRIES

The diets of disadvantaged peoples of the developing world vary from one community to another, but in many regions the main components are cereals and plant foods. Consumption of animal milks and meat is often limited. It would be predicted, therefore, that the Ca and Zn intakes in these communities would be low. Intakes of P and Mg would be expected to be relatively high, as cereals and plants are rich sources of both these minerals. Culinary practices, such as the use of plant ash (e.g. Nyasaland Bantu; American Indians, Papua New Guineans), lime in the making of tortilla (Mexico), and dried baobab leaf in preparation of steamed millet (The Gambia) could make valuable contributions to mineral intakes in some societies (Prentice and Bates, 1994).

In general, only 30–40% of dietary Ca and Zn are absorbed from typical Western diets, while absorption of P and Mg is somewhat higher at 40-60%. Ca absorption from predominantly plant-based diets is thought to be considerably reduced, due to the chelation properties of compounds such as phytates and oxalates.

The extent to which individuals habituated to low mineral intakes have adapted to their diets, is unknown. Positive balances have been reported in children and adults with low Ca and Zn intakes, indicating that absorption efficiency must be high and losses low. It has been suggested that colonic absorption, after degradation of fibre and phytate by bacteria, may play an important role in this context. Adaptation of Ca metabolism to diets containing high amounts of phytate, has been observed. Mg and Zn restrictions are also accompanied by increases in absorption efficiencies and decreases in endogenous losses (Prentice and Bates, 1994).

The diets of children in developing countries may differ from those of adults. Many infants and toddlers are breast-fed for prolonged periods and receive specially-prepared weaning foods. Older children may receive preferential or reduced amounts of certain foods, such as milk or fish, relative to adults. It is, therefore, important to judge the likely adequacy of the mineral supply during childhood by using dietary data collected from children.
These data demonstrate that, as predicted, Ca intakes of children in many disadvantaged communities do appear to be very low.
In contrast, the measured intakes of zinc are not dissimilar to those in affluent societies, due to the fact that unrefined cereals and plant foods contain reasonably high amounts of zinc. The measured intakes of P are moderate to high in older children, resulting in low Ca : P ratios, 1 : 2-1 : 3 mg/mg. Children who are exclusively or partially breast-fed have lower P intakes, and the Ca : P ratio of their diet is higher. In the limited number of studies in which Mg ingestion has been quantified, intakes of children in developing countries appear to be of the same order of magnitude as adult intakes in the UK (Prentice and Bates, 1994).
Breast milk is a major dietary component for many infants and young children in the developing world. Breast milk production by mothers from disadvantaged communities is similar in general to that of mothers in affluent societies, and can be maintained for prolonged periods. Minerals concentrations in mature breast milk decline as lactation progresses in women from both developed and developing countries. This is particularly striking for Zn. There is no evidence of regional variations in P, Mg and Zn concentrations in breast milk, but Gambian women have been shown to have Ca levels that are 20% below those of British women, and low Ca concentrations have been reported from a number of other developing countries. Whether this is a consequence of low maternal Ca intakes is not known. In general, average Ca, P, Mg, and Zn intakes of exclusively breast-fed children at 3 months are approximately 200 mg, 100 mg, 23 mg and 1.8 mg respectively, although it is important to realise that there are wide variations in breast milk mineral outputs between individual mothers. Measured intakes for non-breast-fed children in disadvantaged communities typically are in the following ranges (mg/d): Ca 150-400; P 500-1000; Mg 200-300; Zn 3.0-7.0 while intakes for younger breast-fed children are some what lower (Prentice and Bates, 1994).

3.4 SUPPLEMENTATION STUDIES

Ultimately, the question of whether specific mineral deficiencies may affect the growth and bone development of children in the developing world can only be answered with carefully controlled supplementation studies. To date, there have been relatively few such investigations, and most have involved supplementation with either Zn or Ca. The accumulating evidence suggests that Zn supplementation can increase the height and weight gains of certain groups, particularly infant and adolescent boys, in both developed and developing countries. The response may be limited to individuals with pronounced growth-faltering or low plasma/hair Zn levels. Whether the effect of Zn is a direct consequence of improving Zn supply for tissue growth and metabolism,

or is mediated through stimulation of the appetite is unclear (Prentice and Bates, 1994).
The results of Zn supplementation are more dramatic for children, male and female, recovering from severe malnutrition, when growth is extremely rapid and requirements are much greater than normal. Zn supplementation of customary rehabilitation diets not only improves weight gain but produces proportionately greater deposition of lean tissue. An increase in length gain was noted in one study. In addition, Zn treatment of young children recovering from severe diarrhoea has been shown to enhance length gains (Prentice and Bates, 1994).

The main impression from the few available Ca studies is that supplementation with Ca alone or together with P has little impact on growth velocity but may correct biochemical indicators of marginal Ca status. The comparison of measured mineral intakes of children in the developing world with estimated biological requirements (accretion rates + obligatory losses) can be summarised as follows:
– The average intakes of P and Mg are substantially greater than biological requirements. There is evidence that absorption of these minerals and conservation of endogenous losses are likely to be high. It would appear unlikely, therefore, that inadequate dietary supply of P and Mg contributes to the poor linear growth of Third World children.
– Zn intakes of breast-fed children are close to the biological requirement, if one assumes that there is only limited capacity to reduce losses. Children who are no longer breast-fed have intakes that are 4-5 times above the biological requirement, but Zn supply may be restricted by poor bioavailability. Supplementation studies suggest that the linear growth of vulnerable groups of children, particularly infant and adolescent boys, can be increased by rasing Zn intakes. The mechanism by which this occurs is unknown, but is likely to be related to stimulation of appetite or to metabolic effects, rather than to an improved supply of Zn for bone formation *per se*.
– Ca intakes at all ages are close to the biological requirement for children in many developing countries (less than 1-2 times). In addition, absorption of Ca from Third World diets may be poor, because of the presence of chelating components, such as phytates and oxalates. There is little data on the extent to which children can adapt to low Ca intakes in terms of enhanced absorption and decreased losses, but it must be assumed that substantial adaptation can occur. It may be that slow growth rates represent an adaptation to limited mineral supply. There are indications that marginal Ca status may be reflected in biochemical signs of hyperparathyroidism and in low bone mineral contents, and may induce or predispose children to rickets. The evidence from the small number of Ca supplementation studies on the effects of increasing Ca intakes on bone growth and development is inconclusive.

In reaching these conclusions, a number of assumptions have had to be made which should be borne in mind when interpreting the findings. Firstly, no consideration has been made about the wide differences there are likely to be in requirements, intakes and ability to adapt between individual children.

Secondly, estimating needs on the basis of mineral deposition rates does not take account of the intakes which may be required to maintain optimal function, especially relevant for Zn and Mg. Thirdly, the arguments are based on inadequate data, particularly with respect to the mineral content of the body, the absorption and losses of minerals from children habituated to low intakes, and the identification of marginal mineral status in Third World children.

4 Effects of macrobiotic diets on linear growth in infants and children up to 10 years of age

In order to study the relationship between diet and growth, growth patterns in children 0-10 years old on macrobiotic diets have been assessed. A cross-sectional anthropometric study (0-8 years old children, $n = 243$) indicated that deviation from the reference growth curve occurred during the weaning period. Between 2 and 4 years there was a partial catch-up for weight and arm circumference but not for height. As a next step, a mixed-longitudinal study was performed in 4-18-month-old macrobiotic infants ($n = 53$) and matched omnivorous controls ($n = 57$). For a period of 6 months, data on growth and dietary intake were collected. The data on linear growth supported the findings on growth stagnation observed cross-sectionally. Linear growth was associated with the protein content of the diet, but not with energy intake. On the basis of the first findings nutritional modifictions to the macrobiotic diet (addition of fat and fish) were recommended for all macrobiotic families. Six months later (two years after the first cross-sectional data collection) the anthropometric study was repeated in the same cohort ($n = 194$). This follow-up study revealed that children from families which, since the initial study, had increased the consumption of fatty fish, dairy products, or both, had grown in height more rapidly than the remaining children ($P < 0.05$). Since no indications were found for the presence of adverse social circumstances, infectious diseases or other confounding factors, the data clearly demonstrate that linear growth retardation in children on macrobiotic diets is caused by nutritional deficiencies alone.

From 1985 onwards, growth patterns of children on macrobiotic diets in the Netherlands have been studied, because these children appeared to be significantly lighter and shorter than a control group fed an omnivorous diet. The macrobiotic diet has characteristics similar to the diet of many children in developing countries, in that it is also mainly composed of foods high in starch and fibre but low in protein. In developing countries, however, such a type of diet often coincides with other unfavorable circumstances, which may influence linear growth. In contrast, in the Dutch studies we did not find any evidence for the existence of adverse social circumstances, infectious diseases or other confounding factors. Thus, with this group of macrobiotic children, it was possible to study the effects of diet alone.
Macrobiotic children have a very restricted, almost vegan, type of diet consisting of grain cereals (mainly rice), vegetables, pulses and sea vegetables, with only small amounts of cooked fruits and occasionally some fish. Meat, dairy products and vitamin D supplements are not being used and fish is rarely

given to young children. Intakes of calcium, riboflavin and vitamin D, recorded for the macrobiotically fed children, were substantially below the Dutch RDAs. The aim was to answer the following questions:

1 At what age does growth faltering in height occur in children fed macrobiotic diets?
2 Which nutritional factors are associated with linear growth retardation?
3 What is the effect of modification of the diet on linear growth?

In this paragraph, we will speak of growth retardation when a significant difference ($P < 0.01$) from the median of the Dutch cross-sectional growth reference or from the growth curve of a matched omnivorous control group is observed. Catch-up growth is defined as a positive shift towards the median of the Dutch reference curve or towards the median of the curve of the omnivorous control group.

4.1 CROSS-SECTIONAL STUDY IN 0 - 8-YEAR-OLD CHILDREN

Birth weight
Of macrobiotic children 4.3% had reported birth weights below 2500 g, compared to 2% in a comparable Dutch population ($P < 0.02$). The average birth weight was 3360 g for boys (Dutch median 3500 g; significant difference at $P < 0.001$) and 3250 g for girls (Dutch median: 3390 g; $P < 0.001$) (Dagnelie *et al.*, 1988).

Growth
The curve of length/height for age (Figure 1.6 shows data of girls only, curves for boys were similar) followed the median of the standard until the age of 6-8 months, after which a marked decline was observed, reaching a minimum level (P10) between 1.5 and 2 years. No catch-up was observed at older ages. The curves of weight for age and arm circumference for age showed the same pattern, but now a partial return towards the P50 of the reference was observed after 2 years of age. The curve of weight for height followed the median of the Dutch reference (Dagnelie *et al.*, 1988).

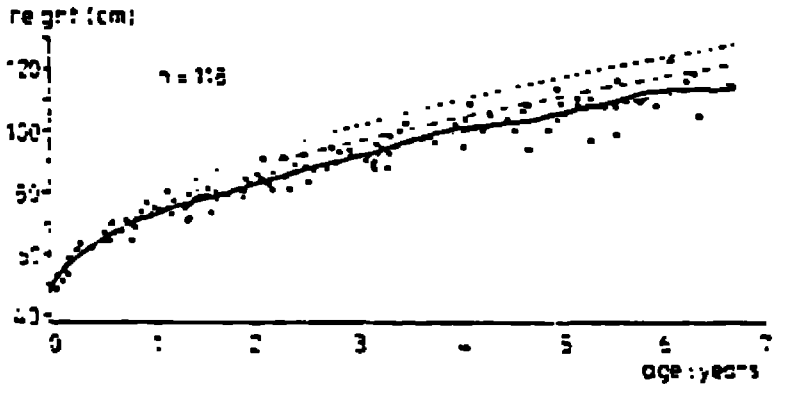


FIGURE 1.6
Height for age of girls on macrobiotic diets in the Netherlands
P10, P50 and P90 of Dutch reference population (Roede & Van Wieringen, 1985).

Relation with diet
Birth weight showed strong positive relationships with both the frequency of consumption of dairy products and of fish by the family. SDS (standard deviation scores) of weight, height and arm circumference were significantly higher in children from families consuming dairy products at least three times a week compared to children from families who rarely or never used dairy products. This association was partly, but not completely, attributed to the difference in birth weight in children from families with or without regular consumption of dairy products. No association was observed between SDS and family consumption of fish, meat or eggs (Dagnelie *et al.*, 1988).
Since the deviation from the normal growth curve occurred during the weaning period, we decided to carry out a mixed-longitudinal cohort study on macrobiotic infants between 4 and 18 months of age.

4.2.2 *Mixed-longitudinal study in 4-18 month-old infants*

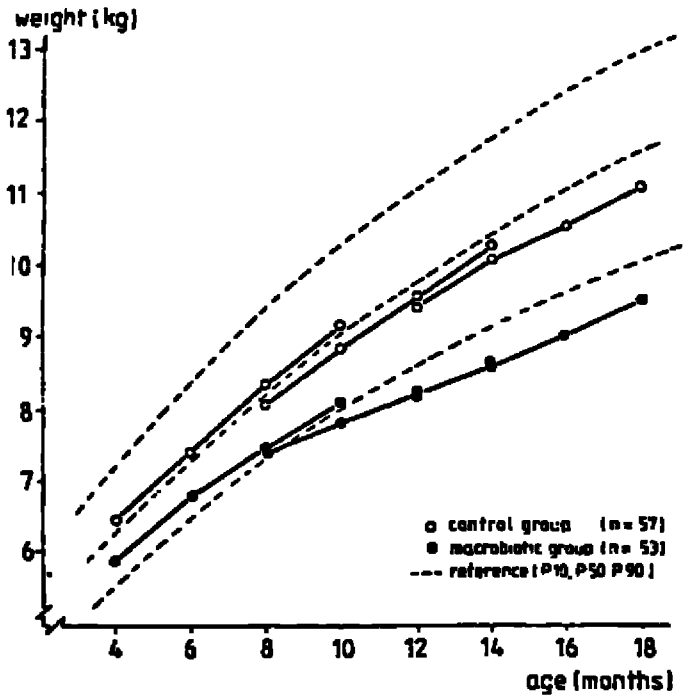
Weaning diet
Macrobiotic mothers continued to breastfeed for an average of 13.6 months (control group: 6.6 months). Complementary feeding in macrobiotic infants started at a mean age of 4.8 months with water-based sieved porridges from whole-grain cereals, followed by vegetables (at 5.7 months), sesame seed (6.4 months) and pulses (8.2 months). Fruits were rarely given and animal products were avoided by most families. In the control group, complementary feeding starting with fruits at a mean age of 2.7 months, followed in the next two months by vegetables and cereals (Dagnelie *et al.*, 1989a).

TABLE 1.4
Intake of energy and nutrients by infants (6-16 months of age) on macrobiotic and omnivorous (control) diets (Dagnelie *et al.*, 1989a)

	Macrobiotic group (n = 49) Mean ± SD	*Control group (n = 57) Mean ± SD*
Energy (MJ)	3.0 ± 0.5	3.6 ± 0.7[a]
En. density (kJ/g)	2.4 ± 0.3	3.4 ± 0.5[a]
Protein		
Animal[b] (g)	4 ± 3	24 ± 8[a]
Total (g)	20 ± 7	32 ± 10[a]
%Energy (%)	11 ± 3	15 ± 3[a]
Fat (g)	22 ± 9	30 ± 7[a]
%Energy (%)	28 ± 12	32 ± 7[a]
Carbohydrate		
Oligosacchar. (g)	47 ± 20	70 ± 17[a]
Polysacchar. (g)	63 ± 41	45 ± 18[a]
Total (g)	110 ± 29	115 ± 25
%Energy (%)	61 ± 10	54 ± 5[a]
Dietary fibre (g)	13 ± 7	7 ± 3[a]
Dietary fibre (g/MJ)	4.1 ± 1.9	2.0 ± 0.7[a]
Calcium[c] (mg)	280 ± 68	751 ± 230[a]
Iron (mg)	5.1 ± 2.8	4.0 ± 1.6[a]
Thiamine (mg)	0.6 ± 0.3	0.4 ± 0.1[a]
Riboflavin (mg)	0.4 ± 0.1	1.1 ± 0.3[a]
Vitamin B_{12} (mg)	0.3 ± 0.2	2.9 ± 1.3[a]
Vitamin C (mg)	53 ± 22	77 ± 40[a]

[a] Difference significant at $P < 0.001$.
[b] Including breast milk.
[c] Based on preparation of foods with water containing 28 mg of calcium per liter.

Table 1.4 shows that for all age groups combined, the daily intake of energy and nutrients in the three cohorts of the macrobiotic group differed significantly from that of the control group. In the macrobiotic group, fat intake decreased from 37% energy at an age of 6-8 months to 17% at 14-16 months, due to the fact that fat from breast milk was not replaced by other fat sources during weaning. With the decreasing amount of breast milk, animal protein intake decreased from 7 g/day at 6-8 months to 2 g/day at 14-16 months, as compared to an increase from 18 to 28 g/day in the control group. The intake of calcium riboflavin and vitamin B_{12} by macrobiotic infants was considerably below that of the control group (Dagnelie *et al.*, 1989a).



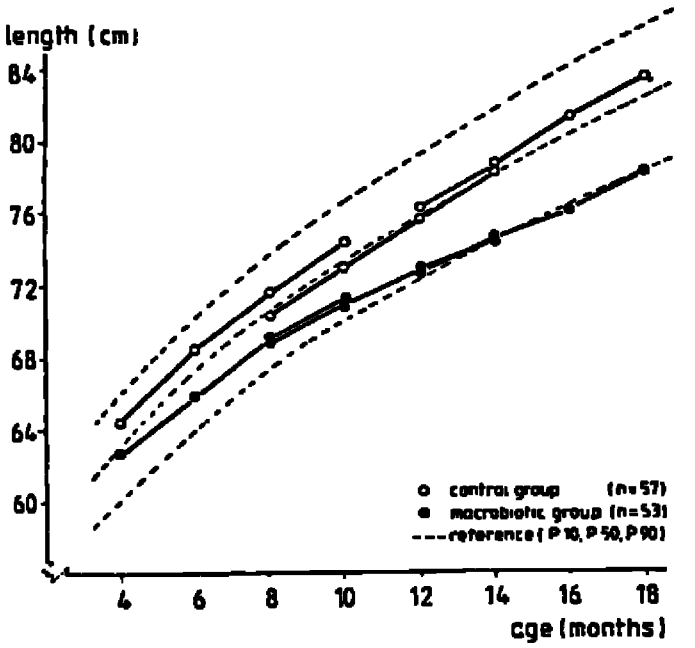


FIGURE 1.7
Growth curves (length for age, weight for age) of infants on macrobiotic or on omnivorous (control) diets in the Netherlands (Dagnelie *et al.*, 1989b)
P10, P50 and P90 of Dutch reference population (Roede & Van Wieringen, 1985).

Growth
Growth curves of length and weight for age for both groups are presented in Figure 1.7. Deviation in linear growth from the P50 of the reference occurred in the macrobiotic infants from four months onwards. From 16 months of age, linear growth stabilized at the 10th percentile of the Dutch references, whereas in the control group growth velocities were similar to the Dutch references (Dagnelie *et al.*, 1989b). Comparison with birth weight data of the macrobiotic infants showed that retardation of weight growth already occurred before the age of 4 months. Weight growth was most depressed between 8 and 14 months,

while stabilization at the P3 level occurred between 14 and 18 months. As shown in Table 1.5 for the combined cohorts, growth velocities for weight, length and arm circumference (expressed as units per year) were significantly lower in the macrobiotic group.

TABLE 1.5
Growth velocities (units per year) of infants (4–18 months of age) on macrobiotic and omnivorous (control) diets)

	Macrobiotic group (n = 52) Mean ± SD	*Control group (n = 57) Mean ± SD*
Weight (kg)	3.1 ± 1.6	4.4 ± 1.4[a]
Length (cm)	13.2 ± 3.9	16.7 ± 3.1[a]
Arm circumference (cm)	1.0 ± 2.2	2.3 ± 2.4[b]
Weight-for-length (kg)	2.4 ± 1.9	3.3 ± 1.8[c]

Differences between groups significant at [a] $P < 0.001$; [b] $P < 0.003$; [c] $P < 0.02$.

Relation with diet

It was analyzed whether the observed growth retardation could be explained by a reduced intake of energy or protein by the macrobiotic infants. Both the energy intake and the protein content of the macrobiotic diet contributed independently to growth in weight and arm circumference (Dagnelie *et al.*, 1989b). In contrast, growth in length was only associated with the protein content of the diet.

The low riboflavin intake by the macrobiotic children was reflected by an elevated activity coefficient of erythrocyte glutathion reductase (EGR) (Dagnelie *et al.*, 1989a). Iron deficiency was observed in 15% of the macrobiotic infants, versus no infants in the control group (Dagnelie *et al.*, 1989c). As a consequence of the extremely low intake of vitamin B_{12} in macrobiotic infants, low plasma vitamin B_{12} concentrations, and elevated plasma levels of methylmalonic acid and homocysteine were found (Schneede *et al.*, 1994) which were associated with a rise in mean corpuscular volume (MCV). In summer, 28% of macrobiotic children showed clinical symptoms of rickets, and in winter 55% (Dagnelie *et al.*, 1990). The data indicated that the high prevalence of rickets is the result of long-term depletion of body calcium stores, caused by a diet with a low calcium, and a high fiber content, in combination with vitamin D deficiency during a part of the year. No indication of an effect of the duration of breastfeeding on the presence of rickets was found (Dagnelie *et al.*, 1994). Major skin and muscle wasting was present in 30% of the macrobiotic infants. Growth velocities in weight and height were lower in these wasted infants ($P < 0.05$). Infants with major skin and muscle wasting were slower in locomotor development than the other macrobiotic infants ($P = 0.05$). The macrobiotic group was significantly later in gross motor development ($P < 0.001$) and, to a lesser degree, in speech and language development ($P < 0.03$) (Dagnelie *et al.*, 1989b).

4.3 RECOMMENDATIONS FOR THE MACROBIOTIC DIET

Based on the findings of the above studies, the following dietary recommendations were given to all macrobiotic families in the Netherlands (Dagnelie *et al.*, 1994a,b):
1 To add fat as an additional source of energy to a total of at least 25-30% of energy as fat. This can be achieved by including 20-25 g of oil per day, or by eating more nuts and seeds.
2 To include fish (2-3 portions per week) as a source of vitamin B_{12}. Especially during winter, fatty fish should be consumed to provide the child with vitamin D.
3 To increase the consumption of plant sources of calcium and vitamin B_2. Consumption of these products is within the macrobiotic philosophy, but they are poor sources of calcium.
At this stage the use of dairy products was not yet explicity recommended since this was considered incompatible with the macrobiotic philosophy. The effects of these dietary recommendations have been evaluated in the 2-year follow-up study.

4.4 TWO-YEAR FOLLOW-UP STUDY

Diet
Few changes were found in the frequency of consumption of foods typical of the macrobiotic diet, but there were some changes in the consumption of animal products, especially dairy products and fish, as well as vegetable oil and vitamin D supplements (see Table 1.6). However, only 6% of those regularly consuming fish had adopted the advice of eating fatty fish (Dagnelie *et al.*, 1994a).

TABLE 1.6
Consumption frequency of selected foods by children in macrobiotic families in 1985 (n = 173) and in 1987 (n = 152) (Dagnelie *et al.*, 1994a)

	Percentage of families					
	1985			*1987*		
	≥3/wk	*1-2/wk*	*<1/wk*	*≥3/wk*	*1-2/wk*	*<1/wk*
Fish	3	41	58	10	64	26
Sunflower/pumpkin seeds	31	32	29	48	27	25
Sesame seeds and pasta	88	3	8	89	5	6
Vegetable oil	75	12	13	92	5	3
Vitamin D supplement in winter	9	1	89	21	1	77
Dairy products	14	5	81	26	12	72
Tofu/tempeh	77	16	8	76	20	3
Leaf vegetables	95	1	4	97	2	2

Growth
Growth velocity, expressed as change in SDS (calculated from the P50 and SD of the cross-sectional Dutch reference curve) of the macrobiotic children in

various age groups is presented in Table 1.7. A marked growth depression for height was observed in the children who, at the time of follow-up, were 2 years old. For children 3-5 years of age, a slight, but significant, positive change in SDS had occurred for both weight and height. In children 6-9 years of age, no changes in SDS occurred, except a slight, but significant, positive trend towards the P50 for height in girls. Thus, these data confirm our earlier observations concerning linear growth retardation during the first two years of life and only partial catch-up (for weight and arm circumference) during the following years.

TABLE 1.7
Change in SDS per year of macrobiotic children in different groups (Dagnelie *et al.*, 1994a)

	Change in SDS per year (mean ± SD)		
Current age (1987)	*2 year*	*3-5 years*	*6-9 years*
Boys	(n = 25)	(n = 40)	(n = 33)
Weight	−0.17 ± 0.11	0.14 ± 0.05[a]	−0.01 ± 0.02
Height	−0.44 ± 0.09[b]	0.09 ± 0.04[c]	0.04 ± 0.04
Girls	(n = 18)	(n = 48)	(n = 30)
Weight	−0.15 ± 0.12	0.16 ± 0.05[a]	0.08 ± 0.06
Height	−0.55 ± 0.11[a]	0.14 ± 0.04[a]	0.11 ± 0.03[a]

Relation to diet

The frequency of consumption of animal products (i.e. fish and dairy products) was positively associated with height ($P < 0.05$) (cross-sectional analysis). In those children whose consumption of fish and dairy products had increased since 1985, linear growth was significantly faster ($P < 0.05$) than in other macrobiotic children (longitudinal analysis) (Dagnelie *et al.*, 1994a). A marked example of catch-up growth in weight and height after the introduction of dairy products and fatty fish in three macrobiotic siblings, aged 3, 5 and 8 years, is shown in Figures 1.8a-c.

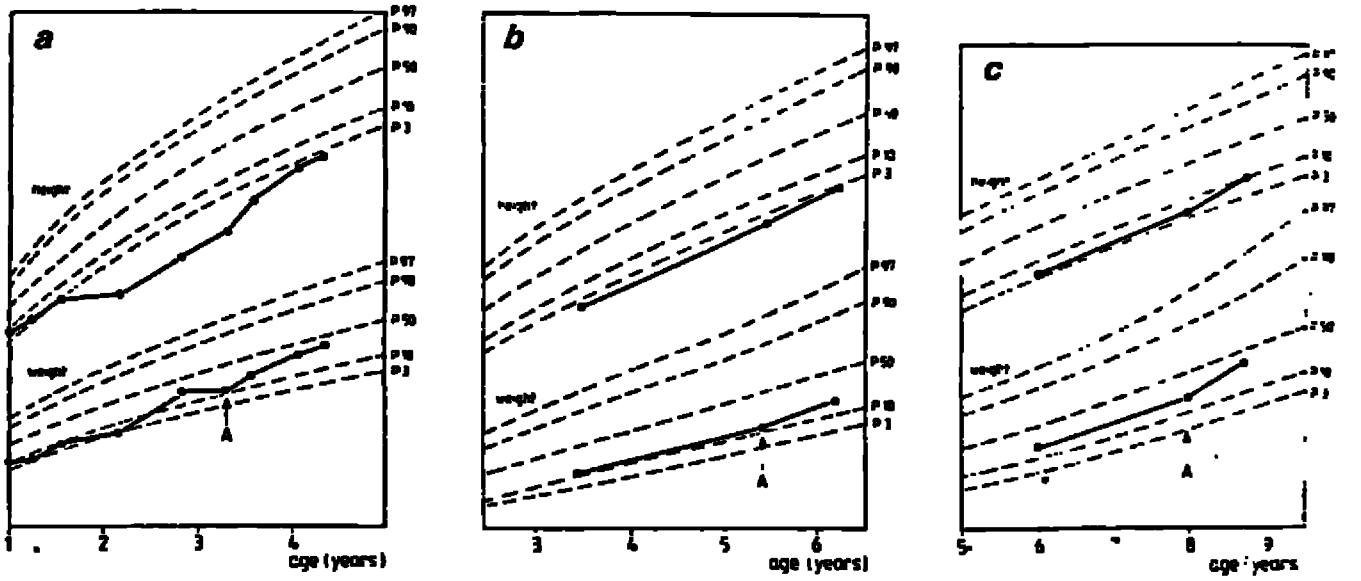


FIGURE 1.8
Growth in weight and height of three macrobiotic siblings in the Netherlands before and after the modification of the macrobiotic diet by introducing dairy products and fatty fish (shown as 'A') (Dagnelie *et al.*, 1994a)

These studies on growth of children on macrobiotic diets have provided the following answers to the questions:
1 *Timing of growth faltering in children fed macrobiotic diets:* A small but significant intrauterine growth retardation was indicated by a lower birth weight of macrobiotic children. Growth velocities in height and weight were most depressed between 8 and 14 months of age. Between 14 and 18 months of age, growth stabilized parallel to the 10th centile of the Dutch references, after which some, but incomplete, catch-up growth was observed for weight and arm circumference. No catch-up growth was observed for height.
2 *Nutritional factors associated with deviations in growth in children on macrobiotic diets:* Low birth weight was associated with a low frequency of consumption of fish and dairy products by the mother. SDS of weight, height and arm circumference were significantly higher in children from families consuming dairy products regularly, compared to children from families which rarely used dairy products. The increase in weight and arm circumference between 4 and 18 months of age was associated with both the energy intake and protein content of the diet. Growth in length was only associated with the protein content of the diet.
3 *Effect of modification of the macrobiotic diet on growth:* Catch-up growth in height and weight occurred after increased consumption of fish and dairy products. Our findings demonstrate that, provided unfavourable nutritional circumstances change, catch-up growth in height is still possible, even at the age of 8 years, even though the original growth channel may not be attained.

These data demonstrate that the observed linear growth retardation in children on macrobiotic diets is caused by nutritional deficiencies alone. By using a matched control group in the mixed-longitudinal study, confounding factors as sex, parity, socio-economic level and region of residence were excluded. The

educational level of the parents was high, and 92% of macrobiotic infants grew up in a two-parent family (control group: 100%). No indications of any other adverse circumstances, such as prevalence of infectious diseases, were observed.
The associations of linear growth with consumption of dairy products and fish suggest the importance of protein, and particularly animal protein, in the diet. It has been suggested that height is affected most by protein deficiency, whereas weight is more sensitive to a low energy intake. However, in real life we cannot disentangle the influence of the protein content of dairy products and fish from the influence of the extra energy, calcium, zinc, or changing bioavailability of iron and other nutrients, which are supplied simultaneously with the consumption of these products. Furthermore, a low utilization of the protein in the macrobiotic diet, due to its low energy and high fibre content, might have played a role in limiting linear growth. Finally, linear growth retardation seems to be related to inadequate weight gain: growth velocity in height was lower for the wasted macrobiotic infants, compared to the non-wasted macrobiotic infants in the mixed-longitudinal study. Thus, this suggests that sufficient energy is also needed for normal linear growth (Dagnelie *et al.*, 1994a).
Catch-up growth is a self-correcting response which occurs as soon as an adequate diet is provided. The catch-up growth in height in children whose diet has been extended with dairy products and fish suggests that before modification the diet was nutritionally inadequate. The influences of separate nutrients can only be studied by intervention. The fact that catch-up growth in height even occurred in macrobiotic children of 8 years of age indicates that also for older children the macrobiotic diet continues to be nutritionally inadequate.
The importance of dairy products is also illustrated by comparison of anthropometric data of children on lacto-vegetarian diets and children on macrobiotic diets. In macrobiotic children, whose diet lacks dairy products, stunting is combined with a normal weight for height, whereas children on lacto-vegetarian diets, who receive dairy products, show some degree of wasting but virtually no stunting (Dagnelie *et al.*, 1994a).

Follow-up in 1993
In 1993, a follow-up study was performed with 268 children who were fed a macrobiotic diet from birth on for a period of 3 to 10 years. These children had participated in at least one of the former studies: the cross-sectional studies of 1985 and 1987, or the mixed-longitudinal study of 1987. The earlier studies reported growth deviations in height and no catch-up growth occurred before the children's tenth year of life. The 1993 follow-up study was performed to answer the question whether the children show a subsequent catch-up growth. The children were between 7 and 17 years of age.
A clear shift was observed in the nutritional habits. In comparison with the earlier studies, the macrobiotic diet was interpreted less strictly by the consumers and more products of animal origin were consumed (dairy products, some meat and fish).
The children showed significant linear catch-up growth compared to the 1985 and 1987 data: height for age showed a clear shift from the P10 towards the P50

of the standard (boys: ΔSDS = 0.59, $p < 0.001$; girls: ΔSDS = 0.56, $p < 0.001$). It can be concluded that significant linear catch-up growth occurred before as well as after the tenth year of life, because for all age intervals the same shift could be assessed. In 1993 height for age was still slightly lower compared to the P50 of the Dutch reference. Due to the fact that almost all families had incorporated at least some animal products in their diet since 1987, no firm conclusions can be drawn on the relation between the diet and the observed linear catch-up growth.

5 Influence of exercise on linear growth

The effects of exercise on linear growth were investigated in preschoolchildren recovering from protein-energy malnutrition (PEM). 20 children, 24-48 months old, under treatment for severe PEM, were assigned to either an Active group (stimulated, but not forced, to participate in games and activities that involved walking uphill, climbing a ramp, running, tumbling and climbing stairs) or a Control group (with the *ad libitum* pattern of physical activity and rest commonly observed in child-care and nutrition rehabilitation centers). Dietary intake was controlled and almost identical in both groups (2.5 ± 0.07 g protein and 117 ± 7 kcal/kg/day). Mean energy expenditure during daytime, assessed by heart rate monitoring and its relationship with oxygen consumption, were 2.0 and 1.7 times basal metabolic rate in the Active and Control groups, respectively ($P < 0.01$). In 6 weeks, both groups gained an average of 1.98 kg. However, the Active group grew more in length (22 ± 8 vs 14 ± 6 mm, $P < 0.05$) and lean body mass (final creatinine-height index: 0.97 ± 0.12 vs 0.89 ± 0.09, $P < 0.05$). The inactivity that accompanies severe malnutrition may contribute to stunting, whereas mild-to-moderate exercise combined with a good diet enhances linear growth. This may be mediated by endocrine growth factors, whose synthesis is prompted by exercise.

Protein-energy malnutrition leads to growth retardation in children, affecting both body mass and stature. Dietary energy deficit has been considered one of the main causes of this growth retardation. However, the amount of dietary energy needed for growth between 1 and 5 years of age is only about 2-3% of the total daily requirement. Furthermore, although it has been shown that children of that age with dietary intakes 20-30% below requirement remain in energy balance by decreasing physical activity, they cease to grow, at least in terms of body mass. This occurred even when dietary intake of all nutrients, except energy, was adequate (Torun and Viteri, 1994).
This suggests that factors, other than dietary, may play a role in the growth retardation seen in malnutrition.

5.1 STUDIES WITH CHILDREN RECOVERING FROM MALNUTRITION

Twenty boys, 24–48 months old, with edematous protein-energy malnutrition, were admitted to INCAP's Clinical Research Center. All were wasted and stunted. The degree of stunting resulted in heights corresponding to those of healthy children 17 ± 3 months old, 19 months younger than the patients'

chronological ages (Table 1.8). After initial recovery, when edema, apathy and irritability had disappeared, and the children were willing to participate in the games and activities that were part of this study, they were randomly assigned to one of two groups (Active and Control), paired according to age, height, and nutritional status (Table 1.8). Ten children were originally assigned to each group, but one of them was transferred from the Control to the Active group, as described below.

TABLE 1.8
Characteristics of patients on admission to the study

	Active group n = 11	*Control group n = 9*
Age (months)	39 ± 8	34 ± 8
Height-age (months)	16 ± 3	17 ± 3
Weight (kg)	9.12 ± 0.94	8.90 ± 0.87
Height (cm)	79.9 ± 3.3	80.5 ± 3.0
Weight-for-height (% of standard)	83 ± 5	80 ± 6
Creatinine-height index	0.76 ± 0.11	0.72 ± 0.08
Serum proteins (g/dl)	7.2 ± 0.6	6.8 ± 0.9

Nutritional and medical treatment, emotional support and other routine activities were the same for both groups. During the six weeks of study, they received a diet similar to that offered at that time in most nutrition rehabilitation centers in Guatemala. It was designed to provide 2.5 g protein/kg per day (1 g from milk, 1 g from egg and 0.5 g from corn) and 500 kJ/kg per day (30% from lipids). The diet was supplemented with vitamins and minerals to satisfy the needs of children recovering from malnutrition. All patients adhered strictly to this dietary protocol, and small amounts of fruit were given when a child requested additional food.

The two groups of patients differed only in relation to physical activity. Children in the Control group followed the pattern of physical activity and rest periods most commonly observed in rehabilitation and child-care centers dealing with malnourished patients. While out of bed, they walked and moved around in their room and in the playing areas, and they were entertained by the staff with toys and games that did not require running or jumping, although such activities were not restricted. Children in the Active group were taken out of bed one hour earlier in the morning and 1/2 hour earlier after the midday nap. In addition to freedom of movement in their room and play areas, these children were encouraged to participate in games and activities that involved walking on a grade, running, tumbling and climbing stairs. Those activities alternated with periods of rest or sedentary play, similar to the Control group, to avoid tiredness and boredom.

No child was forced to remain inactive nor to participate in the game scheme. One child who was initially assigned to the Control group was quite restless and insisted in participating in the more active games. After one week, he was therefore transferred to the Active group.

Physical activity in both groups was examined by continuous heart rate

monitoring, and energy expenditure was calculated from individual heart rate : energy expenditure relationships and periodic measurements of basal metabolic rate. Growth was evaluated through standardized daily measurements of length on two consecutive days. The latter were always measured by the same person.

Dietary intake was almost identical in both groups, averaging during the 6 weeks 2.50 ± 0.07 g protein and 490 ± 30 kJ/kg per day (mean ± standard deviation).

Physical activity raised the daytime heart rate at an average of 23 and 17% above the nighttime heart rate in the Active and Control groups, respectively ($P < 0.01$). Mean energy expenditures during the day were 2.0 and 1.7 times the basal metabolic rate ($P < 0.01$).

The two groups of children showed similar clinical improvement and average weight gains of 1.98 kg over the 6-week period. Nutritional recovery, assessed by weight-for-length, was equally satisfactory, 96 ± 7 and 95 ± 6% of expected. However, the Active group reached a higher creatinine-height index (0.97 ± 0.12, vs 0.89 ± 0.09, $P < 0.05$), indicating greater muscle mass and protein repletion.

The Active group also had a greater linear growth of 22 ± 8 mm, compared with 14 ± 6 mm in the Control group ($P < 0.05$). The difference in linear growth became evident by the fifth week of the study (Figure 1.9). The Active group's increment of 22 mm in 6 weeks was two times greater than the linear growth of about 10 mm expected in normal children of the same chronological age, and 60% greater than the 13-14 mm expected in normal children of the same height-age (i.e. 17 months) (Torun and Viteri, 1994).

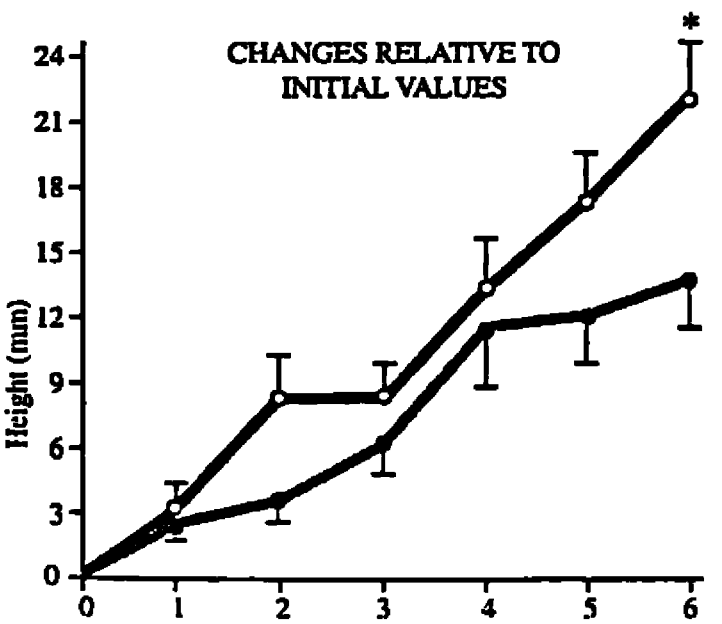


FIGURE 1.9
Cumulative linear growth of Active groups (open circles, n = 11) and Control groups (black circles, n = 9) of children recovering from protein-energy malnutrition

Mean ± SEM.

* = Groups differ;

$P < 0.05$.

The studies in malnourished children recovering from protein-energy malnutrition, indicate that moderate, but consistent, physical exercise enhances linear growth and promotes catch-up from stunting, related to malnutrition. The mechanisms by which exercise enhances linear growth may be mediated by endocrine factors that promote the growth of long bones, such as growth hormone and insulin-like growth factors (somatomedins). These hormones, as well as insulin, also enhance the muscle synthesis that seemed to occur in the studies on children. The fact that physical exercise is an important stimulus for the secretion of growth hormone and the synthesis of insulin-like growth factor I, supports this concept.

Summary

Processes which have taken place in the past have shaped the human populations found in the world today. The most fundamental process has been genetic, namely he shaping of human gene-pools through natural selection . In addition, human population migration has served to isolate different groups across sufficiently long time-spans to allow between-population genetic variation.
Nutritional influences on linear growth are confounded by the fact that when food intake is low, the intake of many other nutrients will also be inadequate. About one third of linear growth failure can be ascribed to illness.
Adequacy of dietary mineral supply for human bone growth and mineralisation is shown by an estimation of the biological requirements of Ca, P, Mg, and Zn for normal growth in the human, and the likely manifestations of an inadequate supply of Ca, P, Mg and Zn in the growing child. There is some evidence that increasing the intakes of these minerals would improve growth and bone development in Third World children.
Effects of macrobiotic diets on linear groth in infants and children up to 10 years of age are shown in comparison with linear growth in third world children.
Even when dietary intake of all nutrients except energy is adequate, a cease to grow has been shown, which suggest that factors other than dietary play a role in the growth retardation seen in malnutrion, for instance lack of exercise.

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