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The Link Between Childhood Undernutrition and Risk of Chronic Diseases in Adulthood: A Case Study of Brazil

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Obesity, cardiovascular disease, and type 2 diabetes mellitus are now prevalent among adults living in developing countries; these chronic diseases affect socioeconomically disadvantaged adults living in impoverished families with undernourished children. This review summarizes data from Brazil—a developing country undergoing the nutrition transition—suggesting an association between childhood undernutrition and obesity and chronic degenerative disease. Potential mechanisms for the association include long-term effects of childhood undernutrition on energy expenditure, fat oxidation, regulation of food intake, susceptibility to the effects of high-fat diets, and altered insulin sensitivity. The combination of childhood undernutrition and adult chronic degenerative disease results in enormous social and economic burdens for developing countries. Further research is urgently needed to examine the effect of childhood undernutrition on risk of obesity and chronic degenerative diseases; one goal of such research would be to determine and provide low-cost methods for prevention and treatment.

Key Words: undernutrition, stunting, obesity, diabetes, hypertension

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Introduction

Epidemiologic studies document increasing socioeconomic disparities worldwide. The gap between rich and poor is growing, and the share of worldwide income obtained by the poorest 20% of individuals decreased from 2.5% in 1960 to 1.3% in 1990.[1] Economic activity has also become highly concentrated; the richest nations now have 15% of the population but produce 50% of the worldwide Gross Domestic Product (GDP), whereas the poorest nations contain 50% of the world population but produce only 14% of the world GDP.[2] Even countries in which economic development has occurred, increased poverty continues to be reported. In Brazil, for example, the economy grew 1.2% per year between 1980 and 1992, but there was a 7.5% decrease in per capita income during the same period, with a marked deterioration in living conditions.[3]

In addition to the increasing gap between rich and poor, there have been profound changes in population size and the proportion of individuals living in rural versus urban areas. In 1970, 35% of the world population lived in urban areas; in 1999 this number increased to 46%.[2,4] In Latin America, 57% of the population lived in urban areas in 1970, whereas in 1998 this number increased to 75%.[3] The increasing population and the shift from rural to urban locations has resulted in many families becoming homeless. As a consequence, shantytowns now flourish. In Brazil, 80% of the population lives in urban areas[3] and this proportion will continue to grow. São Paulo, long considered the motor of Brazilian development, now contains 10 million people and experienced a 2547% increase in the shantytown population (to 2 million individuals) between 1973 and 1993.[5]

This review describes some of the nutritional problems now related to urban poverty in Brazil, a country that reflects conditions faced by countries in that the nutrition transition coincides with the growing pains of fast urban development. We focus, in particular, on the emerging evidence of a link between childhood undernutrition and subsequent obesity, a phenomenon that

may help explain the emergence of obesity in poor countries worldwide.

Increasing Obesity, Type 2 Diabetes, and Cardiovascular Disease

The prevalence of obesity, defined by a body mass index (BMI, kg/m^2) $\geq$30,[6] appears to have increased sharply in many developing countries during the last decade. Although representative survey data on secular trends in BMI are scarce, data from Samoa,[7] Mauricius,[8] and, more recently, from China[9] and Kuwait,[10] have shown adult obesity is increasing at rates comparable to those in developed countries such as the United States.[11] Table 1 shows trends in obesity in Brazil between 1975 and 1997.[12] The greatest increase in prevalence of obesity was seen in poor women from the richest (Southeast) region of the country. There are substantial gender differences in these trends; the prevalence of obesity increases with income in men but with poverty in women (Table 1).

Some investigators[13–15] suggest that using BMI to categorize body fatness may not be appropriate for individuals living in developing countries because of the prevalence of stunting; stunted individuals may have relatively greater trunk and limb length, thereby increasing BMI in relation to body fatness. Although these arguments have not yet been directly addressed with studies relating body fatness to BMI in stunted individuals, changes in BMI over time likely reflect changes in body fatness, suggesting real secular trends. In some childhood cohort studies, marked increase in weight-for-height or BMI did not coincide with increase in height-for-age.[16,17] In one longitudinal study[17] in São Paulo in which two groups of school girls were followed for two years, changes in anthropometry were related to dietary fat intake. Figure 1 shows that a higher increase in weight-for-height was observed among stunted girls compared with non-stunted girls when higher energy from fat was consumed.

Coincident with increasing body fatness in Brazil is the increasing prevalence of diseases closely associated with overweight, including type 2 diabetes mellitus (NIDDM) and cardiovascular disease. Brazil was listed among the "Top 10" countries in a recent study on the global burden of diabetes; 4.9 million adults had type 2 diabetes in 1996 and an estimated 11.6 million adults will be affected in 2025.[18] Deaths from cardiovascular disease are also increasing in Brazil. Coronary heart disease alone accounted for 14.2% of deaths in 1950 and 32.4% of deaths in 1989.[19] Hypertension is also highly prevalent and occurs more frequently among the socioeconomically disadvantaged groups in Brazil.[19] The high death rate from cardiovascular disease in Brazil is consistent with trends worldwide.[20]

Increasing Obesity without Increasing Energy Intake?

The causes of increased obesity in Brazil are not known, particularly among socioeconomically disadvantaged women. In the United States, increasing energy intake has paralleled the rising prevalence of obesity since 1980,[21] suggesting that increased energy intake could be an important underlying cause for the rise in the number of obese people. Similar trends in energy intake have not been reported in Brazil; a comparison of national food intake surveys during 1974–1975 and 1987–1988[22–24] revealed a decrease, rather than an increase, in mean caloric consumption in all regions. These data are summarized in Table 2. Another publication described an 11% decrease in nationwide daily per capita food availability in Brazil.[25] Compositional changes have also occurred during this period: consumption of beans, veg-

Table 1. Secular Trend of the Prevalence (%) of Obesity (BMI $\geq$30) in Two Regions of Brazil According to Per Capita Income Quartiles

Region/Income Quartiles	Men			Women		
	1975	1989	1997	1975	1989	1997
Northeast						
1st quartile	0.7	0.8	1.7	3.0	5.2	8.0
2nd quartile	0.9	1.4	3.8	3.2	8.3	14.1
3rd quartile	1.1	3.0	4.1	4.5	7.8	13.3
4th quartile	2.8	5.2	8.4	7.6	9.9	14.6
Southeast						
1st quartile	1.6	2.9	3.8	6.6	11.6	15.0
2nd quartile	2.2	4.2	9.7	8.0	16.5	12.1
3rd quartile	3.3	7.8	9.6	10.3	14.8	13.2
4th quartile	5.3	8.1	9.5	9.1	13.2	8.2

Taken from reference 12.

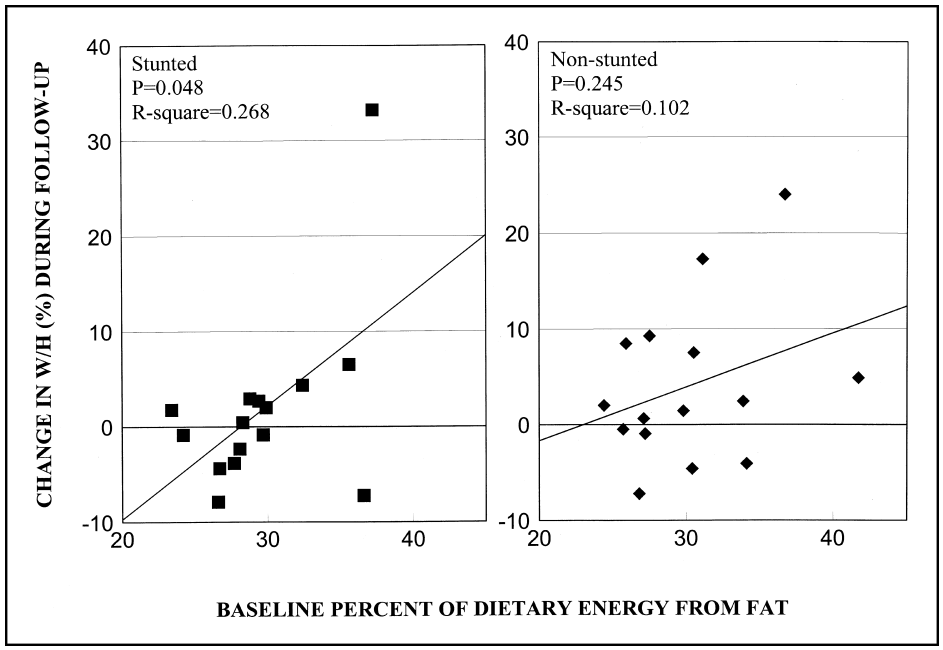

Figure 1. Association between baseline percentage of dietary energy from fat and change in weight-for-height (W/H, percentage of median) during the follow-up period in stunted and non-stunted school girls living in shantytowns in the city of São Paulo, Brazil. Reprinted with permission from the *Journal of Nutrition*.[17]

etables, roots, and tubers (staples of the Brazilian diet) have decreased, and consumption of meat, sausages, milk and other dairy products, sugar, and soft drinks has increased. Reduced consumption of vegetables and other high-fiber foods and increased consumption of meat, dairy, and sugar would be expected to increase dietary energy density as well as dietary glycemic index. Both of these factors promote increased energy intake and can lead to weight gain.[26,27] Although national figures do not suggest increased consumption overall, compositional changes may account for increased energy density that masks increased energy consumption in individuals who are overweight.

Decreased total physical activity, or increased sedentary time, may be associated with the increase in the prevalence of obesity in Brazil. During the 1980s and 1990s, a substantial shift occurred in occupation patterns toward more third-sector jobs (i.e., services) owing to the intense migration from rural to urban areas.[3] Because all service occupations are considered light activity, this is also associated with a decrease in physical activity. Moreover, modernization of agricultural processes has probably reduced physical activity in rural areas.[28]

Association between Childhood Undernutrition and Subsequent Obesity and Chronic Degenerative Diseases

Increasing prevalence of adult obesity in developing countries is found to coincide with high prevalence of childhood undernutrition. In Brazil, 10.5% of the children nationwide under age 5 have moderate/severe stunting (defined as height-for-age below –2 z-score).[29] The highest prevalence of stunting (18%) is found in the poorer Northeast region, but even in the affluent Southern region 5% of children are considered undernourished.[29] Evidence exists of coincident undernutrition and obesity within the same family. In 1995, Sawaya et al.

Table 2. Mean Reported Energy Consumption in the Two Brazilian National Surveys ENDEF (1974–1975) and POF (1987–1988) by Region of the Country

Regions (Cities)	ENDEF	POF	% Difference
North (Belém)	1833	1635	−12.1
Northeast (Recife, Fortaleza, Salvador)	1674	1571	−6.0
Southeast (Rio de Janeiro, Belo Horizonte, São Paulo)	2000	1801	−11.0
South (Porto Alegre, Curitiba)	2043	1712	−19.3
West (Brasilia)	1944	1534	−26.7

Taken from reference 24.

documented 30% prevalence of undernutrition (stunting and/or low weight-for-age) in the same shantytowns with 15% prevalence of obesity.[30] Nine percent of households had at least one member who was underweight and one member who was obese.[30]

The apparent coexistence of undernutrition in children and obesity in adults has several potential explanations, but in particular raises the question of whether undernutrition increases the future risk of weight gain.[30] This possible association is analogous to the postulated effects of low birth weight on adult risk of obesity and the general concept of metabolic programming by early diet;[31] these concepts are thought to be mediated by mechanisms including modification of phenotypic gene expression in terminally differentiated, poorly replicating cells during intrauterine development and are reported in both animal models and humans.[32–36]

Epidemiologic evidence supporting an association between childhood undernutrition and adult obesity and related chronic degenerative diseases can be found in studies reporting an association between nutritional stunting (a marker for early childhood malnutrition[37]) and increased risk of overweight in Brazil, Russia, China, and South Africa.[30,38] In Brazilian school children from a low-income rural community, short stature was associated with overweight even at low reported energy intake.[39] In a further study, 372 women and 161 men with short stature were studied prospectively;[40] for each decrease in z score of stature, there was an increase in the waist-to-hip ratio of 65% in men and 29% in women. The latter study, by using waist-to-hip ratio rather than BMI, attempted to avoid the potential confounding factor of different body proportions between stunted and non-stunted individuals. Sichieri et al.[41] studied a representative sample of 2040 households in the city of Rio de Janeiro and found that stunting was associated with risk of obesity and abdominal fatness in women (odds ratio = 1.77; 95% CI = 1.10–2.83). These findings confirm data from the first prospective study conducted in Senegal,[16] which showed that girls stunted at infancy recovered body weight and subcutaneous fat mass during puberty but did not catch up on stature, sitting height, or skeletal breadths (bi-acromial and bi-iliac diameters). The stunted girls[16] also did not have less subcutaneous fat (sum of six skinfolds) or lower BMI than non-stunted children. Regional variation in subcutaneous fat distribution indicated greater accretion at the biceps and subscapular sites in stunted compared with non-stunted girls.

Low body weight at 1 year, a basic indicator of undernutrition, is associated with increased risk of later cardiovascular disease,[42] higher blood pressure, and adverse changes in plasma concentrations of glucose, insulin, fibrinogen, factor VII, and apolipoprotein B.[35] Postnatal catch-up growth is also a risk factor for subsequent hypertension, cardiovascular disease, and insulin resistance, suggesting that smallness at birth, resulting from environmental influences that restrain intrauterine growth, is more important than genetic smallness per se.[43] Studies in Finland have shown that the path of growth through childhood modifies the risk of disease associated with size at birth.[44] The highest death rates from coronary heart disease occurred in men who were thin at birth but had accelerated weight gain in childhood.

Stunting is also related to changes in blood parameters associated with noninsulin-dependent diabetes and the metabolic syndrome.[45,46] For example, Brown et al.[47] reported that short stature was related to fasting plasma glucose and plasma glucose levels 120 minutes after a glucose load in females. Sichieri et al.[41] reported an association between short stature and hypertension. Gaskin et al.[48] found that stunting, but not low birth weight, was associated with elevated systolic blood pressure in Jamaica. Velasquez-Melendez et al.[49] studied a population near São Paulo, Brazil, in which 20% of men and 15% of women were stunted; the investigators observed that the stunted individuals had higher fasting glucose, higher triglycerides, higher low-density lipoprotein cholesterol, and higher total cholesterol than non-stunted adults. Stunting in women was also associated with higher BMI, waist-to-hip ratio, and central obesity.

Potential Mechanisms for Long-term Influence of Childhood Undernutrition on Body Fatness

A large number of studies demonstrate metabolic alterations in all tissues and body systems in human children suffering from undernutrition, and the majority of these alterations seem to effect energy conservation. Few studies, however, have investigated the permanency of such alterations after nutritional recovery. There is some evidence for a disproportionately greater replenishment of body fat stores than body protein stores during the catch-up growth in infants and children recovering from undernutrition. Ashworth et al.[50] used anthropometric variables to demonstrate a disproportionate increase in body fat at the time when the expected weight-for-height had been reached; after recovery from protein-energy malnutrition, previously undernourished children were fatter than well-nourished children of the same age and weight. More recent studies by Fjeld et al.[51] confirmed these findings using metabolic balance studies combined with measurements of total energy expenditure to determine fat and protein accretion during recovery from severe protein-energy malnutrition. The mean fat content in those studies was approximately 42% of weight

gain,[51] nearly double the expected mean body fat content in young children (i.e., 24%).[52] In the same study, there was no difference in the fat content of new tissue between infants gaining weight at a moderate rate (6 g · kg^{-1} · day^{-1}) or a rapid rate (12 g · kg^{-1} · day^{-1}). This and similar studies indicate that high-energy feeding of undernourished children is relatively easy, implying that the children are hungry, perhaps because their low body fat stores have triggered signals encouraging hyperphagia.[53]

The cause of the very high ratio of fat to protein accretion in children recovering from undernutrition is not known. One possible explanation for this preferential fat deposition is its lower energy cost relative to protein. It is likely relevant that the rates of weight gain encouraged in infants and children recovering from undernutrition are very high, typically 5 to 15 times greater than the usual mean rate of gain in normal children. These high rates of weight gain are necessitated by the fact that slow rates of gain delay recovery with the possible consequence of cognitive impairment, prolonged expensive treatment, and additional opportunistic infections. Whereas important in these respects, however, the high rates of gain probably exceed the metabolic capacity for accretion of lean body mass, and therefore permit disproportionate fat gain. Evidence suggests that at least some, and perhaps most, bone growth in normal children takes place in intermittent spurts rather than consistently and gradually over time,[54] and that bone growth is regulated by a choreographed cast of circulating hormones and local growth factors.[55] Muscle growth is believed to be a natural consequence of bone growth, with muscle stretching acting as one of the primary muscle growth stimulants.[56] In the normally nourished child, therefore, growth can be viewed as an event that occurs in response to a delicate balance of growth hormone and other growth factors. Under these particular metabolic conditions, a relatively high proportion of bone and muscle growth occurs in relation to fat deposition. By contrast, when weight gain or growth occurs in the absence of the correct balance of growth factors, the result is a higher proportion of fat and a lower proportion of lean tissue; this more closely resembles the composition of new tissue, which occurs in non-growing adults when they gain weight.[57]

It is unknown whether these metabolic changes, leading to abnormal composition of tissue deposition during recovery from undernutrition, and equivalent changes, occurring in children with less severe undernutrition, persist in the long term. However, we have observed several abnormalities in stunted Brazilian children aged 8 to 11 that are consistent with long-term adaptations in undernourished children designed to promote energy conservation and excess weight gain.

In the initial 2-year longitudinal study by Sawaya et al., investigators reported a higher susceptibility to gain in weight-for-height when higher-fat diets were consumed in stunted school girls compared with non-stunted ones.[17] Stunted girls had also higher waist-to-hip ratios, a factor that would presumably influence glucose metabolism and later chronic degenerative diseases.

In a more recent 3-day cross-sectional metabolic study,[58] investigators examined resting metabolic rate (RMR), postprandial energy expenditure, respiratory quotient (RQ), and substrate oxidation. Compared with control children, stunted children had lower RMR when the results were expressed as MJ/day. However, RMR values were not significantly different from those for control children when expressed relative to lean body mass (the major site of RMR in humans). Additionally, investigators found normal postprandial thermogenesis in the stunted group. Stunted children showed significantly higher fasting RQ and, consequently, fasting fat oxidation was significantly lower (Figure 2). The authors concluded that childhood nutritional stunting was associated with long-term impairment of fat oxidation, a factor that strongly predicts obesity.[58]

In another set of experiments in the same children, free-living total energy expenditure (TEE) was measured over 7 days using the doubly labeled water method.[59] Investigators found that stunted girls had significantly lower TEE than boys, which may help explain the

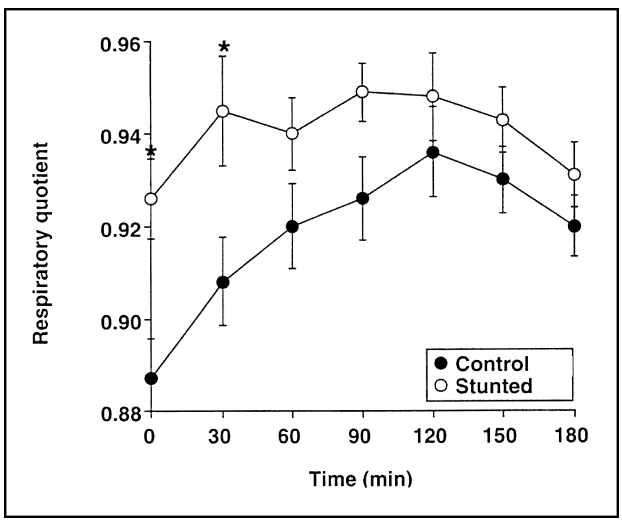

Figure 2. Mean (± SEM) fasting (0 min) and postprandial respiratory quotient in stunted and control children. Reprinted with permission from the *American Journal of Clinical Nutrition*.[60] *Significantly different from the stunted group, $P < 0.05$. The average respiratory quotient did not differ significantly between the 2 groups.

particularly high risk of obesity in stunted adolescent girls and women.

In a third set of experiments, investigators tested the hypothesis that nutritionally stunted Brazilian children have impaired regulation of energy intake. A 753-kJ yogurt supplement was administered at breakfast and its effect on subsequent energy intake was assessed. There were no differences in energy intake between stunted and non-stunted children, even though the stunted children weighed 10% less. Energy intake per kg body weight was significantly higher in the stunted children and the ratio of energy intake to RMR was also significantly higher. In addition, the absolute difference in energy intake between supplement and control days was higher in stunted children compared with non-stunted ones.[60] These findings suggest important metabolic changes present in previously undernourished children (with low height-for-age but normal weight-for-height).

Conclusion

Epidemiologic studies suggest an association between childhood nutritional stunting and increased risks of obesity and chronic degenerative diseases in adulthood. Although questions remain about the extent to which anthropometric measurements can predict body fatness in previously malnourished individuals, the findings from epidemiologic studies to date are entirely consistent with evidence suggesting long-term adverse effects in metabolism associated with undernutrition in childhood. There are enormous economic and social implications of long-term effects of childhood undernutrition on morbidity and mortality, especially because most childhood undernutrition occurs in developing countries that are unable to finance treatment of chronic degenerative diseases. Further research is urgently needed to delineate the role of childhood undernutrition in adult morbidity and mortality, and to provide effective low-cost solutions for chronic degenerative diseases in developing countries.

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