CAUSES OF LOW BIRTH WEIGHT IN LATIN AMERICA*

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SUMMARY

Analysis of the different studies reported in the literature leads to the conclusion that weight of the newborn is remarkably better in the high socioeconomic groups than in the low socioeconomic groups, and that this association also prevails in small poor population sectors of the rural area of Guatemala. In these villages, the association between the score of the socioeconomic scale developed for this research work and the proportion of children with low birth weight, disappears in the groups of tall, well-supplemented mothers during pregnancy. The data presented suggest that both nutritional history since conception, as well as nutritional status of the mother during pregnancy, constitute one of the important mechanisms of the causal relation that exists between socioeconomic characteristics and fetal growth. Another mechanism of great importance in Latin America is the high prevalence of infection in both mother and child from its prenatal stage. It is estimated that the causal complex poverty-malnutrition-infection is responsible for at least half of the newborns with low weight in Latin America. All the other known causes determining most of the babies with low weight at birth in industrialized countries are responsible of no more than one-fourth of these babies in Latin America. For this reason, the strategies used

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in developed countries to decrease the incidence of low birth-wight babies are not applicable in the Region. For example, in many populations of the Subcontinent, very simple indicators such as height, head and arm perimeter, and housing characteristics, can be very useful to select groups of mothers with high risk of delivering low birth-weight babies, and that, for this reason, require priority attention in health programs. The use of these risk indicators will contribute to notably improve the efficiency and effectiveness of these programs, particularly in populations with inadequate health resources.

Based on the above-mentioned statements, the authors conclude that an improvement of the nutritional status and of the health of gestating women, may conduct to a significant decrease of the prevalence of low birth-weight babies in the majority of the Latin American Region. This, in turn, will help reduce the high infant mortality rates observed in these countries, and permit new generations a greater probability of developing all of their genetic potential.

I. INTRODUCTION

The purpose of this work is to discuss the most important determinants of low birth-weight (LBW) babies in Latin America. We consider this step as crucial for the planning, implementation and evaluation of programs oriented to reduce the incidence of low birth weight in the Latin American countries.[1-8] To this effect, we will review the influence of the socioeconomic, nutritional and maternal infection factors during pregnancy on the weight of the newborn. We will then discuss the influence of various miscellaneous factors such as the smoking habit, toxemia of pregnancy, altitude and genetic factors. Finally, we will comment the determinants that should merit priority attention in programs aimed at reducing the incidence of low birth-weight children in the Latin American countries.

II. SOCIOECONOMIC LEVEL AND BIRTH WEIGHT

The relation that exists between socioeconomic factors and birth weight will be discussed in the following paragraphs. The main differences between the high and low socioeconomic levels will be analyzed to this effect, trying to integrate them in a simplified model of causal relations. The differences associated to socioeconomic characteristics of families in the rural villages of Guatemala will then be examined.

Figures 1 to 3 summarize the results of various studies where the weight of newborns and the height of mothers of high and low socioeconomic level are compared.[9-11] Women of the low socioeconomic groups in both rural and urban populations are smaller and give birth to a greater proportion of LBW babies than those of the high socioeconomic groups. Nevertheless, the latter show a height and LBW proportion similar to those of middle-class white women of urban populations of the United States.

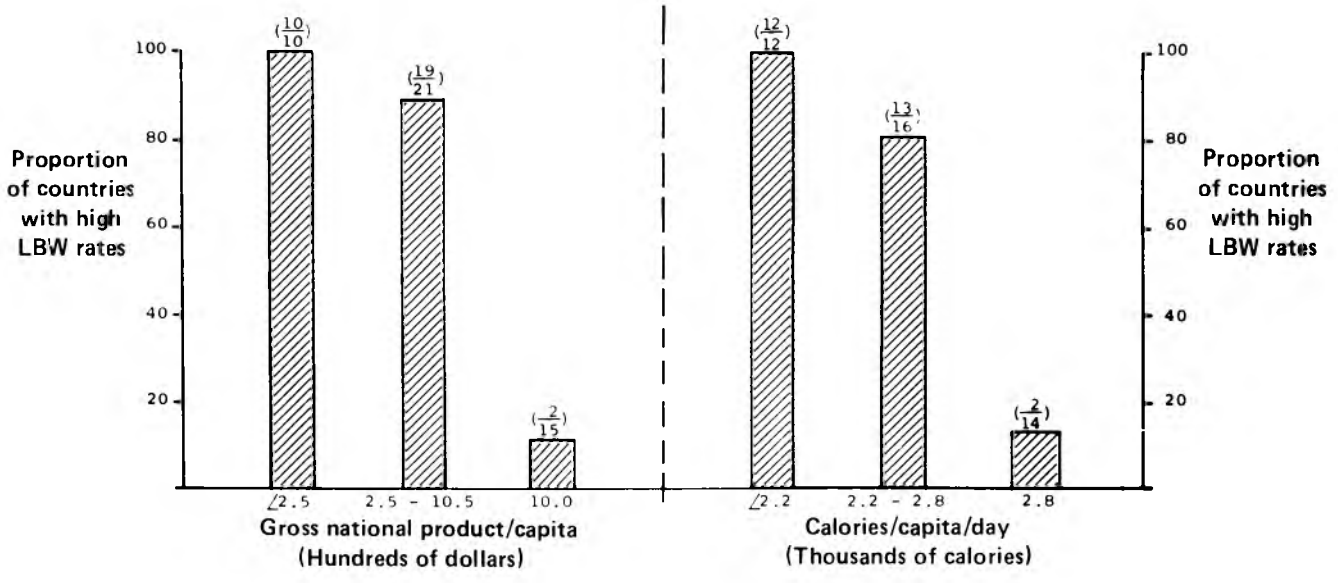


Fig. 1. *Proportion of countries with high LBW ($\leqslant$ 2.5 kg) rates according to national* **per capita** *gross product and* ***available calories*** **per capita/***day*.

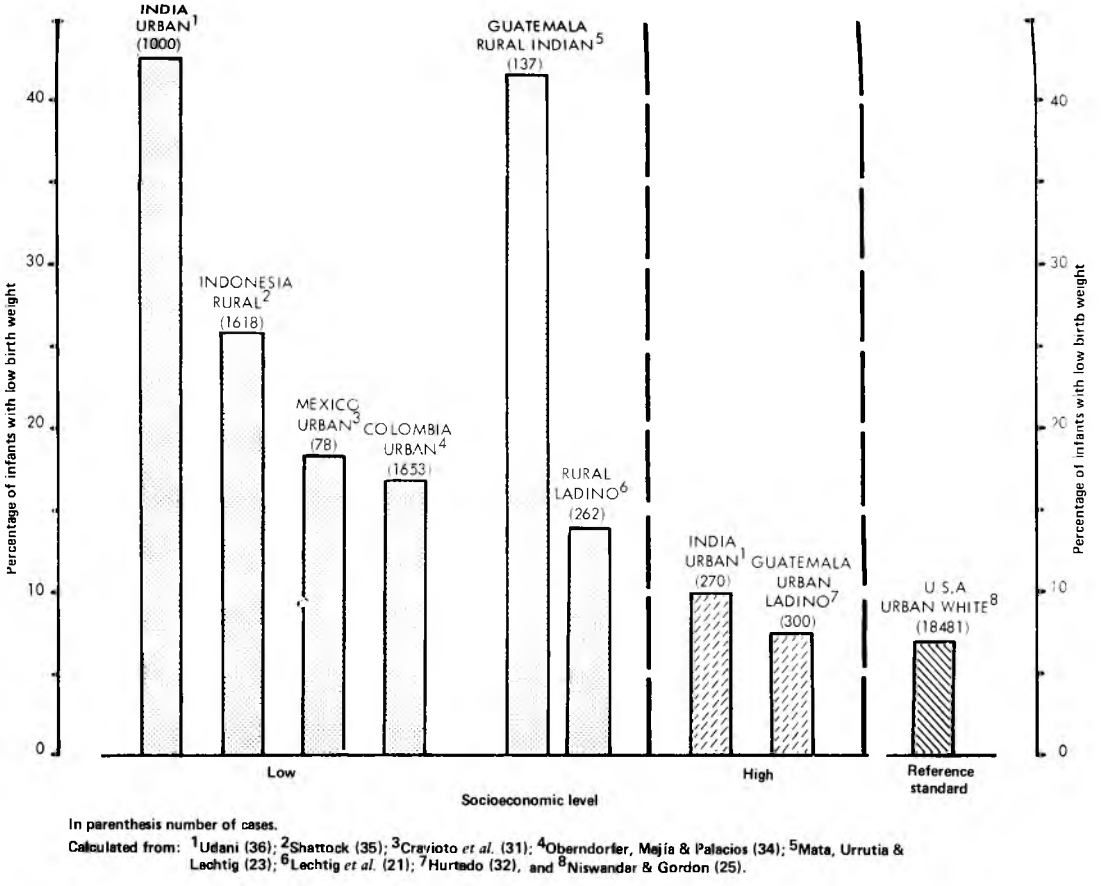
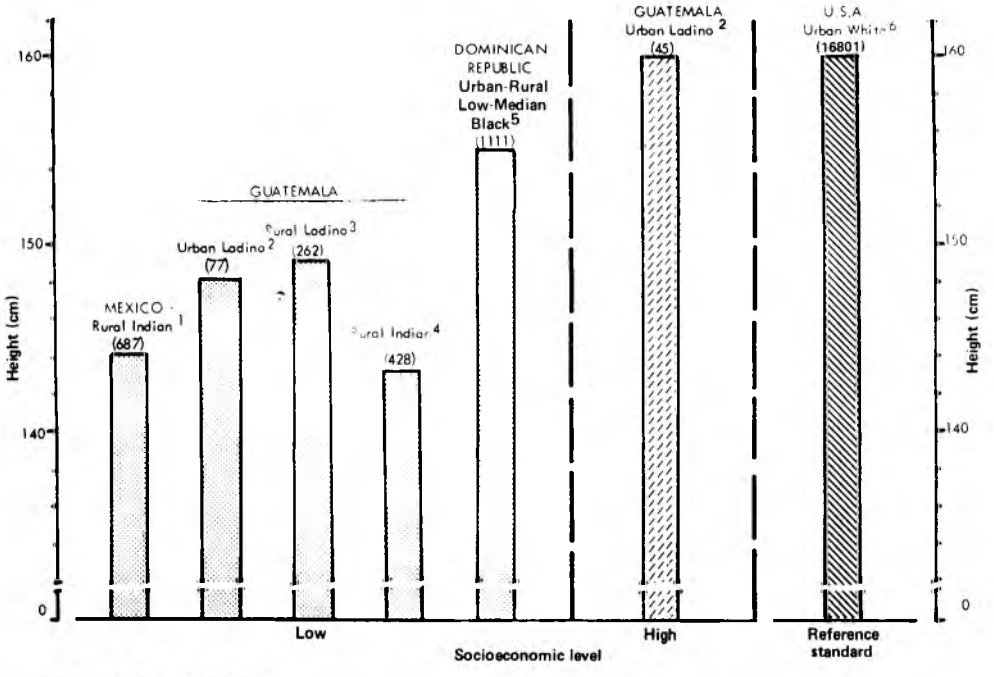


Fig. 2. *Relationship between socioeconomic level and percentage of children with low birth weight.*



In parenthesis number of cases.

Calculated from: [1]Faulhaber (20); [2]Arroyave *et al.* (19), and Lechtig *et al.* (69); [3]Lechtig *et al.* (21); [4]Mata, Urrutia & Lechtig (8); [5]Sebrell *et al.* (26), and [6]Niswander and Gordon (25).

Fig. 3. ***Relationship between socioeconomic level and height of adult women in developing countries.***

In the developing societies, the socioeconomic level is also associated to other maternal characteristics, even within the same ethnic group. Thus, dietary protein and calorie intake,[12-18] weight before pregnancy,[19-26] and weight gain during the gestational period[21, 25, 27-30] are notably lower in mothers of poor rural sectors than in those of high socioeconomic level. As mentioned in the Introduction, in these countries the proportion of low birth-weight babies is much higher in the urban and rural groups of low socioeconomic level than in groups of high socioeconomic level.[21, 23, 25, 31-36]

In the majority of these studies, the socioeconomic status has been almost exclusively defined on the basis of notorious differences in the family income. Practically no information is available on other sociocultural factors that could explain the variations observed in regard to maternal nutrition and birth weight.

However, it must be noted that in the developing societies various common characteristics participate, such as a low gross *per capita* national product; an almost total external dependency in regard to the marketing of raw materials; inefficient systems of land tenure, and a rudimentary technology. Furthermore, these societies are characterized by marked differences between the high and low socioeconomic strata, particularly in terms of purchasing power, food availability and environmental sanitary conditions. These are the causes why malnutrition and infectious diseases are highly prevalent in these populations, principally during the first 5 to 7 years of life.[23] A simplified model of the relation between socioeconomic factors, malnutrition, infection and retardation of development is described in Figure 4. Maternal malnutrition, whether caused directly by dietary deficiencies, or indirectly through increased nutrient losses (due to intense physical activity or to infectious disease) is an importante cause of growth and development retardation which starts in the fetal stage. This retardation, in turn, tends to perpetuate the poverty-malnutrition-poverty vicious cycle through generations.

These interrelations are being explored in the INCAP longitudinal study (ILS) on nutrition and mental development,[37] currently underway in four rural Ladino villages of the East of Guatemala. These villages have a total population of around 3,000 inhabitants, half of whom are under 15 years of age. Fundamentally, these villages have an agricultural subsistence economy and grow mainly corn and beans. The annual income is around $200.00 (US) per family, and the greater part of this amount is used for food and clothing. The environmental sanitation conditions are extremely deficient; drinking water is obtained from brooks or public wells, and only 65% of the houses have latrines.

On a purely empirical basis, a socioeconomic scale (SES) was designed based on the house characteristics, clothing and education of the children. Figure 5 shows that as the score in this scale ascends, the percentage of children with low birth weight diminishes. These results demonstrate that even in small rural villages where almost all of the inhabitants are poor and illiterate, very simple socioeconomic scales can serve to identify groups of mothers at greater risk of delivering low birth-weight babies.[11]

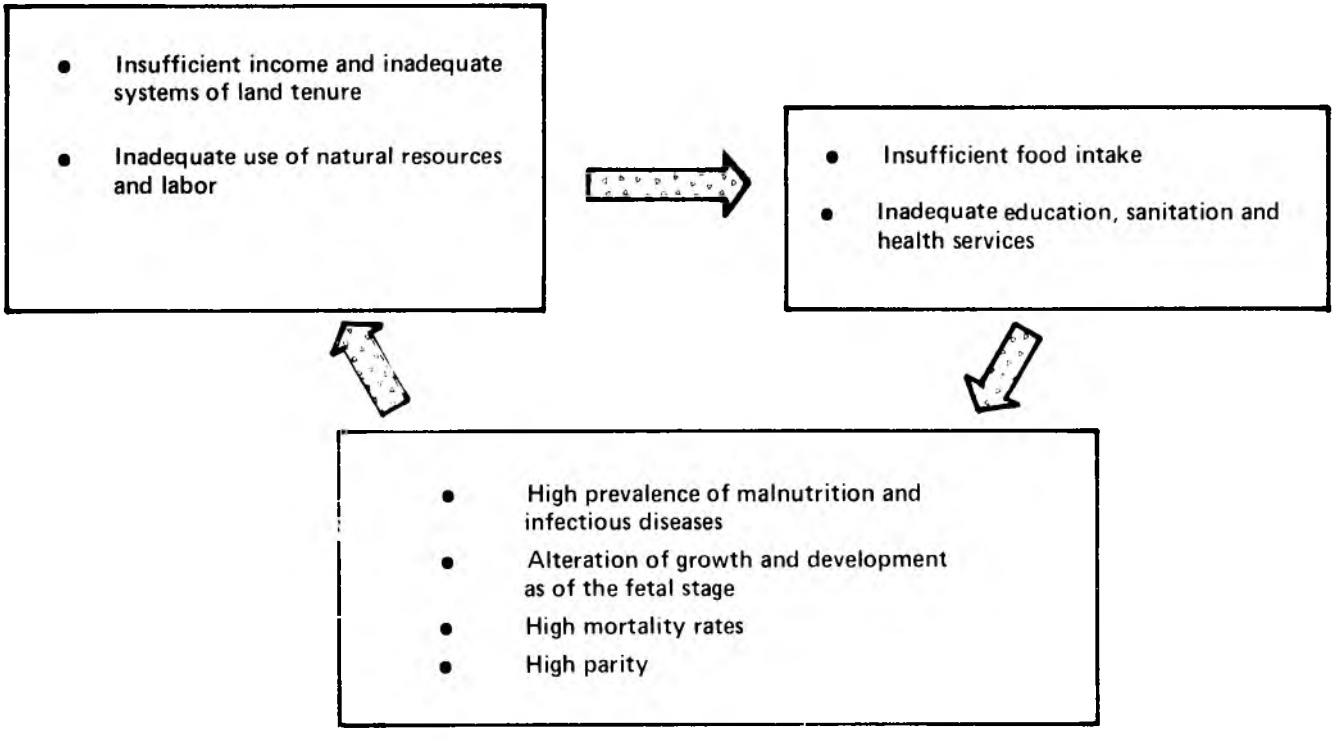


Fig. 4. *Socioeconomic determinants of maternal nutrition and fetal growth in preindustrialized societies.*

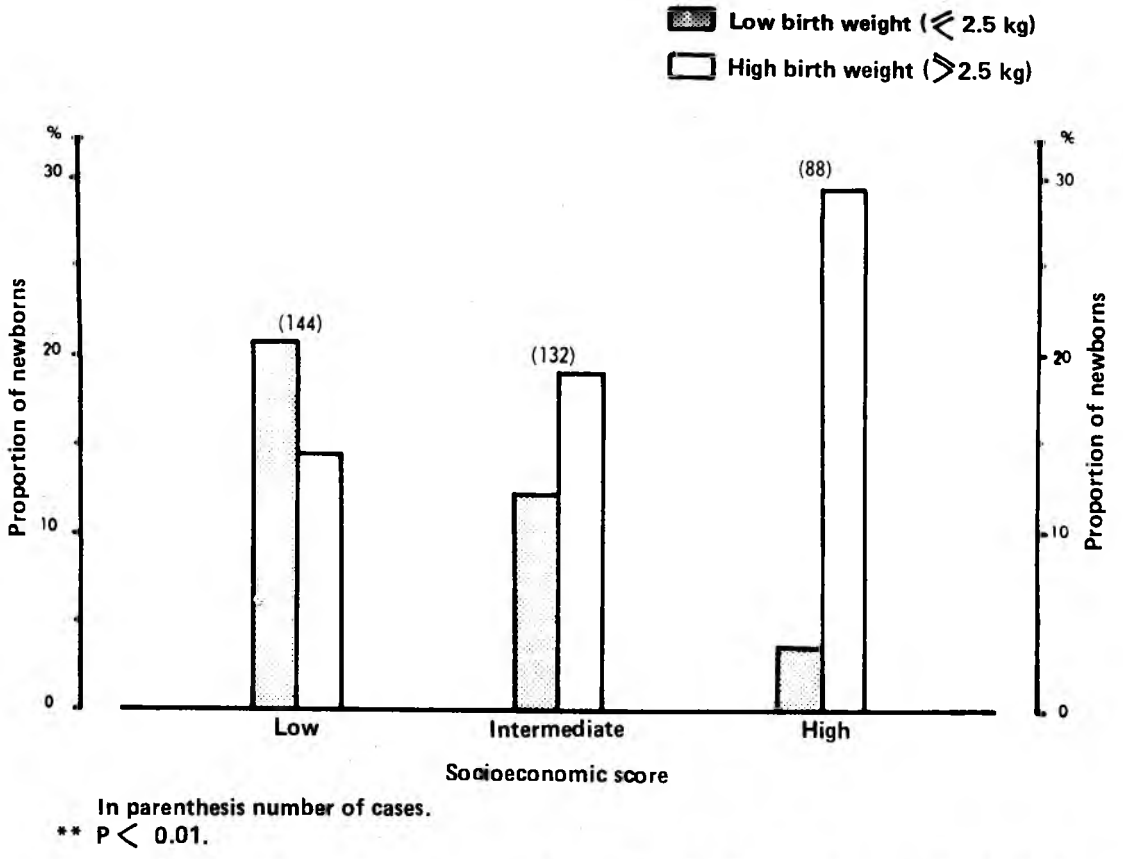


Fig. 5. *Relationship between socioeconomic score and the proportion of children with high and low birth weight in four rural villages of Guatemala.*

The SES score also showed a direct association with maternal height, with the head circumference of the mother, and with weight at the third trimester of pregnancy. In contrast, an inverse relation with maternal morbidity during pregnancy was detected.

The relation between the SES score and the low birth weight of the children, within two categories of the mother's height, is shown in Figure 6. The magnitude of this association is greater in the small mothers than in the tall ones. A similar pattern was observed when instead of using the mother's height, her weight was analyzed together with her cephalic circumference or her morbidity during pregnancy. The fact that the relationship between the SES score and the proportion of children with low birth weight varies when controlled by some maternal characteristics is of great interest, since it suggests that said characteristics can be important mechanisms of the relation between socioeconomic factors and low birth weight.

Thus, a reasonable interpretation of this finding is that the score in the socioeconomic scale reflects economic and cultural conditions which result in malnutrition and other diseases in the mother since the very early stages of her life and which, in turn, produce fetal growth retardation of her child. Of course, there are other possible interpretations of these findings. For example, it could well be that the score in the socioeconomic scale and the maternal characteristics are risk indicators not causally related with the responsible mechanisms of fetal growth retardation. Nevertheless, this is a remote possibility, since there is evidence that improvement of the mother's nutrition during pregnancy is associated with birth weight.[30, 34, 35] Nonetheless, whatever the causal relations between these variables, there is no doubt that in these villages the SES score has a biological significance since it is associated with the risk of low birth weight.

III. INFLUENCE OF MATERNAL NUTRITION ON BIRTH WEIGHT

Animal experiments have demonstrated that the severe calorie and protein malnutrition of the mother delays fetal growth.[38] These effects could be irreversible in the case of those organs where malnutrition has affected the velocity of cellular division.[39]

The effect of maternal nutrition on birth weight in the human beings is clear under severe and acute malnutrition situations. Thus, it has been repeatedly observed that babies born of pregnancies that took place during famine periods had a lower birth weight than those born during periods of adequate food availability.[40-42]

On the other hand, studies on the influence of chronic, moderate malnutrition on fetal growth have rendered less clear-cut results. These studies can be divided into two groups: those that explore the effect of the maternal nutrition history *before* pregnancy (since conception) and those that study the effects of nutritional status *during* pregnancy.

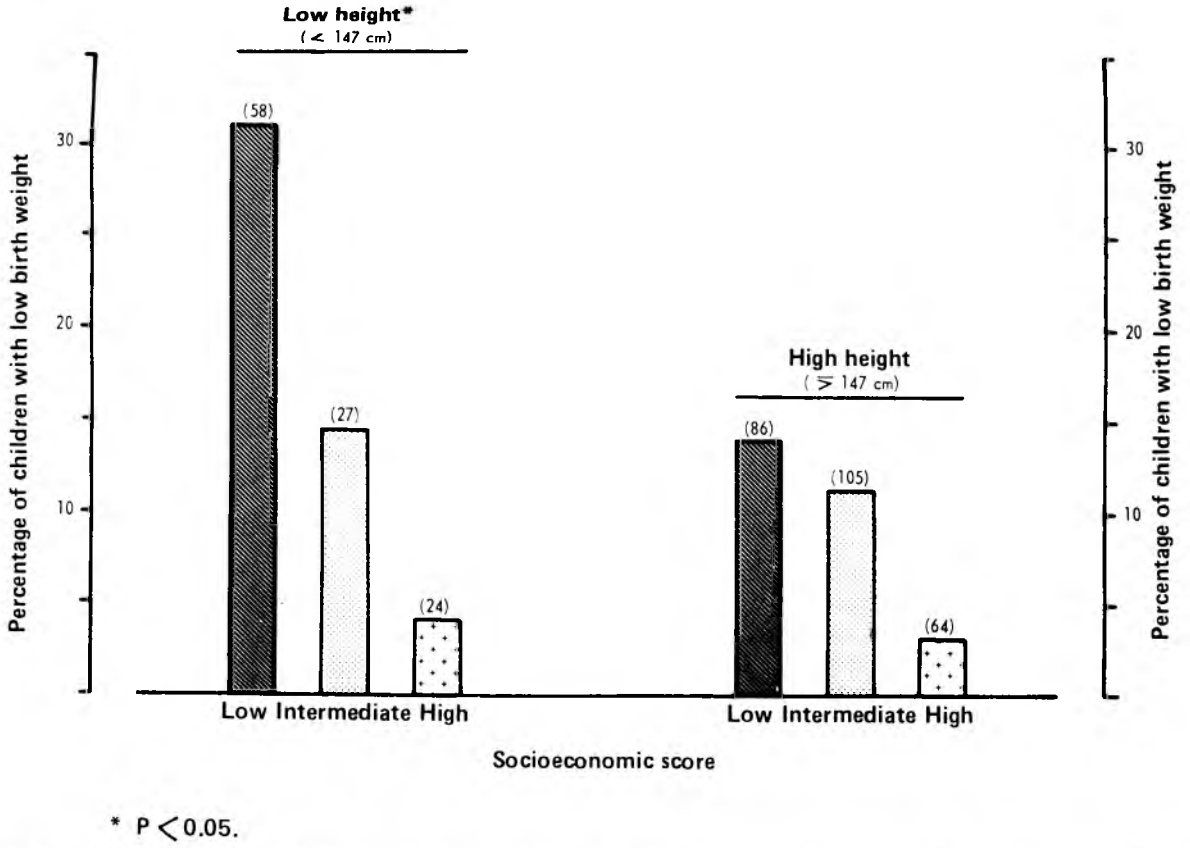


Fig. 6. *Influence of maternal height on the relationship between socioeconomic score and the proportion of children with low birth weight (⩽ 2.5 kg).*

A. Influence of Maternal Nutritional History Since Conception

The indicators used to estimate the nutritional history of the mother are principally anthropometric measurements such as height and weight.

It must be kept in mind that most of the difference in the mean height of adult women between the low socioeconomic groups of Guatemala and the white middle-class populations of the United States of America already exists among 7-year-old children of the same populations. Therefore, it seems that the majority of the height differences found between adult women groups is due to growth retardation during their first seven years of life.[43-46] More still, research work carried out in various technologically underdeveloped countries (TUC) have revealed that the height of the 7-year-old children of high socioeconomic level is similar to that of the standards of industrialized countries, and greater than the height of children of low socioeconomic level of the same ethnic groups.[47-53] These findings suggest that, particularly in the TUC, the environmental conditions associated with socioeconomic level such as malnutrition and infection can be important determinants of height in the adult age. The observation that there is an effect of food supplementation on the growth of preschool children,[53] and the negative association found between the duration of diarrhea and growth in the ILS,[54] offer additional support to the hypothesis that in these population groups, height reflects in part the nutritional history of the mother.

Now, in approaching the relation between maternal nutrition and fetal growth, a consistent association has been found between the mother's height and the weight of the child at birth.[21, 25, 55]

The relation between the mother's height and the proportion of children with low and high birth weight in the four rural villages where the INCAP longitudinal study (ILS) is carried out, can be appreciated in Figure 7. As the data clearly reveal, the proportion of children with low birth weight decreases as the height increases, and the proportion of children with high weight at birth increases.

The weight of the mother before pregnancy has also showed a consistent association with birth weight in mothers of the same height.[25] A similar association has been found between the arm circumference of the mother and the weight of her baby at birth.[56, 57]

Another anthropometric measurement to be considered is the head circumference of the mother. Available information suggests that the differences in head circumference between adult populations are fundamentally due to differences in the growth velocity of the head during the first two years of life. Head circumference of children who have suffered severe malnutrition is very early stages of their lives has been reported to be smaller,[58] and within the same ethnic group, in children of low socioeconomic level.[59, 60] It has also been found that protein-calorie supplementation during early life improves the growth velocity of the head circumference.[56, 61]

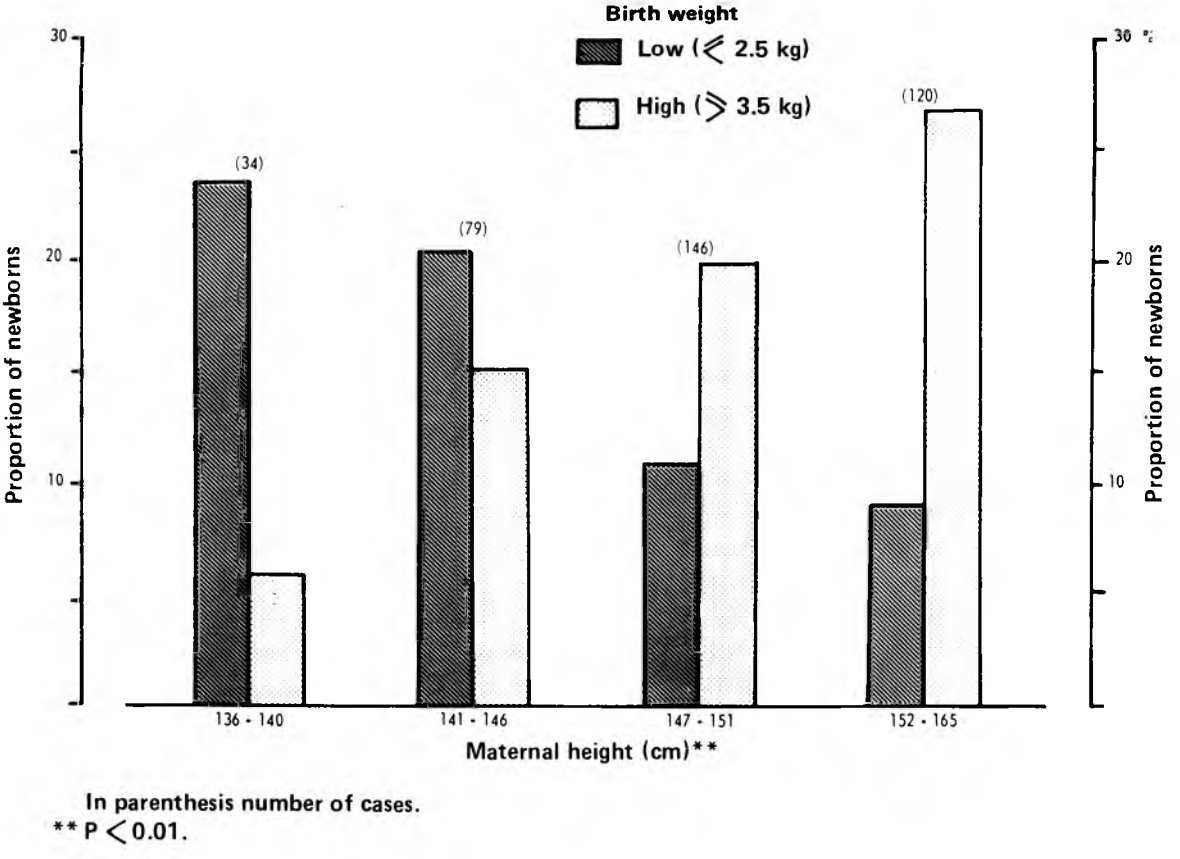


Fig. 7. *Relationship between maternal height and the proportion of children with low and high birth weight.*

The relation observed in the ILS between the mother's head circumference and the proportion of children with low and high birth weights is shown in Figure 8. The reviewed literature does not include other reports on this association, which is of great importance because it continues to be significant even after controlling for height and weight of the mother. Consequently, it could well reflect the specific influence of the very early nutritional history of the mother on the growth of her child.

In summary, maternal height, weight before conception, and the arm and head circumference of the mother show consistent association with birth weight in populations of technically underdeveloped countries. These relationships probably reflect the influence of the maternal nutrition history of fetal growth.

B. Nutritional Status during Pregnancy

Under field conditions, the most commonly used indicators to estimate nutritional status of the mother during gestation are the weight gain during pregnancy and the estimations of dietary intake.

Weight gain during pregnancy is directly related with birth weight, both in industrialized and nonindustrialized countries.[21, 25] On the contrary, in the majority of studies where dietary surveys or food supplementation programs have been used, no association whatsoever has been detected between the intake of nutrients during pregnancy and birth weight.[62, 63] It could be that this lack of association is due to the low reliability of the data on nutrient consumption, and/or to the fact that the majority of the women under study were relatively well nourished.[64]

In the technically underdeveloped countries (TUC), several studies both of a dietary and nutritional intervention nature, have revealed an association between maternal dietary supplementation and weight of the child at birth. However, variables such as infectious diseases and medical care, which could complicate this association, were not explicitly controlled.[64] Thus, the results of Iyengar's experiment in India[65] suggest a strong effect of food supplementation of the mother on birth weight. Nevertheless, these results are difficult to interpret, since in order to develop the food supplementation program, the mothers of the experimental group were hospitalized during the last trimester of gestation. This hospitalization could have resulted in lower infection rates or in less physical exercise, factors which in turn could have been responsible for the observed increment in birth weight.[66-68]

The relation between the dietary intake of pregnant women who have not had food supplementation and birth weight in rural populations of Guatemala is presented in Figure 9.

It is obvious that the average birth weight increased progressively as the dietary intake increased. This relation between the home diet and the weight of the child

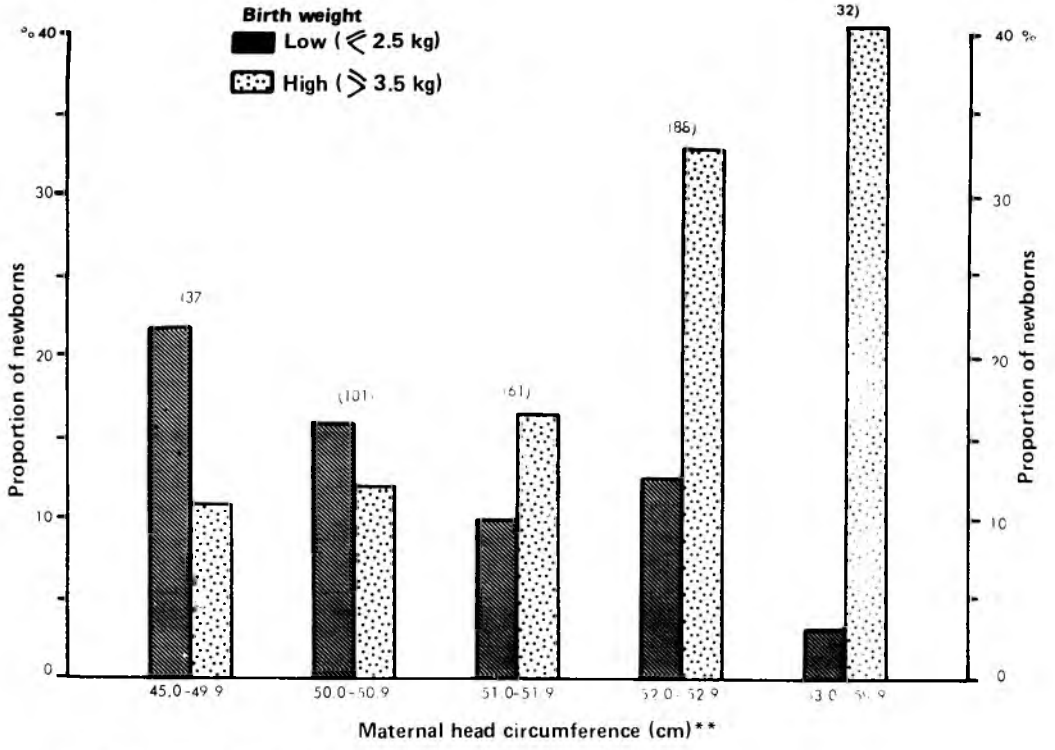


Fig. 8. *Relationship between cephalic circumference of the mother and the proportion of children with low and high birth weight.*

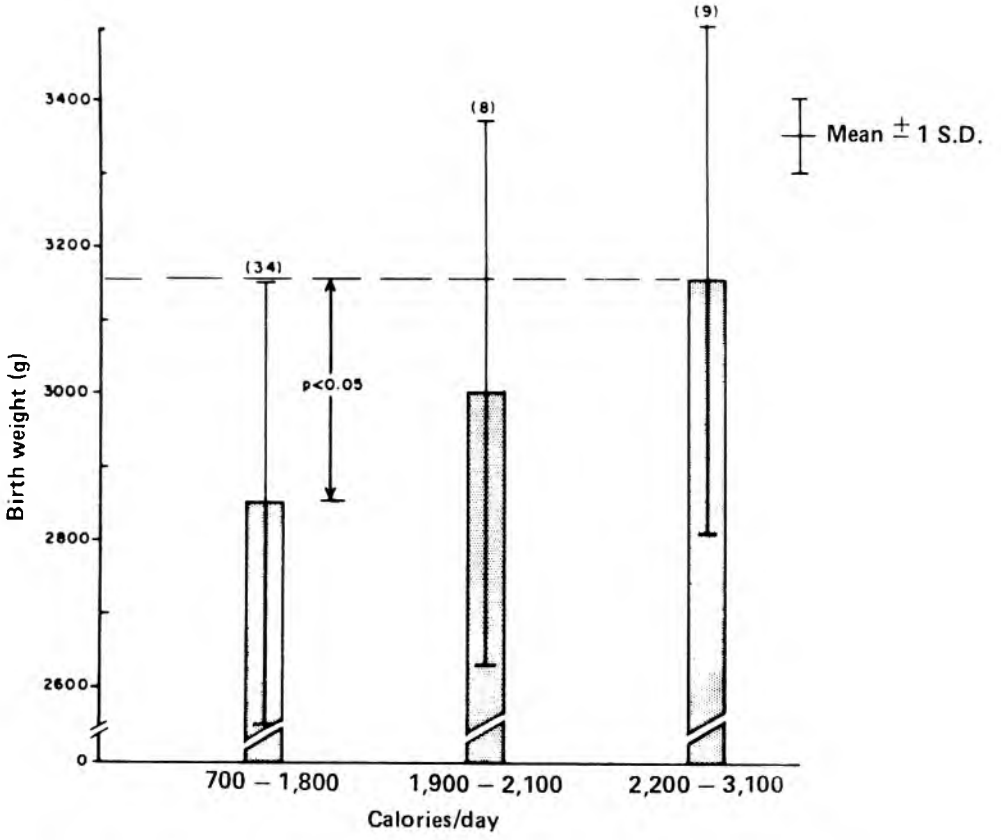


Fig. 9. *Relationship between dietary intake during pregnancy and birth weight.*

at birth was maintained after controlling for the influence of height, parity, duration of diseases of the mother during pregnancy and sex of the newborn. The INCAP longitudinal study to which we have referred has provided additional data on this relationship. It should be noted that this research contemplates administration of two types of supplement: "Atole" and "Fresco." The nutrient content of both preparations is presented in Table 1. As observed, the "Fresco" does not contain protein and its caloric concentration is approximately a third of that of the "Atole."

TABLE 1

NUTRIENT CONTENT PER CUP* (180 ml)

Nutrients	Type of supplement	
	Atole	Fresco
Total calories, kcal	163	59
Protein, g	11	–
Fat, g	0.7	–
Carbohydrates, g	27	15.3
Ascorbic acid, mg	4.0	4.0
Calcium, g	0.4	–
Phosphorus, g	0.3	–
Thiamine, mg	1.1	1.1
Riboflavin, mg	1.5	1.5
Niacin, mg	18.5	18.5
Vitamin A, mg	1.2	1.2
Iron, mg	5.4	5.0
Fluor, mg	0.2	0.2

* Figures approximated to a decimal.

Attendance to the supplementation centers is voluntary and consequently there exists an ample variation in the intake of the supplement during pregnancy. The amounts of supplement ingested both daily and at periodic intervals, were measured as well as the physical growth and mental development of the children. In addition, morbidity, the habitual diet of the families and sociocultural characteristics were also measured.[69]

For the purpose of determining the effect of food supplementation during pregnancy on birth weight, the magnitude of the association between food supplementation and birth weight was first investigated in order to explore if the observed association was an artefact produced by any interfering variable.

The percentage of children with low birth weight for the groups with high and low supplementation is shown in Figure 10. As the data show, this proportion was approximately half in the groups with high supplementation than in those with low supplementation, and no difference was found between the populations who consumed "Fresco" and those who ingested "Atole."

Table 2 presents the observed correlations between caloric supplementation during pregnancy and birth weight. As observed, the values for the slope (or dose-response relationship) both in reference to "Fresco" as well as to "Atole" were very similar. This Table also indicates that a significant correlation between caloric supplementation during pregnancy and birth weight was observed in the total population ($P < 0.01$).

TABLE 2

CORRELATION BETWEEN SUPPLEMENTED CALORIES DURING PREGNANCY AND BIRTH WEIGHT OF THE CHILD

Supplement	r	Dose-response relationship* (weight in g/10,000 supplemented cal)	n	P <
Atole	0.113	23	219	0.10
Fresco	0.123	30	186	0.10
Total (Atole and Fresco)	0.135	29	405	0.01

* Dose-response relationship for Fresco greater than for Atole; covariance test: N.S.

Investigations were then undertaken to determine whether this association was due to a systematic error or to an artefact introduced by interfering variables. For this purpose, approximately 50 maternal variables were studied, including home diet and morbidity during pregnancy, anthropometry, obstetric history and socio-cultural characteristics of the family. As Table 3 shows, the dose-response relationship between the supplemented calories and the weight of the newborn was basically the same after controlling for the influence of the previously mentioned maternal variables. Consequently, these findings reveal that none of these variables can explain the observed association between caloric supplementation during pregnancy and birth weight.

Finally, the possible effect of autoselection of the pregnant women in regard to the supplement intake, as an explanation for the observed association between

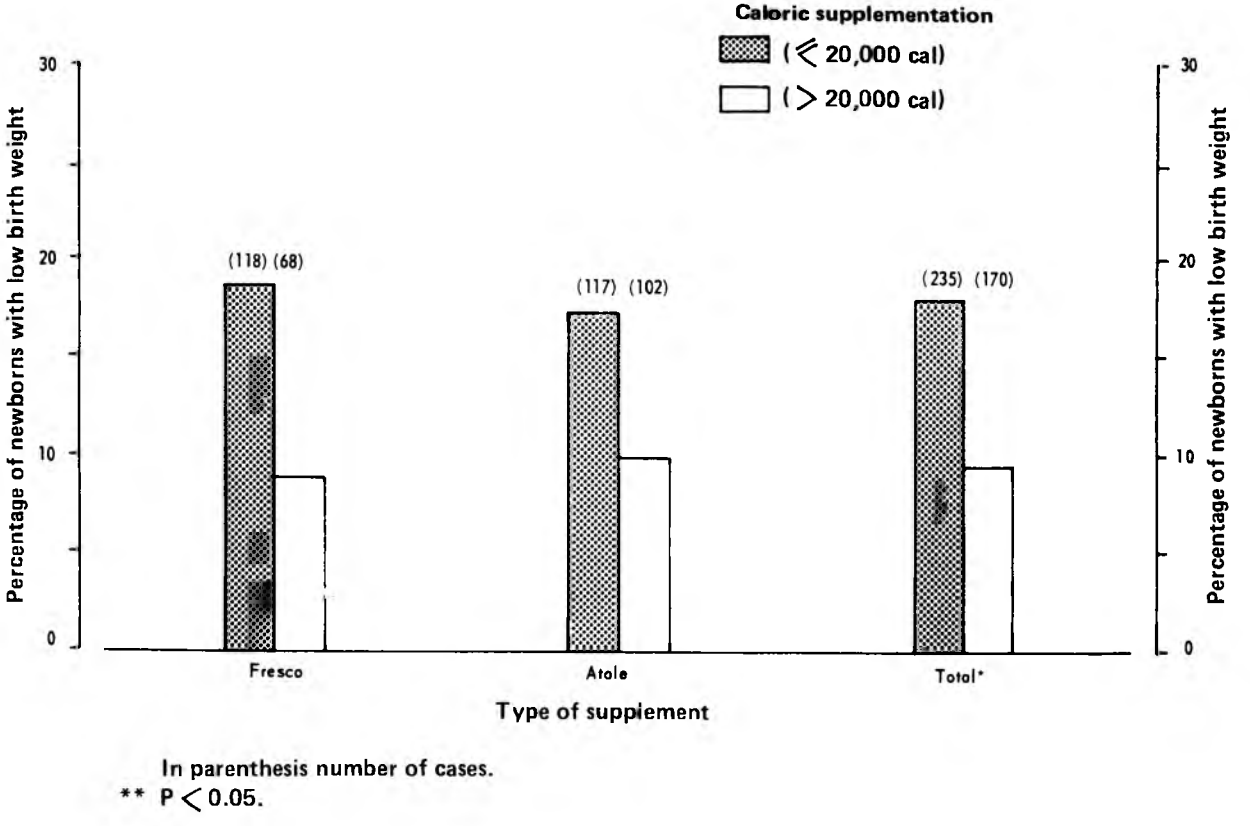


Fig. 10. *Relationship between the amount of supplemented calories during pregnancy and the prevalence of low birth weight (⩽ 2.5 kg).*

TABLE 3

DOSE-RESPONSE RELATIONSHIP BETWEEN CALORIC SUPPLEMENTATION DURING PREGNANCY AND BIRTH WEIGHT (n = 405)

		Dose-response relationship birth weight ($g/10^4$ cal)	S.E.
1.	Before controlling for interfering variables	29**	10.6
2.	After controlling for interfering variables[1] (in multiple correlation)	30**	10.6

** $P < 0.01$.

1 Home diet, height, cephalic and arm circumference, weight at 1st trimester, parity, gestational age, anorexia and diarrhea during pregnancy.

caloric supplementation during pregnancy and birth weight was investigated. Differences in birth weight between consecutive children of the same mother were calculated in order to explore the possibility that any factor not measured in the study could be producing both effects: high food supplementation consumption during pregnancy, and newborns with a higher weight.

The differences in birth weight for the subsample of consecutive siblings, divided into three groups according to differences in regard to caloric supplementation of the mother between the two pregnancies can be appreciated in Figure 11. As the data reveal, when caloric supplementation during the last pregnancy was lower than during the preceding one (bar A), the average birth weight of the last baby was also lower than that of the preceding child. When caloric supplementation in the course of the last pregnancy was higher than during the previous pregnancy (bar C), the mean weight of the last newborn was also greater than that of the preceding child ($r = 0.295$, $n = 82$, $P < 0.01$). Hence, the relation observed between the supplemented calories during pregnancy and birth weight was consistent not only in all the population studied but also between siblings of the same mother. Consequently, it was concluded that calorie supplementation during pregnancy produced an increment in birth weight.[69]

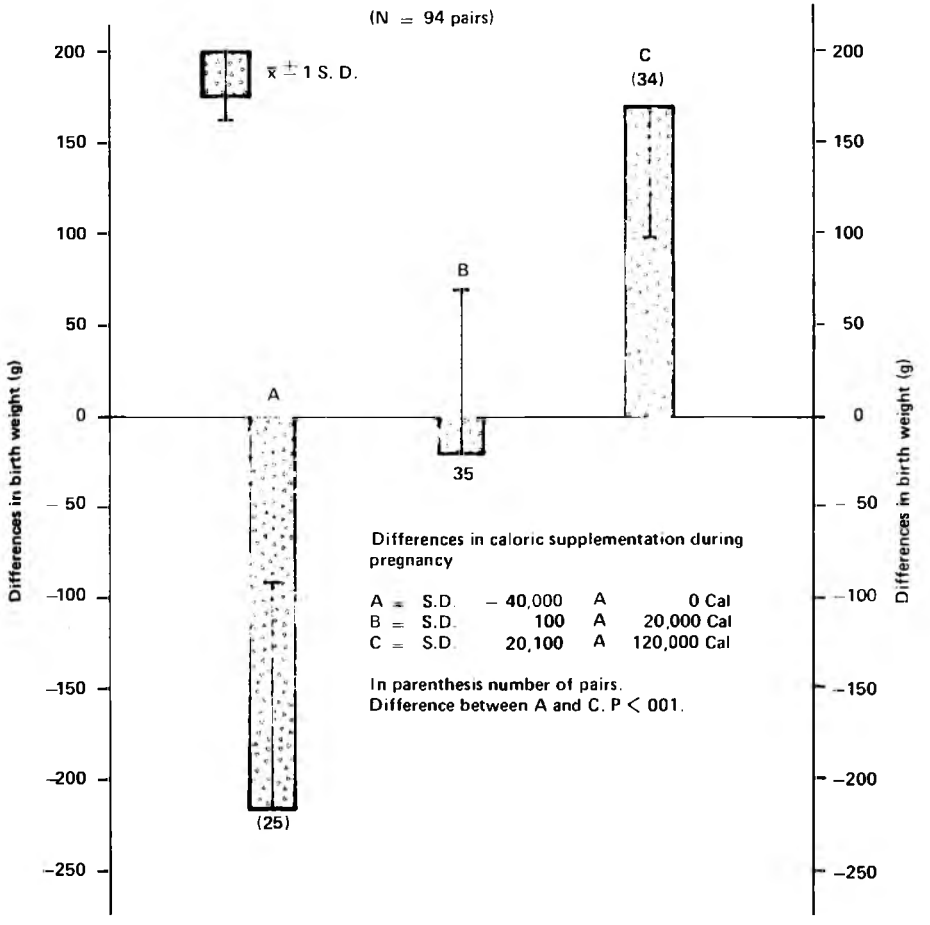


Fig. 11. *Relationship between differences in caloric supplementation during pregnancy and differences in birth weight between two consecutive siblings (last pregnancy minus preceding pregnancy) (n = 94 pairs).*

C. Which are the Mechanisms of this Effect?

It is generally accepted that malnutrition during pregnancy induces changes that lead to a reduction of the materno-fetal transference of nutrients.[22, 70] Furthermore, there is evidence that children of malnourished mothers also present biochemical changes which reflect the nutritional alterations of the mother.[71] Consequently,

reduction of the materno-fetal transference of nutrients would lead to a retardation in fetal growth through metabolic changes in the fetus, which in some aspects would be similar to those produced by malnutrition in the pregnant woman.

It should be noted that in the present study protein did not cause an additional effect to that of calories. This is probably due to the fact that calories are the most important limiting nutrient in the home diet. It is possible, therefore, that part of the protein of the diet is being used to supply calories.[72, 73] Consequently, up to a certain point, the caloric supplementation of this population group is equivalent to a protein-calorie supplementation, since it permits to spare protein for synthesis and growth. It is possible that in populations where the protein-calorie ration is very low,[74] a specific effect of protein supplementation may be observed. The best food supplement for a population is not necessarily the most adequate, and could be even harmful for other populations if their diets are limiting in other nutrients.

The public health implications of the association between food supplementation during pregnancy and fetal growth are obvious. As already mentioned, children with low birth weight present high rates of infant mortality.[8-10] This means that the efficiency of nutritional programs designed to reduce infant mortality could be greatly increased if these were oriented to mothers with a high risk of having low birth-weight babies.[75]

The relationship between the socioeconomic score and the children with low birth weight for two categories of caloric suplementation during pregnancy is shown in Figure 12. As the data reveal, the magnitude of the association between socioeconomic score and low birth weight is higher in mothers with low supplementation than in mothers with high supplementation. More still, in the group with high socioeconomic score, food supplementation practically did not produce differences in the proportion of children with low birth weight. These results clearly indicate that the effects of caloric supplementation are greater in the group with low socioeconomic score. Furthermore, these results suggest that differences in the proportion of children with low birth weight among groups of different socioeconomic score, may be notably reduced if mothers improve their nutritional status during pregnancy.

The relationship between the socioeconomic score and the proportion of children with low birth weight, in regard to two variables, height of the mother and her caloric supplementation during pregnancy, is observed in Figure 13. As the data show, the association between the socioeconomic score and low birth weight is quite strong in the group of mothers of small stature and low supplementation. On the other hand, no association is observed between the socioeconomic score and birth weight in the group of tall, well-supplemented mothers during pregnancy. The two intermediate groups also show an association of intermediate magnitude between the two extremes.

Finally, Figure 14 shows an example of the implications that these considerations have both in terms of effectiveness as well as in terms of the cost of programs

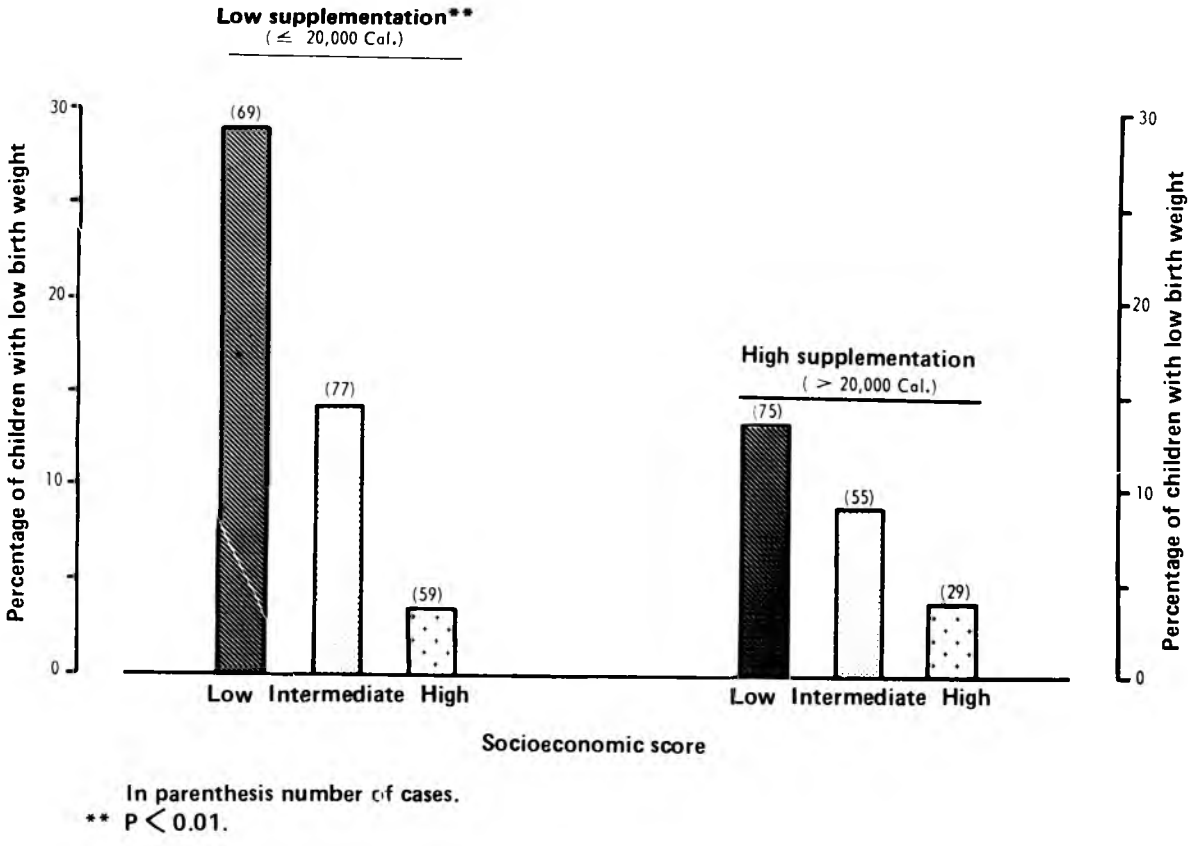


Fig. 12. *Influence of caloric supplementation during pregnancy on the relationship between socioeconomic score and the proportion of children with low birth weight (≤ 2.5 kg).*

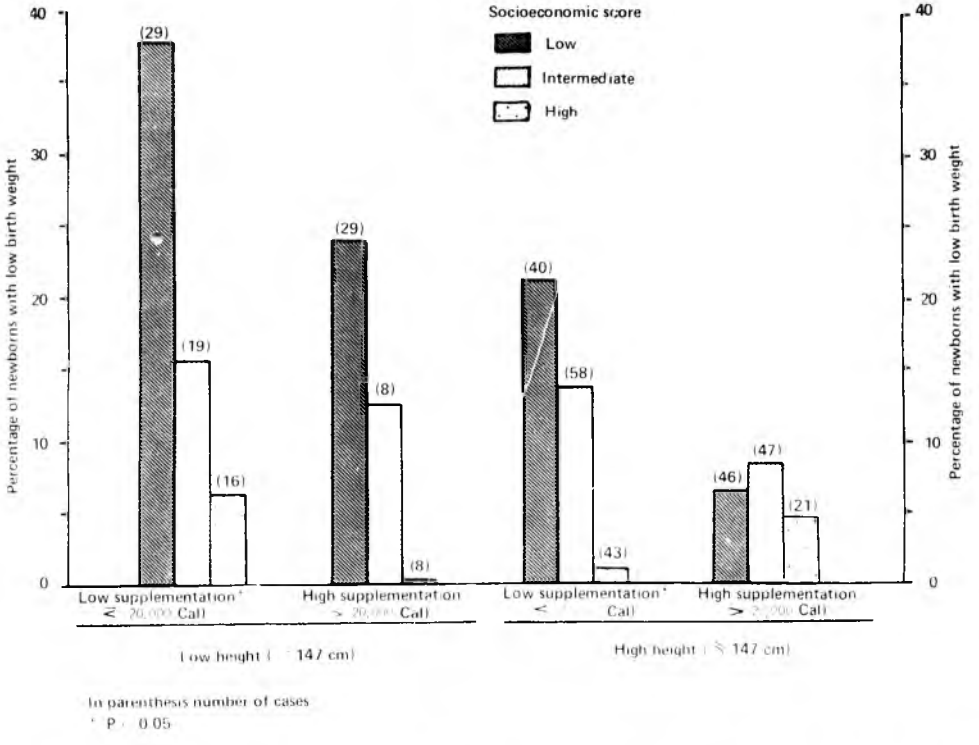


Fig. 13. *Influence of maternal height and of caloric supplementation during pregnancy, on the relationship between socioeconomic score and the proportion of children with low birth weight.*

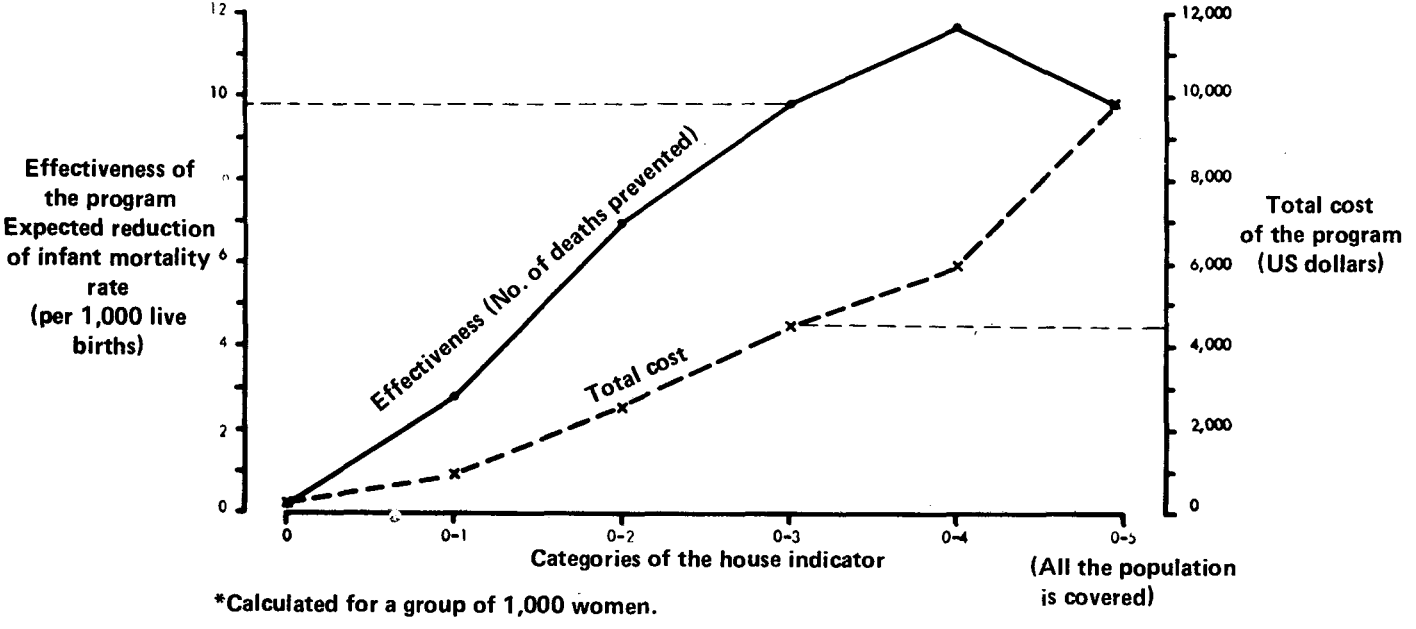


Fig. 14. *Expected changes in the effectiveness and cost of a program* according to the categories used to identify women with high risk of delivering low birth-weight babies.*

aimed at reducing the prevalence of low birth weight or of infant mortality. For this analysis we have selected the house characteristics as a risk indicator, and the reduction in the infant mortality rate as a measure of the effectiveness of the program in a group of 1,000 women.[75] Examination of data in the same Fig. 13 indicates that the expected effectiveness of the program —estimated by the number of prevented deaths— increases in the measure that the superior limit selected to detect groups at high risk increases up to a point beyond which no greater increment is observed. The total cost of the program, however, continues to increase regularly even though its efficacy does not increase any more. In other words, it is evident that if the category 0 to 3 in the housing scale is used to identify women at high risk and the program is applied exclusively to this group, the resulting effect would be similar to that obtained if the program were applied to the total population. Since the cost of applying the program exclusively to the more at-risk group is half the cost resulting from the coverage of the total population, the use of this indicator —house— would permit obtaining twice the expected benefit for the same cost.[75]

IV. INFECTION

Discussion of the association between infectious disease and fetal growth retardation can be divided in two sections: maternal morbidity during pregnancy, and intrauterine infection.

A. Maternal Morbidity During Pregnancy

The available evidence suggests that mothers of low socioeconomic level with endemic protein-calorie malnutrition, also suffer from a high prevalence of infectious diseases.[8, 66, 67]

A preliminary work has shown[66] that morbidity of the mother during pregnancy is inversely related with birth weight. This association disappeared after controlling for the mother's diet during pregnancy, a fact which suggested that the majority of the maternal morbidity effects on birth weight were due to an intake reduction resulting from the anorexia that accompanies almost all of the infectious diseases. However, during that occasion we were unable to investigate which were the most important symptoms.

In a more recent study[67] an inverse relation between common infectious diseases during pregnancy and birth weight was again observed (Fig. 15). The proportion of children with low birth weight increased gradually from 10% in the group of healthier mothers up to 26% in the small group of mothers who reported any type of disease symptoms during more than 50% of their pregnancy. In conclusion, high morbidity levels during pregnancy were associated with a significant increase in the proportion of low birth-weight children, and this association remained constant after controlling for the more important maternal variables.

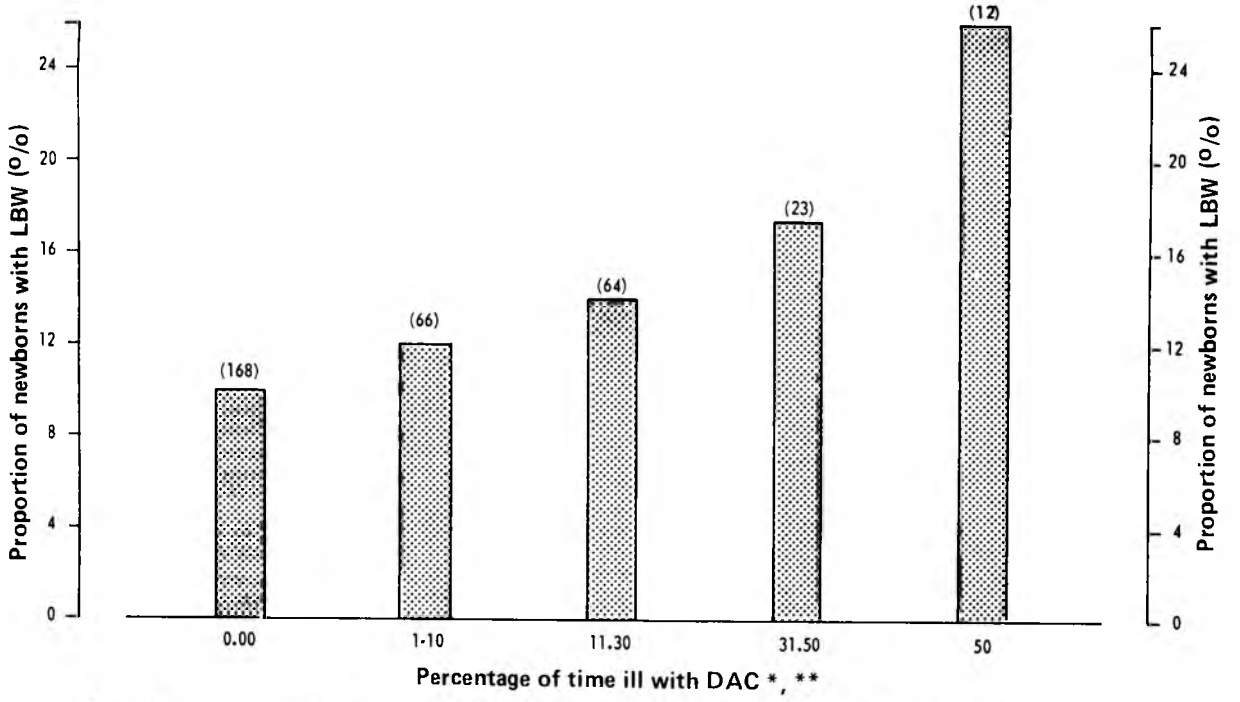


Fig. 15. *Relationship between the percentage of time ill during pregnancy (DAC)* and the proportion of low birthweight (LBW < 2.5 kg) babies** (four Guatemalan rural villages, n = 334).*

The possible mechanism of this effect appears to be the reduction of the nutrient transference from the mother to the fetus. Studies in humans suggest that this can occur due to a reduction in food intake and to the metabolic response to infection.[76, 77] Nevertheless, it should be emphasized that in observational studies such as the ones previously mentioned, assignment of gestating women to determined maternal morbidity categories was not based, of course, on specific criteria designed by the researcher. For this reason it is necessary to interpret the findings with great caution, and to explore in what degree do these results replicate in different populations.

B. Intrauterine Infection

The term "intrauterine infection" will be used in this discussion to indicate the invasion by microorganisms of the fetus tissues, the placenta and its membranes.

1. *Etiology and prevalence*

One of the most serious problems in exploring the effect of intrauterine infection on growth and fetal development lies on the diagnosis of intrauterine infection. Although various techniques have been employed and are available to the researcher, up to this moment there does not exist a totally reliable methodology to make this diagnosis.[78-90]

The more common causal agents of intrauterine infection are shown in Table 4 divided in two main classes: microorganisms that have been wholly demonstrated to be causes of intrauterine infection, and microorganisms that possibly cause this infection.

In relation to the prevalence of intrauterine infection few data are available from underdeveloped populations. In the prospective study of 88 mothers from four rural villages of the East of Guatemala, to which we already referred in a previous paragraph, 66% showed one or more days of infectious disease during pregnancy.[66] The prevalence of antitoxoplasma antibodies was between 60 and 94% in population groups of Guatemala and Costa Rica.[91, 92] Studies carried out in Latin American countries have shown that the IgM levels in cord blood are frequently high in rural or urban populations with deficient sanitary conditions. In these populations the proportion of children with high IgM levels is approximately 50% compared with 5% in Latin American populations with satisfactory environmental conditions.[93] This prevalence is similar to the one found in children with suspected clinical intrauterine infection in Birmingham, Alabama, USA.[82] In Children who have suffered confirmed intrauterine infection, the prevalence of high IgM levels in cord blood is 85%.[80] Taking into account these observations, the total prevalence of intrauterine infection in developing populations is probably much higher than in the developed societies, possibly as high as 10% of all babies born alive.

TABLE 4

ETIOLOGIC AGENTS OF INTRAUTERINE INFECTION

Agent	Demonstrated	Probable
Virus	Cytomegalovirus Rubella Herpes simplex Chicken pox Vaccinia Polio Western equine encephalomyelitis	Coxsackie B Echo Measles Mumps Influenza Hepatitis "Attenuated virus"
Mycoplasma		T strain
Bacteriae	The majority, particularly: Enterobacteriae *Listeria monocitogenes* *Vibrio fetus* *Treponema pallidum* *Mycobacterium tuberculosis*	
Protozoa	*Toxoplasma gondii* *Plasmodium*	
Fungus	*Candida*	

2. *Effects on birth weight*

Low birth weight for gestational age is frequently found associated with intrauterine infection. This association has been particularly evident in infections caused by the rubella virus. The average weight of newborns with congenital German measles is below 2,500 grams,[94] in comparison with 3,300 to 3,500 grams for normal children of the same populations.[95] Other viral agents have been associated with fetal growth retardation. From 30 to 100% of children with cytomegalovirus infection[96] and all those infected by herpes virus[97] have been reported to have fetal growth retardment. Fetal infection by poliovirus is probably a cause of prematurity and low birth weight, especially if it occurs during the first trimester of pregnancy and is clinically severe.[98] A similar observation has been reported in relation to the smallpox vaccine.[99] In cases of fetal infection caused by influenza, mumps, smallpox, chicken pox and measles, the information on this subject is contradictory.[100-102]

In relation to the effects of bacterial infection, an association between the presence of bacteriuria during pregnancy and fetal growth retardation has been reported.[103-105] Nevertheless, more recent information has not confirmed this association.[106-109] Also, the presence of mycoplasma T strains in the cervix or in the urine of gestating women has also shown to be associated with low birth weight.[110] The weight of children with congenital syphilis also is reduced when compared with that of healthy children.[111] Furthermore, an association between low birth weight and the presence of positive seroconversion for toxoplasma during pregnancy has been shown.[112] Lastly, it has been observed that the birth weight of children with placentary infection caused by plasmodium was, as an average, 260 g lower than in the control group.[113]

Table 5 describes the principal routes and action mechanisms on intrauterine infection as well as the factors that influence its final impact.

TABLE 5

PATHWAYS, MECHANISMS AND FACTORS INFLUENCING THE FINAL EFFECT OF INTRAUTERINE INFECTION

A.	**Pathways of intrauterine infection:**
	– Placentary
	– Vaginal
	– Others
B.	**Mechanisms of intrauterine infection:**
	– Reduction of placentary flow
	– Inhibition of the mitosis velocity
	– Chromosomal ruptures
	– Cellular necrosis
	– Increment of catabolic velocity
	– Tissular hypoxia
C.	**Factors influencing the final effect of intrauterine infection:**
	– Nature of causal agent
	– Gestational age at which infection is initiated
	– Severity of the infection (extension, localization, duration)
	– Materno-fetal response (nutrition, immune response)

In the greater part of the reported cases, infection was produced through the placentary pathway, a finding that indicates that the agent must have been first in

the maternal blood.[114, 115] In other cases, particularly of infections produced by herpes virus and bacteriae, infection was produced through the vaginal pathway[116] originating the so-called amniotic infection syndrome.[14] There are other possible infection routes, including transmission through the maternal ovary.[117] The agent is then disseminated in the fetus, producing acute or chronic infection which may not be clinically detectable at birth.[82]

One of the mechanisms which explains fetal growth retardation is the reduction of the placentary blood flow,[118] mainly due to injury of the placenta's endothelium.[119] Another important mechanism is the inhibition of the cellular multiplication which results in hypoplasia.[120] Furthermore, a high frequency of chromosomal ruptures has been reported, and this leads to the production of a great number of nonviable cells and, hence, to low growth rates.[121] In contrast, cellular necrosis does not appear to be an important mechanism in the production of fetal growth retardation.[111] In addition, the increment in the catabolic velocity[122] and the tissular hypoxia[113] can play an important role as mechanisms of the effect of intrauterine infection.

One of the most important factors which influences the final effect of intrauterine infection, naturally, is the agent. Thus, infection by rubella is found consistently associated with fetal growth retardation, while infection producted by cytomegalovirus shows an association with mental retardment independently of the physical growth of the fetus.

The gestational age at which infection occurs is also of importance in determining the magnitude of the injury, its nature and reversibility. For example, intrauterine infection is more dangerous and probably of irreversible effects if it occurs during the first months of pregnancy, since at this stage many organs, including the brain, are in the hyperplasic growth phase.[123]

Another factor is the severity of the infection defined by the extension of the infectious process and the localization of the lesions. Under similar conditions of extension and localization, processes of longer duration will probably produce a more profound effect on fetal growth than relatively short infectious processes.

In addition to the above-mentioned factors, those modifying the physiologic state of the fetus are also important. Among these we can cite nutritional status, which may be reduced due both to maternal malnutrition or to a restriction of the placentary blood flow.[119] Other factors are the immune response capacity of the fetus, the magnitude and efficiency of which determine the final result of the infectious process.

After the third month of gestation, the fetus is capable of producing immunoglobulins and components of the hemolytic system complement.[124] At birth, the fetus can show retarded hypersensibility reactions[125] and a phagocytic activity similar to that of the adults.[126] The efficiency of these mechanisms is fufficient to

protect the newborn, even if he lives in environments with very high infection risks. Demonstration of immunologic reactions of fetal origin has been possible in the majority of intrauterine infections.[127] In some cases,[128] however, reactions have appeared tardily or have not been detected, thus suggesting an alteration of the recognition mechanisms of the agent as strange to the fetal organism. This observation has been reported in some types of infection produced during the first trimester of gestation, and have profound implications for the immunologic theory.[129, 130]

The maternal defense mechanisms against infection also play an important role. The majority of the antibodies produced by the mother are IgG type and, consequently, pass to the fetus and contribute to protect him.[131] In infections occurring through the vaginal route, the passage of antibodies and other factors of the mother to the fetus can also be an important factor in the protection of the product.

It must be emphasized that, excepting the studies carried out during German measles epidemics, these data are originated from studies that have not been designed for the specific purpose of exploring the effect of intrauterine infection on birth weight. For example, the retrospective information on gestational age does not permit to infer if the low birth weight observed was due to fetal growth retardation or to a short-term gestational age. In spite of these difficulties, the reviewed data suggest that fetal infections produced by German measles, cytomegalovirus, herpes virus, toxoplasma and plasmodium exert unfavorable effects on fetal growth. In the case of other infections, evidence is doubtful.

The mechanisms of this effect are principally the reduction of the placentary blood flow and the inhibition of the mitosis velocity in the fetal organisms. The injury produced depends on the type of infectious agent, the time at which the infection occurs and its severity, the nutritional status of the fetus, and the effectiveness of his immune response. Estimates of the prevalence of intrauterine infection vary in accordance to the environmental sanitation conditions, and can possibly be as high as 10% in the alive newborns in technologically underdeveloped societies.

V. OTHER FACTORS

A. Altitude

The Andes region in South America is the area of higher altitude (more than 3,000 m above sea level) more densely populated in the world. Obstetricians working in the Andean Region frequently report that children born in that zone are generally smaller. Various reports from the Andean Region in Peru have consistently shown that a lower birth weight and a greater neonatal mortality correspond to the highest altitude. Thus, a sample of children born in Cuzco (at an altitude of almost 4,000 m) weighed an average of 200 g less than children born in Lima (200 m altitude). More still, children born in Cuzco from mothers of European origin also showed a lower average birth weight than that of populations living at sea level.[132, 133] Similar data have been observed in the United States.[134, 135]

In summary, the available evidence suggests the existence of an inverse relationship between altitude and birth weight. Populations who live at higher altitudes tend to have a high percentage of children with low birth weight. Analysis of the published data suggests that the altitude effect can produce an increase of 4 to 5% in the prevalence of low birth weight for each increment of 1,000 meters above sea level.

B. Genetic Factors

There is consensus in the scientific community as to the importance that genetic factors play as determinants of birth weight. Nevertheless, available data are difficult to interpret given the different genetic or ethnic differences usually found associated to environmental differences. Various authors[136, 137] have found a clear difference in the average birth weight among different ethnic groups. Thus, for example, the North American Indians show the greatest average birth weight while the Mayan Indians and Hindus show lower averages. On the basis of this incidence, it is assumed that there exists a strong genetic component in the causal complex which determines birth weight. The variables to correlate in studies on the genetic influence on intrauterine growth, are the growth potential of the parents and newborns. In the developed societies, environmental conditions can permit a complete expression of the genetic potential for physical growth. This is why it is considered that in the developed countries, variability in height is to a great extent due to a different genetic growth potential.[138] In these societies high correlations between the size of the parents and the size of the children have been found.[138]

It has been shown that the relation between the size of the mother and the size of the newborn is consistent in many mammal species, including the human species.[139] Data collected from various independent groups of researchers suggest that this relationship is mainly a function of the size of the mother, and not of the size of the father, both in animals[140, 141] as in humans.[142, 143] These data suggest that birth weight depends more on the environment provided by the mother than on genetic influences. A possible mechanism of this effect is the placentary blood flow.[144] However, in undernourished populations, the physical growth of both parents and newborns does not appear to be a total expression of the genetic potential for growth. This notion is derived from numerous studies which indicate that chronic malnutrition and the high morbidity rates associated to it, cause physical growth retardation.[53, 54] In other words, in these societies environmental factors, principally malnutrition and infection, determine the extent of how the fetus can develop its growth genetic potential.[145]

C. Miscellaneous Factors

Great attention is paid in the literature originated from the developed countries, to a series of factors that are found with relatively less frequency in the developing countries of the world. These factors will be briefly reviewed in the following paragraphs.

The incidence of pre-eclampsia is three times higher among primigravidae than among multigravidae and occurs with exceptionally high frequency in women who

have had serious systemic diseases previous to initiation of pregnancy. A high incidence of toxemia of pregnancy also exists in low socioeconomic populations where maternal protein-calorie malnutrition is highly prevalent.[146]

In a study of 947 cases of preeclampsia carried out in the United States of America, it was found that both the fetus and the placenta showed important alterations in growth and development in comparison with the conception product of normal women. Furthermore, women with toxemia of pregnancy tended to give birth at a shorter gestational age than normal women.[147]

There is also evidence of association between the cigarette-smoking habit during pregnancy and birth weight. The average birth weight is around 200 g less in mothers who smoke than in those who do not smoke during pregnancy.[148] In a sample of non-smoking mothers of the United States, the incidence of low birth weight was approximately half (3.6%) than that observed in a comparable sample of smoking mothers (7.6%).[149] The cigarette-smoking habit during pregnancy has also been associated to a short gestational age, and it is estimated that around 10% of the effect of the smoking habit on birth weight is due to a short gestational age.[150] The principal mechanisms of this effect seem to be the vaso-constrictor effect of nicotine on the blood vessels of the placenta, a high concentration of carbon monoxide in the blood and, consequently, fetal hypoxia and a small-size placenta.

Besides, various complications of pregnancy can produce low birth weight. These include diabetes, cardiac disease, Rh incompatibility, severe anemia, excessive vomiting or hemorraghes during pregnancy, abortion induced through various means, previous placenta, multiple pregnancies, and previous abortions.[151, 152]

Finally, in some mothers from developed countries, a repetitive tendency to give birth to children with low weight, commonly due to their short gestational age, has been observed. This tendency, found in apparently normal women, has been called idiopatic prematurity in view of the fact that the causes of these phenomenon are unknown.[153]

VI. ESTIMATION OF THE IMPORTANCE OF THE REVIEWED FACTORS

Due to the scarcity of information, it is impossible to provide a precise estimate of the relative importance of the various factors previously described, in respect to their contribution to the high incidence of low birth-weight babies in Latin America. However, some points merit consideration in this regard.

The triad formed by maternal malnutrition, infection and low socioeconomic level constitutes a very complex interaction and it is difficult to estimate the relative importance of each one of its individual components. Thus, in contrast to the developed countries, 70% or more of the developing societies are in the low

socioeconomic level stratum, where a high prevalence of malnutrition and infection exists. Furthermore, in populations of the Andean Region, it is possible that the altitude exerts a negative interaction with malnutrition and maternal infection. However, although the Andes Region is the more populated high-altitude region of the world, its contribution to the high incidence of low birth weight in Latin America appears to be relatively small.

In general, the cigarette-smoking habit is quite uncommon in Latin American mothers, so that this is also a factor of little practical importance as determinant of the total incidence of low birth weight in the Region. Reports on the incidence of toxemia of pregnancy in the developing countries vary between 3 and 26% of the number of born-alive babies,[146, 154, 155] and it has been observed that this condition is more prevalent in the low socioeconomic classes. It is possible that maternal malnutrition be one of the contributing factors to the development of toxemia of pregnancy,[156] and it is also possible that toxemia of pregnancy produce a greater number of low birth-weight babies in the developing countries than in the developed countries. However, due to the high prevalence of malnutrition and infections, it is probable that even under these circumstances, the contribution of toxemia of pregnancy to the total incidence of low birth weight in Latin America is small when compared to the contribution of maternal malnutrition and infection. The same conclusion is applied to the series of miscellaneous factors mentioned previously.

The known causes of LBW are summarized in Table 6, divided into two groups in terms of their relative importance in the Latin American countries.

TABLE 6

DETERMINANTS OF LOW BIRTH WEIGHT IN LATIN AMERICA

A. Predominant	B. Of minor importance
1. Low socioeconomic level	1. Altitude
2. Malnutrition	2. Toxemia of pregnancy
3. Infection	3. Smoking habit
	4. Hemorrhage
	5. Repeated abortions
	6. Previous child with low birth weight
	7. Diabetes
	8. Cardiovascular disease
	9. Multiple pregnancy
	10. Hyperemesis
	11. Genetic factors
	12. Other

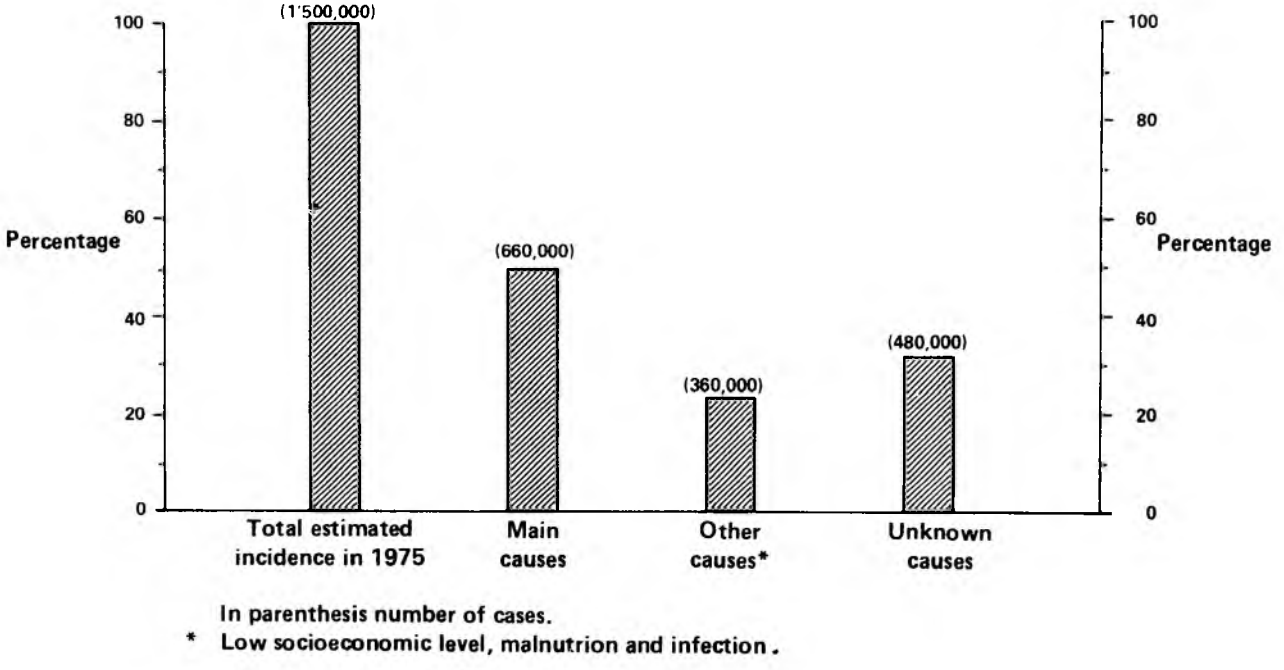


Fig. 16. *Estimated incidence of low birth weight in Latin America, by causes.*

A proximate estimation of the importance of three groups of causes as determinants of the incidence of LBW in Latin America is presented in Figure 16. It is estimated that the causes considered as predominant were responsible for 44% of the babies born with LBW in 1975. All of the other known causes would be responsible for approximately a fourth of the total incidence. The remaining group —a third of the total incidence— would correspond to causes which have not been determined as yet.

In conclusion, the available data suggest that the high incidence of low birth weight in Latin America is primarily the result of the high prevalence of maternal malnutrition, of common infectious diseases during pregnancy, and of factors that interact with poverty or economic, social and cultural deprivation of the majority of the Latin American populations. These three factors interact in a very complex form for the purpose of finally producing a high incidence of low birth weight in our countries.

It is essential to recognize that this high incidence is directly related to the malnutrition, infection and poverty conditions. For these reasons, when adoption of measures for reducing the incidence of low birth weight is considered, it is important to approach the problem not only as a specific public health problem, but also in its global context in relation to the social and economic development of the population.

Many public health specialists have not recognized the contribution of maternal malnutrition to the prevalence of low birth weight, and feel that the problem can be solved by massive immunization programs and with the establishment of curative medical services. Nonetheless, these programs are not only very costly but their effective utilization in the developing countries is quite limited unless there exists a simultaneous improvement of both the environmental conditions and of the basic social and economic parameters of the community. On the other hand, one of the considerations to be kept in mind is the frequent failure of traditional nutritional actions in the Latin American countries. The fact that maternal malnutrition is an important causal factor in the etiology of low birth weight does not necessarily mean that the supplementary feeding programs herein discussed will solve the problem. It must be emphasized that these programs were implemented as research procedures. As routinary service activities such programs are generally very expensive, they consume too much time and personnel, contribute to create dependent populations, and frequently induce unfavorable effects on the local food industry. Consequently, it is possible that such programs are inadequate as unique and massive measures aimed at great population groups and during long time intervals.

RESUMEN

CAUSAS DE BAJO PESO AL NACER EN LATINOAMERICA

Del análisis de la literatura se concluye que el peso del recién nacido es notablemente mejor en los grupos de alto nivel socioeconómico que en los grupos de bajo

nivel socioeconómico, y que dicha asociación también existe en pequeñas poblaciones pobres del área rural de Guatemala. En estas aldeas, la asociación entre el puntaje de la escala socioeconómica desarrollada para esta investigación y la proporción de niños con bajo peso al nacer, desaparece en los grupos de madres con alta talla y bien suplementadas durante el embarazo. Los datos presentados sugieren que tanto la historia nutricional desde la concepción, como el estado nutricional de la madre durante el embarazo, constituyen uno de los mecanismos importantes de la relación causal existente entre características socioeconómicas y crecimiento fetal. Otro mecanismo de gran importancia en Latinoamérica es la elevada prevalencia de infección, tanto en la madre como en el niño desde su vida prenatal. Se estima que el complejo causal pobreza-desnutrición-infección es responsable de por lo menos la mitad de los niños nacidos con bajo peso en la Subregión. Se considera, además, que el conjunto de causas conocidas como responsables de la mayor parte de niños con bajo peso al nacer en los países industrializados, determina no más de la cuarta parte de estos niños en la América Latina. Por esta razón, las estrategias utilizadas en países industrializados para disminuir la incidencia de bajo peso al nacer no son aplicables en Latinoamérica. Por ejemplo, en muchas poblaciones del Subcontinente indicadores muy sencillos tales como la talla, el perímetro de la cabeza y del brazo, y las características de la vivienda, pueden ser muy útiles para seleccionar grupos de madres con alto riesgo de dar a luz niños con bajo peso al nacer y que, por lo tanto, requieren con carácter prioritario, la atención de los programas de salud. El uso de estos indicadores de riesgo contribuirá a mejorar notoriamente la eficiencia y la efectividad de dichos programas, particularmente en las poblaciones con recursos de salud inadecuados.

Se concluye que un mejoramiento del estado nutricional y de la salud de las mujeres gestantes, conducirá a un descenso significativo de la prevalencia de niños con bajo peso al nacer en la mayor parte de la población latinoamericana. Esto, a su vez, ayudará a reducir las altas tasas de mortalidad infantil que se observan en estos países, y permitirá a las nuevas generaciones una mayor probabilidad de desarrollar toda su potencialidad genética.

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