Normal Fetal Growth Regulation: Nutritional Aspects

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NORMAL FETAL GROWTH

To determine the mean fetal growth curve in the human species is theoretically impossible; it would require a precise measurement of fetal weight in utero during the entire fetal life. Fetal growth curves used in clinical practice are based on data obtained from liveborn infants of different gestational ages. Presumably, they provide reasonable estimates of the general pattern of fetal growth, although it is not valid to derive velocity growth curves from cross-sectional data. Longitudinal ultrasound studies on large numbers of patients have now been obtained and have provided no evidence that babies with larger heads or who are large for dates have a significantly shorter duration of gestation (1). All the fetal growth curves obtained by this technique have the same general pattern: they show a regular and rapid growth during the second trimester of intrauterine life, followed by a slight faltering, which becomes more pronounced just before term (2). This faltering in the fetal growth curve does not seem to be an artifact due to the cross-sectional nature of the data collected at birth. This is also apparent on head growth curves, which can be derived from longitudinal measurements made in utero by echography (3).

After delivery, the newborn infant grows faster than just before birth and seems to “catch up” after the preterm growth faltering. This results in a marked irregularity of growth during the perinatal period (4), which is apparent on velocity curves (Fig. 1).

To explain this irregularity, it has been suggested that near term, fetal growth is not optimal and is limited by some unknown maternal factor, in the absence of which the growth curve would have no linear deviation during the perinatal period (2).

That human growth might be suboptimal in the perinatal period is also suggested by epidemiological evidence. In all populations, perinatal mortality is related to birthweight by a U-shaped curve with high values for small birthweights, a minimum in the medium range, and again high mortality for larger newborn infants (5). Birthweight associated with the lowest level of perinatal mortality may be considered as being the “optimal birthweight.” In all the statistics published so far,
this optimal birthweight is higher than the mean birthweight (6–12), suggesting that the mean fetal growth results in lower than optimal birthweights.

To determine normal fetal growth in the human, therefore, is a doubly insoluble problem. First, it is impossible to measure fetal growth directly; even if this were possible, mean growth curves would presumably not reflect optimal fetal growth. In addition, optimal birthweight associated with the lowest perinatal mortality seems to vary considerably from one ethnic group to the other, from one population to the other, and even within the same ethnic group between socioeconomic classes. It would be between 3,800 and 4,000 g for white Americans (6), approximately 2,950 g in the poorest social groups in India (11) but 3,380 g in the upper middle class (11), 3,050 g in Ghana (10), and between 3,500 and 4,000 g in Nigeria (9). The wide range of these figures shows how difficult it is to interpret birthweight statistics. When the level of perinatal mortality for every birthweight class is not known, which is frequently the case in developing countries, it is impossible to know whether the mean fetal growth is normal: in other words, if the difference "optimal birthweight — mean birthweight" is in the usual range or, on the contrary, if there is a real problem of fetal growth retardation in a population.
In the absence of precise data on the value of optimal birthweight, it may be wiser to consider with skepticism the classic idea that a mean birthweight below the standards of industrialized countries is synonymous with insufficient fetal growth. Many nutritionists insist that the same growth standards should be adopted for all populations (13): ethnic factors seem to have little influence, if any, on growth potential before puberty (14,15). To advocate different birthweight standards for every population may seem to be a return to the past, when the extent of malnutrition in a given population could be minimized by using local standards, which included a significant number of malnourished children. Ethnic factors, however, may have an influence on postpubertal growth (14,15). Maternal size is not uniform in different populations and is known to have a more pronounced influence on fetal growth than the genetic factor. There is an important correlation between half-sibs with a common mother ($r = 0.581$), while birthweights of half-sibs with a common father are almost unrelated (16). One cannot expect to have similar birthweight statistics in populations with different maternal sizes, even though, as is likely to be the case, growth potential is the same for all during fetal life.

FACTORS LIMITING FETAL GROWTH

That fetal growth might be limited by some maternal factor does not seem to be specific to humans. In most species, the fetus rarely fully expresses its genetically determined potential for growth (17).

The classic demonstration was made as early as 1938 by crossing Shire horse with Shetland ponies (18). The birthweights of foals born to Shetland dams were similar to those of pure Shetland, while foals born to Shire dams were of similar birthweights to purebred Shires. This maternal influence, independent of genetic factors, was confirmed more recently by experiments of transplantation of fertilized eggs. Eggs of normal sized pigs transplanted into dwarf sows produced lighter than usual piglets. When the experiment is reversed, that is, when eggs from dwarf sows are transferred to normal sized mothers, the piglets are about twice the size of dwarf piglets (19). A similar predominant maternal influence on birthweight has been observed in sheep (20) and rabbits (21).

Comparative physiology provides some clue to the nature of this maternal regulation. Widdowson (22) first suggested that placental blood flow might be the main regulator of fetal growth, since plasma concentration of nutrients does not vary markedly between species, whereas placental blood flows are very different. This hypothesis is supported by the allometric relationship between maternal and fetal weight. When comparing species of different sizes, the relationship between physiological variables and body weight is not necessarily linear (23,24). The best example is basal metabolic rate, which is much lower per unit of body weight in larger species. Some variables, such as energy reserves or muscular mass, are related to body weight, whereas others, such as blood flows, are related to body surface area; others, such as blood pressure, are independent of physical size.
These relationships can be predicted by mathematical calculations, which were discovered as early as the 17th century by Galileo (23). Thus it can be demonstrated that plasma concentration of nutrients is independent of body size, as pointed out by Widdowson (22). In mathematical terms, the relationship between a physiological variable and body weight can be described by the general equation:

\[ X = \text{body weight}^a \]

The coefficient \( a \) is called the "allometry coefficient," and the variable \( X \) is related linearly to body weight if \( a = 1 \), to the maternal surface area if \( a = 0.73 \), and is independent of body size if \( a = 0 \). This allometry coefficient can be estimated from observed values of a given variable in different species. This approach was used by Battaglia and Meschia (25) to determine the relationship between maternal and fetal size. The authors showed that fetal weight (or litter weight for polytocous species) is related to maternal weight by the equation:

\[ \text{Fetal weight} = (\text{maternal weight})^{0.75} \]

This suggests that fetal growth is regulated by an unknown factor related to body-surface area. These authors suggested that fetal growth might be limited by the fact that the fetal oxygen supply should remain only a small fraction of the total maternal oxygen uptake. A limitation of fetal size by the maternal capacity to provide the fetus with oxygen is supported by the persistence of a prolonged lactation period among placental mammals. Lactation presumably appeared earlier than placentation in mammalian evolution (26). When it appeared in early mammals, placentation offered a selective advantage, since the fetus \textit{in utero} is strongly protected against the external environment. That lactation persisted despite the lack of protection offered to the fetus suggests that the mother's capacity to keep the fetus \textit{in utero} is limited by an unknown factor, which could be the oxygen supply to the fetus. All the other nutrients needed for growth are provided by the mother during lactation.

That maternal nutritional reserves do not intervene in interspecies regulation of birthweight and that a factor related to maternal capacity to provide oxygen to the fetus is more likely to be involved suggest that it could be the same within the human species. To speculate on the allometric relationship between maternal and neonatal size in humans is hardly feasible, however. Lean body mass is related to the square of the height and not to its cube as a result of changing morphology in individuals of different sizes. This makes the interpretation of allometric data more difficult than in comparative physiology. It is well known, however, that birthweight is not proportional to maternal weight, as would be expected if maternal nutritional reserves regulated fetal growth. Mean birthweights of term newborn infants for different classes of maternal body weight calculated from Aberdeen standards in the United Kingdom (27) are reported in Table 1.

Heavier women have lighter newborn infants per unit of body weight. The lower birthweight compared to maternal body weight in heavier women has been long noticed but has been interpreted in nutritional terms (28). It has been postulated
that when the mother has low energy stores, there is suboptimal fetal growth with a competition between the deposition of maternal nutritional reserves and fetal needs. When the mother is well nourished, however, the fetus reaches optimal growth and the surplus of nutrients can be stored by the mother without any major further increase of birthweight. This interpretation, postulating a competition between maternal fat reserves and fetal growth with a priority either for the fetus or for the mother, depending on the availability of nutrients, would imply that birthweight would be positively related to maternal fat reserves. If this nutritional interpretation were true, low birthweights should be more frequent among women with low fat stores, whereas fatter women should have bigger newborns. We tested this hypothesis in a survey on birthweight in an underprivileged population of the periphery of Dakar. Results are reported in Table 2. Maternal triceps skinfold, which may be considered a rough estimate of maternal fat reserves, was negatively related to birthweight when adjusted for maternal body weight. In other words, birthweight was lower when maternal fat stores were higher. This result was statistically highly significant.

This result may seem surprising. Most nutritionists would assert that a good maternal nutritional status (i.e., solid energy reserves) is necessary for normal fetal growth. It seems that this inverse relationship between maternal fat stores and birthweight has long been noticed. Classically, it is well recognized that maternal height has a noticeable influence on birthweight and that this relationship is inde-
pendent of maternal weight (27,29). We also found this relationship in our sample (Table 3): adjusted for maternal weight, birthweight is higher in taller women. However, if the influence of maternal height, weight, and triceps skinfold is tested simultaneously, the relationship between maternal height and birthweight is no more significant (Table 2). This suggests that the relationship between maternal height and birthweight would only reflect the negative relationship between maternal fat stores and birthweight; for a given weight, taller women are slimmer.

The inverse relationship between maternal fat stores and birthweight is hardly compatible with the hypothesis that fetal growth is suboptimal when the mother has low energy reserves. It is difficult to explain in nutritional terms why heavier women have proportionally smaller newborns. A vascular interpretation is more attractive. All the oxygen consumed by the fetus is brought to the placenta by uterine blood flow. Uterine blood flow, as any blood flow (24), is likely to be comparatively smaller in heavier women. We suggest that fetal oxygenation limits fetal size in humans.

PLACENTAL BLOOD FLOW AND FETAL METABOLISM REGULATION

All clinical situations resulting in fetal hypoxia are associated with fetal growth retardation. When the pregnancy takes place at high altitude, the birthweight is depressed by about 100 g per 1,000 m of altitude (30). Severe maternal anemia resulting in tissue hypoxia is associated with low birthweight. When the hematocrit is below 30%, birthweight is depressed by about 100 g per 2% decrease in the packed cell volume (31). Tissue hypoxia resulting from narcotic use might be responsible for the birthweight reduction observed in drug addicts (30). Tobacco consumption is also associated with intrauterine growth retardation. This may be caused by a reduced transfer of oxygen to the fetus by a double mechanism. First, carbon dioxide causes a minor but chronic hypoxia; second, nicotine has a vasoconstrictor effect, thus reducing placental blood flow (30). The hypothesis of a decreased infant birthweight among smokers as a result of a decreased food intake does not seem tenable. There is a depression of birthweight even when maternal food intake are maintained (32).

These observations support the hypothesis that oxygen supply to the uterus controls fetal growth. The relationship between oxygen supply and fetal size,

<table>
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*Sample size, 2,456; p < 0.001.
however, is not straightforward. First, there is no evidence that the fetus is suffering from metabolic acidosis, as would be expected if its metabolism were limited by oxygen availability. This has been shown in the ewe, the cow, the mare, and in humans (33–35). Moreover, the fetus is a consumer and not a producer of lactic acid, which means that its metabolism is mainly aerobic (25). Finally, giving pure oxygen to the mother does not increase fetal oxygen consumption, which suggests that, under usual conditions, all metabolic fetal needs are met (36). Apparently, fetal metabolism is regulated by some unknown mechanism, keeping the oxygen demand below the amount brought by the uteroplacental blood flow.

Glucose is intriguing with respect to fetal nutrition because it is the only major substrate of oxidative metabolism that is not transferred actively across the placenta (37). This is in marked contrast with other essential nutrients, such as amino acids, vitamins, and minerals. One may wonder why such an active mechanism did not appear during evolution. A possible explanation could be that the absence of an active placental uptake makes glucose a potential regulator, which could adjust fetal metabolism and fetal oxygen demand to placental blood flow. A transfer of glucose to the fetus by passive diffusion implies that the amount of glucose crossing the placenta at any time is determined by physical factors and is mainly dependent on placental blood flow under usual conditions when maternal and fetal blood glucose levels are tightly controlled. A regulation of fetal metabolism by the rate of glucose transfer would make oxygen demand indirectly related to uteroplacental blood flow. This would mean that even in the absence of any sign of fetal hypoxia, fetal metabolism could be adjusted to oxygen availability.

Glucose regulates fetal metabolism at two levels. First, it is the main substrate of fetal oxidative metabolism (25). In animals, it has been estimated that, under basal conditions, 50% of fetal oxygen is used to oxidize the glucose consumed by the fetus and directly transferred from maternal circulation. Another 25% is used to oxidize lactate produced by the placenta from maternal glucose. Second, glucose stimulates fetal insulin production, which seems to act as a "fetal growth hormone," since it stimulates both fat and protein synthesis (17). Among the factors that may cause the birthweight to deviate from the mean, fetal insulin secretion seems to induce the widest variations. When the mother has a poorly controlled diabetes, a state in which fetal hyperinsulinemia is known to be present, birthweights approaching 6,000 g are not exceptional. On the other hand, diabetic newborn infants from normal mothers but who had a deficient insulin production during fetal life have a severe intrauterine growth retardation and birthweights as low as 1,250 g are reported in the literature (17).

The hypothesis of an adjustment of fetal oxygen demand by glucose transfer is further supported by experiments in sheep which show that making the fetus hyperglycemic results in a definite increase of the plasma lactate of the fetus (38) and in metabolic acidosis (39). In conclusion, if oxygen availability seems to be the factor limiting fetal size, glucose is likely to be the regulator adjusting fetal metabolism to placental blood flow and indirectly to oxygen supply.
ORIGIN OF PRETERM FETAL GROWTH FALTERING

The preterm growth faltering observed in man is intriguing. After birth, growth accelerates through "catch up" growth, as may be seen after an episode of malnutrition (4). Since fetal growth seems independent of maternal nutritional reserves, it is unlikely that the factor limiting fetal growth is nutritional. Moreover, this fetal growth faltering has been described in well-fed populations with no problems of food availability (2). Tanner (4) suggested that this could be an adaptation of the species to make delivery easier. This does not explain, however, why this growth faltering results in lower than optimal birthweights. Moreover, if this were a genetic adaptation of the species, one should observe growth irregularity in preterm newborn infants approaching their estimated date of delivery. This is not the case: growth curves of preterm newborn infants do not falter before 40 weeks of gestational age (40).

This growth irregularity appears much more like an imperfection of the species than an adaptation. According to the laws of evolution, this type of minor imperfection can occur when there is a rapid change in the genetic heritage, giving an important selective advantage to the species. This has suggested the hypothesis that the slight preterm growth faltering could be an imperfection appearing as a result of the acquisition of upright posture (41). This human acquisition with large selective advantages results in perturbations of the cardiovascular system and of the supply of blood flow to the uterus. This could explain why the organism is not able to sustain fetal growth at an optimal level up to the end of intrauterine life. Upright posture is associated with a marked lumbar lordosis, which compresses the aorta before the origin of the uterine arteries. It also results in a decrease of plasma volume and cardiac output, which is corrected by an increased sympathetic activity and does not seem to protect the fetus (42).

Recently, this hypothesis has been questioned, since there is no preterm faltering of abdominal growth curves measured in utero by ultrasound (1). If this fetal growth faltering is attributable to a reduced placental blood flow, abdominal growth should be more affected than fetal head growth, which does not appear to be the case. Actually, fetal growth curves (1,3) are incompatible not only with the above hypothesis but also with the most widely used fetal growth standards. Before 35 weeks of pregnancy, fetal weekly weight gain is estimated to be approximately 300 g and only 100 g between 39 and 40 weeks (43). Ultrasound estimates suggest that fetal head growth velocity peaks at 25 g per week at 30 weeks of gestational age and falls to 15 g per week before term (1). Obviously, fetal head growth faltering does not explain fetal weight gain faltering. Presumably, all organs have a low growth velocity before birth, yet abdominal growth continues steadily. Abdominal circumference measurements in utero are influenced by fetal position (3), which is constantly changing during fetal life. It is more reasonable, therefore, to doubt the general shape of intrauterine abdominal curves. Otherwise, one should have to admit that the 200 g per week decrease of fetal velocity results mainly from the
growth faltering of nonabdominal organs, which is not supported by postmortem studies of growth-retarded stillborns or neonates (44).

African women have a pronounced lumbar lordosis. They give birth to newborn infants lighter than Europeans; this has often been interpreted in nutritional terms. In Table 4, however, we report the birthweight of African babies in a periurban community with no problems of food availability. Birthweights were calculated for different classes of maternal weights which, one may assume, reduces or even eliminates the nutritional factor. These values were obtained with a regression equation derived from our data and compared to Aberdeen standards (27). The difference in birthweight is, on the average, 375 g. This difference may be attributable to an increased compression of uterine arteries by a marked lumbar lordosis. None of the other factors known to influence birthweight could account for such a difference. This may be indirect evidence that the acquisition of lumbar lordosis results in impaired fetal growth.

THE FETUS AS NUTRITIONAL VICTIM

That fetal growth seems to be unrelated to maternal energy reserves and to depend mainly on the mother’s ability to provide oxygen is in agreement with the idea of the fetus being a perfect nutritional parasite. Under certain circumstances, however, fetal growth seems to be sacrificed to protect maternal nutritional reserves.

During the Dutch famine of 1944–1945, there was a sharp birthweight depression of more than 300 g when the mean maternal weight after delivery decreased only 2.5 kg (45). According to usual standards of birthweights related to maternal weight (27), such a minor variation of maternal weight should have resulted in a birthweight depression of less than 50 g.

What was observed in Holland during the famine occurs every year in many rural Third World communities when there is a food shortage just before the harvest, when mothers must sustain heavy physical activity. This phenomenon was described by Prentice et al. (46,47) in The Gambia. Their data show that during the rainy season, there is a depression of birthweight of 160 g when the mothers on average are 3 kg lighter. According to birthweight standards from Dakar, which

<table>
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<th>Maternal weight (kg)</th>
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<tr>
<td></td>
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<td>3,360</td>
<td>80</td>
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*All parity groups  
Data from Thomson et al. (27).
were collected in an ethnically similar population, this diminution of maternal weight should have resulted in a birthweight depression of only 60 g (see Table 2).

Several years ago, a high-protein low-carbohydrate diet was supposed to reduce the incidence of preeclampsia. In Motherwell, Scotland, the obstetrician in charge of the only maternity hospital between 1938 and 1977 insisted that all pregnant women, even in the absence of any sign of preeclampsia, should follow this diet, which resulted in an acute decrease of maternal total energy intake (48). At 20 weeks of pregnancy, women were slightly lighter than in Aberdeen, a nearby community where the diet was not prescribed but which was similar to Motherwell in all other respects. Although this difference of maternal weight was not significant, birthweights in the two communities were very different: newborn infants in Motherwell on average were 300 g lighter. According to Aberdeen standards (27), this birthweight difference is usually observed when differences of maternal weight of approximately 15 kg are seen.

Contrary to previous traditional thought, these observations suggest that the fetus is not a parasite but is a victim when there is decreased maternal food intake. This is not contradictory with our hypothesis about fetal growth regulation—that birthweight might decrease when maternal energy reserves are hardly depressed. This may even be considered evidence of birthweight regulation independent of maternal reserves.

Acute food shortage is the common characteristic of all situations, suggesting that the fetus is a victim when the mother is malnourished. Metabolic adjustments occurring during an acute depression of food intake were studied extensively in animals. These result in faltering of fetal growth, presumably by the following mechanism (25,49). Maternal fasting is associated with a decrease of maternal glucose plasma levels. Since glucose crosses the placenta by a facilitated diffusion mechanism, this results in fetal hypoglycemia. Fetal insulin production is depressed, and there is a reduction of fetal metabolism and growth.

That glucose could regulate fetal metabolism makes the fetus sensitive to maternal fasting, regardless of the extent of maternal fat reserves. In mammals, there is no enzymatic system allowing a transformation of fatty acids into glucose (49). When the 70 or 90 g of hepatic glycogen reserves are exhausted, that is, after a few hours, fasting results in hypoglycemia. Keeping glucose to a tolerable level is possible only by gluconeogenesis from muscle amino acid. During maternal fasting, the fetus can presumably use some alternate fuels, such as fatty and ketonic bodies (25,49). These substances do not stimulate fetal insulin production, however, and allow only limited fetal metabolic activity. The slowing down of fetal metabolism in only a few hours, well before maternal energy reserves are seriously depressed, suggests that during fasting, the conservation of maternal energy reserves is a priority compared to sustaining optimal fetal metabolism.

All the metabolic adjustments that occur during maternal fasting are associated with modifications of cardiovascular physiology, which combine with the depressed plasma nutrient levels to decrease the nutrient flow in the placenta. In man, fasting results in decreased blood volume (50), decreased cardiac volume, and lowered
blood pressure (51). These vascular modifications are likely to reduce placental blood flow. They occur well before maternal energy reserves are seriously depleted. In animals, the same physiological adjustments to fasting have been reported, and their effects on placental perfusion have been measured. In pregnant rats (52), when maternal food intake is reduced by 50%, there is an inadequate plasma volume expansion during pregnancy, a reduced cardiac output, and a reduced placental blood flow. In the pregnant ewe (53), the cardiac output remains unchanged compared to controls when food intake is reduced, but there is a redistribution of cardiac output toward the liver at the expense of uteroplacental blood flow, which decreases by about 25%.

When the cardiovascular function is deficient, the organism usually reacts by an activation of the sympathetic nervous system with an increased secretion of catecho-
lamines. The type of vascular redistribution observed in the pregnant ewe during fasting suggests that this reaction is also activated by acute malnutrition (53). The involvement of the sympathetic nervous system would make the fetus a victim during maternal fasting. This reaction is activated in emergency situations only, when maternal life is in danger. Animal experiments suggest that it does not protect placental perfusion (42). Hard muscular work could have the same effect (54). Physical activity, especially if performed in a hot environment, results in increased sympathetic nervous activity, which likely provokes a reduced placental blood flow (42).

THE FETUS AS PERFECT PARASITE

If one excepts fasting, during which maternal metabolism is disturbed, the plasma level of glucose is under the tight control of a complex hormonal mechanism. If fetal growth is regulated by the placental glucose flow, this control makes the fetus a perfect parasite, especially when considering that it plays a role in regulating maternal hormonal balance.

At the beginning of pregnancy, when fetal energy needs are minimal, progesterone produced by the placenta results in maternal fat storage following an increased dietary intake and a reduction in energy expenditure (30). Progressively, during the third trimester of pregnancy, this deposition of fat decreases; this has been attributed to a progesterone antagonist, estriol, also produced by the fetoplacental unit (55). At the end of pregnancy, there is a lipolysis, with fasting plasma fatty acid levels up to 5 times those observed in nonpregnant women. This appears to be due to the action of human placental lactogen (HPL), which induces an increased peripheral resistance to insulin (55). This alteration in fat metabolism provides an alternative fuel source for the energy needs of maternal tissues and so spares glucose for use by the fetus. At this stage, the fetus seems to have an absolute priority over the deposition of fat by the mother. Since there is an increased peripheral resistance to insulin, the mother can lay down fat only when there is a frank hyperglycemic peak, during which the fetus itself becomes hyperglycemic and fetal growth is stimulated by an increased fetal insulin production. The fetus
might also be able to stimulate muscle protein breakdown by a hormonal mechanism and to reuse muscle amino acids for the synthesis of new tissues.

At the end of pregnancy, there is a raised excretion of 3-methylhistidine by the mother, which seems to reflect an increased muscle catabolism (55). This increased amino acid turnover probably is related to an upsurge in estrogen production by the fetoplacental unit. It may protect the fetus against the variations of maternal protein intake, muscle mass being a virtually limitless reserve of amino acids, which can be transformed rapidly and efficiently into fetal proteins.

In conclusion, under usual conditions, the fetus may be considered as a perfect parasite. In contrast, when there is maternal fasting and when the mother becomes hypoglycemic, there is a depression of cardiovascular function and the fetus is victimized.

ENERGY REQUIREMENTS OF PREGNANT WOMEN

According to FAO/WHO recommendations (56), a pregnant woman should receive a daily supplement of 1.2 MJ (or 285 kcal), which amounts to a total of 335 MJ for the entire period of pregnancy (80,000 kcal). This is in addition to a diet providing 9.2 MJ per day (2,200 kcal) and is equivalent to a total daily intake of 10.4 MJ (2,485 kcal).

In most developing countries, food intakes of pregnant women are much lower. In West Africa and in India, for instance, daily energy intakes of about 1,400 kcal are often reported, and a daily intake below 2,000 kcal appears to be the rule in most developing tropical countries (46). This difference between observed energy intakes and internationally recommended values is reported constantly from one survey to another; it is difficult to believe that it results from an underestimation of food consumption.

This difference may be interpreted in several ways. Women can be considered as having grossly insufficient energy intakes. This would imply that they produce a fraction of the energy they need from fat stores or, alternatively, that they reduce their energy expenditure by feeding a small fetus with reduced energy needs.

The first interpretation would mean that in societies where energy intakes are low, and pregnancies are frequent and followed by a prolonged energy-demanding lactation, there should be a progressive deterioration of maternal nutritional status with parity. In West Africa, where all these conditions are met, one should observe a rapid maternal wasting in rural zones, since most women are energy deficient according to international standards. This is far from being the case, however. Table 5 shows the mean body weights of a sample of rural women in the poorest zones of Upper Volta and Mali. Their weight remains constant with parity, although the survey showed that the average interval between two deliveries was approximately 2.4 years. In rural Gambia, similar results were obtained from a smaller sample (47). It seems that despite energy intakes well below internationally recommended allowances, these women are in energy balance during all their reproductive years.

Pregnancy and lactation are notably successful in populations with low energy intakes. The main difference compared to affluent societies is that mean birthweight
is lower (47). This does not mean that there is a birthweight deficit, however. To interpret a low mean birthweight, one must compare it with the local optimal birthweight associated with the lowest perinatal mortality. Our data on the relationship between perinatal mortality and birthweight in poor communities with no possibility of cesarean section suggest that this deficit, if present, may be much lower than usually assumed by a crude comparison of mean birthweights with European standards.

A low mean birthweight may be seen from a teleological point of view as a maternal adaptation to produce an infant with lower nutritional needs when food is scarce. It may seem more advantageous for the species that a mother give birth to a small baby with low energy needs rather than to a normal sized baby (57). This interpretation is debatable: after birth, the mother can tap the energy she needs for lactation from her fat stores, in contrast to what happens during pregnancy. Adjusting the size of the newborn to maternal lactating capacities would imply a regulation of birthweight by maternal fat stores, which does not seem to be the case.

So far, there is no evidence that energy intakes below internationally recommended allowances result in altered reproductive ability. An alternative interpretation must be sought considering that these women are able to give birth to a child every 2 years, to breastfeed him for 18 months or more without losing weight during the reproductive years, and have energy intakes nearly 4 MJ (1,000 kcal) below their theoretical requirements. A possible conclusion is that their needs are overestimated.

To estimate the energy cost of pregnancy, several approaches are possible. One can observe healthy, well-nourished pregnant women, estimate the energy value of the tissues synthesized by the mother and the fetus, and add to it the energy required to cover the extra metabolic needs. This approach, used by the 1973 WHO/FAO committee (56), has several limitations. First, the women who were used to calculate the recommended allowances had newborns with a birthweight higher than the mean birthweight observed in less affluent communities. This resulted in higher estimates of energy requirements. It seems inappropriate to set these as international standards, since mean birthweights observed in industrialized coun-

### TABLE 5. Body weight and parity in rural Sahelian women

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<td>54.7 6.2</td>
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*Data from E. Bénédice and A. Briand (unpublished data).*
tries are higher than optimal birthweight in other communities. On the other hand, it is by no means clear whether the women consumed during pregnancy the exact quantity of energy they needed and no more. Approximately half the energy needs estimated by FAO/WHO are intended to cover the cost of the deposition of 3.5 kg of fat by the mother, which is supposed to be a prerequisite for good lactation. Most women in poor societies do not lay down that much fat and yet breastfeed their babies successfully (47). One wonders whether all this extra fat is necessary.

An epidemiological approach would be more appropriate to estimate the energy needs of pregnant women. Theoretically, the ideal method would be to observe pregnancy in populations with various energy intakes, to determine at which level pregnancy is less successful, and to test whether energy supplementation will improve its outcome.

Increasing maternal energy intake does seem to improve fetal growth in situations of acute food shortage. In The Gambia, the birthweight depression observed during the rainy season could be corrected by an appropriate nutritional intervention (58). In chronic situations, where maternal energy intakes are low but regular, the situation is not as clear.

One of the first supplementation studies carried out in Guatemala (59) on women who had energy intakes below 1500 kcal before intervention is often quoted as evidence that energy supplementation in undernourished populations increases birthweight. It is not clear, however, whether this study, conducted in a rural community, dealt with a chronic situation and if the reported effects of food supplementation were due to the correction of periods of acute shortage occurring throughout the year.

This intervention initially was designed to test the influence of a protein supplement on fetal growth. The supplement was distributed in two of four experimental villages. At the end of the intervention, when it appeared that this protein supplement had no effect on birthweight, the data were used to test whether there was a relationship between energy supplementation during pregnancy and birthweight. In the original publication, there was a small correlation \( r = 0.135 \) which, taking into account the large sample size, was statistically significant. The authors deduced from this result that there was a causal link between energy supplementation and increased birthweight. The design of the study, however, did not allow this conclusion. The protein supplement was randomly given, but the energy supplement was determined by the mothers themselves. In other words, this study, as far as energy was concerned, was not a supplementation of randomly selected women but an observation of self-selected patients. A bias due to the selection of women who tended to have heavier newborns must be considered. The authors tried to overcome this problem by testing whether this relationship might be explained by the effect of some confounding factor.

The potential confounding variables that were analyzed accounted for only 16% of birthweight variance. None was related to maternal cardiovascular characteristics, which were the most likely to influence birthweight. A noncausal interpretation of the observed correlation between birthweight and energy supplementation was
not ruled out. To estimate a posteriori the results of this intervention, the best approach would be to compare the mean birthweight in the villages before and after supplementation. This estimation from available data (59) gives an increase of mean birthweight of about 50 g. A similar increase of mean birthweight was also observed in most nutritional experiments carried out in women with low energy intakes in Colombia (60), Taiwan (61), New York (62), and Montreal (63). There was no increase of the mean birthweight during the dry season in The Gambia (58).

All these interventions had a low efficiency (64). On average, the increase of birthweight was about 30 g for 10,000 kcal, which is extremely low considering that according to international estimates (56), the energy cost of a normal pregnancy resulting in the birth of a 3,300 g newborn is 40,000 kcal, if one excludes the cost of maternal fat deposition. Obviously, a minor fraction of the energy supplement is used for fetal growth. This does not support the hypothesis that these interventions increased the mean birthweight by correcting a fetal energy deficit, especially when one considers that when there is no acute maternal wasting, the fetus seems to have priority over the constitution of maternal energy stores.

Presumably, the effect of these supplementations on birthweight is to result in higher postprandial hyperglycemic peaks, which promote the synthesis of fetal tissues through the secretion of insulin by the fetus. Since maternal glucose level is tightly controlled in normal nondiabetic women, the effect of such supplementations is bound to be limited.

In principle, women involved in supplementation studies were given as much food as they wanted. Assuming that the small birthweight increase resulting from supplementation was associated with lower perinatal mortality, the food intake after supplementation would be equivalent to the energy needs of the mothers. In none of these studies did energy intake after supplementation approach the internationally recommended allowances. In Guatemala (59), after supplementation, women consumed an average of 1,525 kcal/day; in Colombia (60), 1,765 kcal; and in The Gambia, 1,900 kcal (58). This suggests that if international allowances were derived from observations on Third World women eating ad libitum, the conclusion would be that pregnant women in affluent societies eat too much.

There is evidence that internationally recommended energy intakes for pregnant women are overestimated. There is no solid epidemiological basis, however, to give more reasonable estimates. The small birthweight increase obtained by maternal supplementation in populations with low energy intakes is not sufficient to conclude that these women are energy deficient.

PRIORITIES

In communities where cereals are the staple food, there is no evidence that increasing protein intake results in an improved pregnancy outcome (59). Even among the poorest, increasing the maternal protein intake during pregnancy is not a priority. No intervention has been attempted to increase the protein intake of
women living on a diet with roots as a staple food and who are the most likely to have insufficient protein intake.

With respect to energy, the present attitude of most international bodies, namely, that increasing maternal energy intake is a priority in communities with a low mean birthweight, must be debated. It is controversial to consider that fetal growth is independent of maternal energy reserves, the reverse opinion being almost a dogma among nutritionists. This, however, is our conclusion; it implies a less straightforward attitude toward maternal energy supplementation.

In communities where there is an acute food shortage, such as observed in many Third World rural communities before harvest or during wars or natural cataclysms, giving food to pregnant women is a priority. There is much evidence that in these situations, the fetus is a victim and suffers severely, well before maternal nutritional reserves are seriously depressed. If women take part in heavy agricultural work, they should stop working or reduce their activity at the end of pregnancy. This could be even more important than giving them extra food: it is possible that muscular work results in reduced uteroplacental blood flow, even if the mother is not malnourished (42). “Rest is best” could be the most appropriate message for these communities.

In communities with chronically low energy intakes below those internationally recommended and where the mean birthweight is lower than Western standards, the need for an untargeted maternal supplementation is debatable. Recommended food intakes may be overestimated, and birthweight standards from affluent societies may be irrelevant in these communities.

In poor countries with limited health budgets, any nutritional program competes with other programs. What is the priority? To give the possibility to all women living in developing countries to deliver their babies under hygienic conditions with a possibility of cesarean section and blood transfusion when needed, even in the most remote areas? Or to insist on these women receiving an energy intake equivalent to the theoretically estimated needs? We know that in terms of maternal and neonatal mortality, the first option is rewarding. So far, there is no evidence that random nutritional intervention, when there is no acute food shortage, has much effect.

REFERENCES


DISCUSSION

Dr. Waterlow: From the data you have produced, the evidence suggests that the birthweight of the baby is related to the mother’s lean body mass. This would explain the kind of relationship you have shown to both weight and height.

Dr. Lechtig: The hypothesis that maternal nutrition is related to fetal growth does not exclude the importance of other factors on fetal growth, such as diarrhea during pregnancy, intrauterine infections, bacteriuria, smoking, and hard physical work. These factors usually interact in a complex way, and most act through nutritional mechanisms.

In large samples from Latin American populations, there is evidence of a consistent association between subcutaneous fat and arm muscle measurements with birthweight, after controlling for maternal height and sex of the baby. These data suggest that maternal “reserves” could be used to some extent for fetal growth.

In the human species, the reproductive process has a remarkable capacity to adapt to chronic, moderate deficits in dietary intake. The price, however, is low weight gain during pregnancy, low birthweight, postnatal stunting, low maternal height, lower nutrient requirements, and some degree of suboptimal mental development. This adaptation process, however successful it is to keep the species alive in an unfavorable environment, should not be a reason for not improving the dietary intake in these populations.

Finally, a question: did you explore the contribution of weight gain during pregnancy to birthweight prediction in addition to that of prepregnancy weight? Were there any significant interactions between both independent variables?

Dr. Briend: The results you quote about the relationship between maternal skinfold and birthweight do not seem to be in conflict with my data. I observed a negative correlation between these two variables after controlling for maternal weight and not for maternal height. That an even stronger association exists between birthweight and the indicators of lean body mass is in support of my hypothesis of an indirect regulation of birthweight by lean body mass.

I have no personal data on the relationship between maternal weight gain during pregnancy and birthweight. In most studies published so far, there is a strong correlation between these two variables. It is unwise, however, to take for granted that this relationship should be interpreted in nutritional terms only. Water storage and plasma volume expansion are both related to birthweight and to maternal weight gain. This suggests that the relationship between maternal weight gain and birthweight might be indirect and due mainly to the interaction of an unknown vascular variable.

Dr. Lechtig: Most of the mechanisms responsible for the effect of intense physical activity during pregnancy on birthweight are of a nutritional nature, for example, higher energy expenditure or lower provision of blood nutrients to the cells. Thus data supporting an effect of physical activity on birthweight do not conflict; indeed, it may contribute evidence to the nutritional hypothesis. In poor populations, resting daily during 2 to 3 hr may be equivalent to supplementing 100 to 200 kcal per day.

Dr. Waterlow: Would Dr. Lechtig or Dr. Briend expect a Guatemalan woman who is very small to produce under normal circumstances a child of the same birthweight as a tall West African woman? I am not suggesting that these are ethnic differences in birthweight, because the small size of the Guatemalan woman is probably largely imposed by environmental influences in the past, but is a 2.5 kg baby from a small mother necessarily any worse than a 3 kg baby from a larger mother?
Dr. Lechtig: As mentioned in my chapter, one way of estimating impact on birthweight is through changes in the proportion of low birthweight babies. Its public health significance arises from the known relationship between low weight at birth and higher risk of infant and neonatal mortality. We have found in a sample of Guatemalan babies that about 90% of neonatal deaths occurred in the group of low birthweight infants. Thus it appears that in poor populations, when a baby weighs less than 2.5 kg at birth, his risk of dying is notably higher than that of babies with a higher birthweight. Although maternal height, parity, birth interval, and other characteristics influence the magnitude of the association between low birthweight and risk of death, they do not change the basic conclusion.

Although maternal height is associated with birthweight, short mothers (less than 147 cm) may show less than 5% of low birthweight babies when they are supplemented during pregnancy or pertain to the high socioeconomic group in rural villages. Also, tall mothers (≥ 147 cm) may have as high as 20% of low birthweight babies when they pertain to the low socioeconomic group and do not have appropriate food supplementation during pregnancy. Therefore, although short mothers show a trend toward lower birthweight babies, they are able to decrease the proportion of these babies down to figures usually seen in middle class, white populations in the United States.

I would also like to point out that the average increase in birthweight needed to decrease the proportion of low birthweight babies is relatively small. In most poor populations, it ranges between 100 and 300 g. Under these circumstances, the maximum increment expected in head circumference (about 1 cm) would not be enough to significantly increase the risk of cephalopelvic disproportion. This may be the reason for not observing an increase in the incidence of cephalopelvic disproportion after successful nutritional interventions.

Dr. Briend: To estimate the impact of a nutritional intervention, one must take into account the situation of the community where it takes place. If there is an acute food shortage, the intervention is bound to be effective. In situations where food intake is low but regular, the effects of such an intervention are not so clear. This was apparent in The Gambia, where food supplementation was effective in increasing birthweight only during the rainy season, before the harvest.

Dr. Whitehead: I will briefly summarize what we have recently published in The Lancet. When food intake during pregnancy in rural Gambian mothers is 1,600 kcal/kg/day or more, the average birthweight of babies is remarkably normal. It is only during times of the year when average energy intakes fall well below this average, particularly during the last trimester, that birthweight is seriously affected. If a dietary supplement is given to the mother during this period of extreme food deprivation, then a significant increase in birthweight can be produced. In our study, this increase was on average 225 g; we also reduced the incidence of small-for-dates babies from 30% down to about 5%. Our data thus demonstrate the tremendous ability of a mother to adapt to low energy intakes as well as the fact that there is a threshold to this adaptation below which the growth and development of the fetus are adversely affected.

Dr. Briend: Is this a threshold effect or an acute shortage effect? If the intake of a mother who is obese and whose intake is adjusted to 2,200 kcal drops to 1,800 kcal, she would still be well above the mean energy intake observed in The Gambia; this fasting effect, however, will reduce blood volume and blood perfusion of the placenta.

Dr. Whitehead: We do not suggest that the “threshold” value we found in The Gambia is applicable all over the world. It is important that this phenomenon be studied in a number of countries with differing socioeconomic backgrounds. We must also know more about the range of individual requirements within these environments. Only when we have all this
information at our disposal will we be able to provide recommended dietary allowances for pregnant women with a greater degree of confidence than we can at the moment.

Dr. Mata: Dr. Briend's chapter enlightens us on the physiological approach to understanding the genesis of low birthweight in developing countries. There is much skepticism about the relationship between diet in pregnancy and birthweight. For instance, Australian workers cannot explain the relatively good birthweight of infants from aboriginal women in the presence of poor food intake during pregnancy and low pregnancy weight gain. What is fascinating in Dr. Briend's chapter is the emphasis given to uteroplacental blood flow in the dynamics of fetal growth. In our studies with Mayan women, who consume 1,800 to 2,000 kcal normally, but who are very short, no correlation was observed between low birthweight and pregnancy diet, but a correlation was noted with maternal weight and especially with height. Over 4 years, during which 40% of the entire village population consumed the best possible mixture of soya flour supplemented with lysine, vitamins, and iron, no changes were induced in birthweight or in postnatal physical growth. On the other hand, women in the Guatemalan highlands spend half their time inside homes, cooking and inhaling smoke from the hearth, a situation that may contribute to the high incidence of intrauterine growth retardation. This risk has disappeared in Costa Rica and Panama (due to electrification), where a drop in the incidence of low birthweight has occurred within the last two or three decades. Furthermore, is anxiety due to scarcity of food during the dry season a factor? If so, how can we measure stress? Stress might explain the increase of low birthweight and infant mortality in recent times in virtually all the socialist countries, particularly in the USSR. Infant mortality in the USSR in 1981 was about 34 per 1,000, while it is declining, for instance, in Sri Lanka, Costa Rica, and in Cuba, countries that certainly are poor, and where the diet has not changed significantly in the last 15 years. These controversial issues should be taken into consideration in future studies, and should focus on lifestyles of people, infection, and other variables that nutritionists usually do not measure.

Dr. Waterlow: Dr. Briend has produced a detailed study from which he has made certain propositions about the regulation of birthweight. The conclusion that I draw from his chapter is that the most convincing regulator of birthweight at the physiological level might well be the infant's insulin secretion, since this is an anabolic hormone for all nutrients; and that the infant's insulin secretion might be influenced by the maternal blood glucose level. This leads me to the question: in the intervention studies, such as those in the Gambia, is there any relationship between the intake of the supplement and maternal blood glucose levels?

Dr. Whitehead: Data of the type you require are at present being prepared for publication. You know, of course, that we have published this type of data covering lactation. We have suggested that the high level of circulating energy metabolites in the blood is related to the greater sense of health and well-being which the mothers claim when their diet is being supplemented.

Dr. Waterlow: I repeat my question: Do measurements of blood glucose in women provide an indication of (a) those who are at risk if they had low glucose levels, and (b) whether a supplementary program was needed or was likely to work?

Dr. Whitehead: So far we have emphasized the importance of regularly weighing women during the course of pregnancy. Such measurements are simple and can be informative. The problem with routine measurements of biochemical components, such as blood glucose, is that the collection of the blood must be done under highly standardized conditions; otherwise, misleading values can be obtained.