# The Risk of Maternal Nutritional Depletion and Poor Outcomes Increases in Early or Closely Spaced Pregnancies[1]

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ABSTRACT An adequate supply of nutrients is probably the single most important environmental factor affecting pregnancy outcome. Women with early or closely spaced pregnancies are at increased risk of entering a reproductive cycle with reduced reserves. Maternal nutrient depletion may contribute to the increased incidence of preterm births and fetal growth retardation among these women as well as the increased risk of maternal mortality and morbidity. In the past, it was assumed that the fetus functioned as a parasite and withdrew its nutritional needs from maternal tissues. Studies in both animals and humans demonstrate, however, that if the maternal nutrient supply is inadequate, the delicate balance between maternal and fetal needs is disturbed and a state of biological competition exists. Furthermore, maternal nutritional status at conception influences how nutrients are partitioned between the mother and fetal dyad. In severe deficiencies maternal nutrition is given preference; in a marginal state the fetal compartment is favored. Although the studies of nutrient partitioning have focused on energy and protein, the partitioning of micronutrients may also be influenced by the maternal nutritional status. Marginal intakes of iron and folic acid during the reproductive period induce a poor maternal status for these nutrients during the interpregnancy interval. Poor iron and folic acid status has also been linked to preterm births and fetal growth retardation. Supplementation with food and micronutrients during the interpregnancy period may improve pregnancy outcomes and maternal health among women with early or closely spaced pregnancies. J. Nutr. 133: 1732S–1736S, 2003.

KEY WORDS: • *pregnancy* • *interpregnancy interval* • *adolescent pregnancy* • *undernutrition* • *maternal nutrition depletion*



An adequate availability of nutrients during gestation is probably the single most important environmental factor influencing pregnancy outcome. Although physiological adjustments in nutrient utilization and metabolism are geared to improve the utilization of dietary nutrients during pregnancy, these adjustments may be insufficient to meet the demands for pregnancy and lactation if the woman is in poor nutrient status at conception. An adequate supply of nutrients is required to maintain the delicate balance between the needs of the mother and those of the fetus. An inadequate supply will cause a state of biological competition between the mother and the conceptus in which the well-being of both organisms is at serious risk. The consequences of this undesirable situation on the fetus are well known; the consequences of undernutrition on the mother are less well documented.

Maternal undernutrition due to an insufficient food supply places a mother and her fetus at risk. However, there are two other groups of women at risk for having an supply of nutrients inadequate to meet the needs for pregnancy. One group is young girls who conceive within 2 y of menarche and who, consequently, may enter pregnancy with low nutrient reserves because of the recent use of nutrients for their own growth. Another group is those women who have short interpregnancy intervals (<18 mo) and may not have had sufficient time to replace nutrients used during the previous pregnancy. In both cases, the mother's nutritional status at conception may be compromised and her ability to support fetal growth and development may be less than optimal. Most of the research in this area has focused on maternal protein and energy status (1,2). It seems reasonable to assume, however, that micronutrients may also be depleted in women with early or closely spaced pregnancies.

The purpose of this paper is to review the effect of early pregnancies or short interpregnancy intervals on the fetus and maternal health and to evaluate how those conditions may affect nutrient partitioning between the maternal and fetal dyad.

### *Pregnancy outcomes in young women or women with short interpregnancy intervals*

Women with short interpregnancy intervals or early pregnancies are at increased risk for delivering preterm, low-birthweight or small-for-gestational age (SGA)[3] infants (3–8).

[1] Manuscript prepared for the USAID-Wellcome Trust workshop on "Nutrition as a preventive strategy against adverse pregnancy outcomes," held at Merton College, Oxford, July 18–19, 2002. The proceedings of this workshop are published as a supplement to *The Journal of Nutrition*. The workshop was sponsored by the United States Agency for International Development and The Wellcome Trust, UK. USAID's support came through the cooperative agreement managed by the International Life Sciences Institute Research Foundation. Supplement guest editors were Zulfiqar A. Bhutta, Aga Khan University, Pakistan, Alan Jackson (Chair), University of Southampton, England, and Pisake Lumbiganon, Khon Kaen University, Thailand.

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[3] Abbreviations used: SGA, small for gestational age.

Among adolescents, low birth weight and preterm deliveries are more than twice as common as in adult pregnancies and the neonatal mortality rate is almost 3 times higher (9). In the United States, women with interpregnancy intervals of <8 mo were 14–47% more likely to have very premature and moderately premature infants than were women with intervals of 18–59 mo (10). In a study of >810,000 infants born to Michigan women between 1993 and 1998, both white and black women with interpregnancy intervals of <6 mo were 50% more likely to have a low-birth-weight infant, 20% more likely to have a preterm birth and 30% more likely to have an SGA infant than were women with intervals of 18–23 mo (11). Similar results were found for singleton infants born to women in Utah from 1989 to 1996 (5). For those women an interpregnancy interval of <6 mo increased the risk of low birth weight by 40%, preterm birth by 40% and SGA by 30%. Data from women in North Carolina and Chicago also show that the risk of preterm birth or SGA infant is increased about 50–80% in women with short interpregnancy intervals (3,12). Thus, the risk of low birth weight or preterm birth among women with early or closely spaced pregnancies in the United States is at least 50% greater than that of adult women with a interpregnancy interval of 18–23 mo.

Short interpregnancy intervals also increase of the risk of adverse maternal outcomes. A recent comprehensive analysis of the effect of interpregnancy interval on maternal morbidity and mortality was just completed using a data set of 456,889 parous women delivering singleton infants in Latin American and the Caribbean between 1985 and 1997 (13). After adjusting for major confounding factors (i.e., age, reproductive history, marital status, education, cigarette smoking, prenatal care, maternal body mass index before pregnancy) women with interpregnancy intervals of <6 mo had a higher risk for maternal death (odds ratio [OR] 2.54; 95% confidence interval [CI]: 1.22–5.38), third trimester bleeding (OR 1.73; 95%CI: 1.42–2.24), prelabor rupture of membranes (OR 1.72; 95%CI: 1.53–1.93), puerperal endometritis (OR 1.33; 95%CI: 1.22–1.45) and anemia (OR 1.30; 95%CI: 1.18–1.43) than did women with interpregnancy intervals of 18–23 mo. Pregnant adolescents under age 15 y also are at higher risk for maternal complications than are adult mothers (9). Some of the most common problems are abnormally high maternal weight gains, pregnancy-induced hypertension, anemia and renal disease (6,9,14,15).

The cause of poor pregnancy outcomes and maternal complications among women with early pregnancies or short intervals between pregnancies has been debated. Some attribute the increased risk of poor pregnancy outcomes to various factors associated with being young or having short intervals (i.e., socioeconomic status, lifestyle, stress, adequacy of prenatal care, etc.). Others attribute the poor outcomes to an independent factor related to some aspect of the woman's physiology, such as biological immaturity, competition for nutrients or incomplete recovery of the physiological and anatomical adaptations in the reproductive system so that the woman is not biologically prepared for conception (5). Accumulating evidence from studies done in both groups suggests that these poor pregnancy outcomes are not explained by sociodemographic or behavioral risk factors (6,11). For example, the association between poor fetal and maternal outcomes and short interpregnancy interval persists after the data are stratified for sociodemographic, behavioral and reproductive risk factors (3–5,10–13,16).

A study of young pregnant women also showed that biological immaturity increased the risk of poor outcomes after sociodemographic factors were controlled for (17). Competition for nutrients between the mother and fetus may account for the negative effect of a young gynecological age on outcome. Before 1980 most thought that the growth of adolescents ceased when they became pregnant. However, in 1981 Naeye (18) hypothesized that the fetuses of growing teens are smaller than fetuses of mature women because growing teens compete with their fetuses for nutrients. Frisancho et al. (19) provided support for that hypothesis when they reported that infants born to young, growing Peruvian mothers were smaller than those born to adult women. More recently, Scholl et al. (20,21) documented that pregnant teens continue to grow during gestation by measuring changes in knee height length during gestation. They also showed that growing teens give birth to smaller infants even though they tend to gain more weight (**Table 1**).

Pregnant teens who continued to grow during gestation gained more maternal fat reserves during the last trimester, had higher gestational weight gains and retained more weight postpartum than did nongrowing teens (21). Generally among adult women, an increased weight gain is associated with larger birth weights. However the growing teens had infants that weighed about 155 g less than infants of nongrowing teens. Scholl et al. (22) subsequently found that growing teens have a surge in maternal leptin concentrations during the last trimester, which may reduce the rate of maternal fat breakdown during late pregnancy and thereby increase the mother's use of glucose for energy. This would result in less energy being available for fetal growth. This partitioning of metabolic fuels among growing pregnant teens so that more energy is used for maternal growth at the expense of that available for fetal growth would account for higher maternal fat gains and lower birth weights among the younger, growing teens. Data from subsequent pregnancies in adolescents show that birth weight increases about 75% for every 1% increase in maternal weight for height in their second pregnancy compared to their first (14). In other words, the more mature the adolescent at conception, the lower the risk of gaining excessive amounts of fat and delivering a low-birth-weight infant.

**TABLE 1**

*Maternal growth, fat gain, and birth weight in pregnant adolescents*[1]

| | Growers (n = 144) | Nongrowers (n = 174) |
|---|---|---|
| Age at conception, y | 15.9 ± 0.1 | 16.0 ± 0.1 |
| Gestational weight gain, kg[2] | 15.2 ± 0.6 | 12.8 ± 0.5 |
| Triceps skinfold thickness change PP to 28 wk[3] | +0.7 ± 0.4 | –1.2 ± 0.4 |
| Subscapular skinfold thickness change PP to 28 wk[4] | +0.02 ± 0.4 | –1.3 ± 0.4 |
| Arm-fat area ($cm^2$) change PP to 28 wk[3] | +1.6 ± 0.5 | –1.5 ± 0.5 |
| Infant birth weight, g[4] | 3050 ± 42 | 3189 ± 39 |

PP = pre-pregnancy.

[1] Mean ± SEM. Models (weight gain, skinfold thickness, arm-fat area) are adjusted for maternal age, ethnicity, and parity by analysis of covariance.

[2] Significantly different from nongrowers: $p < 0.01$.

[3] Postpartum – 28 wk gestation value. Significantly different from nongrowers: $p < 0.005$.

[4] Significantly different from nongrowers: $p < 0.05$.

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### *Nutrient partitioning in women with early or closely spaced pregnancies*

Several decades ago it was assumed that nutrients were distributed among the various tissues based on the different metabolic rates of those tissues (23). Organs with higher metabolic rates drew a larger proportion of the available nutrients, and if the nutrient supply was limited, organs with the higher metabolic rates were thought to compete more successfully than organs with lower metabolic rates. This principal regarding the distribution of nutrients was applied to pregnancy, and because the fetal-placental unit has a higher metabolic rate than any of the maternal organs except the brain, it was assumed that fetus would compete effectively with the mother for a limited amount of nutrients. This assumption led to the conclusion that only extreme degrees of undernutrition retard fetal growth, especially in humans. However, both animal and human studies done during the past three decades show that this assumption is not valid and that the more severe the dietary restriction, the greater the impairment of fetal growth. For example, when rats were restricted to 75% of their unrestricted intake, the mothers gained weight and fetal weight equaled that of controls (24). When restricted to 50% of their normal intake, the mothers lost 8% of their initial weight while fetal weight decreased approximately 12%. When mothers were restricted to 25% of their normal intake, they lost about 30% of their initial body weight and fetal weight was reduced by about 50%. Thus, in the food-restricted rat, fetal growth is only sustained when the food supply is sufficient to support some maternal weight gain. However, if the food restriction is more severe, both maternal and fetal tissue gains are affected and the fetus is more deprived than the mother.

Data from studies in pregnant women also show that malnourished women can protect their body stores of nutrients from fetal parasitism. The pregnancy outcomes of women giving birth during the Dutch famine in 1944–1945 have been cited as evidence that the human fetus is an effective parasite (25). The birth weights of infants born to women exposed to the famine during the second and third trimester and consuming only about 1200 kcal/d decreased by about 250 g. This relatively small 10% reduction in birth weight under such extreme conditions has been interpreted as evidence that the human fetus is a parasite or that the mother adapts to reduced food intake to support fetal growth. A reanalysis of the data by Rosso (23) that included changes in maternal body weight showed that fetal growth is more reduced than maternal body weight (**Table 2**). The women exposed to the most severe conditions during the second and third trimester lost about 3% of their initial body weight whereas the mean reduction in birth weight among the infants born to these women was about 10%. Thus, the human data are consistent with the animal data. When food is restricted during pregnancy, fetal parasitism does not sustain fetal growth at the expense of maternal tissue.

**TABLE 2**

*Estimated changes in maternal body weight and birth weight among Dutch women exposed to famine conditions in World War II*

| | Postpartum body weight, kg | Change in body weight, kg | Birth weight, g |
|---|---|---|---|
| Prefamine | 59.0 | +1.0 | 3338 |
| Famine during 3rd trimester | 57.6 | −0.4 | 3220 |
| Famine during 2nd and 3rd trimesters | 56.5 | −1.5 | 3011 |
| Famine during 1st and 2nd trimesters | 61.0 | +3.0 | 3370 |
| Famine during 1st trimester | 61.6 | +3.5 | 3312 |

Data from reference 23.

Maternal nutritional depletion at the outset of pregnancy is more likely to be a problem for women with short interpregnancy intervals or early pregnancies. Maternal nutritional depletion is defined as a negative change in maternal nutritional status during a reproductive cycle going from nonpregnant, nonlactating to pregnancy; to lactation; to partial lactation; and back to nonpregnant, nonlactating (1). In general, the negative effect of maternal depletion is increased with a shorter period of potential repletion during the interpregnancy interval or low nutritional reserves at the outset of pregnancy. Maternal nutritional depletion, defined in this way, differs from the undernutrition seen in women with extremely inadequate diets; those women do not have sufficient food to replete the reserves mobilized during pregnancy and lactation even with lengthy interpregnancy intervals. Those women are nonrepletable whereas those who have a negative change in nutritional status due to a short interpregnancy interval or competition with maternal growth needs among young mothers are incompletely repleted.

To fully understand the relationship between maternal depletion and pregnancy outcome, the overall change in maternal nutritional status across a full reproductive cycle should be evaluated along with measures of birth weight and the maternal food intake. When this long-term framework is applied to pregnancy outcomes among Pakistani women (26), undernourished women gained weight during a reproductive cycle while showing a negative trend in infant birth weight (i.e., the weight of the second infant is lower than that of the first). Marginally nourished women lost weight during a reproductive cycle concurrent with a positive trend in infant birth weight. Well-nourished women had little change in maternal weight or infant birth weight. Other studies of women in developing countries also show that women with lower initial maternal weight for height or less initial subcutaneous fat experience larger gains in maternal weight or subcutaneous fat during a reproductive cycle (26–30). Animal studies support these findings that undernourished women gain weight during a reproductive cycle in comparison with well-nourished women. When rats were fed unrestricted amounts or 75% or 60% of the food intake of their unrestricted controls, the two food-restricted groups gained a modest amount of weight during partial lactation and nonpregnancy or nonlactation whereas the rats with unrestricted food lost weight (31). In sum, these studies show that nutrients are partitioned differently between mothers and their offspring depending on the initial nutritional status of the mother. Those who are severely depleted tend to gain weight in the interpregnancy period where as those more marginally underfed do not.

If maternal nutritional status influences the partitioning of nutrients between the mother and fetus, the effect of a nutritional supplement on pregnancy outcome should also vary with the mother's initial status. Winkvist et al. (2) studied this question in 176 complete reproductive cycles of rural Guatemalan women who were either malnourished (i.e., very low weight), marginally nourished (i.e., low weight), or well nourished (>50 kg). Supplementation of very-low-weight women prevented an otherwise negative trend in birth weight from one sibling to the next, but supplementation of low-weight women benefited the mother by preventing a negative trend in maternal weight over the cycle. This suggests that low-weight

(marginally malnourished) women replete themselves during reproduction under conditions of chronic moderate-to-severe undernutrition but that there is a negative effect on the birth weight of the offspring. Nutrients were preferentially partitioned to the mother, protecting her at the expense of the fetus. The underlying mechanism for partitioning nutrients between the maternal and fetal dyad depending on the mother's initial nutritional status or current food supply is unknown. However, policy makers and program planners need to remember this relationship when planning nutritional interventions for undernourished women around the world.

The effect of interpregnancy nutrition on maternal and fetal outcomes has received very little attention in developed countries. To the best of my knowledge, Caan et al. (32) are the only researchers who have studied the effects of providing food supplements between pregnancies on pregnancy outcome among U.S. women. Plans to reduce the funds available for the federal Women, Infants, and Children (WIC) food supplementation program provided an opportunity to compare the effect of interpregnancy supplementation on the outcome of a subsequent pregnancy. Two groups were studied—those receiving supplements for 0–2 or 5–7 mo postpartum. Both groups received the WIC package during two consecutive pregnancies. The second infant born to the mothers supplemented for 5–7 mo postpartum had a higher mean birth weight (131 g) and birth length (0.3 cm) and a lower risk of low birth weight than did the women receiving supplements for only 0–2 mo postpartum. Also, at the onset of the second pregnancy, the women supplemented for 5–7 mo had a higher mean hemoglobin concentration. This study shows that interpregnancy nutrition can improve the outcome of subsequent pregnancies even among reasonably well-nourished women.

### *Micronutrient depletion and pregnancy outcome*

The studies reviewed above have focused on food restriction or maternal protein and energy depletion and pregnancy outcome. The effect of the depletion of micronutrients on pregnancy outcome has not been studied as extensively as that of protein and energy. One would expect, however, that nutrients mobilized from maternal reserves to meet the needs for pregnancy and lactation must be replaced during the interpregnancy interval. If that interval is too short or if there a competition for the use of those nutrients for maternal and fetal growth, a deficiency of those micronutrients could develop and influence pregnancy outcome. Both folic acid and iron are mobilized from maternal reserves during pregnancy and lactation and must be replaced in the interpregnancy period. If the maternal folate and iron status is poor at conception, an insufficient supply of these micronutrients could increase the risk of poor maternal or fetal outcomes.

The concentration of folic acid in maternal serum and erythrocytes declines from midpregnancy until 3–6 mo postpartum (33). During pregnancy folic acid is needed for cell division; during lactation it is required for the synthesis and secretion of milk. If the dietary supply of folate is low, circulating levels begin to decline during the fifth month of pregnancy and continue to decline until several weeks after delivery. Among women in developed countries, 20% have low serum folate levels 6 mo after delivery (33). Epidemiological studies in the United States have found an association between preterm births or SGA deliveries and lower concentrations of folate in the serum or erythrocytes (34). A poor maternal folic acid status at conception may contribute to the poor reproductive outcomes in women with early or closely spaced pregnancies.

Iron is another nutrient that is mobilized from maternal stores during pregnancy, and the stores of iron tend to remain low for several months after delivery (35). Iron deficiency anemia is a prevalent problem among pregnant adolescents (6) and is associated with preterm delivery and associated low birth weight. The excess preterm birth rate among women with short pregnancy intervals or early pregnancies may be due in part to poor maternal iron stores resulting from insufficient repletion after a previous pregnancy or to recent growth demands (35).

The circulating concentrations of other nutrients, such as zinc, vitamin A, vitamin B-6 or vitamin B-12, also decline during pregnancy, but the concentrations of those nutrients return to normal shortly after delivery, suggesting that they are less likely to be low at the beginning of a subsequent pregnancy or in pregnant adolescents (33). However, because low plasma zinc concentrations have been associated with low birth weight or preterm birth (36), further study of the relationship between maternal zinc status and pregnancy outcome in women with early or closely spaced pregnancies is warranted.



### *Conclusion*

A short interval between pregnancies or an early pregnancy within 2 y of menarche increases the risk for preterm birth and growth retarded infants. Maternal nutrient depletion has been proposed as a possible cause of these poor pregnancy outcomes. Maternal depletion of energy and protein resulting from short interpregnancy intervals or early pregnancies leads to a reduction in maternal nutritional status at conception and altered pregnancy outcomes (1,2,33). Partitioning of the available supply of protein and energy between the maternal and fetal dyad is influenced by the initial degree of maternal undernutrition. Nutrients appear to be preferentially deposited in maternal tissue in marginally depleted women whereas fetal needs take precedence in severely depleted women. Poor maternal micronutrient status also is likely to influence pregnancy outcome. Poor maternal iron and folate status has been associated with preterm births and intrauterine growth retardation, two outcomes for which women with early or closely spaced pregnancies are at high risk. Populations are at risk of poor nutritional status at conception because of recent maternal growth or a recent pregnancy may benefit from receiving food and micronutrient supplements during the interpregnancy period.

### *Research needs*

Research is needed on the following topics:

- Efficacy of micronutrient supplementation prior to gestation (i.e., during the interpregnancy interval versus only during pregnancy alone)
- Association between maternal micronutrient depletion at conception and pregnancy outcome
- Effect of biological immaturity on the metabolic response to pregnancy and nutrient metabolism among young mothers
- Effect of micronutrient status on the physiological and metabolic differences among young and mature pregnant women

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