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Studies of Nutrition Intervention in Pregnancy

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ABSTRACT: *The main conclusion of this review of 8 nutritional intervention studies during pregnancy is that, in mothers with protein-energy malnutrition—either acute or chronic—food supplementation during pregnancy can improve birthweight and decrease the incidence of low birthweight babies. It is stressed that programs to reduce the incidence of low birthweight babies must be aimed at the major causes of low birthweight, which differ among populations. For example, in Harlem the major probable cause of low birthweight is not dietary protein-energy deficiency but short birth intervals, very young primiparas, high parity, and smoking.* (BIRTH 9:2, Summer 1982)

This paper reviews the results published during the seventies on the relationship between maternal nutrition and birthweight, with a view to: (1) building articulate knowledge useful to improve current nutritional programs; and (2) identifying the main gaps in our knowledge and the corresponding research needed.

To this aim, results from eight maternal nutrition intervention studies were reviewed (Bogotá, Guatemala, India, Mexico, Montreal, New York, Taiwan and the Dutch Famine Study).

Nutrition Intervention in Pregnancy

As seen in Table I, seven of the eight projects included a planned nutrition intervention; the eighth was based on the results of an imposed famine and recovery period. They differed in the nature of the population under study and in the outcomes of central concern. Among the latter were birth weight, survival, and physical and psychosocial development of the infants.

Four of these eight studies were randomized, controlled trials. In three of them (Bogotá, New York, Taiwan) the unit of randomization was the individual, while in the fourth (Guatemala), the unit of randomization was the village. Each of the four projects followed experimental designs based on:

1. **Identification of a target group.**
2. **Incorporation of a carefully matched control group.**
3. **Delivery of a defined nutritional supplement.**
4. **Evaluation of the impact of treatment in terms of maternal weight gain, birth weight, and health and development of the child.**

At the time these four projects were designed, sample sizes were projected on the basis of data from pilot studies and public health records. The changes in birth weight proved to be less than those anticipated, so that sample sizes sometimes were inadequate to yield statistically significant results.

In the course of these studies a major question that had to be confronted was that of determining the nutritional status of the populations under study. Among the measures used were anthropometric and biochemical variables, dietary intakes, and evidence of specific nutrient deficiencies. Questions may be raised concerning comparability between studies in terms of the use of these measures, their reliability and validity in some cases, and how they may be used to distinguish between the consequences of lifelong malnutrition versus malnutrition of recent onset.

Examination of the eight studies considered as a group shows that four different approaches were taken in the design of nutrition interventions:

1. **Provision of unlimited freely available liquid supplements with individual intakes measured at the delivery center.**
2. **Distribution of beverages to pregnant women, which were especially developed to supply the**

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estimated deficit in energy and protein when compared to levels consumed by high-income groups; intake was measured indirectly.
3. Distribution of customary foods to the individual or the family, the quantity having been calculated to cover the estimated deficit based on dietary enquiries, and
4. Consumption of hospital diets plus additional food supplements designed to increase the energy and protein intake to the RDA levels.

The basis on which the estimated deficiencies in energy, protein, or specific nutrients were calculated for individual women or communities differed markedly in the various studies. Two important variables influencing nutritional requirements which were not included in these studies were energy output (including physical activity) and energy losses related to chronic and acute infections. Additional questions that were raised in regard to some but not all of the studies include:

1. The problem of compliance, and its measurement.
2. Self-selection for a higher or lower intake of the supplements.
3. Replacement of home diet by the supplements.
4. Availability, acceptability and cultural appropriateness of the supplement, and
5. Use of the supplement by other family members.

These studies differed in terms of research strategy, target population, sample size, assessment of nutritional supplementation, and control of potential confounding factors. Notwithstanding the criticism that can be addressed to each individual study, as a whole, these eight projects offer the best information presently available. The following pattern emerges from a review of their results.

(1) In mothers with protein-energy malnutrition, either acute or chronic, appropriate food supplementation during pregnancy can improve average birthweight and decrease the incidence of low birthweight babies.

(2) The increase in average birthweight may range between 40 and 298 g depending on the prior level of malnutrition (moderate or severe), type of malnutrition (chronic or acute) and total amount of net nutrient supplementation provided during pregnancy.

(3) The effect on birthweight is greater in populations with moderate to severe malnutrition, as detected through anthropometric measures (weight, height, head and arm circumference), simple social scales (house quality, accessibility to health services, literacy and environmental sanitation), dietary surveys, or through monitoring food availability at family level.

(4) Prenatal supplementation in combination with postnatal supplementation and with availability of health care services is associated with improved survival, physical growth and mental development of the offspring.

(5) The nutrient content of the food supplements should be tailored to provide the most limited nutrients in the home diet. Protein-rich supplements are desirable when the home diet protein-calorie ratio is grossly below 11% such as in cassava- and sweet potato-fed populations. Where energy is the main limiting nutrient, the supplement should be similar in protein content to the home diet. It is suggested that when information on main limiting nutrients is missing, the protein-calorie ratio of the supplements should average 11%.

(6) No detectable evidence exists of harmful effects of protein-energy supplementation provided through regular foods ingested in quantities within the present range of the recommended dietary allowances.

(7) Prenatal food supplementation or food deprivation during the last trimester of pregnancy may suffice to produce an effect on birthweight. If nutritional supplementation begins earlier in pregnancy and is sustained throughout gestation the effects on birthweight may be greater.

(8) Sufficient data now exist to anticipate a beneficial impact of maternal nutritional programs on maternal and infant well-being in malnourished populations. Lack of complete knowledge on this issue should not be used as an excuse for not intervening or not developing appropriate programs.

(9) Main areas that require additional work are to develop suitable techniques to: (a) select women at high nutritional risk; (b) assess participants' compliance with the program; and (c) to estimate degree of participants' self-selection.

Research is needed to gain a better understanding of: (a) the influence of sex and gestational age on the nutritional effect on birthweight; (b) the effect of the nutritional intervention on functional outcomes related to health and development of the infant and the mother, including role of changes in birthweight as an intermediate variable between maternal nutrition and functional outcomes; and (c) the cost-effectiveness, side effects and long-term stability of the impact of food supplementation programs.

TABLE 1. SUMMARY OF STUDIES ON THE IMPACT OF MATERNAL NUTRITION INTERVENTIONS DURING PREGNANCY ON INFANT AND CHILD HEALTH

	Dutch Famine Study (1, 2)	Bogota, Colombia (2 4)	Guatemala/INCAP (2, 3, 5, 6)	India (7,8)	Mexico (3,9)	Montreal (2, 10)	New York City (2, 3, 11)	Taiwan (12, 13)
STUDY OBJECTIVE	Impact of acute starvation during pregnancy on birth weight and subsequent development in 18-year-old men.	Effect of prenatal and postnatal nutritional supplementation on birth weight and child development.	Effect of prenatal and postnatal nutritional supplementation on birth weight, child development and infant morbidity and mortality	Impact of maternal supplementation on birth weight.	Impact of supplementation during pregnancy and lactation on birth weight, lactation, and development in the young child	Impact of prenatal dietary improvement program on birth weight and infant survival.	Impact of prenatal supplementation on birth weight and infant development.	Impact of prenatal and postnatal nutritional supplementation on birth weight and child development.
RESEARCH DESIGN (Strategy)	Retrospective study of records from maternity hospitals, vital records, and military services for cohort of all births to women exposed to acute famine during World War II. Records available of weekly rations provided to population segments. Control groups from comparable maternity hospitals and for males whose mothers were not exposed to famine.	Prospective intervention study of offspring of women supplemented in third trimester and/or during lactation with available foods to meet recommended dietary allowances; medical care provided.	Prospective intervention study of offspring of women supplemented in pregnancy and lactation and children supplemented to 7 years of age. Liquid supplements consumed in community center; medical care provided.	Poor malnourished women identified in last trimester and hospitalized to assure supplement intake Project consists of several small clinical studies.	Prospective studies of matched pairs of non-supplemented and supplemented pregnant women living in rural villages; medical care provided.	Prospective study of patients entered through public prenatal clinic; supplementary foods based on dietary and clinical characterization; education and health care provided.	Prospective study of nutritional intervention of public prenatal clinic patients with follow-up of infants to one year of age; medical care provided. Randomized control trial.	Prospective study of liquid nutritional supplements or placebo provided to women for consumption in community health center. First child not treated; second child assigned randomly to treatment groups. Medical care provided.
DESCRIPTION OF POPULATION	n = 40,000 births. Dutch cities under Nazi occupation; well-fed up to 1940; food rationing 1941-4; near starvation 1944-5; rehabilitation 1945-6.	n = 413 births. Urban slums. Pregnant women identified as having prior malnourished child. Their estimated average daily intake was: 1,600 calories 35.5 g protein.	n = 1,536 pregnancies in 4 rural villages. Estimated average daily intake for pregnant women was: 1,400 calories 45 g protein.	Urban subjects. Basal intake was: 1,600-1,800 calories 40 g protein.	n = 39 pregnancies. Rural village. Estimated daily intake of pregnant women was: 1,950 calories 50 g protein. Clinical indicators of malnutrition and anemia.	n = 1,213 white urban patients. Generally low income women with prior history of low birth weight.	n = 769 poor black urban women identified as being "at risk" for low birth weight upon entrance to public prenatal clinic. Daily dietary intake at start was: 2,200 calories 80 g protein.	n = 294 enrolled; 169 completed two pregnancies and consumed adequate supplements. Population from 14 poor rural rillages. Married women only with 1 child prior to male child. Basal daily intake of women was: 1,200 calories 40 g protein.
DIETARY MODIFICATION	Starvation due to stoppage of external food supplies (1944-1945); then restoration to high dietary intake.	Selected foods provided for entire family. Net increment for pregnant woman was 133 calories and 20 g protein daily.	Liquid supplements. 1) Fresco = low calorie, no protein, vitamin — mineral fortified. 2) Atole = proteins plus calories, vitamin-mineral fortified. *Ad libitum* intake measured at level of individual	Regular hospital foods (2,000 cal) plus up to 500 calories in additional foods or supplements.	2-3 glasses partly-skimmed milk to provide average daily supplement in pregnancy of: 205 calories 15 g protein. During lactation about 50% greater. Mineral supplement also provided.	Free foods provided on "prescription basis" coupled with nutrition education, dietary histories taken regularly.	Liquid "Supplement": 470 calories plus 40 g protein plus vitamins and minerals. Liquid "Complement": 322 calories plus 6 g protein plus vitamins and minerals. Control: no supplement; routine vitamins and minerals	Supplement A. 800 calories 40 g protein Suplement B: 80 calories no protein Control: no nutrition intervention.

TABLE 1. *continued*

INCREASE IN BIRTH WEIGHT FOLLOWING DIETARY IMPROVEMENT	Yes: 271 g average when diet improved for last half of pregnancy. Moreover, as the famine continued, birth weight declined to a maximal mean decrement of 300 g from the pre-famine level.	Yes: average mean increment of 50 g for all supplemented, 77 g for those supplemented one trimester or more. Data suggest increased birth weight associated with increased protein intake.	Yes: 111 g average increment, or 28 g per 10,000 supplemental calories consumed during pregnancy (based on 405 births). Data suggest increased birth weight associated with increased energy intake.	Yes: 298 g average increment.	Yes: 180 g average increment in supplemented groups; marked decrease in number of low birth-weight infants reported.	Yes: 40 g average increment.	Yes: 41 g reported with Complement (not statistically significant). No increase with Supplement. Heavy smoking decreased birth weight; Supplement and Complement overcame the decrease in birth weight due to heavy smoking.	Yes: 74 g in "good supplement" group, e.g. woman consumed more than 50% of Supplement A (not significant). Yes: 60-100 g increment (not statistically significant) for those consuming more than 50% of Supplement A compared to Supplement B and controls.
INFLUENCES OF GESTATIONAL AGE ON RESPONSE TO DIETARY CHANGE	Nutritional rehabilitation during third trimester was sufficient to restore mean birth weight to pre-famine level.	Last trimester or more showed effect.	No effect detected; birth weight increment depended on total calories ingested during pregnancy.	Treatment limited to third trimester.	None reported.	No effect detected.	Birth weight not related to gestational age at which supplements were started.	Treatment before and during pregnancy; no effect reported.
INFLUENCE OF SEX OF INFANT ON RESPONSE TO DIETARY CHANGE	At height of famine decrement, birth weight was greater for males than for females.	Increment in males (100 g) greater than in females (12 g).	None detected.	None reported.	None reported.	Not analyzed.	None detected.	No clear differences demonstrated.
EFFECTS ON MOTHER	Measure of maternal weight at 10 days post-partum showed maternal weight decrement preceding decrease in birth weight. During alleviation of famine, maternal weight increased before birth weight did, and continued to increase as full feeding continued.	Greater maternal weight gain associated with supplementation.	Supplement intake associated with: increased weight gain during pregnancy; placental weight; placental RNAase activity and with shorter post-partum amenorrhea and birth interval.	Maternal weight gain with supplement.	Supplemented women gained 6.4 kg more than unsupplemented women.	Maternal weight gain not significantly increased by added dietary intake.	Maternal weight gain greatest in women entering program early in pregnancy.	No effect of Supplement A on maternal weight gain. Mothers on Supplement A excreted 1.2 g N more than those on Supplement B, but consumed 4.8 g N more.
ADVERSE EFFECTS OBSERVED	An excess in the number of very early premature and increased perinatal mortality was reported when starvation occurred in the first trimester with refeeding in second and third trimesters.	None reported.	None detected.	None reported.	None reported.	None reported.	Large number of premature babies (IUGR) and excess neonatal deaths observed in some women on high-protein supplement, especially those with prior low birth-weight infants.	Not examined.

It should be stressed that, although malnutrition is one important determinant of fetal growth, it is not the only one. Its relative importance as a cause of low birthweight will vary between populations. Short birth intervals, diarrhea during pregnancy, young primiparas, excessive parity, malaria, bacteriuria—all are important depending on their distribution in each specific population group. Other interventions besides protein or calorie supplements are perhaps more appropriate to poor populations in the U.S., particularly in the Harlem population studied by Rush et al. Where women eat an average of 2200 calories and 80 g of protein daily,[2,11] which is above what is required during pregnancy, there is no reason to supplement the diet with either energy or protein. There the main problem is short birth intervals (less than one year), smoking, mother's age less than 16 years, and high parity (over 4 children). If one can decrease these segments of the childbearing population in Harlem, a notable decrease in the proportion of low birthweight babies will occur. Without any nutritional change, and even without improving the level of medical care, the population of Harlem could come out with figures of perinatal mortality similar to Sweden's. There may be other populations in the U.S. which do have nutritional deficits, but in the population studied by Rush et al., the main causes of low birthweight are young primiparas, birth intervals of less than one year, smoking, and high parity.

Programs should be based upon repairing the major damage occurring within *that* population. For example in rural Guatemala, where the major cause of low birthweight is energy limitation, the emphasis should be on providing foods rich in energy. In New Guinea, where the main cause of low birthweight is protein limitation, protein-rich foods should be provided. In populations like those of Bangladesh, where the main causes of low birthweight and perinatal mortality are protein-energy malnutrition and very short birth intervals, and where there are mothers of 11–15 years of age, the main effort should be family planning and nutrition. Nutrition alone will not make a very important difference in Bangladesh. In rural areas of Africa where malaria is the main problem, no matter what nutritional program is begun, unless anti-malarial treatment is used one will not be able to decrease the prevalence of low birthweight babies and the high infant mortality rates. Thus, one must be sure one is attacking the primary agents which are the cause of low birthweight and perinatal and infant mortality in each specific target population.

In summary, the population that was studied by Rush et al., and was used as an example to argue that nutritional supplementation programs are not effective, was not the most appropriate population to test the effects of nutritional supplementation. Family planning and smoking control programs would be more appropriate in such a population.

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