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FINAL REPORT

SUBMITTED TO INTERNATIONAL CENTER FOR RESEARCH ON WOMEN

MATERNAL DEPLETION PROJECT

TECHNICAL SECTION

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Overview

Maternal depletion was first described by Jelliffe and Maddocks in 1966 (1), although it had been recognized as a potential risk of reproduction for mothers much earlier. Even though the term "maternal depletion" caught on, very little research has been conducted with the mother as the focus of study. Recently there has been increasing recognition of the importance of maternal health. Researchers have just begun to incorporate some of the complexities inherent in the interrelationships of maternal nutritional status and reproductive cycling in their study techniques. The research reported here attempts to further that process. Three articles will be referred to in this report.

1) "Frequent Reproductive Cycling: Does it Lead to Nutritional Depletion of Mothers?", Merchant K and R Martorell, Progress in Food and Nutrition Science, 12:339-369. (2)

2) "Maternal and Fetal Responses to the Stress of Lactation Concurrent with Pregnancy and of Short Recuperative Intervals", Merchant K, Martorell R, and JD Haas, American Journal of Clinical Nutrition, (in press). (3)

3) "Maternal and Fetal Responses in Consecutive Pregnancies to the Stress of Lactation Concurrent with Pregnancy and of Short Recuperative Intervals", Merchant K, Martorell R, and JD Haas, to be submitted for publication by October.

These three articles are attached to this report in Appendix A. In addition to summarizing the research we have conducted, an important aim of this report is to assess future research directions. Therefore, this will be a major theme of the report.

Is frequent reproductive cycling (episodes of pregnancy and/or lactation) in poor women from developing countries a cause of poor maternal nutritional status (maternal nutritional depletion)? This question forms the basis for this research. First, a thorough review of the literature was conducted to examine the evidence available to answer this

question (article 1). From this information it was possible to set research priorities which led to the two studies reported in article 2 and article 3, addressing specific situations postulated to lead to the nutritional depletion of mothers. As defined previously, maternal nutritional depletion refers to nutritional consequences postulated to result from the stresses of frequent reproductive cycling. In particular, this research addresses potential energetic stress imposed by frequent reproductive cycling. Energy is not created in metabolic processes; therefore, when the burdens are high and resources are low the balance will be negative. Negative consequences of energy deficits for the mother and the family is the major concern.

The review examined evidence regarding the existence of maternal nutritional depletion by considering 1) the energetic cost of pregnancy and lactation and various explanations for how this cost is met; 2) the issues of measurement of both reproductive cycling and maternal nutritional status; 3) the various patterns of change in anthropometric measures and estimation of body fat during pregnancy and the postpartum period, and finally 4) the conceptualization and evidence of the more direct attempts to establish the presence or absence of maternal nutritional depletion. The following conclusions were drawn from this critical examination of the literature.

Conclusions Drawn from Review of Literature

The characterization of reproductive cycling (and its corresponding demand) using parity and time intervals between pregnancies or births is too simplistic. In spite of shortcomings, virtually all investigations characterizing maternal reproductive stress use birth interval (or interpregnancy interval) and /or parity. Parity is used to indicate the number of

pregnancies, but actually only captures information about the number of live births because miscarriages, abortions, and stillbirths are not counted. Another problem with parity is that it does not provide information on the timing or spacing between births.

And yet, a single birth interval is not a satisfactory measure of reproductive cycling since it is only the time interval between two successive births and does not take into account the spacing of previous births. In previous studies, the focus of research is usually the child, and the variables of interest frequently are the previous or subsequent interval relative to the index child. However in this research, we are concerned with the mother and hence, each birth interval she experiences is relevant, especially when the investigation addresses her cumulative reproductive experience.

A shortcoming of both parity and intervals as measures of the "energetic challenges" of reproductive cycling is that lactation is disregarded. In actuality, full breastfeeding on demand has a higher energetic cost than pregnancy. The use of birth or interpregnancy interval as a measure of the duration of a replenishment period for the mother contains the implicit assumption that lactation behavior has either no effect or a beneficial effect on nutritional status. Parity as a gross measure of reproductive stress also can be misleading because lengthy lactation periods between births may (depending on the amount of milk produced) have a more depleting effect on nutritional status than frequent pregnancies. If replenishment is the crucial factor, then the lactation behavior of the mother during birth intervals must be taken into account.

There is great variation and complexity in the reproductive patterns (number of births, spacing, and the length and intensity of each lactation period) between women. These measures miss the great variation and complexity of reproductive cycling (particularly

because neither considers the lactation behavior of the mother). The most promising improvements that have been introduced recently are the use of proportions of time spent pregnant or lactating within a specified period of time, and the definition of recuperative intervals based on lactation status.

Not enough effort has been devoted to the characterization of maternal nutritional status during pregnancy and lactation. The most difficult technical problems are created by the physiological alterations of water balance and tissue hydration during pregnancy and the early postpartum period and the presence of tissue that is not maternal (i.e. the fetus and the placenta) during pregnancy. Fatfold thicknesses and limb circumferences are more informative measurements than absolute weight or weight gain for characterizing maternal nutritional status during pregnancy. Reference data for these measures are needed for pregnancy, the postpartum period and various stages of lactation in healthy populations living in a variety of contexts.

The patterns of change in fatfold thicknesses are highly variable. In attempting to characterize anthropometric changes during pregnancy and lactation, it is crucial to distinguish various patterns and to identify maternal and environmental characteristics associated with the different patterns. Some studies indicate that a large increase in fatfold measures occurs during the early postpartum period in some populations; this should be examined further. Some studies indicate an increased mobility of fat stores of lactating women relative to non-pregnant, non-lactating women, another result worthy of further investigation. In addition, prepregnant measures rarely have been obtained to establish an appropriate baseline to assess gestational changes. A greater effort should be made to

extend the time frame of measurement (to collect more measures before conception and following birth).

Information on the relative energetic demand imposed by pregnancy, lactation, both and neither will provide a more accurate picture of the nutritional stress imposed by reproductive cycling. Estimating the energetic costs of pregnancy and lactation has been a topic of interest for many, although success has been limited. Recent evidence suggests that the estimated cost has been inflated (although it is not clear which components have been overestimated).

Fat gain and resting or basal metabolic rate are the two largest maternal components of the energetic cost of pregnancy; there is some evidence that both have been overestimated in the past. The average fat gain in healthy women originally estimated to be 4 kg may be closer to 2.5 kg. With respect to the basal or resting metabolic rate, some unexpected trends (reductions) during pregnancy have been observed (particularly in the Gambian population) and are worthy of further investigation to determine the range of adjustment that is common and under what circumstances the adjustments occur. Further understanding of the hormonal influences on energy balance and the metabolic changes during periods of pregnancy and lactation is needed.

Studies regarding fat changes and metabolic rates during lactation are particularly lacking. It is crucial for the determination of the energetic cost of lactation, that the fat gain during the corresponding pregnancy be well characterized because it is expected that these additional fat stores are accumulated during pregnancy in order to offset the energetic cost of lactation (reducing the amount of energy required from the diet during lactation). The

contribution of physical activity to the energy balance equation has been virtually impossible to measure, but new methods using doubly-labelled water may change this situation.

The cumulative effect on the mother of multiple pregnancy and lactation cycles within short periods of time has not been examined adequately. The short-term effect of pregnancy and/or lactation on maternal nutritional status has not been clarified adequately, either. The evidence reviewed in article 1 clearly demonstrates that the relationships of cumulative maternal nutritional depletion due to the high demands of reproductive cycling are too complex to be established merely by a relationship (or lack thereof) between parity and maternal weight. Longitudinal anthropometric measures and information on lactation status (in addition to birth and pregnancy intervals) should be used. Patterns of anthropometric change must be examined in relation to the changing reproductive status (physiological states) of the women.

Introduction to the Specific Research Issues Addressed

The review of the literature exposed some of the difficulties researchers have faced in documenting the presence of maternal nutritional depletion due to frequent reproductive cycling. Some factors contributing to these difficulties are easily postulated. It is expected that biological systems will attempt to compensate for the energetic stresses imposed by reproduction through various strategies such as increasing intake, mobilizing stores and/or decreasing physical activity in order to maintain energy balance. It has even been suggested that stores are acquired early (during pregnancy) in anticipation of later need (late gestation and lactation). This suggests a high level of organization and control in the biological system. Bauman and Currie (4) used a term for this control, "homeorhesis",

defined as "orchestrated changes in metabolism of body tissues necessary to support a physiological state."

It is only when this system coordinating nutrient flow is particularly stressed that depleting effects are likely to be observable. Therefore it is important to consider situations of particularly high stress in the study of maternal nutritional depletion. Frequent reproductive cycling in a context of poverty is one such situation. One important aspect of frequent reproductive cycling is close birth spacing. This results in a shortening of the non-pregnant/non-lactating interval in a reproductive cycle. In some cases the non-pregnant/non-lactating interval may be eliminated entirely with breastfeeding of the previous child continuing concurrent with the subsequent pregnancy.

Both potential conditions, a shorter non-pregnant/non-lactating interval and the overlap of lactation with subsequent pregnancy, lead to increased energetic demands. A shorter non-pregnant/non-lactating interval before conception would be expected to reduce the opportunity for nutritional recuperation of the mothers and lead to poorer maternal status and fetal outcomes (2, 5, 6). Women who overlap lactation with pregnancy must supply energy for milk production and fetal growth in addition to their own needs. Study of these situations of expected high energetic stress became the focus of the studies of article 2 and article 3.

Surprisingly, little is known about the frequency and extent to which pregnancy and lactation overlap. Where information is available however, indications are that overlap is a common occurrence. Lactation and pregnancy are each energetically-demanding processes. Therefore, when these two physiological states occur simultaneously, the risk of nutritional depletion of the mother or growth retardation of the fetus might increase,

particularly among women with limited access to food. There is also the possibility that the breastfed child will be harmed if breastfeeding patterns are altered or if milk volume is reduced. No one, to our knowledge, has assessed the nutritional implications of the overlap of pregnancy and lactation for the mother, the fetus, or the breastfeeding child.

Summary of Key Findings

A rich, longitudinal data set from a Guatemalan community supplementation trial (conducted from 1969 to 1971) was used to examine the prevalence and responses to lactation concurrent with pregnancy and short recuperative intervals. The prevalence of the overlap of lactation with pregnancy was found to be very high, 50.2% in the Guatemalan women studied (3). The mean supplement intake of women who experienced the overlap of lactation with pregnancy was higher than that of women who did not. These differences persisted when examined across pregnancies in the same woman and after the short birth interval was controlled in the analyses. In addition, the presence of overlap seemed to affect fat stores negatively. By pairing consecutive pregnancies within women, it was possible to control for inherent characteristics of the mothers that could confound the relationships of interest (between the presence of overlap, short recuperative intervals and maternal and fetal responses). The results indicate that overlap is most stressful, short recuperative interval follows, and long recuperative interval is least energetically stressful on the mother.

There is some evidence from these data of chronic effects of frequent reproductive cycling. Women with long recuperative intervals (non-pregnant/non-lactating intervals ranging from 6 months to 8 years between cycles, with a mean of almost 4 years) had

measurably higher fat stores than women with short recuperative intervals between cycles. There were significant differences in supplement intake between women who experienced long recuperative intervals (intake is lower) and women who did not. These differences also persisted across consecutive pregnancies in individuals.

The research design of the Guatemalan supplementation trial made food supplements available ad libitum. Within each village supplementation centers were set up which served the supplement drink (fresco or atole depending on which supplement type the village had been assigned) twice daily between meals. Any member of the village was welcome to attend and consume as much of the supplement drink as they wished. This supplementation intervention was present in the villages for all eight years of the intervention study period. Therefore, the resources available for energy intake of the individuals of these villages were increased. In spite of this, the stress of frequent reproductive cycling was demonstrated.

Public Health Implications

Mothers experiencing long recuperative intervals between births (subsequent conception occurring > 6 months following weaning of the previous child) had the largest fat stores (measured by thigh fatfolds). Although research in this area is just beginning, the results suggest two practical recommendations: 1) that women living in circumstances of high energetic stress space their births so that subsequent conceptions occur more than 6 months following weaning of the previous child and 2) if pregnancy occurs sooner than this, that an effort be made to consume additional food that is calorically dense.

Issues for Future Research

A major portion of the maternal depletion project study period was required for preparation and construction of the data files. All previous work using the INCAP data tapes from the supplementation trial had been directed at child outcomes. Therefore major restructuring was required to construct data files which were referenced to the mother rather than individual child and appropriate for addressing maternal outcomes, the focus of the maternal depletion project. At this point in time we have produced three journal articles, 1-published, 1-in press, and 1-submitted (see Appendix A). Unfortunately, key issues remain that could be addressed in a relatively short period of time, but the duration of this project has been too short. Several of the remaining issues are described below.

It is important first to identify who is most negatively affected by the two factors of close birth spacing --presence of overlap and short recuperative intervals-- that are postulated to lead to greater energetic stress during pregnancy. It is also important to identify who receives the benefits of a nutritional intervention.

The three most immediate recipients of negative effects of energetic stress during pregnancy and positive effects of nutritional supplementation during pregnancy are the mother, the fetus and the breastfeeding child. The previous work has been restricted to the mother and the fetus due to limitations of the data available and to complexities of defining and then isolating the effects of close birth spacing on the breastfeeding child. The research reported in article 2 and article 3 begins the process of determining who is most jeopardized by situations of high energetic stress. The results consistently showed effects of energetic stress on the <u>mother</u> (intake increased and stores decreased in situations of higher stress) and not the fetus (the birthweights did not differ significantly between groups

experiencing differing stresses). This suggests that, the mother may be buffering the energetic stress and therefore protecting fetal growth. Effects on the breastfeeding child remain to be examined.

Building on this initial investigation, the issues of nutrient partitioning between mother and fetus can be explored further using the Guatemalan data set. The interrelationships among maternal supplement intake, fat stores and fetal growth within the subgroups should be examined directly. It may be possible to determine if fetal growth is protected by increased maternal intake, maternal fat mobilization and/or both. And yet, more complete information on other components of energy balance --such as physical activity and total dietary intake-- is necessary to fully explore the complexities of nutrient partitioning during reproduction.

This research demonstrates that evidence of maternal nutritional depletion due to a demanding reproductive history is found when the reproductive stress is characterized adequately. It is time to abandon the use of parity as the sole indicator of previous reproductive stress experienced by a woman. One of the conclusions of the literature review (2) was that parity and a single previous birth interval are not adequate methods. The research reported in articles 2 and 3 was specifically aimed at refining the characterization of reproductive cycling in order to improve the understanding of reproductive stress and its consequences. A major contribution of this research was a reassessment of the nature and timing of reproductive cycling so it could be quantified accurately, no longer ignoring the contributions of components such as lactation to reproductive stress. When this was done, responses to the postulated stress were seen.

Efforts to accurately characterize reproductive cycling and the resulting stress should be continued.

Several other important implications for future research in this area can be derived from this work. As anticipated in the review of the literature and demonstrated in the subsequent studies, it is crucial to consider the presence of overlap --particularly when assessing the effects of birth spacing (otherwise there may be an overestimation of the effect of birth spacing attributed to recuperation). The phenomenon of overlap of lactation with pregnancy should no longer be overlooked. It appears to occur frequently in populations with close birth spacing and relatively low socioeconomic status (7-9). This study has provided evidence of a high prevalence (50.2%) of overlap in 4 rural Guatemalan communities during the 1970's. The duration of overlap of lactation with pregnancy extended beyond the first trimester (the period during which a woman may not recognize her pregnancy) for 44.3% of the cases of overlap. This indicates that many women made the decision to breastfeed during at least some portion of their subsequent pregnancy.

As with the characterization of reproductive cycling, this research exposed the importance of accuracy in the characterization of maternal nutritional status and dramatically illustrated in several cases how easy it is to misinterpret data on maternal nutritional status and to oversimplify crucial complexities of reproductive cycling. Misinterpretations are common, particularly when a woman's nutritional status is assessed at one point in time during the reproductive years without consideration to her location in the reproductive cycle. Maternal nutritional status is very dynamic during the reproductive years. The fluctuations are wide and can influence interpretations of the data. A simple categorization of pregnant, lactating, pregnant <u>and</u> lactating, or non-pregnant/non-lactating is not enough. (And yet,

the pregnant and lactating category has generally been overlooked or entirely forgotten.) Division into these categories is not adequate because variation can be expected among non-pregnant/non-lactating women based on duration since weaning, initiation of partial breastfeeding, or previous birth. More effort should be devoted to develop ways of accurately characterizing maternal nutritional status during the reproductive years given these complexities.

New studies could be designed to examine crucial aspects of the situation of lactation occurring concurrent with pregnancy. In particular, examination of the attitudes and beliefs regarding breastfeeding during pregnancy and decisions regarding weaning and the consequences for the breastfeeding child (as well as the mother and the growing fetus) would be useful. Measures of milk production by the mother, milk composition, and milk intake by the breastfeeding child during various stages of overlap are needed. Information regarding the prevalence and duration of overlap of lactation with pregnancy in various cultural subgroups should be obtained. Finally, recommendations should be developed and disseminated based on the research findings.

Conclusion

It is clear that the question "frequent reproductive cycling: does it lead to nutritional depletion of mothers?" is no longer the major question of interest. Evidence provided by the analyses reported in articles 2 and 3 demonstrate that there are responses (increased intake) to and consequences (reduced stores) of the stresses of frequent reproductive cycling. Now the questions can be expanded to: what conditions and combination of factors result in nutritional depletion --mild, moderate and severe--, how prevalent are these,

what are the functional consequences of this depletion, how long does it persist and what factors facilitate recovery?

Functional meaning is needed for maternal nutritional status measures. Assessing functional consequences of depletion is the central challenge in investigations of maternal depletion that remains largely untouched. For example, it is known that the measures of fat are very low in the Guatemalan women relative to healthy British women (13 mm thigh fatfold vs. 35 mm thigh fatfold), but it is not known what the consequences are when a Guatemalan mother loses several millimeters of fat due to the stress of pregnancy with lactation or a short recuperative interval. Frequent reproductive cycling over many years may lead to very subtle consequences or readily apparent and yet difficult-to-measure consequences. Inadequate attention has been given to potential consequences such as, increased morbidity, reduced work output, exhaustion, decreased "well-being", accelerated aging and/or premature death. It is clear that the range of outcomes of maternal depletion studied must be expanded.

Ultimately the rest of the family and particularly the young children are likely to suffer from a worn out or depleted mother, but more importantly the women, themselves, suffer. Although progress is being made to shift more attention to research on the health of women in the context of poverty, clearly much work remains to be done in this area.

APPENDIX A

Index of attached articles:

1) "Frequent Reproductive Cycling: Does it Lead to Nutritional Depletion of Mothers?", Merchant K and R Martorell, Progress in Food and Nutrition Science, 12:339-369. (2)

2) "Maternal and Fetal Responses to the Stress of Lactation Concurrent with Pregnancy and of Short Recuperative Intervals", Merchant K, Martorell R, and JD Haas, American Journal of Clinical Nutrition, (in press). (3)

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FREQUENT REPRODUCTIVE CYCLING: DOES IT LEAD TO NUTRITIONAL DEPLETION OF MOTHERS?

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ABSTRACT

Is frequent reproductive cycling (episodes of pregnancy and/or lactation) in poor women from developing countries a cause of poor maternal nutritional status? This review seeks to examine the evidence available to answer this question. The measurement of reproductive cycling, maternal nutritional status, and the energetic costs of pregnancy and lactation are reviewed. The data available on the anthropometric changes during pregnancy and lactation are described. Against this background, the evidence in support of the hypothesis that repeated reproductive cycling leads to a maternal depletion syndrome is examined. It is concluded that although the data are inadequate to unequivocally establish or rule out the existence of maternal nutritional depletion due to a demanding reproductive history, the data suggest this relationship does exist. Weaknesses of current measurement and study design methodologies are identified and priorities for future research aimed at clarifying the extent to which reproductive cycling affects maternal nutritional status are identified.

KEY WORDS: Maternal nutrition, Pregnancy, Lactation, Energy balance, Energy cost, Birth spacing

MATERNAL DEPLETION SYNDROME

The energetic and nutrient demands placed on women during pregnancy and lactation frequently have been identified as major nutritional stresses in the lives of women (1-3). How these stresses are accommodated has been an active area of research recently. The expectation has been that women cope with the increased demands arising out of the reproductive process through one or more of the following mechanisms: increased dietary intakes, reduced activity levels and catabolism of maternal tissues (4). More recently, some investigators suggest that metabolic adaptations during pregnancy and lactation also enable women to maintain energy balance (5-7).

Key questions remain unresolved including the following: To what degree do women need to increase dietary intakes and/or decrease activity levels to cope with reproductive stress without compromising maternal health? Are recovery periods between reproductive cycles necessary for women's health? How are women --who live under conditions where dietary intakes are marginal and where physical labor demands are high-- able to accommodate the nutritional stresses of reproduction? Is it by increasing intake, decreasing activity and/or spacing pregnancies? To what extent are metabolic adaptations complementary or alternative coping mechanisms? Although these questions clearly have relevance

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to all women and children, the focus of this article is on women of marginal nutritional status living in poverty in developing countries.

Reproductive cycling is the term used in this article to refer to both the frequency and duration of periods of gestation, as well as the frequency, duration and intensity of periods of lactation. The term maternal nutritional status can be used to encompass biochemical measures of levels and stores of vitamins and minerals, clinical signs of deficiency, as well as more general anthropometric measures of body tissue stores. The emphasis of this article is on the anthropometric measures of body tissue stores --because more data of this type are available and because anthropometric measures provide a useful summary indicator of long-term energy balance.

The extent to which reproductive cycling affects maternal nutritional status is the primary focus of this review. The impact of one pregnancy-lactation cycle or a portion of this cycle (short-term) as well as the cumulative impact of a number of cycles (long-term) on a woman's nutritional status is examined.

Unfortunately, little research has focused specifically on the relationship between reproductive history and maternal nutritional status. This review article begins by introducing in greater detail the concept of maternal depletion syndrome, followed by a review of recent work on energy balance during pregnancy and lactation. Next, methods of measuring maternal nutritional status during pregnancy and lactation are reviewed briefly and a detailed presentation of key studies of anthropometric changes during pregnancy and lactation is made, followed by an evaluation of current approaches to the measurement of reproductive cycling. Then, after drawing from these varied yet related topics, the limited evidence regarding the relationship between reproductive cycling and nutritional depletion is examined. Finally, the information reviewed is summarized and priorities for future research aimed at clarifying the extent to which reproductive cycling affects maternal nutritional status are identified.

Women in developing countries, are pregnant, lactating or both during large portions of the reproductive years (i.e. menarche to menopause) with --it is believed-- detrimental effects on maternal nutritional status. Some researchers have used the term "maternal depletion syndrome" to refer to these repercussions on maternal health (8), but others question whether this characterization is appropriate (9-11). In the nutritionally-based model of maternal depletion syndrome, it is hypothesized that the greater energetic and nutrient demand on the mother during pregnancy and lactation results in a compromised nutritional status when many cycles of pregnancy and lactation occur within a short time-interval under conditions of relatively poor dietary intakes (12).

The increased biological stress may be accompanied by social/environmental stress for the mother due to the increase in family size which results from frequent reproductive cycling. Specifically, the increase in family size further limits resources of time and money, potentially reducing the quality of care of the children while increasing the burdens on the mother. In spite of the recognition that a larger context exists, the focus in this review is on the stress of reproductive cycling on maternal nutritional status.

Figure 1 provides a simple conceptual framework to describe the major factors related to reproductive behavior which deplete or benefit the nutritional status of women. It is not meant to provide an exhaustive description, but rather a scheme for organizing key concepts. Poverty directly (e.g., poor diets, heavier workloads, greater rates of infection) or indirectly (e.g., reduced access to and demand for family planning methods and therefore increased frequencies of conception) determines the negative demands on maternal nutritional status.

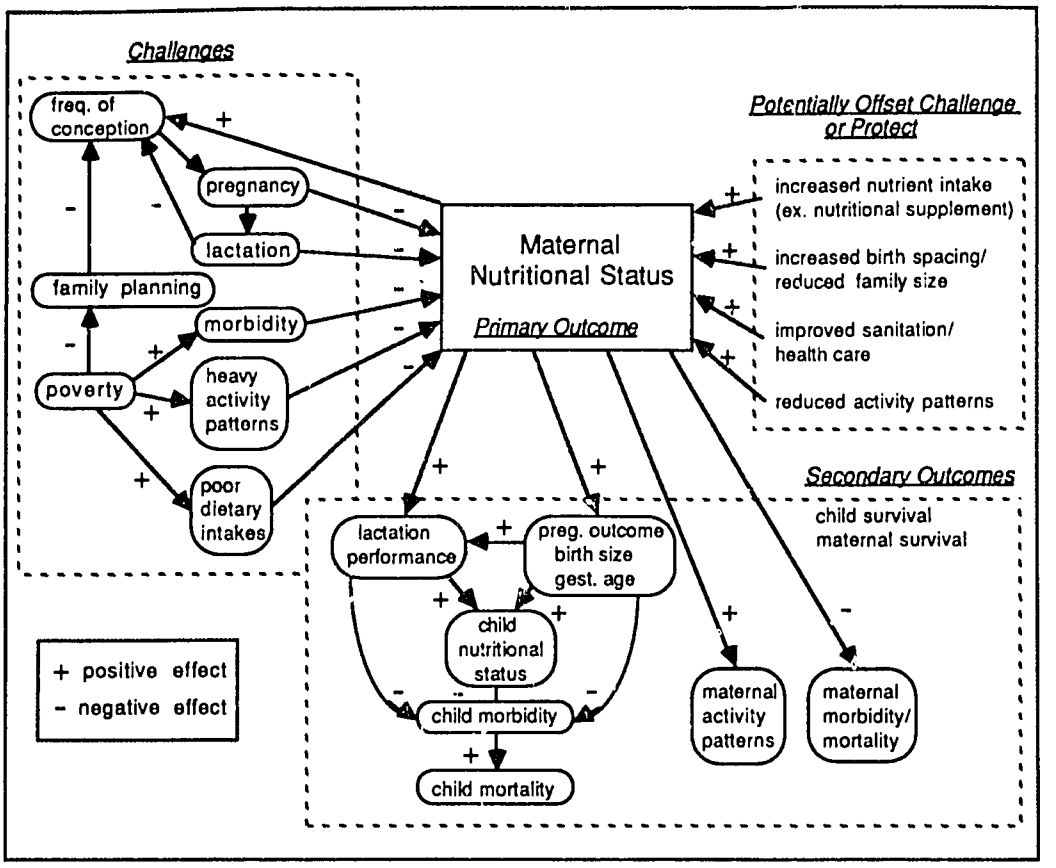

FIG. 1: Model of Context of Maternal Nutritional Depletion

These challenges may be offset or prevented through various strategies such as nutritional supplementation, increased time intervals between births, improved environmental sanitation, greater access to health care and reduced activity levels. Maternal nutritional status leads to secondary outcomes affecting both mother (e.g., activity patterns, morbidity and mortality) and child (e.g., pregnancy outcome --birth size, gestational age--, lactation performance, the child's nutritional status, morbidity and ultimately mortality).

ENERGY BALANCE

It is important to consider the stress of reproductive cycling on maternal nutritional status in the wider context of energy balance because energy is such a fundamental component of metabolism. The various flows of energy of four physiological states are diagrammed in Figure 2. Two sources may contribute to the available energy pool, dietary intake (following ingestion, digestion, and absorption) and maternal tissue (following mobilization from storage). Use of the pool of circulating energy depends upon the physiological status of women. In a non-pregnant, non-lactating state, energy metabolism is regulated by homeostatic mechanisms; work and body tissue are the two potential targets of input energy (as shown in panel A).

The mechanisms regulating energy metabolism during pregnancy and lactation can be more accurately described as homeorhetic rather than homeostatic because

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they coordinate a directed flow of energy. Homeorhesis is defined by Bauman and Currie (13) as "orchestrated changes in metabolism of body tissues necessary to support a physiological state." During pregnancy, an additional target for the available energy is fetal growth (panel B). Similarly, during lactation, the process of milk production claims a share of the available energy (panel C). When a woman is both pregnant and lactating, the potential use of the available energy is most diverse (panel D).

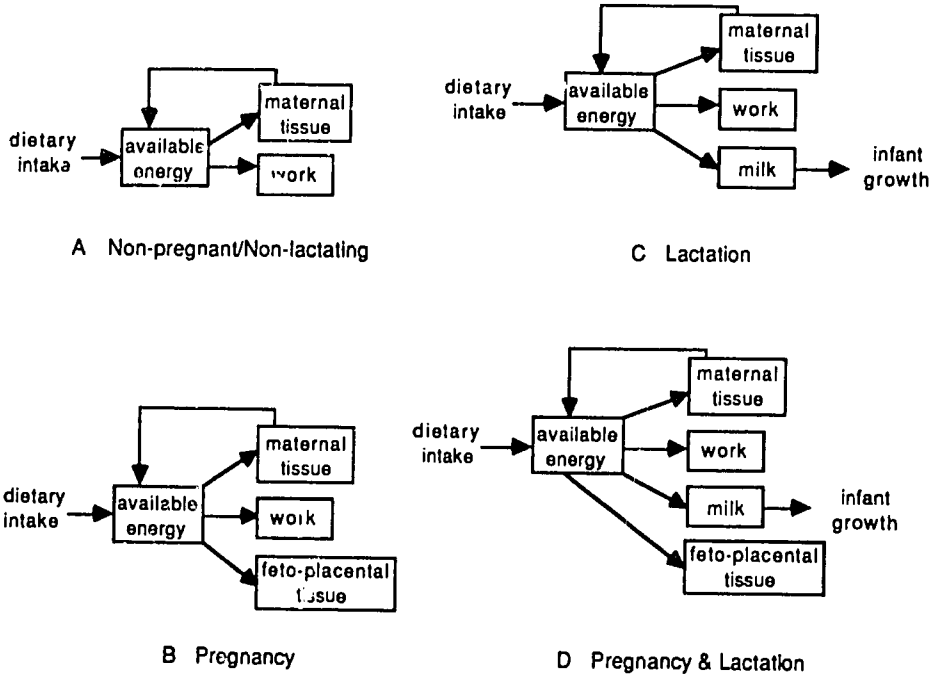

FIG. 2: Components of Energy Balance During Reproduction

Pregnancy

Some of the commonly-held beliefs concerning the energetic needs of pregnancy are being challenged (5, 14-16). The theoretical estimate of the total energetic cost of pregnancy made by Hytten and Leitch (4) using a factorial approach (the cost of each component of use is estimated and summed) was 312 MJ (approx. 75,000 kcal). This estimate was later revised to 355 MJ (approx. 85,000 kcal, (17)). The FAO/WHO/UNU (18) use 335 MJ (80,000 kcal) as the theoretical estimate of the increased cost of pregnancy.

Newer evidence from a variety of countries suggests that the current estimates of the energetic cost of pregnancy are inflated. The results of a five country study were published recently in a series of articles coordinated by Durnin (5, 19). Studies were conducted of pregnant women from Scotland (20), the Netherlands (21), Thailand (22), the Gambia (23), and the Philippines (24); it was concluded that the energy cost of pregnancy is more likely to be about 250 MJ (60,000 kcal).

Major discrepancies between theoretical estimates and experimental results from Durnin's multicenter study occur in the case of two components of energetic cost: maternal fat gain and basal metabolism during pregnancy. Hytten and Leitch (4) estimated that 148 MJ (approx. 35,500 kcal) were needed for increased maternal fat tissue and that 121 MJ (29,000 kcal) were required for increased oxygen

consumption during pregnancy. These are 47% and 39%, respectively, of the total estimated energy cost. The value for increased oxygen consumption later was revised to 164 MJ (approx. 39,500 kcal) (17), making the increased maternal fat and increased oxygen consumption cost 42% and 46% of the total estimate, respectively.

A summary table (Table 1) of the results from the five-country study demonstrates that in no case was the mean fat gain more than 2.3 kg, or 38% of the total observed/calculated energetic cost. An interesting aspect of these data is that in spite of tremendous diversity of conditions, varying techniques to estimate fat and differing absolute mean fat gains among the study populations, there is remarkable consistency in the percentage (31 to 38%) of the total energy cost that was used for maternal fat deposition. In order to demonstrate the importance of the magnitude of the maternal fat gain component in the estimation of the energetic cost of pregnancy, the cost has been calculated (Table 1) for each sample as if the mean gain had been 4.0 kg (C_4). Note that the energy gap between the expected theoretical cost (C_t = 312 MJ) and the C_4 estimate is much smaller (particularly in the case of Thailand, the Philippines and the Gambia) than the gap between the theoretical cost (C_t) and the measured cost (C_m). It appears that the theoretical cost is overestimated mainly due to the assumption of a 4 kg gain in fat during pregnancy.

TABLE 1
Fat Gain, Relative Energy Cost of Fat, Total Energy Cost and Total Energy Gap during Pregnancy from a Five-Country Study

	sample size n	fat gain (kg) Mean	SE	energy cost fat %	total energy cost (MJ) C_m	C_4	total energy gap (MJ) C_t-C_m	C_t-C_4
Scotland	88	2.3	(0.3)	37.7	281	327	31	-15
Netherlands	57	2.0	(0.3)	32.2	286	346	26	-34
Gambia	52	0.6	(0.3)	35.4	78	202	234	110
Thailand	44	1.4	(1.1)	31.0	208	296	104	16
Philippines	51	1.3	(0.3)	33.0	181	273	131	39
Theoretical		4.0		48.7	C_t^* = 312			

C_t = theoretical estimate of total energy cost (4)
C_m = measured total energy cost (5)
C_4 = Five-country estimates of total energy cost <u>if</u> 4.0 kg of fat had been gained rather than what was actually gained.

The Gambian absolute mean fat gain is strikingly low compared to the mean fat gain in each of the other four samples. Seasonality and food availability are important determining factors of patterns of fat gain and loss in the Gambian population. Although the mean fat gain of the Gambian women in this sample was 0.6 kg, those who received an energy-rich supplement had a mean fat gain of 2.0 kg after adjustment for seasonality. This is similar to the mean fat gain of the Scottish and the Dutch women (Table 1).

The results of this five-country study challenge the commonly-accepted estimation that a "normal" pregnancy results in a mean storage of 4 kilograms of fat. Rather, there appears to be tremendous variation between women and across cultures and socioeconomic strata and there is no evidence of adverse functional outcomes associated with fat gains in the range of 2 to 2.5 kg.

The other major component of the energetic cost of pregnancy is the basal metabolic or resting metabolic rate. The "normal or average" range of this

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component is also controversial. Results from two (the Gambia and Scotland) of the five countries studied suggest that women have lower metabolic rates early in pregnancy (6, 25) than originally expected (4). These investigators suggested that the lower resting metabolic rate may be an adaptation to the high energy cost of pregnancy. In the case of the Gambia, it has been suggested that adaptation (or accommodation to adverse circumstances) of a population that experiences chronic, cyclic and severe food shortages has occurred. Illingworth and coworkers (15) recently reported a 28% reduction in postprandial energy expenditure during the middle trimester of pregnancy in seven healthy women relative to the values obtained post-lactationally in the same women. The specific physiological mechanisms for proposed adaptations or accommodations have not been delineated.

Women completing "successful, normal" pregnancies do not appear to be increasing their dietary intake to the degree that currently is being recommended (6, 14, 16, 20, 21, 23, 24). This discrepancy may be largely a result of the fact that energy requirements allow for an unrealistic increase of 4 kg of maternal fat during pregnancy.

The energetic cost of physical activity during pregnancy is the component of energy balance remaining to be explored in the effort to explain the apparent discrepancy between measured intakes and estimations of the total energetic cost of pregnancy. Most studies of activity patterns indicate that major alterations do not occur during pregnancy and the postpartum period in most societies (16, 26). Yet, minor changes may play an important role in determining requirements if sustained over several months. McNeill and Payne (27) reported that patterns of physical activity from 115 rural south Indian women (using 24 hr recall) "suggest that pregnant and lactating women spend more time in personal activities (mainly resting) and less time in social activities, working in the fields, and travel than do non-pregnant, non-lactating women." The degree to which energy spent on physical activity can be reduced is dependent on the level of activity normally engaged in. McNeill and Payne (27) suggested that "where the normal level of physical activity is high, significant changes (15-20% lower than non-pregnant, non-lactating)" in activity may occur. The problem however, is that current methods lack the necessary precision for recording such changes.

Not only can women's use of time change during pregnancy but also the cost associated with a particular activity can change. The increase in maternal body weight which occurs during pregnancy will increase the cost proportionately of weight bearing activities (28). Banerjee and coworkers (29) showed no significant differences between 42 pregnant and 37 non-pregnant women in the energetic cost per unit of body weight of eight common daily activities.

Several investigations indicate that the energetic cost of non-weight bearing activity (pedaling on a bicycle ergometer) does not differ for women between pregnancy and the postpartum period (30, 31). In contrast, Pernoll and coworkers (32) reported a significant increase in oxygen consumption and in the length of the recovery period (or oxygen debt) for women pedaling a bicycle ergometer during pregnancy compared to the postpartum period.

The conflicting results may be due to the fact that the timing of the measurement in the postpartum period differed between the studies, 6 wk (30), 3 mo (31) and 6 mo (32) following birth. Another problem is that it is extremely difficult to standardize exercise conditions for even a carefully controlled oxygen consumption measurement. As Illingworth and coworkers (15) point out "any changes in posture act as a potent stimulus for the release of noradrenaline which will itself promote a significant increase in metabolic rate" (33). In addition, the energetic cost and therefore oxygen consumption is affected by mechanical efficiency (which varies as a function of posture) and by training.

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These difficulties prevent a conclusive statement on the contribution of physical activity to the energy-balance equation. The measurement of energy expenditure using doubly labelled water appears to be a promising technique for the clarification of pregnancy-related changes (34-36). Davies and coworkers (37) used this method for making serial measurements at 6-week intervals in 7 well-nourished pregnant British women (following prepregnant baseline measurements). Prentice (36) summarized the major finding as "the metabolic and behavioral responses to pregnancy are extremely variable", and also stated that "none of the subjects showed any energy-sparing decreases in the cost of physical activity."

Lactation

Investigations addressing the energetic costs of lactation have been reviewed thoroughly by Prentice and Prentice (38) and is dealt with only briefly here. As in the case of pregnancy, the recommended dietary intake for this period seems to be substantially higher than observed values (16). This discrepancy occurs in spite of the fact that recommendations for dietary intake during lactation assume that some of the energetic need will be supplied by maternal fat mobilization, as demonstrated by Thomson and coworkers (39).

The recommended energy intake during lactation of 2092 kJ/d (500 kcal/d) is based on the expectation that 150 MJ (36,000 kcal) will be available from the 4 kg of fat deposited during pregnancy. This energy store is expected to provide 837 kJ/d (200 kcal/d) for 6 months, reducing the additional energy required to sustain lactation from 2929 kJ (700 kcal/d) to 2092 kJ/d (500 kcal/d). Of course, if the average fat gain during pregnancy is 2 kg and not 4 kg, the net energy contribution of fat losses would be reduced from 200 kcal/d during the first six months. The total energetic cost of lactation is estimated using data derived from the results of the WHO Collaborative Study on Breastfeeding (40) which are summarized in Table 2 (18). This estimate is consistent with the estimate reported by Gopalan and Belavady (41) of an increased energetic requirement for a sample of lactating Indian women on "the order of 500 to 700 calories per day".

TABLE 2
Median Breast-milk Secretion and Energy Cost of Lactation

Month of Lactation	Median volume [a] (ml/d)	Energy content of milk [b] (kcal/d)	(kJ/d)	Energy cost of lactation [c] (kcal/d)	(kJ/d)
0-1	719	503	2105	629	2630
1-2	795	556	2326	695	2908
2-3	848	594	2485	742	3105
3-6	822	575	2405	719	3008
6-12	600	420	1757	525	2197
12-24	550	385	1610	481	2012

[a] Data from the results of WHO Collaborative Study on Breastfeeding (40).
[b] Taken as 0.7 kcal (2.9 kJ)/ml.
[c] Assumed efficiency of conversion = 80%.

These calculations are highly dependent on the amount of milk produced. Measurement of the amount of milk produced daily is a challenge. Traditional methods such as weighing the infant before and after each suckling period are notoriously difficult to carry out and are obtrusive in such a way as to change patterns of breastfeeding and even milk output on the measurement day. New techniques using deuterium oxide show promise but require further development (42, 43). Also, the measurement of dietary intake and energy expenditure due to physical activity remain problematic during lactation as in pregnancy.

As with pregnancy, investigators have looked for evidence of energy-sparing adaptations to lactation. The evidence regarding changes in basal metabolic rates during lactation is inconsistent. Although an increase in basal metabolic rates would be expected (due to milk synthesis), some studies have not only shown no evidence of an increase but rather a decrease (38). In addition, Illingworth and colleagues have observed lower postprandial thermogenesis in lactating women compared with women who are not lactating (44).

Generally lactation is recognized to lead to weight loss and some of these data will be presented in the following section. Data from Gambian women (45) however, suggest that fat loss during lactation does not always occur and that it is dependent on other components of energy balance (particularly, dietary intake). As previously mentioned, seasonality affects food availability and physical activity in Gambian women. Weight loss (shown to be highly correlated with fat changes) was observed in lactating women in this population during the wet season (the season in which food availability is decreased and physical demands are increased) and weight gain was observed in lactating women during the dry season. There are also data of postpartum weight changes from women in affluent societies demonstrating that weight loss in lactating women was not greater than that of non-lactating women (38). Prentice and Prentice (38) suggest that "it is probably more realistic to view women's large adipose tissue stores as an emergency buffer against acute restriction of food intake."

In a small sample (n=18) of Guatemalan women it appears that the energetic cost of lactation was supplied almost entirely by fat tissue mobilization (rather than by increased dietary intakes) (46). A comparison with 6 non-lactating Guatemalan women of similar size from the same communities showed no significant differences from the lactating women "in terms of daily energy intake, daily energy expenditure, the energy cost of specific activities, or the pattern of activities throughout the day." However, it is possible the sample sizes were inadequate to show actual differences between the groups.

MATERNAL NUTRITIONAL STATUS DURING PREGNANCY AND LACTATION

This section begins with a discussion of various approaches and difficulties encountered in the assessment of maternal nutritional status during pregnancy and lactation. Problems associated with the use of anthropometry are considered and reference is made as well to measurement difficulties related to more direct measurements of body composition. Next, studies of body fat changes during pregnancy and/or lactation are reviewed.

Measurement Techniques

Generally, attained weight and height are considered to be the minimal measures necessary to assess a person's nutritional status. However, the assessment of a woman's nutritional status using weight measurements during pregnancy is complicated by the fact that a measure of weight is a composite measure of maternal and fetal tissue. Weight gain during pregnancy has generally been studied in relation to (as a predictor of) fetal growth or birthweight, not as an indicator of maternal nutritional status, and many attempts have been made to develop weight gain charts that are appropriate for pregnant women (4, 47-52).

Measures of limb circumferences and fatfolds at various sites on the body avoid the problem of including fetal components and give information regarding a person's body composition, but have not been used extensively in investigations of maternal nutritional status. Fatfold thicknesses are not easy to measure reliably and therefore it is crucial to standardize measurement techniques and

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to train anthropometrists carefully. Because the magnitude of changes in the measures are small, imprecisions easily can obscure meaningful relationships.

Reference data for fatfold measurement sites are not available for pregnant women, nor have methods for estimating total body fat from fatfolds been developed for pregnant women. Because of the lack of data, reference data and methods of body fat estimation for non-pregnant, non-lactating women (53, 54) have been applied to pregnant women (55, 56), in spite of indications that body fat distribution is altered during pregnancy (57).

More-sophisticated approaches to body composition determination can be used: techniques which estimate body composition based on the water content of the body, such as, densitometry, hydrometry, gamma ray spectrometry, and new methods such as neutron activation, dual-photon absorptiometry, ultrasound, infrared interactance, bioelectrical impedance, and total body electrical conductivity. (See Lukaski (58) for a review of these techniques.)

There are problems of applicability with each of these techniques (given considerations of safety, convenience and/or practical limitations of expense and availability of equipment) for women who are pregnant. Questions can be raised as to the biological validity of the required assumptions in a physiological state such as pregnancy for most of these techniques. The implications of the inherent assumptions that are least likely to be valid during pregnancy are discussed below. The newer methods have the additional problem that they are still in the development stage and require further study before general application can be recommended.

Another problem associated with the measurement of maternal nutritional status is created by the unidentified or unknown sources of variation in body water which occur during pregnancy. This will lead to inaccuracy and imprecision, particularly in the measurement of weight but also in the most common techniques for estimating body composition (densitometry, fatfolds, hydrometry and gamma ray spectrometry).

Because assessment of body composition is crucial to understanding the nutritional status of both mother and fetus, investigators have attempted to measure total body water. The most common method used is a deuterium dilution technique. Using this technique, Hytten and coworkers (67) demonstrated (in 93 Scottish women with normal pregnancies) that the mean total body water of women with no clinical edema rose by 6.8 kg (15 lb) from 10 to 38 weeks of pregnancy compared to a mean 9.8 kg (22 lb) increase for women with generalized edema. Forty-six of the ninety-three women showed clinical signs of edema (20 leg edema and 26 generalized edema). All 93 women "whether or not they had edema, were perfectly well throughout pregnancy and had normal healthy babies" (5`). In order to confirm this surprisingly high incidence of edema during pregnancy, Thomson and coworkers (60) conducted an epidemiological study and found a similar incidence in women who also were categorized as normotensive (showing neither hypertensive nor pre-eclamptic signs).

It is not clear where the additional water of pregnancy is stored. It has been estimated that 5,800 ml of additional water are associated with the various tissue changes of pregnancy, but an average of 1,700 ml, 2,100 ml and 2,700 ml remain unaccounted for in women with no clinical signs of edema, leg edema and generalized edema, respectively (59). Robertson (61) examined the changes in compressibility of tissue in 39 clinically-normal primigravid women and postulated that "generalized edema may occur because of a hormonally activated change in the extracellular ground substance" of connective tissue.

Given the magnitude of variation in "normal" pregnancies and the poor understanding of the changes in total body water and tissue hydration during

pregnancy, determination of total body fat during pregnancy using current techniques is shaky at best. Although no assumptions are made regarding the (constant) level of hydration of fat free mass using fatfold measurements (unlike densitometric, gamma-ray spectrometric and hydrometric techniques of total body fat estimation) these measurements may be affected by water retained subcutaneously, but this should be minimal. Robertson (61) reported that "edema of the lower limbs is easily displaced by pressure" and Taggart and coworkers (57) found that the presence of edema had no consistent effects on the pattern of change in fatfold measures.

A problem of greater concern (than edema) when using fatfold measures to predict total body fat is the assumption that subcutaneous fat storage is representative of internal fat storage. Although there are no data for women, in a study of fat partitioning in dairy cows during pregnant, lactating and "dry" periods, it was concluded that subcutaneous fat measures should be good indicators of body fat reserves and that "the distribution of subcutaneous fat between seven defined regions of the carcass was not affected by differences in total fatness in different physiological states" (62).

Probably the most difficult problem is how to combine measures from differing sites in a biologically meaningful way. Durnin and Wormersley (54) developed prediction equations for total body fat of adult men and adult non-pregnant women from fatfolds using densitometry as the "gold standard". Direct measurement of body fat has been done on only a limited number of cadavers, none of which were pregnant (63). Some investigators have avoided the problems of predicting total body fat from fatfolds by using the measures at the various sites to describe changes for each measured site (not attempting to combine the measures in order to predict total body fat) (45, 57, 64, 65).

One of the two major complications in the assessment of nutritional status of pregnant women is clearly not a problem for lactating women. Since the women have given birth, all of the tissue is maternal tissue and measures such as mass are no longer composite measures of maternal and feto-placental tissue. The other major complication in pregnancy --tissue hydration-- still may apply, though. Although, body water balance was reported to have returned to prepregnant status by two weeks postpartum by Durnin (66), earlier work suggests that altered body water balance may persist in women with generalized edema even 6 to 8 wk postpartum (67). Since specific data are not reported in one case (66), it is not possible to explain the conflicting conclusions (although one possibility is that none of the women had generalized edema in the investigation to which Durnin refers).

Anthropometric Changes

Reference is made in this review only to those studies with more-complete information (known length of gestation at time of measurement, longitudinal measurements, and an emphasis on studying changes in maternal nutritional status, body composition and/or fat during pregnancy and/or lactation.

Longitudinal measurement is essential in the study of these changes because variation in patterns of change among women is high. Investigators examining anthropometric measures longitudinally frequently have identified subgroups of women with respect to patterns of change.

The first comprehensive study of maternal fat changes during pregnancy was conducted by Taggart and coworkers (57). Measurements were made on 84 healthy British women at four points during pregnancy and at two points postpartum. The investigators chose seven sites (triceps, biceps, scapula, costal, suprailiac, mid-thigh, and knee-cap) determined (in preliminary trials) to be appropriate for use during pregnancy. In addition, these investigators measured both body

weight and total body water in 48 of the subjects using the deuterium dilution technique.

Two differentiating characteristics created the following subgroups: 1) overweight/underweight and 2) primiparous/multiparous women. A greater increase in fatfold measures of the underweight and primiparous groups was reported. As mentioned previously, no differentiating patterns of change were observed with respect to the presence or absence of edema.

Increases in fat occurred between 10 and 30 wk of gestation at all sites (Figure 3). Most measures either decreased slightly or remained unchanged from 30 to 38 wk. All the measurements at all sites declined between 38 wk of gestation and 6 wk postpartum; later the changes were variable. The proportional change (relative to values at 10 weeks of pregnancy) was greatest at the suprailiac site (Figure 4).

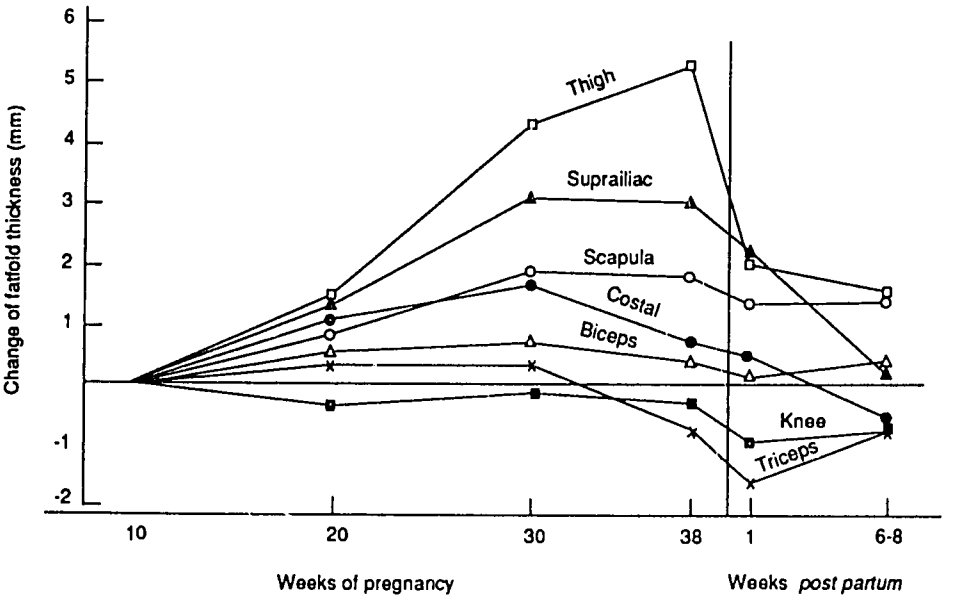

FIG. 3: Absolute changes (from initial measurement at 10 weeks) in fatfold thicknesses during and after pregnancy. (Adapted from Taggart, et al. (57), p. 444)

No study provides as much information on site-specific changes in fat during pregnancy as that of Taggart and coworkers (57). But, other studies have expanded our knowledge of the diversity of patterns of changes among populations and of relationships with levels of intake, season of the year, and activity patterns. In some cases, information is available across longer periods of time, including lactation and even through the subsequent pregnancy and lactation period. It appears that due to the varying nature of factors influencing body composition changes, there is great heterogeneity in patterns of fat deposition among populations (although comparisons are often made difficult because of variation in methods).

Arroyo and coworkers (64) compared patterns of change between the well-nourished Scottish women of Taggart's study and a sample of potentially under-nourished Mexican women. These investigators measured the same seven fatfold sites on 57 pregnant women at 24, 30 and 35 wk of gestation and divided the sample into two groups: overweight (n=26) and low weight (based on weight-for-height

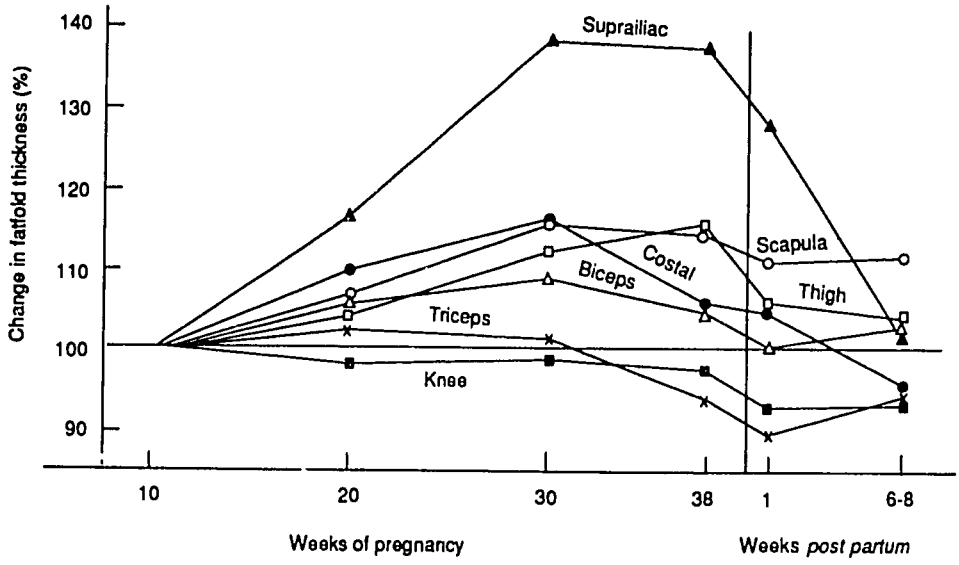

FIG. 4: Proportional changes (from initial measurement at 10 weeks) in fatfold thicknesses during and after pregnancy. (Adapted from Taggart et al. (57), p. 446.)

values at 24 weeks of gestation). Within both the overweight and the low weight groups they observed three additional subgroups of women: those who increased, those who decreased and those who showed no change in the sum of their fatfold measures between the 24th and the 35th week of gestation.

The average pattern of change of the sum of the seven fatfold measures for both of the weight groups is illustrated in Figure 5 with the corresponding

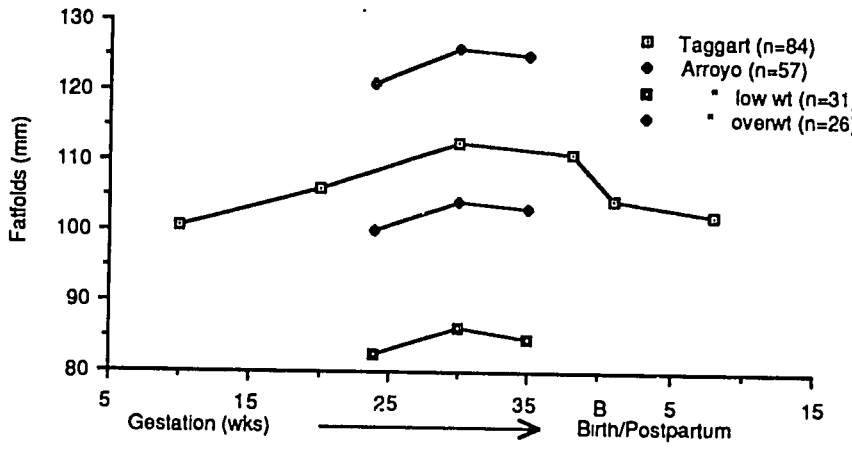

FIG. 5: Changes in total fatfold measures at 7 sites. (Data from Taggart et al. (57) and Arroyo et al. (64))

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measures from Taggart's study shown for comparison. In addition, using the data reported by Arroyo and coworkers, the average of the entire sample (n=57) has been calculated and plotted in Figure 5. Although Taggart's data are over a longer time span, the values fall between the overweight and the low weight groups and are surprisingly similar to those from the women in Arroyo's study.

Pipe et al. (55) and Dibblee and Graham (56) made estimates of fat and fatfree (lean body) mass for samples of women from the United States (n=27 and n=16, respectively). Both sets of investigators used the formulas developed by Durnin and Wormersley (54) to estimate total body fat of women (non-pregnant) based on four fatfold measures (triceps, biceps, subscapular and suprailiac). The ranges and magnitudes of change are surprisingly similar across the two studies (Figure 6).

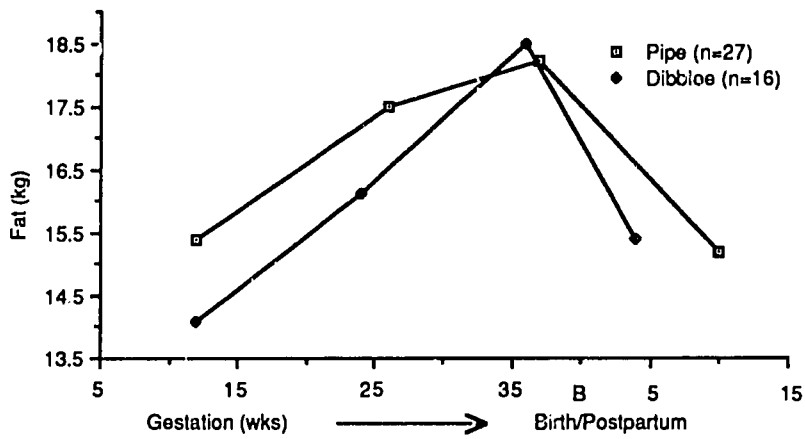

FIG. 6: Changes in total maternal fat mass during pregnancy. (Data from Pipe et al. (55) and Dibblee and Graham (56)).

Taggart and coworkers (57) report the measurements at each site, therefore it is possible to sum values for the four sites (used by Pipe) and to compare these to the data reported by Pipe and coworkers (55). As can be seen in Figure 7, the sums of the 4 fatfold measurements in the women in Taggart's study appear to be lower than the measures in Pipe's study but the pattern of change is similar in both studies.

Prentice and coworkers (45) and Adair and coworkers (7) investigated anthropometric changes over pregnancy and lactation in Gambian and Taiwanese samples, respectively. In the study conducted by Prentice and coworkers, patterns of change were clearly different between the two major Gambian seasons (the dry and the wet season), as shown in Figure 8. The wet season is characterized by low food availability and heavy physical work demands and hence the marked fat losses observed in women who were pregnant or breastfeeding during this season. The dry season is less demanding from a nutritional point of view and fat changes are positive for women who were pregnant or breastfeeding during this season. The investigators note that "the lactating women appeared to have a raised mobility of their fat stores compared with non-pregnant, non-lactating women" (greater fat deposition during the dry season and, greater fat utilization during the wet season). This result is very interesting and worthy of further study.

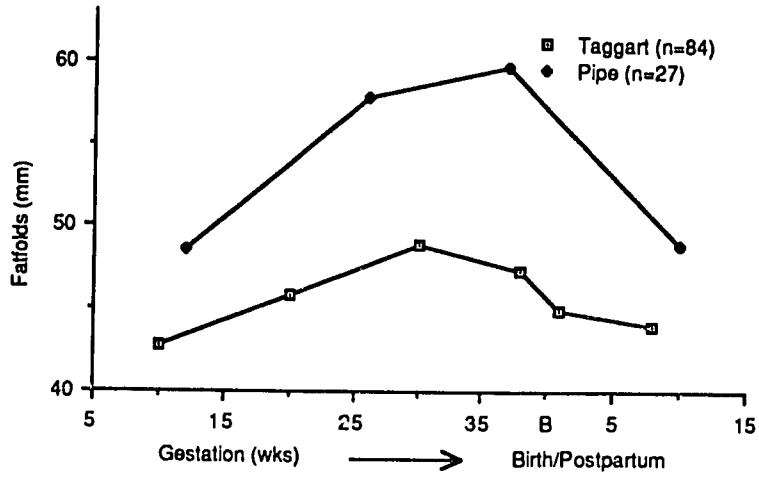

FIG. 7: Changes in total fatfold measures at 4 sites. (Data from Taggart et al. (57) and Pipe et al. (55)).

Adair and coworkers (7) used data from the Bacon Chow supplementation trial conducted in Taiwan to investigate maternal anthropometric changes during pregnancy and lactation. Although there were supplemented and unsupplemented women in the study sample, other analyses had demonstrated no significant difference in fatfolds between treatment groups (65), so the two groups were combined for this analysis. A unique feature of these data is that the final trimester of one pregnancy and the following lactation period as well as the complete subsequent pregnancy and lactation period were studied for each of the women. Longitudinal changes in maternal triceps and subscapular measures across pregnancy and lactation periods are shown in Figure 9. The pattern of change during pregnancy follows the general pattern (a gain during the first two trimesters followed by a loss during the third trimester) demonstrated by Taggart et al. (57) and Arroyo et al. (64).

Adair and coworkers were able to provide data for two successive lactation periods in the same women. Fatfold measures increased from birth to one month postpartum but decreased subsequently in lactation. Even though mean fatfold measures decreased over lactation, increases occurred in a substantial proportion (generally over half) of women. Individual women generally maintained the same pattern of fat change during the second postpartum period as they had during the first postpartum period. In addition, women who had gained more fat during pregnancy seemed to lose more fat during the postpartum period compared to women who had gained less fat during pregnancy.

The investigators divided the sample into net-gain and net-loss groups (based on fatfold changes) during the first twelve months of the first and second lactation periods (Figure 10). Dramatic increases in fatfold thicknesses occur immediately following birth; Adair and colleagues provide this explanation, "mothers no longer need to meet the metabolic demands of the placenta, early milk production is low and total energy intake is higher than in the third trimester of pregnancy. These factors, along with dramatic hormonal shifts could favor rapid fat deposition in the first postpartum month." A possible explanation for the greater intakes following birth is that the fetus and placenta cease to limit gastric capacity, allowing the mother to eat more.

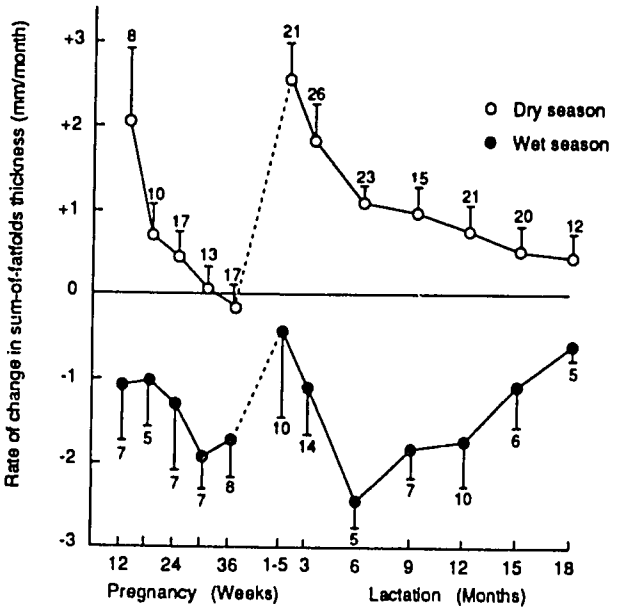

FIG. 8: Rate of change in sum-of-fatfold (triceps, subscapular, and suprailiac sites) of pregnant and lactating women. Values are means -+ SE, and no. of subjects. (Adapted from Prentice, A.M., et al. (45), p. 2795.)

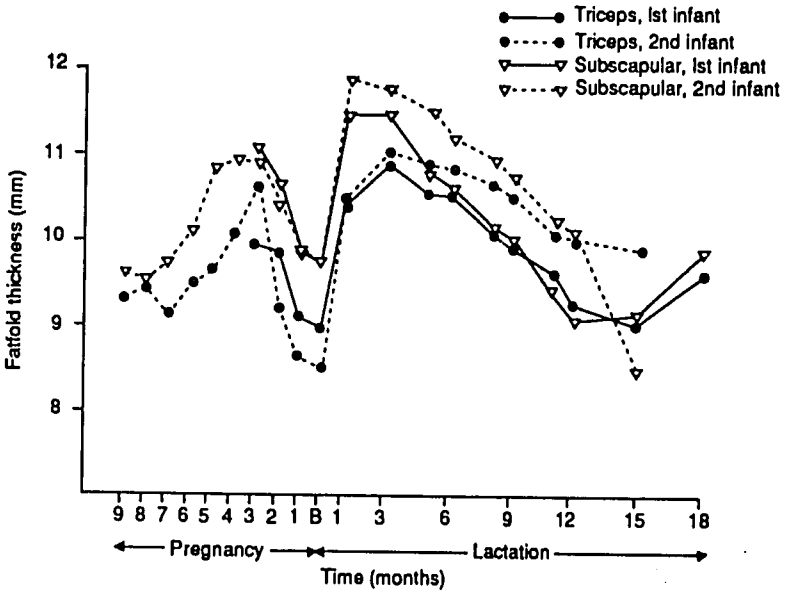

FIG. 9: Mean maternal triceps and subscapular fatfold thicknesses during pregnancy and lactation.
(Adapted from Adair,L.S., et al. (7), p. 777.)

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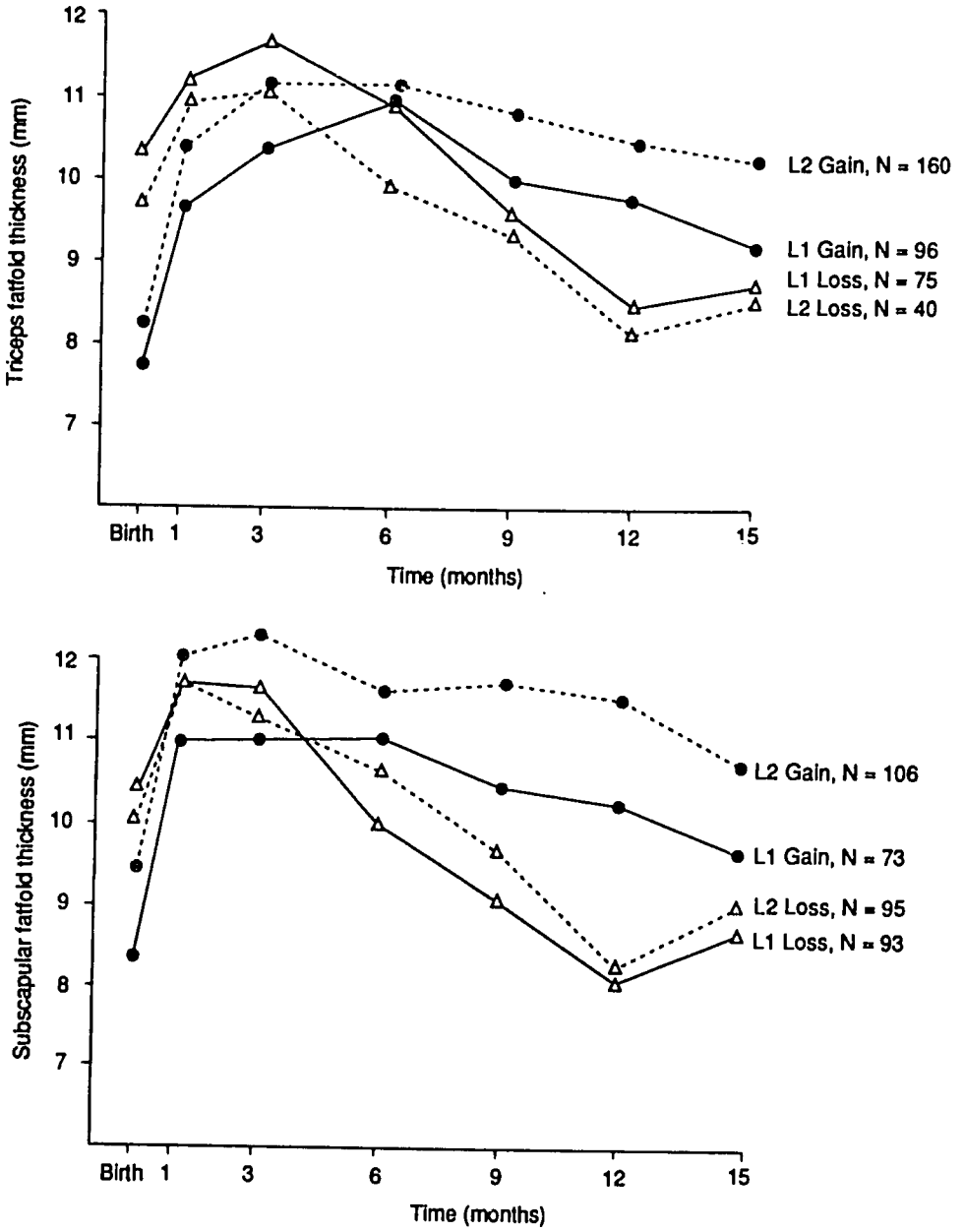

FIG. 10: Mean triceps (top) and subscapular (bottom) fatfold thicknesses in mothers who lost vs. gained fat during lactation. Shown for two consecutive lactation periods (L1 and L2). (Adapted from Adair et al. (7)).

An immediate postpartum increase in fat stores also seems to occur in Gambian women (45) during the dry season and even though fat is lost during the wet season, rates of loss are markedly reduced for the period immediately following birth (Figure 8). On the other hand, this phenomenon is not observed in several studies (57, 68, 69). Clearly, the early postpartum changes in fat deposition or mobilization require more-thorough investigation.

Quandt examined postpartum anthropometric changes in relation to feeding patterns and found that women who lost fat in the postpartum period breastfed their infants more frequently compared to women who gained fat during the postpartum period. She postulated that the increased prolactin levels caused by frequent suckling probably influences the activity of lipoprotein lipase in various tissues as has been seen in studies of pregnant rats (70). A measure of prolactin levels would be the first step in testing this hypothesis. In addition, it would be of interest to compare other components of energy balance between these two groups of women such as dietary intake, energy expenditure and the growth rates of the infants (controlling for the caloric intake from foods other than breast milk if they are not being exclusively breastfed).

It is clear from this survey of studies that there is tremendous variability in patterns of change of fat (energy stores) during pregnancy and lactation among women and yet there is surprising consistency in the general trends among studies. The functional significance (in terms of maternal health, pregnancy outcome and lactation performance) of the differing levels of maternal nutritional status must be identified.

PARITY, INTERVAL MEASURES AND REPRODUCTIVE CYCLING

Virtually all investigations of interest characterize reproductive stress using birth interval (or interpregnancy interval) and/or parity. Parity is used to indicate the number of pregnancies, but actually only captures information about the number of live births because miscarriages, abortions and stillbirths are not counted. Another problem with parity is that it does not provide information on the timing or spacing between births.

A single birth interval is not a satisfactory measure of reproductive cycling since it is only the time interval between two successive births and does not take into account the spacing of previous births. In previous studies, the focus of research is usually the child, and the variables of interest frequently are the previous or subsequent interval relative to the index child. However in this review, we are concerned with the mother and hence, each birth interval she experiences is relevant, especially when the investigation addresses her cumulative reproductive experience.

Other time interval measures combining various components of the reproductive cycle have been constructed in order to refine the information being characterized. For example, interpregnancy interval, the time span between the previous birth and the successive conception, has been used as a measure of the non-pregnant interval of the cycle. Another problem with interval measures is that the length of pregnancy is variable with consequences of its own on fetal growth and ultimately child health.

A shortcoming of both parity and intervals as measures of the "energetic challenges" of reproductive cycling is that lactation is disregarded. In actuality, full breastfeeding on demand has a higher energetic cost than pregnancy (18). The use of birth or interpregnancy interval as a measure of the duration of a replenishment period for the mother contains the implicit assumption that lactation behavior has either no effect or a beneficial effect on nutritional status. Parity as a gross measure of reproductive stress also can be misleading because lengthy lactation periods between births may (depending on the amount of milk produced) have a more depleting effect on nutritional status than frequent pregnancies. If replenishment is the crucial factor, then the lactation behavior of the mother during birth intervals must be taken into account.

There is great variation and complexity in the reproductive patterns (number of births, spacing, and the length and intensity of each lactation period) between women. A woman can be viewed as potentially cycling through four states (Figure 11): 1) initially, neither pregnant nor lactating (N), 2) a woman may become pregnant, 3) at the end of pregnancy, a woman may begin lactation (L) or not (N) and 4) a woman may become pregnant again while breastfeeding the previous child (L_1 + P_2), or may wean the child and return to the non-pregnant/non-lactating state (N).

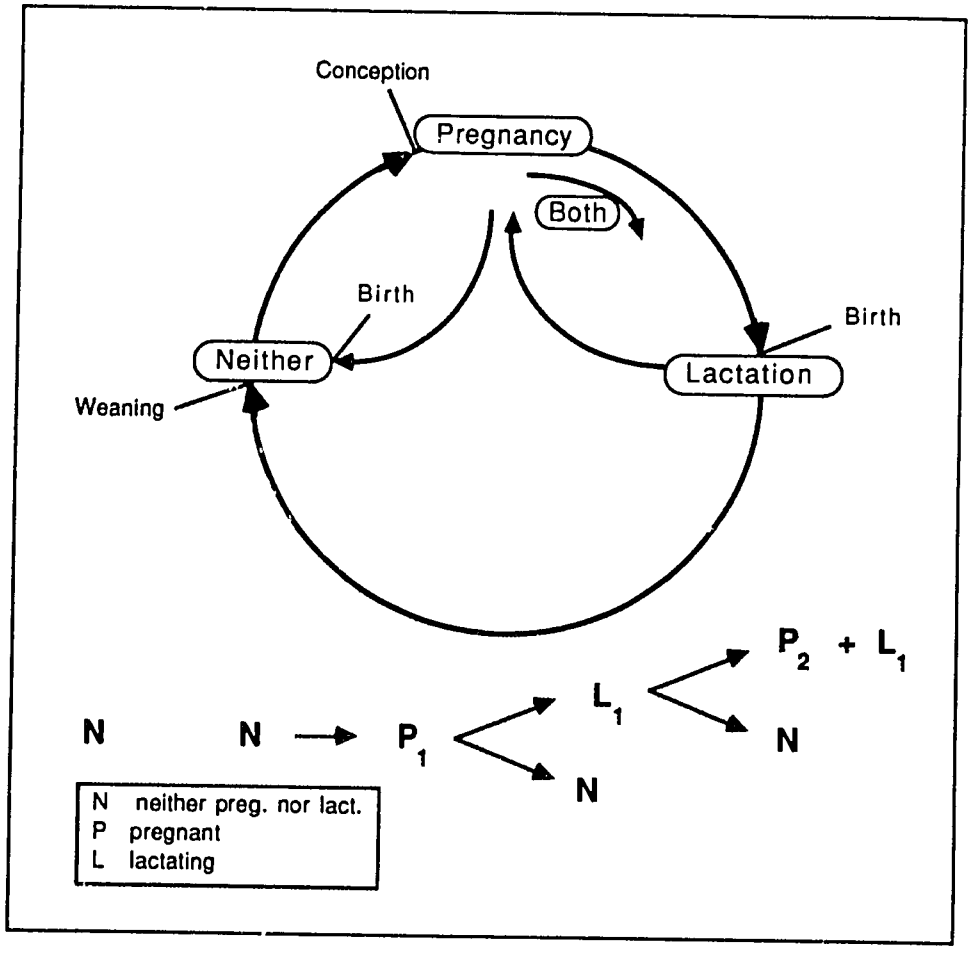

FIG. 11: Reproductive Cycling

REPRODUCTIVE CYCLING AND NUTRITIONAL DEPLETION

The evidence that nutritional depletion of mothers occurs from frequent reproductive cycling within short intervals of time will be addressed in this section.

The assertion that continual reproductive cycling depletes a mother nutritionally, even under conditions of poverty in developing countries, is being challenged by several investigators (9-11, 71). These authors have called attention to the fact that very little evidence exists in the published literature either for or against the existence of these deleterious effects.

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Jelliffe and Maddocks (8) are credited with advancing the "maternal depletion syndrome" hypothesis. They postulated that a state of impairment results "from the increasing and cumulative nutritional stresses of successive pregnancies and lactation." This was based on observations of the harsh lifestyle and very poor physical condition of women living in a remote mountainous region of New Guinea

The term "maternal depletion" has been quite popular since its introduction. It is frequently used (particularly in the demographic literature but also in the nutrition literature) both as a descriptor of the consequences of frequent childbearing under difficult living conditions and as an explanation for other relationships. For example, short birth intervals have been associated with increased child mortality in several populations (72-76) and maternal nutritional depletion has been postulated as a possible mechanism. Maternal depletion could operate to decrease nutrient availability to the fetus (thereby leading to low birthweight and increased risk of death) or it could reduce nutrient availability for milk production. Also, poor maternal nutritional status could restrict maternal activity and affect adversely the quality of child care.

Not only infant mortality, but also low birthweight, poor infant and child growth and increased morbidity are in some cases attributed to the effects of nutritional depletion of mothers (1). These adverse conditions are more-commonly investigated than the malnutrition of women, which is the direct effect of the state of depletion. (Figure 1.)

Given the frequent use of the concept of the nutritional depletion of women due to the stress of reproduction and lactation, it is important first to review the existing evidence carefully, to develop the concept further and finally to test it more thoroughly.

Thirty years of investigations provide information regarding reproductive cycling and maternal nutritional depletion. In 1958, Gopalan (77) published a report of a series of studies on lactation in poor Indian communities. In the first two studies of this series, it was determined that lactational performance was fairly satisfactory as evidenced by breast milk output and resulting infant growth at various stages of lactation. But given the low protein intake of these women and the adequate protein content of the milk, Gopalan postulated that "if the needed protein is not forthcoming from the diet, the maternal tissues are raided to meet the protein requirement." To investigate this possibility, he studied the nitrogen balance of 6 of the women over the final 3 days of consuming a protein supplement for a total of 10 days. Gopalan reported "that nitrogen retention increased as protein intake was raised. This might not be a specific attribute of the lactating state but could be the result of relative tissue-protein depletion of the subjects investigated."

Initially the most common method for assessing the nutritional status of women was the observation of the prevalence of clinical signs of malnutrition in women and their relationship to reproductive histories and/or performance (1, 8, 78, 79)). Jelliffe and Maddocks gave a fairly general and descriptive account of what they observed and learned from other investigators during a visit to the New Guinea Highlands. Using an ecological framework, they linked the severe living conditions and demanding reproductive histories to the very poor nutritional status and physical condition of these women and provided the first description of the maternal depletion syndrome.

A technical group was convened to consider critically the different aspects of maternal nutrition and its relationship to patterns of reproduction (1). After reviewing data available (such as "the incidence of three signs related to malnutrition in seven Latin American and Caribbean countries, in relatively small samples of pregnant, lactating and other women"); they concluded that "facial

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lesions may be more common in pregnant and lactating women. Similarly, the incidence of thyroid enlargement appears to increase during pregnancy."

On the other hand, Rajalakshmi (78) concluded that "the clinical status of the subjects was no different at 6 months of lactation and two years after its cessation without an intervening pregnancy." In addition he reported that "the bone status of women as judged by cortical thickness and width of the second metacarpal bone as well as femur also did not seem to be affected by lactation performance although there was a distinct difference between poor and upper class women." Other investigators have had a similar lack of evidence of depletion through bone demineralization (80-84).

In another study of the nutritional status of women from rural India, 501 subjects were randomly sampled from a group of similar villages (79). A clinical assessment of nutritional status was made based on an examination focusing on 13 signs of malnutrition. A relatively sophisticated conceptual model was proposed and tested. Multivariate techniques were used to analyze the effects of socio-economic status, family structure, demographic characteristics, subcultural norms of food consumption habits, and fertility behavior. Fertility behavior, measured by total number of pregnancies, explained 10% of the variation in nutritional status. In addition, "it was seen that nutritional deficiency was higher among older women than among younger women. In each of the age categories, the higher the parity was, the higher was the nutritional deficiency."

The most common simple method to examine a study sample of women for evidence of maternal depletion has been to test for an association between the body weight of the women and the number of live births (parity) they have had. Some investigators have observed a significant negative relationship between these two characteristics (3, 85) and others have not (45, 78, 86).

When a relationship is found between maternal body weight and parity, the question can be raised --is this in actuality a relationship between body weight and maternal age? In the study reported by Rizvi (85) two parity groups were contrasted, those with parity less than or equal to 2 and those with parity greater than or equal to 3. It would be useful to compare the age distribution between these two groups. Chowdhury (3) demonstrates a negative relationship between parity and maternal weight within two age groups of women, those younger than thirty and those thirty and older.

In investigations where evidence for a simple relationship between parity and maternal body weight has not been found, questions regarding appropriateness of measures, sample sizes and the assumption of a linear relationship between the two have been raised. The issue of appropriateness of measures has been addressed in previous sections. Regarding sample size, in the case of Rajalakshmi's investigation (78) the sample size is relatively large (829 women of low socioeconomic status and 81 women of upper socio-economic status), although the Gambian sample (45) was smaller (143 women total, approx. 10 women per parity group).

Parity may not show a simple linear relationship with maternal weight. Some investigators have suggested that if a women's nutritional status deteriorates, her fecundity is reduced, resulting in a lower parity. Therefore a subgroup of women with lower parities may be of poorer nutritional status. This could have the effect of reducing the overall mean and increasing variation at lower parities. As discussed previously, parity is a poor measure of reproductive cycling and may not be complex enough to capture subtleties such as these. Alternatively, it may be that the inconsistency in reports of a negative relationship between parity and maternal body weight represents true differences between the sample groups.

Although Chowdhury (3) concluded that there were long-term negative effects of reproductive cycling on nutritional status (a negative relationship between maternal weight and parity). This study did not contain clear evidence of nutritional stress during the first year of lactation when triceps fatfold measures and maternal body weights were measured monthly.

Another method of investigating short-term effects has been to examine the relationship between maternal nutritional status at one birth and the duration of the previous birth interval. This method treats the time following birth as a time of replenishment (regardless of lactation status). In a Taiwanese (7) and in a Bolivian (87) sample a significant positive relationship has been observed between birth interval and the maternal measures of fat taken at the birth which closes the interval.

Although the concept of maternal nutritional depletion originated in the field of public health and nutrition, it has been most carefully investigated in recent years by demographers. The two most recent, thorough conceptualizations and systematic investigations for evidence of maternal depletion have been conducted by Costello (71) within a sample of Ugandan women and by Pebley and DaVanzo (88) within a sample of Guatemalan women. In both cases, these investigators postulated that maternal depletion may partially explain poor child health and/or survival.

Costello (71) used data from the 1970 Ugandan Demographic Research Project. The sample was composed of rural Ugandan women from two different regions (Ankole, n=228 and Teso, n=173). Information was collected from a household survey, a series of fertility histories, and medical exams conducted on a sub-sample of women. The medical exams provided some anthropometric measures and hemoglobin levels. In the initial analyses, the relationships of parity and age to the ponderal index (wt/ht^3), triceps fatfold, mid-upper arm muscle circumference and hemoglobin were examined in each of the two districts.

Within broad age-groupings (15-29, 30-44, and 45-59 years), a U-shaped relationship between parity and some of the measures of nutritional status was seen but the results were inconsistent between districts, age groups and measures of nutritional status. Costello suggested that this U-shaped relationship could be interpreted as evidence of the selectivity of higher parities for women of better health until a point where increased parity becomes a liability. For example, the women past reproductive age (46-60) of Ankole, "the healthiest group tends to be those of parity 4 to 6, the least healthy of parity 1 to 3".

Costello concluded the results of the initial analyses with the following statement, "overall, from these results there is little support for the simple hypothesis that nutritional status deteriorates with increasing parity, or that cumulative maternal depletion occurs in these populations. The frequent observance of U-shaped patterns in both districts indicates that there may be other influential factors intervening in the relationship that are not controlled by this type of analysis."

Next Costello conceptualized a multivariate model of maternal depletion. She improved the measure of reproductive cycling by dividing the reproductive years into periods of pregnancy, lactation and "a resting state" (when the woman is not pregnant or lactating), reasoning that the nutritional stress of reproduction is absent during this period. A weakness of her conceptualization is the assumption that pregnancy and lactation are mutually exclusive when it is known that these two states can and do occur simultaneously, particularly in populations where depletion is likely to occur. She measured the short-term component of reproductive cycling as "the time elapsed since last leaving a depletion state, or the current presence in that state."

The multivariate analyses "reveal that there are significant factors related to maternal nutritional status in these rural populations, but cumulative depletion due to extensive periods of pregnancy and lactation is not of major importance. There is no predominant long-term depletion effect associated with the parity-related measure of pregnancy months evident in most cases, nor with the spacing effect of the pregnancy proportion, nor with the lactation variables. However, the short-term depletion status variables do show some significant association with a deterioration of nutritional status."

Short-term nutritional depletion of mothers is one of the main postulated explanations for the observed relationship between short birth spacing and increased child morbidity and mortality. Previously, birth interval has been the major measure used to demonstrate the presence of short-term depletion. Pebley and DaVanzo (88) refined the approach to investigations of short-term maternal depletion by considering the role of lactation in the birth interval. In addition to the interpregnancy interval, two "recuperative" intervals were defined, the "non-breastfeeding" and the "non-full breastfeeding" recuperative intervals.

Using data from the longitudinal supplementation trial conducted by INCAP in four Guatemalan communities, they examined the relationship between the intervals described above (and illustrated in Figure 12) and indices of maternal nutritional status (weight at time of conception and maternal weight gain during pregnancy) as well as two pregnancy outcome indicators, birthweight and length of gestation.

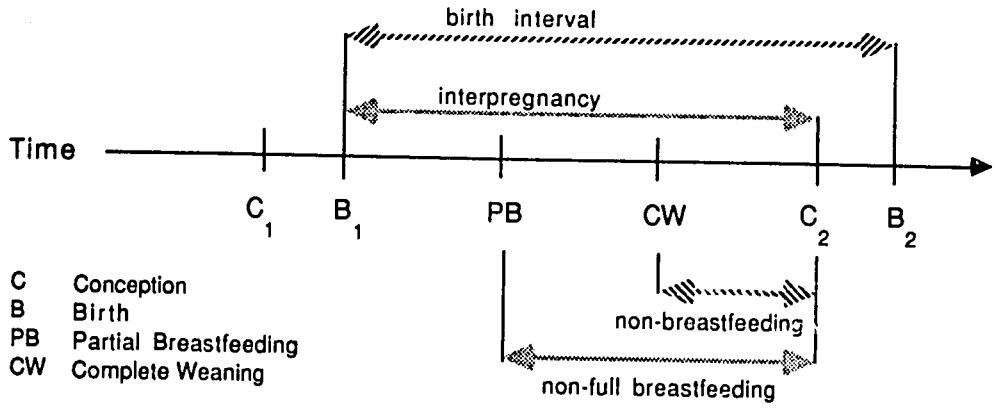

FIG. 12: Recuperative Intervals

Their investigation "suggests that only weight gain during pregnancy is affected by the length of the previous pregnancy interval." Contrary to their expectations, they found "that women with shorter previous intervals tend to weigh more at conception, to gain less weight during pregnancy, and to have babies who weigh the same as women with longer previous intervals." In addition, they found "that women with shorter previous intervals have longer lengths of gestation, as do women with shorter recuperative intervals."

Pebley and DaVanzo (88) suggest that these results may indicate that a selection for healthier women is occurring in the process of becoming pregnant. "In other words, women who are better off nutritionally or in better health may both become pregnant more quickly and are more able to bring the pregnancy to term than women in poorer nutritional status or health." In an attempt to further clarify the relationship between postpartum maternal weight changes and

lactation status, the investigators find "strong evidence of an important role of the duration of full breastfeeding in determining a woman's weight." They further conclude that this evidence "suggests full breastfeeding may be an important factor bringing about depletion (or preventing repletion) of maternal nutritional resources during the interpregnancy interval."

It is crucial to determine when the next conception occurs in relation to weaning or the nadir of weight change. Generally there is a pattern of maternal weight loss following birth as was shown previously. This is illustrated in Figure 13. If two women (woman 1 and woman 2 in Figure 13) are following a normal course of weight loss following birth and during lactation, it is not surprising that the weight at conception would be higher when the interval following the previous birth is shorter (see Figure 13, $Wt_1 > Wt_2$). If a woman (woman 3 in Figure 13) has stopped breastfeeding and has started to replenish her nutritional stores and gain weight, it is still possible that at the time of the next conception her weight is not yet higher than a woman (woman 1 in Figure 13) who is breastfeeding and has a shorter interpregnancy interval (see Figure 13, $Wt_1 = Wt_3$). (For the sake of illustration the example is very simple and only one curve of weight change is shown and all three hypothetical women fall at some point on this curve. Initial nutritional status could be expected to influence the position and shape of this curve, for example, under-nourished women may begin and end at a lower weight relative to well-nourished women.)

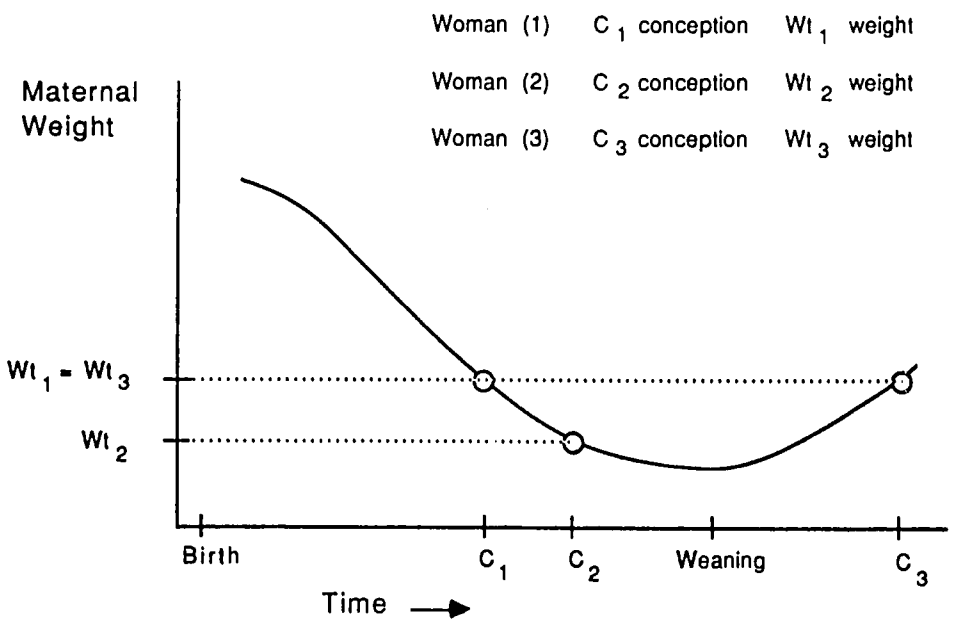

FIG. 13: Hypothetical example of pre-conception measures of 3 women

The potential for bidirectional causality between maternal nutritional status and 1) the likelihood of conception and 2) the duration of lactation, as well as the tremendous variation in patterns of weight and fat change make it clear that the relationships are complex and require a careful consideration of the time sequence of events. Therefore, conceptualizations must not be simplistic (for example, direct parity-to-maternal weight relationships) and conclusions drawn from them must not be accepted without further study.

The description of reproductive cycling and the relative costs have not been adequate, although progress in this area is being made. There is a need to distinguish short-term and long-term depletion within investigations and discussions of maternal nutritional depletion and to clarify the expected outcomes. Whereas nutritional depletion originally meant visible or clinical signs of ill-health, premature aging or malnutrition, later it was measured by maternal weight or changes in maternal weight. Measures of changes in maternal fat stores have not been used in the study of this topic but should be. In spite of these severe weaknesses of the current literature, it is still possible to conclude that there is some indication that under some conditions the nutritional demands of reproductive cycling negatively affect maternal nutritional status.

SUMMARY AND RESEARCH NEEDS

The relationship between maternal nutritional intake and the health outcome for the child, particularly birthweight, growth and mortality has been explored extensively (through the major nutritional supplementation trials as well as other investigations). It generally is postulated or assumed that a mother's nutritional status is the biological link between the positive impact of increased dietary intake (nutritional supplementation) of the mother or the negative impact of short birth intervals on various child outcomes such as birthweight or child mortality. But maternal nutritional status is rarely treated as an important outcome in and of itself.

> Because women are seen mainly as vehicles for child health rather than as primary health care beneficiaries in their own right, long term effects on women's health have been ignored. ... Not only are maternal/child health (MCH) resources limited, when MCH does research the puerperium, it addresses outcomes for the fetus, not for the mother. As an illustration of this bias, an extensive review of MCH literature found that out of 22,080 articles, only four percent dealt with maternal health issues. (Howard (89))

This biased emphasis alone could be considered a major weakness in the literature, and more importantly, in health services and nutritional planning programs that affect women, but in addition, attempts rarely are made to establish that the actual effects of increased dietary intake and short birth intervals truly are operating through the postulated pathway of improving or impairing maternal nutritional status.

The neglect on the part of the scientific community is not due entirely to oversight, it is partially a reflection of the difficulty of measuring maternal nutritional status (and particularly during changing physiological states such as pregnancy and lactation) versus the relative ease of measuring birthweight or child mortality. A more compelling and important reason for this biased emphasis is the recognition that the early years of life are a period of particular susceptibility to those factors threatening survival. Clearly, the well-being of mother and child are linked and the relevant research issues are interrelated.

Investigators now should begin to take a broader view of adverse outcomes that may result from maternal depletion besides low birthweight and child mortality. There are more immediate adverse outcomes such as poor maternal nutritional status and morbidity. In the general conceptual model presented in Figure 1, maternal nutritional status is the central and primary outcome of sources of nutritional stress such as frequent reproductive cycling, morbidity, high activity patterns and low dietary intakes. In this conceptualization the adverse consequences to the child are outcomes secondary to the maternal nutritional status.

This review has examined evidence regarding the existence of maternal nutritional depletion by considering 1) the energetic cost of pregnancy and lactation and various explanations for how this cost is met; 2) the issues of measurement of both reproductive cycling and maternal nutritional status; 3) the various patterns of change in anthropometric measures and estimation of body fat during pregnancy and the postpartum period, and finally 4) by examining the conceptualization and evidence of the more direct attempts to establish the presence or absence of maternal nutritional depletion.

It is concluded that:

- The characterization of reproductive cycling (and its corresponding demand) using parity and time intervals between pregnancies or births is too simplistic. These measures miss the great variation and complexity of reproductive cycling (particularly because neither considers the lactation behavior of the mother). The most promising improvements that have been introduced recently are the use of proportions of time spent pregnant or lactating within a specified period of time, and the definition of recuperative intervals based on lactation status.

- Not enough effort has been devoted to the characterization of maternal nutritional status during pregnancy and lactation. The physiological alterations of water balance and tissue hydration during pregnancy and the early postpartum period as well as the presence of feto-placental tissue during pregnancy create the most difficult technical problems. Weight is the least useful and fatfold thicknesses and limb circumferences are the most useful measurements for characterizing maternal nutritional status during pregnancy. Reference data for these measures are needed for pregnancy, the postpartum period and various stages of lactation in healthy populations living in a variety of contexts.

- The patterns of change in fatfold thicknesses are highly variable. In attempting to characterize anthropometric changes during pregnancy and lactation it is crucial to distinguish various patterns and to identify maternal and environmental characteristics associated with the different patterns. Some data indicate that a large increase in fatfold measures occurs during the early postpartum period in some populations; this should be examined further. Some data indicate an increased mobility of fat stores of lactating women relative to non-pregnant, non-lactating women, another result worthy of further investigation. In addition, prepregnant measures rarely have been obtained. A greater effort should be made to extend the time frame of measurement (to collect more measures before conception and following birth).

- Information on the relative energetic demand imposed by pregnancy, lactation, both and neither will provide a more accurate picture of the nutritional stress imposed by reproductive cycling. Estimating the energetic costs of pregnancy and lactation has been a topic of interest for many, although success has been limited. Recent evidence suggests that the estimated cost has been inflated (although it is not clear which components have been overestimated).

Fat gain and resting or basal metabolic rate are the two largest components of the energetic cost of pregnancy; there is some evidence that both have been overestimated in the past. The average fat gain in healthy women originally estimated to be 4 kg may be closer to 2.5 kg. With respect to the basal or resting metabolic rate, some unexpected trends (reductions) during pregnancy have been observed (particularly in the Gambian population) and are worthy of further investigation to determine the range of adjustment that is common and under what circumstances the adjustments occur. Further understanding of the hormonal influences on energy balance and the metabolic changes during periods of pregnancy and lactation is needed.

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Data regarding fat changes and metabolic rates during lactation are particularly lacking. It is crucial for the determination of the energetic cost of lactation, that the fat gain during the corresponding pregnancy be well characterized because it is expected that these additional fat stores are accumulated during pregnancy in order to offset the energetic cost of lactation (reducing the amount of energy required from the diet during lactation). The contribution of physical activity to the energy balance equation has been virtually impossible to measure, but new methods using doubly-labelled water may change this situation.

The cumulative effect on the mother of multiple pregnancies and lactations within short periods of time has not been examined adequately. The short-term effect of pregnancy and/or lactation on maternal nutritional status has not been clarified adequately, either. The evidence reviewed here clearly demonstrates that the relationships of cumulative maternal nutritional depletion due to the high demands of reproductive cycling are too complex to be established merely by a relationship (or lack thereof) between parity and maternal weight. Longitudinal anthropometric measures and information on lactation status (in addition to birth and pregnancy intervals) should be used. Patterns of anthropometric change must be examined in relation to the changing reproductive status (physiological states) of the women.

A thorough investigation of the effect of reproductive cycling on maternal nutritional status therefore should include: longitudinal maternal anthropometric measurements during pregnancy, lactation and intervening periods across successive reproductive cycles; information on maternal dietary intake and work patterns; infant growth measures; and functional outcomes (such as incidence of morbidity and mortality) of maternal health status. This is a demanding list of requirements for a single investigation, particularly for the time span over which the information is desired (although specific areas of the research agenda can be addressed separately).

Thorough study of the topics reviewed can call attention to the unique health and nutrition problems of women, more specifically it can help a) define what are appropriate "repletion" periods between births and lactation periods, b) identify when in the cycle it is most appropriate to intervene nutritionally, c) identify mothers at risk who require special attention in primary health care and public health programs and d) formulate reasonable recommendations for weight gain during pregnancy, and for levels of dietary intake and physical activity during pregnancy and lactation.

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MATERNAL AND FETAL RESPONSES TO THE STRESS OF LACTATION CONCURRENT WITH PREGNANCY AND OF RECUPERATIVE INTERVALS

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Running Head: Lactation Concurrent with Pregnancy

ABSTRACT

In many regions of the world, women breastfeed one child while pregnant with the next. Among rural Guatemalan women participating in a nutritional supplementation trial, lactation overlapped with pregnancy in 50.2% (253/504) of the pregnancies. For cases where overlap occurred, 41.4% continued to breastfeed into the second trimester, and 3.2%, in the third trimester.

The maternal and fetal responses to the energetic stresses of the presence of overlap and of the duration of the recuperative (non-pregnant/non-lactating) interval were assessed. Overlap resulted in increased supplement intake. Short recuperative periods (< 6 months) resulted in increased supplement intake and reduced maternal fat stores. The energetic stresses of overlap and short recuperative periods did not significantly affect fetal growth. The mother appears to buffer the energetic stress, protecting fetal growth. This research demonstrates that evidence of maternal nutritional depletion due to a demanding reproductive history is found when reproductive stress is characterized adequately.

KEY WORDS: Maternal Depletion, Pregnancy, Lactation, Birth Spacing, Supplementation, Infant Feeding, Birthweight, Maternal Anthropometry, Maternal Nutrition

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INTRODUCTION

Lactation and pregnancy generally are studied as separate phenomena. To an extent, these physiological states are incompatible because of antagonistic effects produced by their corresponding hormonal controls. For example, the steroids of pregnancy inhibit the onset of lactation (1); breastfeeding in turn delays cyclic ovarian activity through poorly-understood hormonal mechanisms (2). But, pregnancy and lactation can --and do-- overlap. Lactation is not prevented by pregnancy if it has been established before conception.

In traditional societies with long durations of lactation, conceptions will occur in spite of breastfeeding. This is not to negate the fact that breastfeeding generally prolongs the period of postpartum amenorrhea. Ovulation may be delayed for many months but eventually it will reappear among women who breastfeed, generally after the introduction of other foods to the infant's diet. Therefore, in societies where the use of artificial contraceptives is rare, many women will become pregnant while breastfeeding unless there are strong taboos against sexual intercourse during the period of lactation.

Behavioral studies in the Third World indicate that pregnancy is cited frequently as a reason for weaning (3). The belief is widespread that pregnancy and lactation are incompatible states. For example, breast milk sometimes is viewed as harmful to the fetus; conversely, pregnancy sometimes is thought to spoil or damage the milk. The fetus, the toddler, or even the mother may be viewed as being at risk if pregnancy and lactation overlap. But, overlap is probably common because many women may not realize they are pregnant for several months after conception. Also, not all women may choose to wean their children upon discovering they are pregnant.

Surprisingly, little is known about the frequency and extent to which pregnancy and lactation overlap. Where information is available however, indications are that overlap is a common occurrence. A study of breastfeeding practices in Central Java found that 40% of the mothers who weaned their children were known to be pregnant (4). In Senegal, 30% of the study sample who

were breastfeeding became pregnant. A substantial proportion of these women continued to breastfeed a previous child: 62% were breastfeeding at 3 months, 19% at 6 months, and over 4% breastfed into the ninth month of pregnancy and even beyond (5). Using cross-sectional data from Bangladesh, it was estimated that 12% of the women who were pregnant at the time of one survey also were breastfeeding a previous child. The cumulative probability of lactation during pregnancy was calculated using data from several successive surveys in the same study. These calculations indicate that among women who were pregnant and breastfeeding a previous child, 45% continued breastfeeding through the sixth month of pregnancy and nearly 20% were breastfeeding at the beginning of the ninth month (6).

Lactation and pregnancy are each very energetically-demanding processes. Therefore, when these two physiological states occur simultaneously, the risk of nutritional depletion of the mother or growth retardation of the fetus might increase, particularly among women with limited access to food. There is also the possibility that the breastfed child will be harmed if breastfeeding patterns are altered or if milk volume is reduced. No one, to our knowledge, has assessed the nutritional implications of the overlap of pregnancy and lactation for the mother, the fetus, or the breastfeeding child.

A longer non-pregnant/non-lactating interval before conception could permit nutritional recuperation of the mother and lead to improved maternal status and fetal outcomes (7,8). A condition of overlapping lactation with pregnancy is more likely to occur and less recuperation is possible when birth spacing is close. Therefore, it is important to isolate the effects of the higher energetic demands of overlap per se from those resulting from short recuperation intervals when identifying causes of maternal nutritional depletion.

Using longitudinal data from a nutritional supplementation trial conducted in four rural communities of Guatemala, this investigation examines the phenomena of lactation concurrent with pregnancy and of recuperative intervals, and assesses their nutritional implications for mother and

fetus. Specifically, the following questions are addressed: To what extent does lactation during pregnancy occur in rural Guatemala? Do mothers consume more supplement when overlap occurs? Are maternal fat stores affected by overlap? Is fetal growth reduced when overlap occurs? Finally, for those women who do not lactate while pregnant, does the recuperative interval –non-pregnant/non-lactating interval–affect supplement intake, maternal fat stores and/or fetal growth?

METHODS

Data

This investigation uses data from a nutritional supplementation trial conducted by the Instituto de Nutrición de Centroamérica y Panamá (INCAP) in four rural communities in the Guatemalan department of El Progreso. The period of the health and nutrition intervention was 1969 through 1977. Two communities each were assigned randomly to receive either a high-protein (11 g/180 ml), high-energy (163 kcal/180 ml) supplement called "atole" or a low-energy (59 kcal/180 ml), no-protein supplement called "fresco".

The supplements were free and available twice-daily to all inhabitants at centrally-located feeding centers in each community. A cup (180 ml) was offered initially; more was provided if requested. Leftovers were measured and actual amounts consumed were recorded for pregnant and lactating women as well as for children up to the age of seven years. Twenty-four hour dietary recall surveys were used at 3-month intervals to measure the home dietary intakes of the women.

A health center was set up in each village to provide free primary health care to all community members. Anthropometric examinations were scheduled at three-month intervals during pregnancy and the first 24 months of lactation from 1971 to 1977. All measures were made by the same individual. Birthweight was measured within 24 hours after delivery. Duration of lactation was determined through maternal recall for all children 7 years or younger at the beginning of the study period (1/69) and prospectively during home visits occurring bimonthly for all those born within the study period. Pregnancies were identified as early as possible (also during home visits).

Gestational age was calculated as the difference between the date of birth and the date of onset of the last menstrual period. The date of conception was estimated by first subtracting two weeks from the gestational age as calculated above, and then subtracting this value from the date of birth. Several surveys were conducted during the intervention period to assess the socioeconomic status of all households. A more-detailed description of the specific data collected and methods used is given by Lechtig et al. (9) and Delgado et al. (10).

Sample Selection

A total of 1529 births were recorded in the 4 study villages during the study period (1969-1977). Of these, 504 births were selected for study in this investigation (Figure 1). The study sample was selected for the following characteristics: term, singleton pregnancies of mothers with a previous child with a known birthdate and lactation duration. Data for previous siblings were only available for children seven years or younger. Birth date and lactation duration for the previous child were required to establish unequivocally whether or not overlap in pregnancy and lactation had occurred. Pre- and post-mature births were excluded on the grounds that these were either truly special subpopulations or cases with errors in the measurement of gestational age. Some women (48%) contributed more than one pregnancy to the study sample.

The selected study sample (n=504) was comparable to the total sample (n=1529) for the following general characteristics, lactation duration of the previous child (C_{n-1}), birth interval, mother's height and head circumference, father's height and head circumference, distance from home to supplementation center, average energy intake from the home diet, proportion receiving each supplement type (fresco or atole) and proportion of male and female newborns. Of those examined, three characteristics differed between the selected study sample and the total sample. The mean maternal age, gestational age and lactation duration of the current child (C_n) were higher in the selected subsample by 2 years, 1/2 week and 1 month, respectively. All mothers of the selected study sample were multiparous, therefore the age difference would be expected. The

minimum maternal age for the total sample was 12.7 years and the selected study sample 16.1 years. The restriction of the study sample to term births is the likely explanation for the slightly longer mean length of gestation; the minimum gestational age recorded for the total sample was 25 weeks and for the selected study sample was 37 weeks.

Analytic Approach

Classification - Pregnancies were divided into two groups based on time of weaning of the previous child (C_{n-1}) relative to the conception of the index child (C_n). Group A (no overlap) was made up of cases in which C_{n-1} was weaned before 2 weeks following the date of conception of C_n and Group B (overlap) was composed of cases in which C_{n-1} was weaned after 2 weeks following the date of conception of C_n. A conservative definition of overlap (> 2 weeks) was used to minimize the possibility of misclassification of those who did not overlap in the overlap group.

Differences between group A and B in maternal and fetal outcomes (the central contrast in this study) cannot be attributed solely to the higher nutritional demands of concurrent lactation and pregnancy versus only pregnancy. The overlap group also has a shorter mean birth interval than the no-overlap group (as would be expected). In an effort to separate the effects of overlap from short recuperative intervals, the main groups were subdivided (Figure 2). Group A (no overlap) was divided into: Subgroup A1 - cases where C_{n-1} was weaned more than 6 months prior to the conception of C_n and Subgroup A2 - cases where C_{n-1} was weaned within the 6 months before the date of conception of C_n. Group B (overlap) was divided into cases where C_{n-1} was weaned during the first trimester of pregnancy (Subgroup B3) or during the second (104 cases) or third (8 cases) trimester (Subgroup B4) of pregnancy.

Contrasts of Interest - The contrast between subgroups A1 (no overlap, long recuperation) and A2 (no overlap, short recuperation) allow for an estimation of the unique effect of short recuperation intervals on maternal and fetal outcomes. On the other hand, the contrast between subgroup A2 (no overlap, short recuperation) and group B (overlap) estimates the unique effect of

overlap. Within group B, the contrast between subgroup B3 (short overlap) and subgroup B4 (long overlap) is made to explore the implications of duration of overlap on maternal and fetal outcomes. The net effect of close birth spacing, whether due to recuperation or overlap is estimated by contrasting the long recuperation - subgroup A1 with the other three subgroups (A2 - short recuperation, B3 and B4 - no recuperation).

Outcome Variables - Although ideally maternal dietary intake should be based on home dietary intake plus supplement intake, supplement intake has been chosen as the preferred maternal intake variable in this study. The precision and accuracy of these data are much higher and the completeness of these data is greater than that of the home dietary data (which were measured by 24-hour recall). The original daily maternal supplement intake data have been summarized by trimester of pregnancy and data are available only for average intake across each trimester in the INCAP data tapes. This poses some limitations (as will be discussed later) for the analytic approach. Maternal fat stores were assessed using the thigh fatfold (an average of the medial thigh and the lateral thigh measures). Of the seven fatfold sites –triceps, biceps, subscapular, suprailiac, knee, thigh and calf– Taggart et al. (11) demonstrated that the thigh fatfold measure shows the largest absolute change across pregnancy. In addition, preliminary descriptive analyses of this Guatemalan study sample revealed that the thigh fatfold measures showed the largest absolute change across pregnancy. For a thorough discussion of the measurement of maternal nutritional status as well as description of previously observed values of various measures of maternal fat stores during pregnancy and lactation, see the review by Merchant and Martorell (8). Fetal growth was assessed by birthweight.

Statistical Methods - Two-tailed Student's t-tests using $\alpha = .05$ were used to assess differences between group means for continuous descriptive characteristics. Chi-square analyses were used to assess differences in proportions between groups for categorical descriptive characteristics. Pearson's correlation coefficients were calculated to evaluate the relationship

between home dietary intake and supplement intake. To address the research questions, first a prevalence of overlap was calculated, and second, two-tailed t-tests (α = .05) were made to test the significance of the contrasts of interest between group or subgroup means (adjusted for potential confounders) for the outcome variables: supplement intake at each trimester of pregnancy and at 3 months postpartum, thigh fatfold at each trimester of pregnancy and at 3 months postpartum and birthweight. Among the variables identified as potential confounders, only those related to the outcome variables with $p < .20$ (using an F-test on the coefficients calculated by linear regression) were retained as covariates to calculate adjusted means. Assuming an ordinal scale with equal intervals, the p-value of the regression coefficient for the subgroup rank (1 to 4) for birthweight was calculated using a one-tailed F-test to test for a trend. The Statistical Analysis System (SAS Institute, Inc., Gary, NC) was the computer software system used for data analyses. (The adjusted means and the corresponding standard errors were calculated using PROC GLM with LSMEANS/STDERR of SAS).

RESULTS

Sample Description

Descriptive statistics for selected variables for group A (no overlap) and group B (overlap) are shown in Table 1. Anthropometric characteristics of mothers and fathers, walking distance from home to the supplementation centers, and gestational length of C_n pregnancies did not differ between groups. Maternal age and parity at the time of birth of C_n children, birth interval (equivalent to age of C_{n-1} at birth of C_n) and lactation duration for the C_{n-1} children differed between groups.

As shown in Table 1, information on the energy intake from the home diet for <u>all</u> three trimesters of pregnancy was available for 89 pregnancies. The mean intake of the home diet (averaged over pregnancy) for the overlap group was 1409 kcal/day/pregnancy and 1410 kcal/day/pregnancy for the no-overlap group. No relationships between the home diet and the

supplement intake for any of the trimesters of pregnancy were demonstrated. The Pearson's correlation coefficient between home dietary intake and supplement intake was not statistically significant for any trimester of pregnancy or for the average values across pregnancy (1st: $r = -0.032$, $p = .76$, $n = 97$; 2nd: $r = 0.055$, $p = .45$, $n = 201$; 3rd: $r = -0.037$, $p = .57$, $n = 234$; average: $r = 0.042$, $p = .70$, $n = 89$). Adjusting supplement intake for home diet using this limited sample did not alter the results reported in the supplement intake section.

Lactation during Pregnancy

Lactation overlapped with pregnancy in 50.2% (253/504) of the pregnancies in this study sample. For cases where overlap occurred, 55.7% (141/253) breastfed only during the first trimester of pregnancy, 41.1% (104/253) continued to breastfeed into the 2nd trimester and 3.2% (8/253) continued into the 3rd trimester. A histogram of the duration (wk) of overlap of lactation with pregnancy (n=253) is shown in Figure 3.

Maternal Supplement Intake

Main Groups - The amount of supplement ingested during pregnancy was related to lactation (Figure 4). Group B --women with overlap of pregnancy and lactation-- had a significantly-higher mean supplement intake for all three trimesters of pregnancy than Group A --women with no overlap. Differences in supplement intake between groups were no longer present 3 months after the birth of C_n. Multiple regression analyses revealed that supplement intake was not associated with mother's height, mother's age, parity, or distance in minutes from the home to the supplementation center. The type of supplement (atole or fresco) and time since the beginning of the study (study month) were significant explanatory variables for supplement intake (i.e. intake was greater in atole villages and increased through the years) and were retained in the model to calculate adjusted group means of supplement intake. Adjusted means for the main groups are plotted in Figure 4. The adjustment for these potential confounders did not alter the results.

Subgroups - Mean supplement intake of subgroup A1 (long recuperation, no overlap) is significantly lower than subgroup A2 (short recuperation, no overlap) during the first two trimesters of pregnancy but not during the third trimester of pregnancy or at 3 months postpartum (Figure 5). However, subgroup A1 was lower than subgroups B3 and B4 (short and long overlap) for all three trimesters of pregnancy. Subgroup A2 was significantly lower than subgroups B3 and B4 only during the 1st trimester. Subgroups B3 and B4 never differed significantly from each other. None of the subgroups were significantly different at the postpartum measure.

Maternal Body Stores

Rates of missing data were high for maternal anthropometry. In part this is due to the fact that collection of maternal anthropometric data was begun in early 1971, 2 years after the beginning of the study. Only a subsample of cases had data for all three trimesters and at 3 months postpartum. Values can be reported in two formats: all available data at any of the four measurement periods (mixed longitudinal), reported elsewhere by Merchant (12), and values for cases with data for each of the four measurement periods (longitudinal subsample) as reported in Table 2. The patterns described below and in the accompanying figures are for the longitudinal sample (for brevity), but they apply as well for the mixed longitudinal sample. Maternal height, gestational length and supplement type were not associated with the thigh fatfold at any trimester of pregnancy or at 3 months postpartum. The reported means are adjusted for maternal age, parity, relative measurement date and study month. The relative measurement date refers to the timing of the anthropometric exam relative to conception.

Main Groups - The group A (no overlap) mean thigh fatfold thickness was slightly but consistently greater than the group B (overlap) mean thigh fatfold thickness for all three trimesters of pregnancy. Following birth, mean thigh fatfold thickness was similar in both groups (Figure 6).

Subgroups - When the main groups were divided into subgroups, a more complex pattern was revealed (Figure 7). Subgroup A1 (long recuperation, no overlap) has higher mean thigh fatfold

measures than the other subgroups at all times. The other three subgroups were similar to each other throughout pregnancy (the largest difference between any two subgroups reaching only 1 1/2 mm). Although the three subgroups were not statistically different, they maintained a constant ordering (subgroup B4 - highest, subgroup B3 - lowest and subgroup A2 falling between). Postpartum, subgroups A1 and B4 converged and subgroups A2 and B3 converged: the no-overlap subgroups (A1 and A2) lost fat and the overlap subgroups (B3 and B4) maintained fat.

Fetal growth

Main Groups - Although not statistically significant, a difference of 30 g in mean birthweight between groups was observed (no overlap 3,143 ± 455 g, n=211; overlap 3,113 ± 488 g, n=243). Study month, supplement intake, and type of supplement were not associated with birthweight. Maternal height, age and parity, and sex and gestational age of the newborn were significant predictors of birthweight. When the sample size was restricted to cases with complete information on maternal height, age and parity, the difference between unadjusted means increased to 52 g (no overlap 3,156 ± 458, n=197; overlap 3,104 ± 468, n=234). The difference is 57 g and is still not statistically significant ($p = .19$) after adjusting for gestational age, sex, maternal height, age and parity (no overlap 3,159 ± 449; overlap 3,102 ± 459).

Subgroups - Adjusting for maternal height, age, and parity, as well as sex and gestational age of the newborn, the mean birthweights for subgroups A1 through B4 are shown in Table 3. The mean birthweight decreases across subgroups (A1 to B4) as the postulated energetic stress increases across subgroups (A1 to B4). This trend across the four subgroups approaches statistical significance ($p = .10$).

DISCUSSION

A potential source of bias was identified when pregnancies classified by presence or absence of overlap were compared on a range of general characteristics. The presence of overlap was associated with a shorter birth interval than the absence of overlap (mean difference of about 1

year). Although this was expected because close birth spacing increases the opportunity for overlap to occur, it is of particular concern because close birth spacing also results in a short interval of time for the mother to recuperate from the previous pregnancy and lactation cycle. The potential confounding of two consequences of close birth spacing (overlap and short recuperative intervals) was of enough concern to warrant an additional set of analyses to assess the impact of the recuperative interval on the three outcomes of interest: maternal supplement intake, maternal fat stores and fetal growth.

The potentially confounding of the effect of recuperative interval with overlap was minimized by eliminating those with a long recuperative interval (subgroup A1) from the contrast to assess the effect of overlap. This reduced the mean difference between no-overlap (subgroup A2) and overlap (subgroups B3 and B4) from one year to three months. This strategy eliminated the other potential sources of bias, maternal age and parity. The mean maternal age and parity were not significantly different between these three subgroups (A2, B3, and B4), indicating that this strategy was effective.

Maternal Supplement Intake

Supplement intake was higher among those of the overlap group than those of the no-overlap group during the 1st trimester of pregnancy. This relationship persisted after controlling for potential confounding with birth interval. It would be expected that the effect of overlap would be most clearly demonstrated in the first trimester because this is when the maximum proportion of the overlap group was actually breastfeeding. By the second trimester 55.7% had weaned and by the third trimester 96.8 % had weaned. As mentioned previously, available supplement intake data were summarized by average intake over the trimester of pregnancy, therefore it was not possible to assess the intake of those who are actually lactating while pregnant at any given point of time in the stage of pregnancy. The result of categorizing pregnancies by absence or presence of any overlap is to reduce the precision with which the potential overlap effect is estimated, particularly during the later trimesters.

To evaluate the potential strength of the duration of overlap (dose response) on the outcomes, subgroups B3 and B4 were contrasted. However, no dose response of supplemental intake was detected (the means did not differ). There are several possible explanations for this. It may be that the duration of overlap does not accurately represent the energetic stress of lactation during pregnancy. Data on milk production by the mother or milk intake by the infant would represent this stress more precisely. Unfortunately, there are no data from this study or in the literature on the breastfeeding behavior of mothers during pregnancy. It may be that the second-trimester feedings were progressively less frequent, with the goal of weaning foremost in the mother's mind. It also may be that milk production was reduced (through the interaction with pregnancy or through decreased feeding frequency), resulting in subgroup B3 resembling subgroup B4 in energetic stress more than originally anticipated.

Had the effect of the recuperative interval not been taken into account (e.g., had only the group A vs. group B contrasts been made), the effect of overlap on supplement intake would have been overestimated because the intake for those of the overlap group was higher than for those of the no-overlap group during all three trimesters of pregnancy. When the effects were separated, supplement intake was higher for the first two trimesters among those with a short recuperative interval (subgroup A2) than those with a long recuperative interval (subgroup A1).

Conversely, if the effect of overlap were not separated from the effect of a long recuperative interval (and therefore long birth intervals), one might contrast subgroup A1 with subgroups A2, B3 and B4 and overestimate the effect of a long recuperative interval on the maternal supplement intake during pregnancy.

Although there is limited information regarding home dietary intakes, given the data available, there is no evidence to suggest that marked replacement of the home diet by the supplement occurred. The fact that the supplements were liquids and that they were made available only

between regular meal times probably minimized effects on home food consumption. Also, there is no reason to believe that replacement rates varied by study subgroup.

There are two additional considerations for the interpretation of the supplement intake results. Intake may not represent appetite. Women who were pregnant and lactating may have chosen to consume more supplement based on the belief that it was particularly important for them. Another behavior that may influence the results (particularly the first trimester supplement intake) is that women who were lactating right up to the time of conception and women who had been lactating recently (subgroups A2, B3 and B4) may have been in the habit of consuming supplement more frequently. The supplement was always available to all members of the communities, but participation (particularly early in pregnancy) could have been influenced by length of time since weaning. It may be that neither of these factors are exerting much of an influence though, because all pregnant and/or lactating women were encouraged to participate. And even the women who were neither pregnant nor lactating just prior to conception, had young children (all women of this study had children under 7 years of age who were a major target of the supplementation program) and so their participation was also encouraged.

Maternal Fat Stores

If the contrast between no overlap (group A) and overlap (group B) is made without regard to potential confounding due to recuperative intervals, the results suggest that those with no overlap had slightly more fat than those with overlap; but when the groups were sub-divided (controlling the effect of the recuperative interval) a different picture emerged. If the subgroups were the same at baseline (pre-pregnancy), it would be expected that those under the greatest energetic stress would mobilize more fat if the dietary intake were not increased proportionately and/or if the physical work were not decreased proportionately. The ordering of increasing energetic stress postulated for the subgroups is from the lowest, subgroup A1 (long recuperation, no overlap) to subgroup A2 (short recuperation, no overlap) to subgroup B3 (short overlap) to the highest, subgroup B4 (long overlap).

A corresponding inverse relationship between postulated stress and fat accumulation by subgroup was not observed.

A possible explanation for the ordering observed is that the subgroups may not have been the same at baseline. Women appear to be tracking from a baseline position of thigh fat that actually differed between subgroups. There is no crossover between subgroups during the three trimesters of pregnancy and the postpartum measures at 3 months for the four subgroups do not converge. In the original study, women were not measured anthropometrically if they were neither pregnant nor lactating, so direct measures of baseline status are not available. The baseline measure is particularly crucial because fat is a cumulative measure.

If it is accepted that the women are following different tracks, what might explain their relative positions? Maternal nutritional status during the reproductive years is dynamic. This is theoretically depicted in Figure 8, which shows three hypothetical women who are all following the same course of fat change beginning at birth. It was assumed that a decrease in fat occurred from birth to the time of weaning. The nadir of fat change is drawn to coincide with the time of weaning. (This exact correspondence is not necessary to the point being made, although it is seen within this Guatemalan data set.) The different relative fat measures at the time of the subsequent conception for each women (a, b, and c) are marked on the y-axis. What varies between the women is the length of the interpregnancy interval (time between pregnancies). Note that for this example, both woman-a and woman-b conceive before weaning. The nadir of change has occurred for woman-c and she is on a course towards repletion, but has not yet reached the status of woman-a.

Note that the same relative ranking that would be postulated, was seen in the maternal stores data of this study: interpret woman-a as subgroup B4, woman-b as subgroup B3 and woman-c as subgroup A2. This is supported by the fact that, on average, subgroup B4 conceived the earliest after the previous birth (12.9 months), subgroup B3 conceived next (15.7 months) and subgroup A2 conceived the latest (17.3 months). Although the relative rankings of the subgroups were

maintained during pregnancy, they were not statistically significant for the longitudinal subsample. This may be a limitation of small sample size. When data of the larger mixed longitudinal sample were used the relative rankings were statistically significant.

As expected the women with long periods of recuperation (subgroup A1) had significantly higher fat stores than women with short periods of recuperation (subgroup A2). Although the difference between groups were relatively small (≈2mm), the absolute measures of Guatemalan women in this sample are low relative to the average measures seen in a sample of healthy British women where the means ranged from 34.8 mm ± 10.7 at 10 wk, to 40.1 mm ± 10.2 at 38 wk of gestation (11). Because the Guatemalan study population is already at a marginal nutritional status, small differences may be of greater practical importance.

In addition to being in the expected direction, the magnitude of the difference between subgroups A1 & A2 was larger than that between subgroups B3 & B4, suggesting that the effect of recuperation is more critical than the overlap effect on attained maternal fat stores.

It is crucial to remember that subgroup B3 & B4 consumed more supplement --quite possibly offsetting the potential risk of mobilization of maternal fat stores due to the higher energetic demand of lactation with pregnancy. It is not known what would have happened had a convenient, freely-available energy supplement not been available.

Fat stores have been observed to increase with maternal age in several populations (13), a potential concern because the mean maternal age was significantly higher in subgroup A1. And yet, the effect of recuperation on maternal fat stores does not appear to be due to confounding with maternal age or parity, because the effect is seen regardless of statistical adjustment for these factors.

Finally, a comment regarding the method of assessing maternal body fat is in order. Maternal fat stores were assessed using the thigh fatfold measure. This single measurement site may not accurately represent the relative level of fat storage of a mother. However, during pregnancy the

thigh fatfold shows the greatest absolute change compared to other sites. No attempt was made to estimate total fat stores of the mother. There are no pregnancy-specific prediction equations available for such a calculation.

Fetal Growth

As in the case with supplement intake and maternal fat stores, it was postulated that presence of overlap represents a greater energetic stress and that fetal growth may be reduced under these circumstances. The main contrast between overlap and no overlap would have required an 85-g difference between means for a statistically-significant effect (one-tailed, $\alpha = .05$) to be detected with this sample size but only 30 to 50-g differences were seen depending on the sample used. The difference --although not statistically significant-- was in the expected direction.

When subgroups were analyzed, a similar situation resulted. Again although none of the differences were significant, they were in the expected directions. Longer recuperation for the mother was expected to result in better fetal growth, and absence of overlap and a shorter duration of overlap were expected to result in better fetal growth. The trend of postulated stress across subgroups --increasing from A1, to A2, to B3 and then to B4-- was not significant ($p < .10$). The practical significance of the birthweight differences among subgroups is minimal given the small magnitude of the differences, as well as the moderately satisfactory birthweight means for each subgroup. In addition, the prevalence of low birthweight (< 2,500 g) did not differ significantly between subgroups. Although insignificant, the observed trend in birthweight should not be dismissed entirely. Given the limiting sample size, the results are suggestive that recuperative interval and presence of overlap both could have slightly influenced fetal growth as indicated by birthweight in term gestations, particularly if the supplement had not been available.

The lack of a relationship between supplement intake and birthweight may surprise some readers given a previous publication by Lechtig and coworkers (9) reporting a relationship between these variables. Two important characteristics differ between the current study sample and the

sample used in Lechtig's article. Lechtig's sample was made up of the births occurring during the first half of the study (1/69 - 2/73). Although an important relationship between maternal supplement intake and birthweight was seen in this half of the study (and confirmed by an independent set of analyses by Marks (14)), births from the second half of the study (3/73 - 12/77) did not show such a relationship (14). The sample of the present study includes births from both halves of the study in approximately equal proportions. In addition, the current study sample is restricted to term births, whereas Lechtig's sample was not. This may be an important distinction if supplementation effects differ by length of gestation. When these characteristics are taken into account, the relationships between birthweight and supplement intake are consistent between all three studies and therefore the selected sample of this study is not anomalous.

CONCLUSION

The phenomenon of overlap of lactation with pregnancy should no longer be overlooked. This study has provided evidence of a high prevalence (50.2%) of overlap in 4 rural Guatemalan communities during the 1970's. The duration of overlap of lactation with pregnancy extended beyond the first trimester (the period during which a woman may not recognize her pregnancy) for 44.3% of the cases of overlap. This indicates that many women made the decision to breastfeed during at least some portion of their subsequent pregnancy. Given the higher energetic demands of this situation --which appears to occur frequently in populations with close birth spacing and relatively low socioeconomic status (4, 5, 6)-- the risks of maternal nutritional depletion and poor child growth and development may be increased.

The data indicate that the presence of overlap resulted in increased supplement intake during the 1st trimester of pregnancy. A shorter recuperative period appears to have resulted in increased supplement intake during the 1st and 2nd trimesters of pregnancy and in lower maternal body stores. Although differences in birthweight between groups or among subgroups were not large or statistically significant, the data suggest that both the absence of overlap and the longer

recuperative period might favor fetal growth somewhat. It appears that the responses of the mother (increase intake, mobilize stores) to the energetic stresses of the overlap of lactation with pregnancy and short recuperative intervals protects fetal growth.

These relationships were demonstrated in a population for which a nutritional supplement was available freely and conveniently between meals each day of the eight-year study period. In addition, primary health care was free and available. Depending on when in the study period their pregnancy occurred, supplementation and health care could have been available for up to 7 years. The presence of this nutritional supplement would be expected to reduce the impact of energetic stresses due to short recuperative intervals and to the overlap of lactation with pregnancy. This is suggested also by the evidence of increased supplement intake under both of these circumstances. Without a freely-available energy supplement, it would be expected that the negative effects on maternal stores and fetal growth would be greater than those found here. On the other hand, it is difficult to predict the extent to which overlap and short recuperative periods would be detrimental to women in more advantaged circumstances.

Although research in these areas is just beginning, the results suggest two practical recommendations: 1) that women living in circumstances of high energetic stress space their births so that subsequent conceptions occur more than 6 months following weaning of the previous child and 2) if pregnancy occurs sooner than this, that an effort be made to consume additional food that is calorically dense.

In addition to the formal research questions, three other results have been demonstrated in this study. 1) Maternal nutritional status is very dynamic during the reproductive years. The fluctuations are wide, are to be expected and can influence interpretations of the data dramatically. 2) It is crucial to consider the presence of overlap --particularly when assessing the effects of birth spacing (otherwise there may be an overestimation of the effect of birth spacing attributed to recuperation). 3) Parity alone is a poor way to characterize reproductive history. When the

reproductive cycle is examined closely and characterized adequately, evidence of maternal nutritional depletion is seen.

For further study of lactation concurrent with pregnancy, specific and general research needs can be identified. The questions of practical importance are who (mother, fetus, breastfeeding child) is most negatively affected by energetic stress and who (mother, fetus, breastfeeding child) benefits from nutritional intervention. Building on this initial investigation, the issues of nutrient partitioning between mother and fetus can be explored further. The interrelationships among maternal supplement intake, fat stores and fetal growth within the subgroups should be examined. And yet, more complete information on all components of energy balance is necessary to fully explore the complexities of nutrient partitioning during reproduction. Data on total dietary intake, milk production and energy expenditure of the mother would be particularly useful.

In general, all studies of lactation or pregnancy should incorporate the fact that these conditions can and do occur together; efforts should be made to estimate the prevalence and duration of overlap of lactation with pregnancy; attitudes, beliefs and behaviors regarding the practice of breastfeeding during pregnancy should be elucidated; measures of milk production by the mother, milk composition, and milk intake by the breastfeeding child during various stages of overlap are needed; the consequences in various ecological settings to mother, fetus, and breastfeeding child of weaning versus continuing to breastfeed a child after a woman discovers she is pregnant must be examined; and, finally, recommendations should be developed and disseminated based on the research findings.

ACKNOWLEDGEMENTS

Thanks are expressed to David Rush and Henry Mosley for their valuable input at very early stages of the analysis, and to Michael Kramer, Frank Hytten, Hollis Erb, Alan Bell, Juan Rivera, Teresa González-Cossío, Joanne Leslie, Kathleen Rasmussen and Jean-Pierre Habicht for their thorough reading and helpful suggestions in the final stages of this work. The research was supported by grant IC-58/03 from the International Center for Research on Women through Cooperative Agreement Number DAN-1010-A-00-7661-00 with USAID.

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Table 1: Descriptive Statistics by Groups

	Group A No overlap				Group B Overlap		
	n	Mean	SD		n	Mean	SD
C_{n-1} Lactation Duration (mo)	251	15.7	6.5	**	253	17.7	3.9
Birth Interval (mo)	251	35.0	16.9	**	253	23.4	4.3
Mother's Age (y) at Birth of C_n	249	30.2	6.8	*	252	28.7	6.7
Parity	247	5.8	3.0	*	253	5.4	2.8
C_n Gestational Age (wk)	251	39.7	1.3		253	39.8	1.4
C_n Lactation Duration (mo)	247	17.4	7.3		252	17.0	7.0
Mother's Height (cm)	229	148.6	4.9		248	149.4	5.6
Mother's Head Circumference (cm)	229	51.2	1.2		248	51.1	1.4
Father's Height (cm)	202	160.1	5.6		185	160.9	6.3
Father's Head Circumference (cm)	202	54.2	1.5		185	54.3	1.7
Distance to Supplement (min)	236	2.5	1.1		247	2.5	1.1
Average Maternal Home Diet (kcal/day)	45	1410	432		44	1409	418
<u>Proportion</u>							
Atole / Fresco		.53/.47				.60/.40	
C_n Male / C_n Female		.55/.45				.52/.48	

C_{n-1} = Previous Child, C_n = Index Child

* Probability of t < .05, ** Probability of t <.0001

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Table 2: Main Group and Subgroup Thigh Fatfold Means* for Longitudinal Subsample

	Group A No Overlap (n=85)	Subgroup A1 Long recup. (n=29)	Subgroup A2 Short recup. (n=56)	Group B Overlap (n=130)	Subgroup B3 Short overlap (n=74)	Subgroup B4 Long overlap (n=53)
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Trimester						
First	13.3 (4.4)	15.5 (4.4)	12.2 (4.2)	12.6 (4.4)	12.0 (4.1)	13.3 (4.3)
Second	14.7 (4.6)	16.3 (4.6)	13.9 (4.5)	13.8 (4.7)	13.2 (4.5)	14.7 (4.6)
Third	16.6 (5.4)	18.1 (5.5)	15.9 (5.4)	16.0 (5.5)	15.4 (5.4)	16.8 (5.5)
3 months Postpartum	15.6 (5.0)	17.1 (5.1)	14.8 (4.9)	15.8 (5.1)	15.2 (5.0)	16.6 (5.0)

* Adjusted for maternal age, parity, relative measurement date and study month

Table 3: Subgroup Birthweight Means
Adjusted for Sex and Gestational Age of Newborn
and Maternal Height, Age, and Parity

Subgroup	n	Birthweight (g) Mean	SD
A1 - Long Recup.	85	3,204	470
A2 - Short Recup.	112	3,120	466
B3 - Short Overlap	131	3,105	458
B4 - Long Overlap	103	3,089	457

FIGURE LEGENDS

Figure 1: Sample selection criteria.

Figure 2: Classification strategy. C_{n-1} = previous child, C_n = index child.

Figure 3: Frequency distribution for the duration of overlap of lactation with pregnancy within the overlap group (n=253).

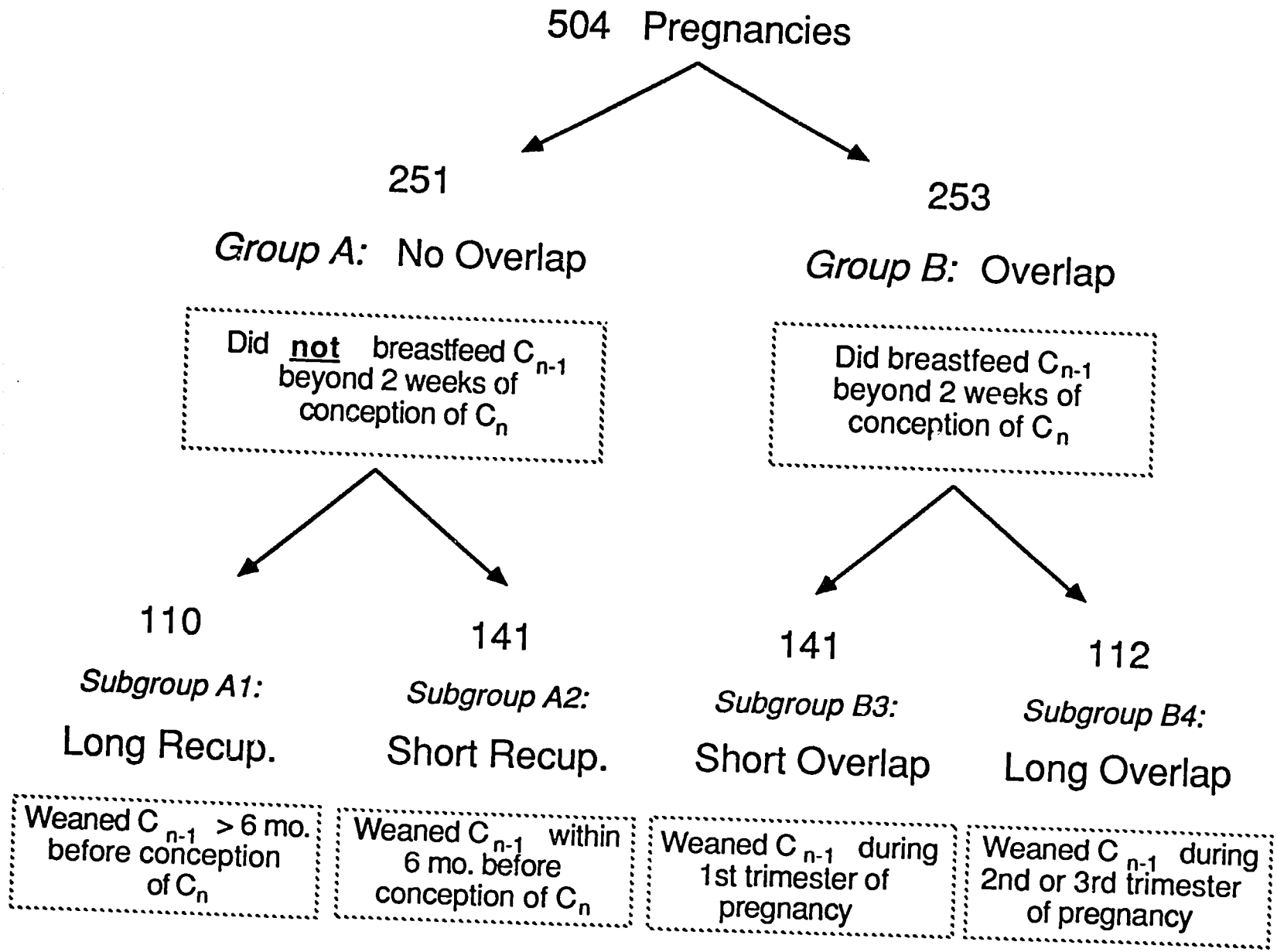
Figure 4: Mean maternal supplement intake across pregnancy and early postpartum for overlap and no-overlap groups. (Mean ± SEM.) Means are adjusted for supplement type and study month.

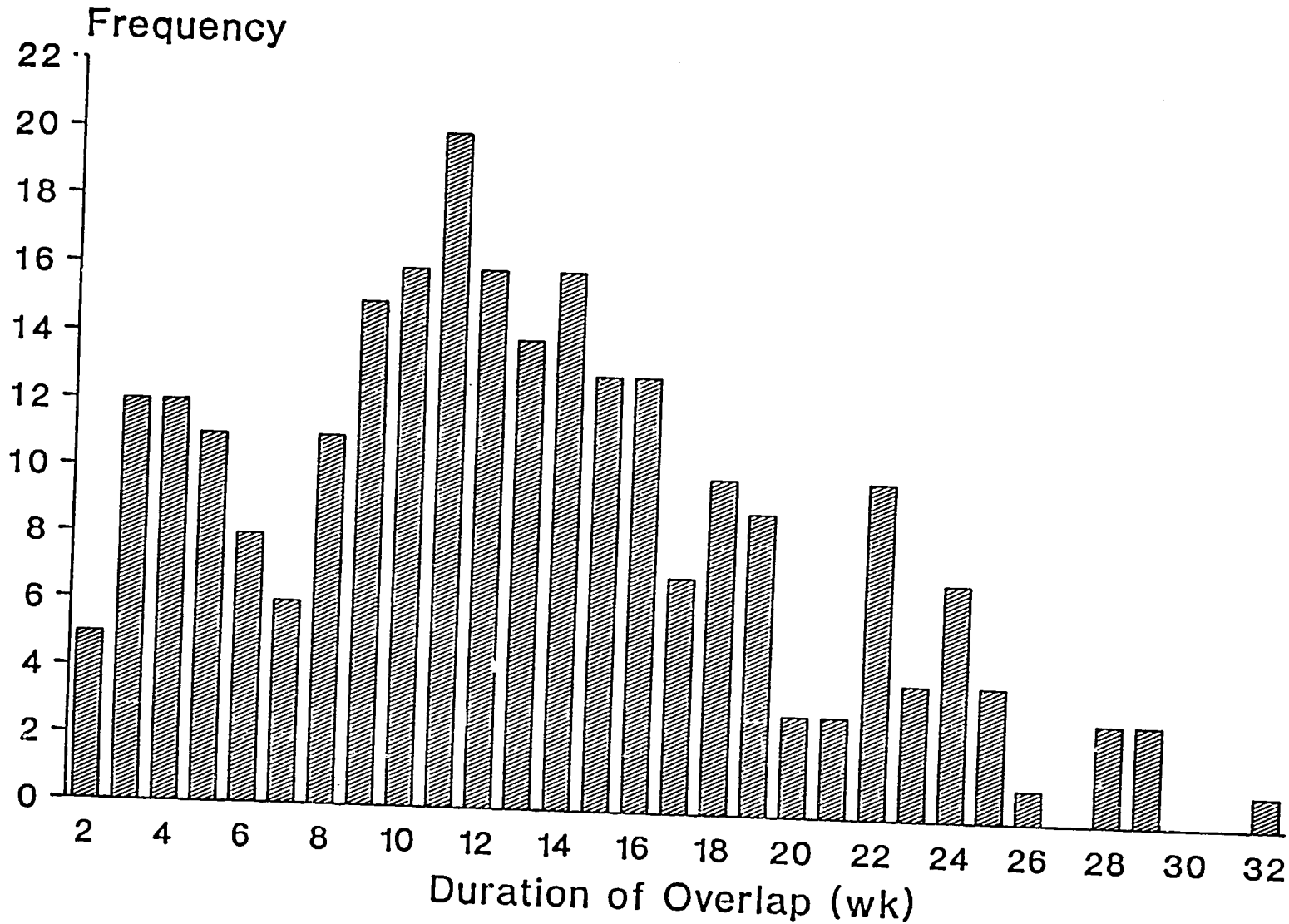
Figure 5: Mean maternal supplement intake across pregnancy and early postpartum for each subgroup. Means are adjusted for supplement type and study month.

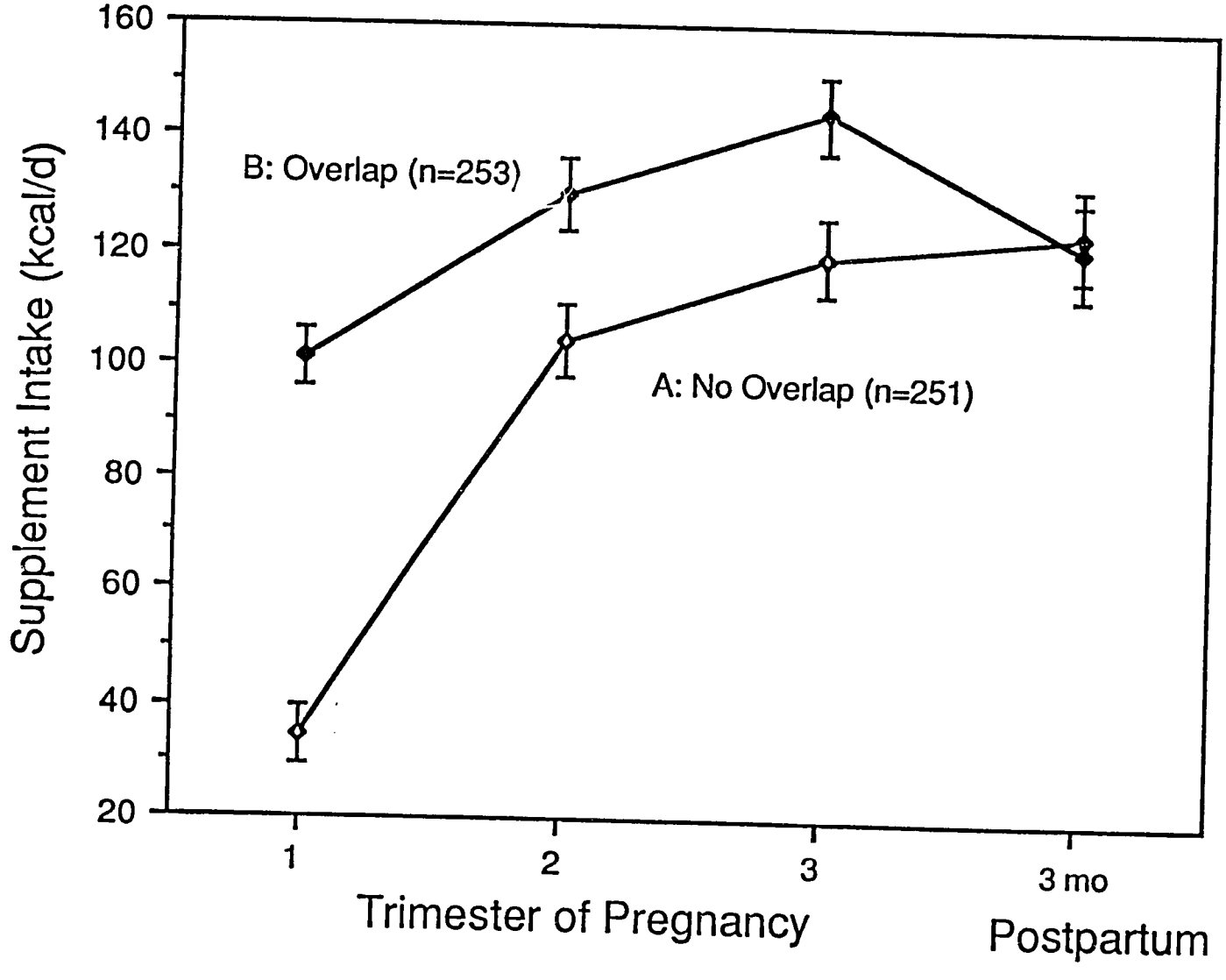
Figure 6: Mean maternal thigh fatfold across pregnancy and early postpartum for overlap and no-overlap groups. (Mean ± SEM.) Means are adjusted for maternal age, parity, pregnancy stage and study month.

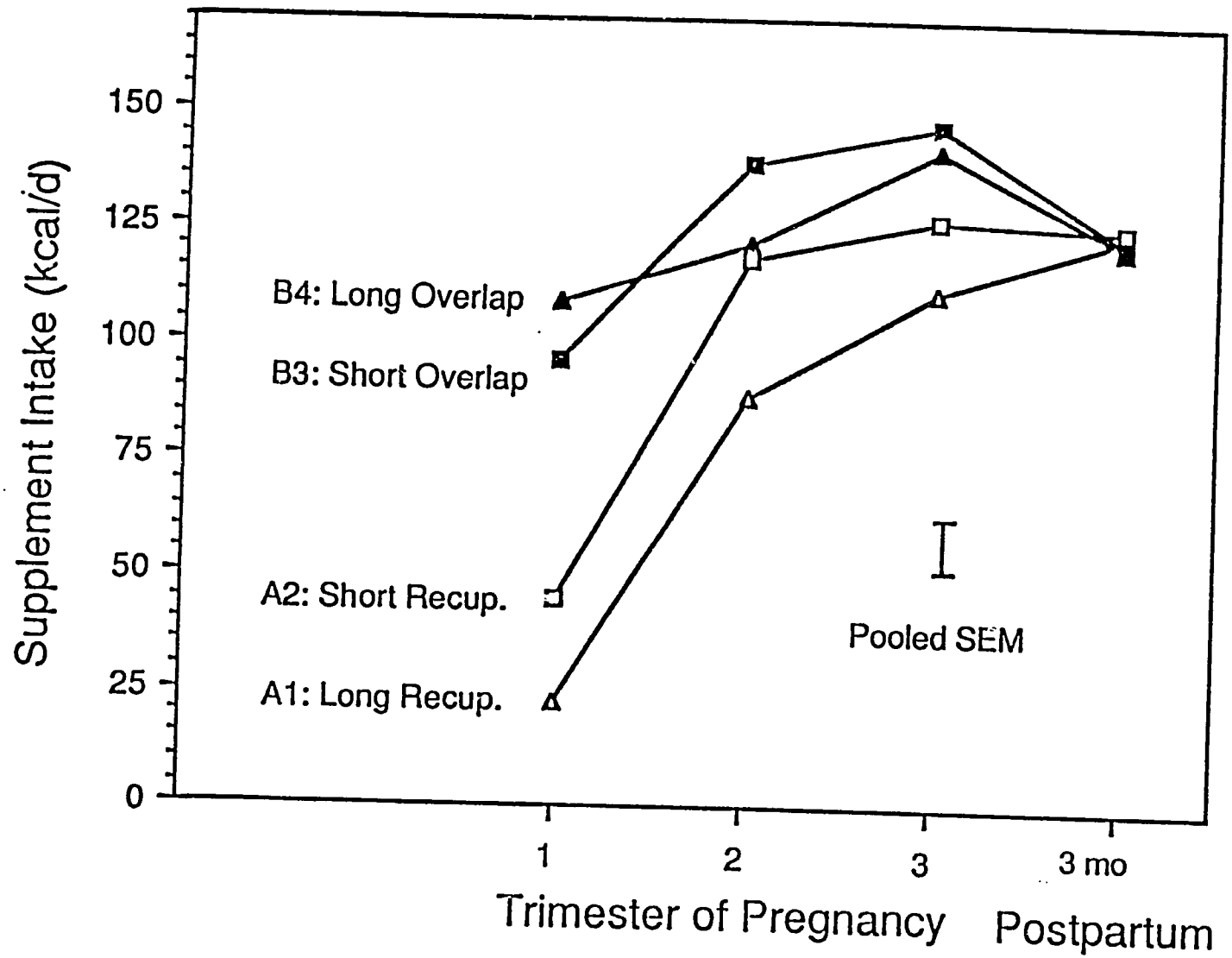
Figure 7: Mean maternal thigh fatfold across pregnancy and early postpartum for each subgroup. Means are adjusted for maternal age, parity, pregnancy stage and study month.

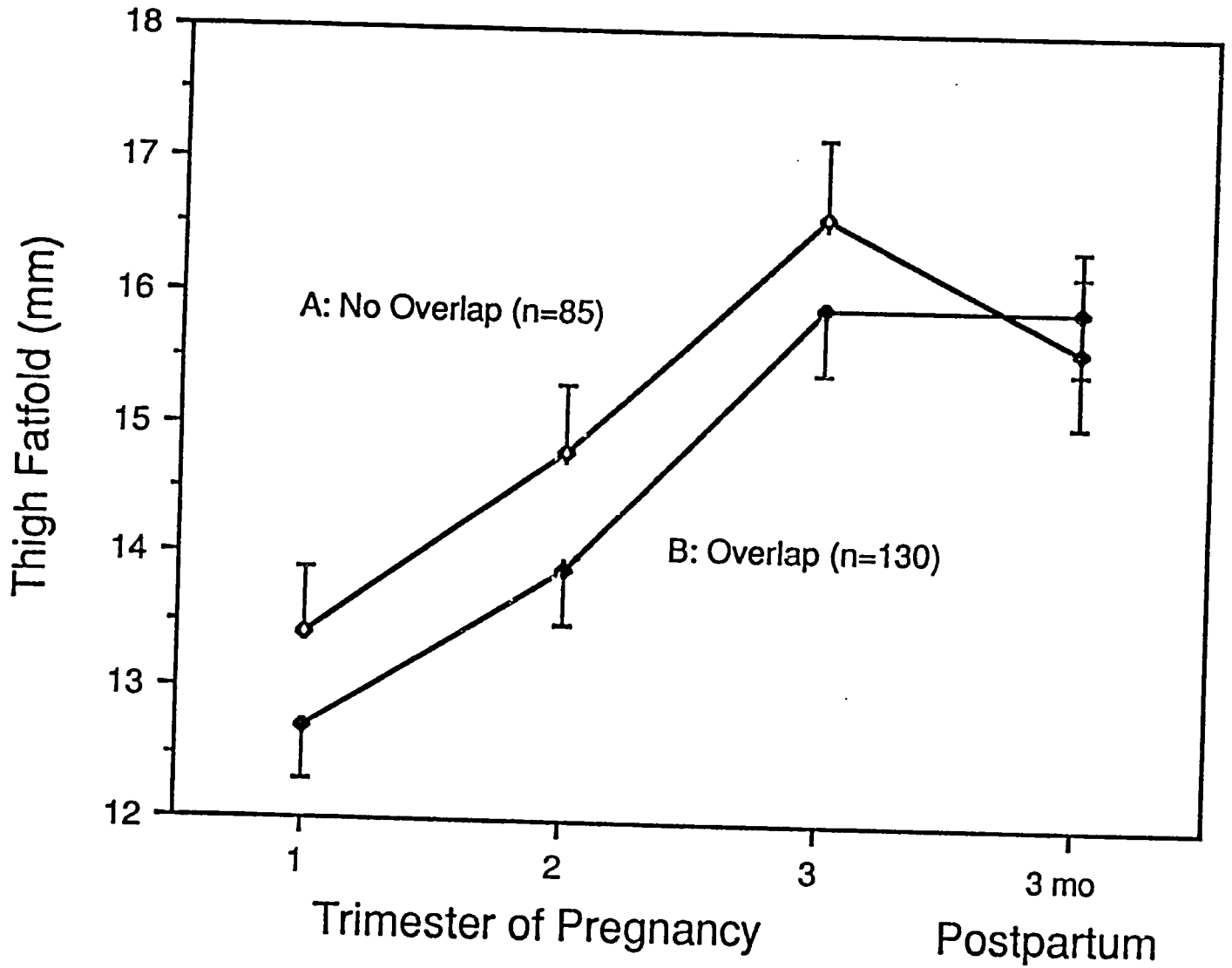
Figure 8: Theoretical maternal fat changes through a reproductive cycle. F = a measure of fat, C = time of subsequent conception.

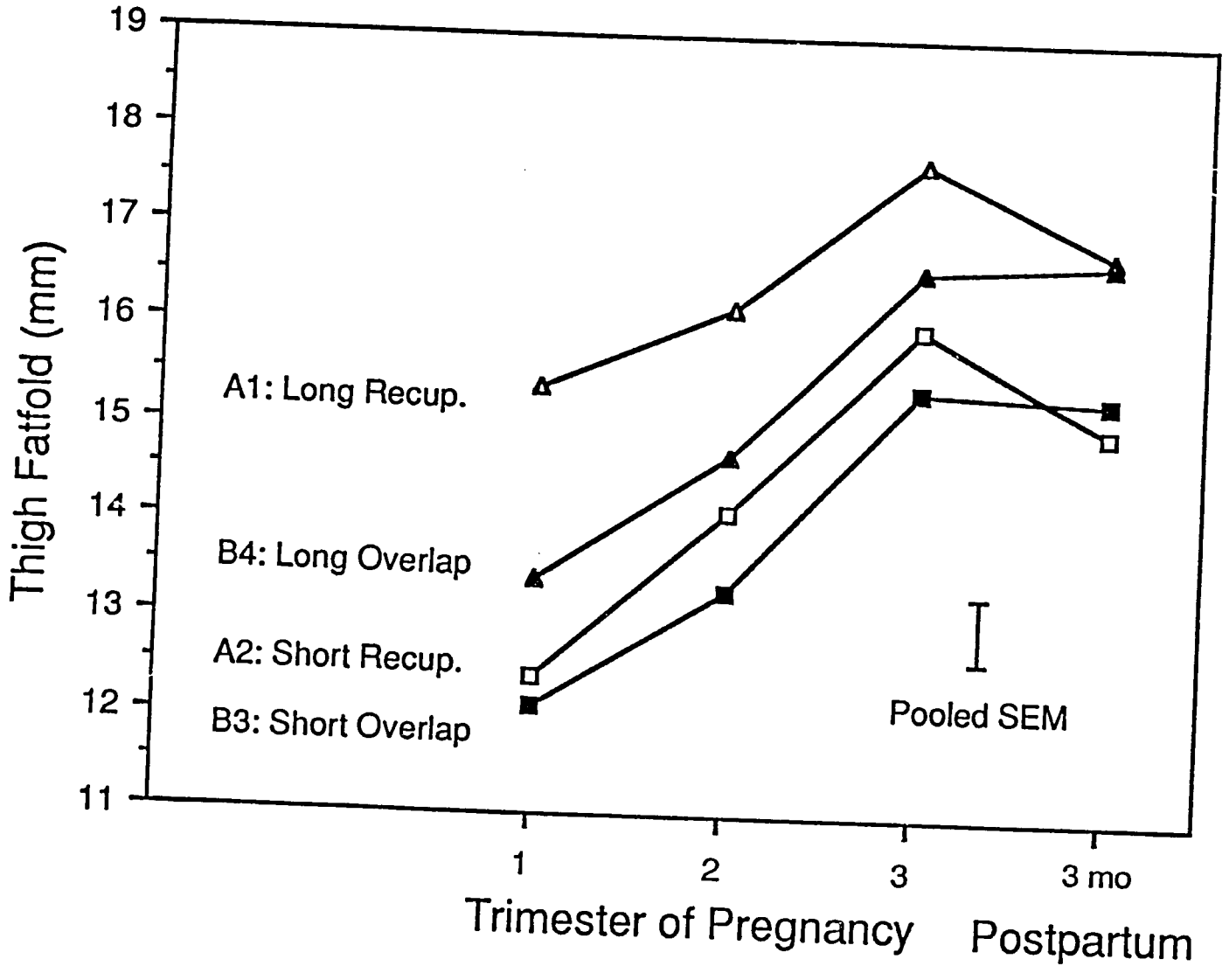

504 Pregnancies
251
Group A: No Overlap
Did not breastfeed C_{n-1} beyond 2 weeks of conception of C_n
253
Group B: Overlap
Did breastfeed C_{n-1} beyond 2 weeks of conception of C_n
110
Subgroup A1:
Long Recup.
Weaned C_{n-1} > 6 mo. before conception of C_n
141
Subgroup A2:
Short Recup.
Weaned C_{n-1} within 6 mo. before conception of C_n
141
Subgroup B3:
Short Overlap
Weaned C_{n-1} during 1st trimester of pregnancy
112
Subgroup B4:
Long Overlap
Weaned C_{n-1} during 2nd or 3rd trimester of pregnancy

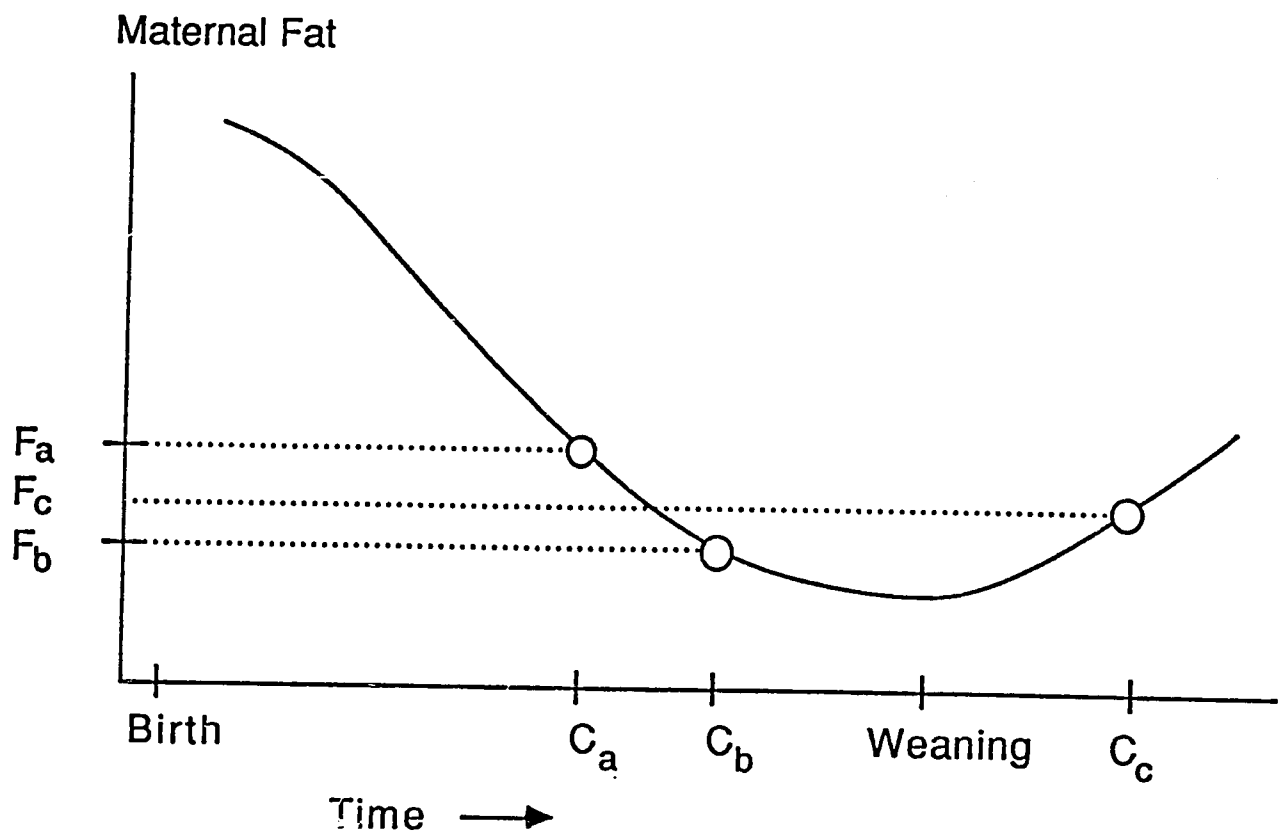

Frequency
22
20
18
16
14
12
10
8
6
4
2
0
2
4
6
8
10
12
14
16
18
20
22
24
26
28
30
32
Duration of Overlap (wk)


160
140
120
100
80
60
40
20
Supplement Intake (kcal/d)
B: Overlap (n=253)
A: No Overlap (n=251)
1
2
3
3 mo
Trimester of Pregnancy
Postpartum


Supplement Intake (kcal/d)
150
125
100
75
50
25
0
B4: Long Overlap
B3: Short Overlap
A2: Short Recup.
A1: Long Recup.
Pooled SEM
1
2
3
3 mo
Trimester of Pregnancy
Postpartum


18
17
16
15
14
13
12
Thigh Fatfold (mm)
A: No Overlap (n=85)
B: Overlap (n=130)
1
2
3
3 mo
Trimester of Pregnancy
Postpartum


Thigh Fatfold (mm)
19
18
17
16
15
14
13
12
11
A1: Long Recup.
B4: Long Overlap
A2: Short Recup.
B3: Short Overlap
Pooled SEM
1
2
3
3 mo
Trimester of Pregnancy
Postpartum


Maternal Fat
F_a
F_c
F_b
Birth
C_a
C_b
Weaning
C_c
Time

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MATERNAL AND FETAL RESPONSES IN CONSECUTIVE PREGNANCIES TO THE STRESS OF LACTATION CONCURRENT WITH PREGNANCY AND OF SHORT RECUPERATIVE INTERVALS

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Running Head: Lactation Concurrent with Pregnancy

-9

ABSTRACT

Frequent reproductive cycling often leads to the overlap of lactation with subsequent pregnancy and the shortening of potentially recuperative (non-pregnant/non-lactating) intervals within the reproductive cycle. This increased energetic stress may lead to maternal nutritional depletion among populations living in poverty.

Although differing responses to the above conditions of energetic stresses from frequent reproductive cycling have been demonstrated previously, it is important to control for inherent characteristics of the mothers. This is accomplished in this study by contrasting the responses to differing stresses of consecutive pregnancies within individual Guatemalan women. The results indicate that overlap is most stressful, short recuperative interval follows, and long recuperative interval is least energetically stressful on the mother. Maternal responses to the stresses are increased supplement intake and reduced fat stores but fetal growth in term gestations is not affected, as measured by birthweight. The results indicate that fetal growth is being protected at the "cost" of maternal nutritional status.

KEY WORDS: Maternal Depletion, Pregnancy, Lactation, Birth Spacing, Supplementation, Infant Feeding, Birthweight, Maternal Anthropometry, Maternal Nutrition

INTRODUCTION

Frequent reproductive cycling increases energetic stresses experienced by women (1). One dramatic illustration of the increased stress resulting from frequent reproductive cycling is the phenomena of lactation occurring concurrent with pregnancy. When births are closely spaced the prevalence of the overlap of lactation with pregnancy increases. Although evidence is accumulating that in many cultures women are often breastfeeding the previous child during some portion of their current pregnancy (1 - 4), study of the energetic stress of this situation on women has just begun.

In a sample of Guatemalan women, it was shown that lactation concurrent with pregnancy (overlap) resulted in increased supplement intake during the first trimester of pregnancy (1). Another result of frequent reproductive cycling is the shorter recovery time available to women between reproductive events such as pregnancy and lactation. The Guatemalan study also demonstrated that short recuperative periods (non-pregnant/non-lactating < 6 months prior to conception) resulted in increased supplement intake during the first and second trimesters of pregnancy and slightly reduced maternal fat stores relative to long recuperative periods (non-pregnant/non-lactating > 6 months prior to conception). The results also suggested that long recuperative periods (> 6 months) and the absence of overlap may favor fetal growth very slightly (1).

A potential bias within the design of the Guatemalan study is that women who are likely to have long recuperative intervals may be different from women who are likely to overlap lactation with pregnancy in certain unmeasured factors. These potential differences between women may affect the outcomes (maternal supplement intake, maternal fat, and fetal growth) independent of the postulated effects of presence or absence of overlap and

of length of recuperative intervals. Using a subsample of the same study population, the analysis reported here eliminates this potential confounding by using each mother as her own control in analysis of consecutive pregnancies. By taking advantage of the fact that women vary from pregnancy to pregnancy in terms of the nutritional stresses they confront, this approach allows for maternal and fetal responses to a particular stress, such as overlap of pregnancy and lactation, to be contrasted to that of another stress, for example short recuperative interval. The strength of this analysis is that it controls for all aspects associated with each woman that do not change appreciably from pregnancy to pregnancy (e.g. genetic predisposition, maternal height, socioeconomic status, etc.).

Hypotheses

Presence of overlap is expected to lead to greater energetic stress on pregnant women. Women who are lactating while pregnant must supply energy for milk production <u>and</u> fetal growth in addition to their own needs. A longer non-pregnant/non-lactating interval before conception would be expected to allow for nutritional recuperation of the mothers and lead to improved maternal status and fetal outcomes (5 - 7).

Based on these postulated energetic stresses and on previous research, the following relationships are hypothesized. These hypotheses are predicting the relative impact of three types of pregnancies (overlap, short recuperative interval, and long recuperative interval) on each outcome of interest.

1) Mothers consume more during a pregnancy with overlap than during a pregnancy preceded by a short recuperative interval; and even more relative to the amount consumed during a pregnancy preceded by a long recuperative interval.

2) Mothers have lower fat stores during a pregnancy with overlap than during a pregnancy preceded by a short recuperative interval; and even lower fat stores relative to those during a pregnancy preceded by a long recuperative interval.

3) Fetal growth during a pregnancy with overlap is poorer than during a pregnancy preceded by a short recuperative interval; and even poorer relative to fetal growth during a pregnancy preceded by a long recuperative interval.

METHODS

Data

This investigation uses data from a nutritional supplementation trial conducted by the Instituto de Nutrición de Centroamérica y Panamá (INCAP) in four rural communities in the Guatemalan department of El Progreso. The period of the health and nutrition intervention was 1969 through 1977. Two communities each were assigned randomly to receive either a high-protein (11 g/180 ml), high-energy (163 kcal/180 ml) supplement called "atole" or a low-energy (59 kcal/180 ml), no-protein supplement called "fresco".

The supplements were free and available twice-daily to all inhabitants at centrally-located feeding centers in each community. A cup (180 ml) was offered initially; more was provided if requested. Leftovers were measured and actual amounts consumed were recorded for pregnant and lactating women as well as for children up to the age of seven years. Twenty-four hour dietary recall surveys were used at 3-month intervals to measure the home dietary intakes of the women.

A health center was set up in each village to provide free primary health care to all community members. Anthropometric examinations were scheduled at three-month intervals

during pregnancy and the first 24 months of lactation from 1971 to 1977. All measures were made by the same individual. Birthweight was measured within 24 hours after delivery. Duration of lactation was determined through maternal recall for all children 7 years or younger at the beginning of the study period (1/69) and prospectively during home visits occurring bimonthly for all those born within the study period. Pregnancies were identified as early as possible (also during home visits). Gestational age was calculated as the difference between the date of birth and the date of onset of the last menstrual period. The date of conception was estimated by first subtracting two weeks from the gestational age as calculated above, and then subtracting this value from the date of birth. Several surveys were conducted during the intervention period to assess the socioeconomic status of all households. A more detailed description of the specific data collected and methods used is given by Lechtig et al. (8) and Delgado et al. (9).

Sample Selection

A total of 1529 births were recorded in the 4 study villages during the study period (1969-1977). From this total sample of births, the study sample was selected for the following characteristics: women with two consecutive, term, singleton pregnancies, each with a known birthdate and lactation duration for the previous child. In addition, it was required that all study women were lactating during at least one of the two consecutive pregnancies. Data for previous siblings were only available for children seven years or younger. Birth date and lactation duration for the previous child were required to establish unequivocally whether or not overlap in pregnancy and lactation had occurred. Pre- and

post-mature births were excluded on the grounds that these were either truly special subpopulations or cases with errors in the measurement of gestational age.

Study Sample - Of the 304 women who contributed at least one pregnancy to the study sample of the previous investigation (1), 102 women had at least two consecutive pregnancies, of which at least one was a pregnancy in which lactation occurred concurrently. These 102 paired pregnancies form the study sample for this investigation (204 of the 504 births of the sample selected for study previously (1)).

The selected study sample of births was comparable to the total sample of births for the following general characteristics, lactation duration of the previous child (C_{n-1}), birth interval, mother's height and head circumference, father's height and head circumference, distance from home to supplementation center, average energy intake from the home diet, proportion receiving each supplement type (fresco or atole) and proportion of male and female newborns. Of those examined, three characteristics differed between the selected study sample and the total sample. The mean maternal age, gestational age and lactation duration of the current child (C_n) were higher in the selected subsample by 2 years, 1/2 week and 1 month, respectively. All mothers of the selected study sample were multiparous (parity of at least 3), therefore the age difference would be expected. The minimum maternal age for the total sample was 12.7 years and the selected study sample 18.0 years. The restriction of the study sample to term births is the likely explanation for the slightly longer mean length of gestation; the minimum gestational age recorded for the total sample was 25 weeks and for the selected study sample was 37 weeks. More thorough information regarding the descriptive characteristics of the total sample (n=1529) is reported elsewhere by Merchant (10).

Analytic Approach

Classification - Initially, both pregnancies of each mother were divided into three categories (overlap, short recuperative interval and long recuperative interval). These groups were defined by the time of weaning of the previous child (C_{n-1}) relative to the conception of the index child (C_n). The overlap category (O) was defined as pregnancies in which C_{n-1} was weaned after 2 weeks following the date of conception of C_n. The short recuperative interval category (SRI) was defined as pregnancies in which C_{n-1} was weaned within the time period of 6 months before the date of conception of C_n to 2 weeks following the date of conception of C_n. Therefore, the duration of the non-pregnant/non-lactating interval was less than six months. The long recuperative interval category (LRI) was defined as pregnancies in which C_{n-1} was weaned more than 6 months before the date of conception of C_n. Therefore, duration of the non-pregnant/non-lactating interval was more than six months. A conservative definition of overlap (lactation > 2 weeks past conception) was used to minimize the possibility of misclassification of those who did not overlap in the overlap group.

The pairs of consecutive pregnancies of each mother were then classified into five possible combinations of these categories: (1) first birth - O, second birth - LRI, (2) first birth - O, second birth - SRI, (3) first birth - O, second birth - O, (4) first birth - SRI, second birth - O, and (5) first birth - LRI, second birth - O (Figure 1). The five categories created by the various combinations of pairing were ordered from 1 to 5 by the postulated trend of difference in energetic stress between the two consecutive pregnancies, creating the "stress difference category". The predictions for differences between births (2nd birth minus 1st birth) of each outcome by the stress difference category are described in Figure 2. The

diagrammatic representation of the times of weaning in Figure 2 are drawn to fall precisely in the middle of the appropriate interval. This implies that the absolute value of the differences in the specified outcomes between successive pregnancies in categories 1 and 5 as well as categories 2 and 4 would be equivalent. In actuality, the time of weaning falls somewhere within the marked interval and the mean time of weaning may not be equivalent between categories 1 and 5 or categories 2 and 4, particularly because the sample sizes are small in several categories in this study. Therefore, no predictions regarding equal magnitude of the differences of outcomes between successive pregnancies for categories 1 and 5 as well as categories 2 and 4 are being made.

Outcome Variables - Although ideally maternal dietary intake should be based on home dietary intake plus supplement intake, supplement intake has been chosen as the preferred maternal intake variable in this study. The precision and accuracy of these data are much higher and the completeness of these data is greater than that of the home dietary data (which were measured by 24-hour recall). For a more thorough discussion of the implications and rationale for this decision, see the previous investigation (1). The original daily maternal supplement intake data have been summarized by trimester of pregnancy and data are available only for average intake across each trimester in the INCAP data tapes. Maternal supplement intake per day was averaged by trimester of pregnancy and during the 3 month postpartum period. The average supplement intake per day over pregnancy was calculated by averaging the three trimester values --(1st T intake + 2nd T intake + 3rd T intake)/3. Each of the five resulting supplement intake variables (1st, 2nd, 3rd trimesters, average over pregnancy, 3 mo. postpartum) for both births of each pair were then adjusted for the study month using linear regression to calculate the residual

values. This adjustment was made because it has been previously shown that mean maternal supplement intake increased over the 7-year study period (11). (It has been previously shown that supplement intake was not associated with mother's age (1), therefore adjustment for maternal age was not necessary.) The difference between paired supplement intake residual values were then calculated (2nd birth of pair minus 1st birth of pair). These five differences were used as the maternal supplement intake outcome variables.

Maternal fat stores were assessed using the thigh fatfold (an average of the medial thigh and the lateral thigh measures). Of the seven fatfold sites --triceps, biceps, subscapular, suprailiac, knee, thigh and calf-- Taggart et al. (12) demonstrated that the thigh fatfold measure shows the largest absolute change across pregnancy. The thigh fatfold measures were taken during each trimester of pregnancy and at 3 months postpartum. The average thigh fatfold measure over pregnancy was calculated by averaging the three trimester values --(1st T fatfold + 2nd T fatfold + 3rd T fatfold)/3. Each of the five resulting thigh fatfold measures (1st, 2nd, 3rd trimesters, average over pregnancy, 3 mo. postpartum) for both births of each pair were then adjusted for the study month and the stage of pregnancy at exam time using linear regression to calculate the residual values. (It has been previously shown that thigh fatfold was not associated with gestational length over the range of values observed in this sample of term births (1).) The difference between paired fatfold residual values were then calculated (2nd birth of pair minus 1st birth of pair). These five differences were used as the maternal fat outcome variables.

Fetal growth was assessed using birthweight. Birthweight was adjusted for the newborn's sex and gestational age and for the age of the mother at the time of birth using

linear regression to calculate the residual values. (It has been previously shown that birthweight was not associated with study month, supplement intake or type of supplement in this sample (1).) The difference between paired birthweight residual values were then calculated (2nd birth of pair minus 1st birth of pair) and used as the fetal growth outcome variables.

Statistical Methods - A test for trend (α = .05) was made on each of the eleven outcome variables, using linear regression and calculating the p-value of the regression coefficient of the expected trend variable. The expected trend variable was assigned by assuming an ordinal scale of equal intervals for the postulated trend of difference in energetic stress across paired categories from 1 to 5 (Figure 2). The Statistical Analysis System (SAS Institute, Inc., Cary, NC) was the computer software system used for data analyses.

RESULTS

Sample Description

Descriptive statistics for general characteristics of the study sample are given in Table 1. Descriptive statistics for general characteristics for the study sample by stress difference category are given in Table 2. The paired mean differences between consecutive births for general characteristics are given in Table 3. The general characteristics do not differ in substantial or unexpected directions between the stress categories of the study sample or the consecutive birth pairs of the subsample.

Maternal Supplement Intake

A trend for differences in maternal supplement intake between consecutive births (2nd birth - 1st birth) across stress difference categories is highly significant for all three trimesters of pregnancy and the average over pregnancy, but not for the first three-month postpartum period (Table 4). The type of supplement did not modify these relationships.

Maternal Fat

A trend for differences in maternal thigh fatfold between consecutive births (2nd birth - 1st birth) across stress categories is highly significant for the first two trimesters of pregnancy, but not for the third trimester of pregnancy or for the first three-month postpartum period (Table 5).

Fetal Growth

A trend for differences in birthweight between consecutive births (2nd birth minus 1st birth) across stress categories is not significant (Table 5).

DISCUSSION

When examining the descriptive characteristics for the study sample by stress category (Table 2), it can be seen that certain patterns hold for all the pregnancies in which overlap occurred. (Overlap occurred during the pregnancies for the 1st birth of the pair in stress categories 1, 2 and 3, and for the 2nd birth of the pair, stress categories 3, 4 and 5. Non-overlap pregnancies occurred for the 2nd birth of stress categories 1 and 2 and the 1st birth for stress categories 4 and 5. Refer to Figure 1.) The mean of the lactation

duration for the previous child was higher in overlap pregnancies than for the non-overlap pregnancies. The mean birth interval was lower in overlap pregnancies than non-overlap pregnancies. Although the differences in both of these cases are generally small, they are consistent and would be expected. A longer duration of lactation for the previous child and a shorter birth interval increase the likelihood that overlap between lactation and the subsequent pregnancy will occur. Differences across stress categories for the other characteristics are variable and generally of small magnitude, particularly relative to the variation and the small sample sizes within some categories. The paired mean differences between consecutive births are minimal with the exception of maternal age, which necessarily must be higher for the second birth of the pair.

The highly significant trend ($p < .0001$) of differences in supplement intake between consecutive births across pregnancy was in the expected direction. This supports the findings of the previous study (1). In addition, the trend of supplement differences between consecutive births in the postpartum (first 3 month period) period was not significant. This confirms the expectation that the increased intake is a response to the stress of overlap rather than a lasting change in the eating patterns of the mothers. It is particularly interesting that a strong trend was seen in spite of the small sample sizes in some categories.

Clearly significant trends were seen across stress difference categories for the differences in thigh fatfolds between consecutive pregnancies during the first and second trimesters ($p < .01$). The trend was in the expected direction again, with the overlap pregnancies showing lower thigh fatfold measures. During the third trimester of pregnancy this trend difference disappears. Possibly the increased intake of the earlier trimesters

helped close the gap in terms of an energy deficit by the third trimester. In addition, fatfold measures taken close to the time before birth may not accurately reflect the fat layer. Some dramatic and unexplained changes in fatfold measures have been observed between late pregnancy and early postpartum (12) that may be physiological changes of maternal tissue interfering with measurement. The sample sizes are noticeably smaller when thigh fatfold is the outcome. Rates of missing data were high for maternal anthropometry. In part this is due to the fact that collection of maternal anthropometric data was begun in early 1971, 2 years after the beginning of the study. In addition, in this analysis paired measures from corresponding measurement periods were required for each pregnancy of the pair in order to calculate the differences, creating a further limitation. A stress-related trend for change in thigh fatfolds was not present at 3 months postpartum. It would be expected that such a trend would not be present at this point in time, particularly since it was not present in the third trimester of pregnancy.

Note that maternal age is always higher for the second pregnancy of the pair. And yet, regardless of birth order, the differences in maternal outcomes --supplement intake and thigh fatfold-- between consecutive pregnancies occur in the expected directions --based on the ordering of what is postulated to be the more stressful pregnancy.

The postulated trend in birthweight was not demonstrated, although given the relatively large variation seen with birthweight, the sample size may have been a limitation. Additional support for the postulated stress of presence of overlap and a short recuperation on birthweight has not been provided by these results. However, this is consistent with the suggestion of the previous work (1) that fetal growth is being protected at the "cost" of maternal nutritional status.

CONCLUSIONS

Further examination of the maternal and fetal responses to the stress of lactation concurrent with pregnancy and of short recuperative intervals has provided additional support for the hypothesis that these are stressful conditions for the mother –increasing supplement intake and reducing fat stores. The stress of these conditions on fetal growth was not demonstrated in these analyses, although there was a suggestion of it in previous analyses (1). It is important to control for inherent characteristics of the mothers that could confound the relationships of interest (among maternal and fetal responses to the presence of overlap, and the duration of recuperative intervals). This was accomplished in these analyses by pairing consecutive pregnancies within women. The results indicate that overlap is most stressful, short recuperative interval follows, and long recuperative interval is least energetically stressful on the mother. Data on three consecutive pregnancies for each woman (the two pregnancies of the consecutive births, in addition to the pregnancy prior to the first pregnancy of the pair) were required to address the questions of this study and the Guatemalan data set provided a rare opportunity to do this. In future research, a larger sample size would be desirable to examine more thoroughly the birthweight differences between consecutive pregnancies. More research is needed to address the consequences of frequent reproductive cycling, particularly the overlap of lactation with pregnancy and the length of recuperative intervals on mothers and their children.

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Table 1: Descriptive Statistics for Study Sample

	Paired Births - n	1st Mean (SD)	2nd Mean (SD)
C_{n-1} Lactation Duration (mo)	102	16.9 (4.9)	17.8 (4.8)
Birth Interval (mo)	102	26.9 (9.0)	25.6 (8.0)
Mother's Age (y) at Birth of C_n	102	28.3 (6.3)	30.4 (6.5)
Parity	100	5.0 (2.5)	6.0 (2.5)
C_n Gestational Age (wk)	102	39.8 (1.3)	39.6 (1.3)
C_n Lactation Duration (mo)	102	17.8 (4.8)	17.1 (7.6)
Mother's Height (cm)	101	149.8 (5.4)	
Mother's Head Circumference (cm)	101	51.2 (1.3)	
Father's Height (cm)	82	160.6 (6.1)	
Father's Head Circumference (cm)	82	54.3 (1.6)	
Distance to Supplement (min)	102	2.4 (1.0)	
<u>Proportions</u>			
Atole / Fresco		.63 / .37	
C_n Male / C_n Female		.51 /.49	.53 /.47

C_{n-1} = Previous Child, C_n = Index Child

Table 2: Descriptive Statistics for Subsample by Stress Category

	Stress Category 1			Stress Category 2			Stress Category 3			Stress Category 4			Stress Category 5		
		Paired Births			Paired Births			Paired Births			Paired Births			Paired Births	
		1st	2nd		1st	2nd		1st	2nd		1st	2nd		1st	2nd
	n	Mean (SD)	Mean (SD)	n	Mean (SD)	Mean (SD)	n	Mean (SD)	Mean (SD)	n	Mean (SD)	Mean (SD)	n	Mean (SD)	Mean (SD)
C_{n-1} Lactation Duration (mo)	7	16.3 (5.4)	13.8 (9.5)	14	17.8 (3.3)	16.0 (6.0)	40	17.2 (3.2)	17.8 (4.1)	21	15.6 (6.8)	20.0 (3.7)	20	17.1 (6.1)	18.6 (2.4)
Birth Interval (mo)	7	21.4 (6.4)	40.6 (21.7)	14	24.2 (3.8)	26.9 (6.9)	40	22.8 (3.2)	23.3 (4.1)	21	26.0 (6.5)	25.4 (4.5)	20	39.9 (10.3)	24.3 (3.0)
Mother's Age (y) at Birth of C_n	7	29.7 (8.2)	33.1 (9.3)	14	28.1 (7.0)	30.4 (7.1)	40	26.3 (6.0)	28.3 (6.1)	20	29.8 (6.0)	31.9 (6.2)	20	30.2 (5.4)	32.2 (5.5)
C_n Gestational Age (wk)	7	40.1 (1.9)	38.8 (0.4)	14	40.1 (1.5)	39.8 (0.7)	40	40.0 (1.2)	39.3 (1.3)	21	39.1 (0.8)	39.3 (1.4)	20	40.0 (1.4)	40.7 (1.0)
C_n Lactation Duration (mo)	7	13.8 (9.5)	12.0 (8.2)	14	16.0 (6.0)	17.7 (5.9)	40	17.8 (4.1)	16.2 (7.8)	21	19.6 (3.7)	17.8 (7.2)	20	18.6 (2.4)	19.3 (8.1)
Mother's Height (cm)	7	149.5 (4.2)		14	150.9 (5.4)		40	149.7 (5.4)		21	148.8 (6.1)		20	150.6 (5.6)	
Mother's Head Circumference (cm)	7	51.8 (1.3)		14	51.2 (1.4)		40	51.0 (1.5)		21	51.4 (1.1)		20	51.2 (1.2)	
Father's Height (cm)	5	160.5 (3.6)		12	160.6 (3.8)		31	161.1 (7.1)		19	160.6 (7.0)		15	159.7 (5.2)	
Father's Head Circumference (cm)	5	53.8 (2.0)		12	53.3 (0.6)		31	54.4 (1.4)		19	54.6 (2.0)		15	54.6 (1.4)	
Distance to Supplement (min)	7	2.6 (1.3)		14	2.2 (0.9)		40	2.3 (1.0)		21	2.2 (0.9)		20	2.6 (1.0)	
Proportions															
Atole / Fresco		.43 /.57			.50 /.50			.70 /.30			.52 /.48			.75 / .25	
		Paired Births 1st	Paired Births 2nd		Paired Births 1st	Paired Births 2nd		Paired Births 1st	Paired Births 2nd		Paired Births 1st	Paired Births 2nd		Paired Births 1st	Paired Births 2nd
C_n Male / C_n Female		.43 /.57	.29 /.71		.43 /.57	.43 /.57		.52 /.48	.58 /.42		.62 /.38	.62 /.38		.45 /.55	.50 /.50

C_{n-1} = Previous Child, C_n = Index Child

Table 3: Mean Differences Between Consecutive Births (2nd Birth of Pair minus 1st Birth of Pair) for General Characteristics

	n	Mean	SD
C_{n-1} Lactation Duration (mo)	134	-0.88	6.87
Birth Interval (mo)	134	-0.83	12.20
Mother's Age (y) at Birth of C_n	133	2.29	0.77
C_n Gestational Age (wk)	134	-0.17	1.72
C_n Lactation Duration (mo)	134	-0.49	8.18

Table 4: Tests for Trend Categories in Differences Between Consecutive Births (2nd Birth of Pair minus 1st Birth of Pair) for Supplement Intake

Stress Difference Category	1		2		3		4		5			
	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	ß p-value	Model R^2
Trimesters												
1st	7	-122 (105)	14	-46 (83)	40	-27 (77)	21	83 (128)	20	76 (125)	.0001	.25
2nd	7	- 43 (130)	14	-15 (108)	40	-22 (99)	21	49 (120)	20	58 (95)	.002	.09
3rd	7	9 (139)	14	-59 (14)	40	-39 (97)	21	36 (89)	20	70 (102)	.0005	.11
All	7	- 52 (116)	14	-40 (85)	40	-30 (70)	21	56 (89)	20	68 (86)	.0001	.21
Postpartum	5	- 44 (127)	14	9 (53)	38	-10 (95)	20	4 (123)	18	-32 (114)	.69	.002

Table 5: Tests for Trend Categories in Differences Between Consecutive Births (2nd Birth of Pair minus 1st Birth of Pair) for Thigh Fatfold and Birthweight

Stress Category	1		2		3		4		5			
	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	ß p-value	Model R^2
Thigh Fatfold												
Trimesters												
1st	2	7.9 (9.3)	5	0.3 (2.2)	21	-1.0 (2.3)	6	-0.3 (2.8)	2	-3.7 (2.4)	.005	.19
2nd	2	4.2 (5.9)	8	1.4 (1.5)	23	-1.1 (2.8)	8	-1.6 (3.7)	5	-1.9 (3.7)	.007	.15
3rd	2	-1.3 (0.6)	8	-0.1 (4.2)	23	-1.6 (2.5)	7	0.7 (3.8)	6	-1.4 (3.6)	.98	0
All	1	-0.4 (NA)	4	-0.2 (3.0)	16	-1.1 (1.9)	6	-0.9 (2.1)	2	-4.4 (2.5)	.15	.08
Postpartum	2	4.4 (4.9)	11	0.7 (3.5)	30	-1.0 (2.1)	8	2.0 (2.1)	7	-2.0 (5.0)	.12	.04
Birthweight												
	6	32 (506)	13	36 (440)	36	-34 (469)	16	114 (410)	15	-110 (456)	.63	.003

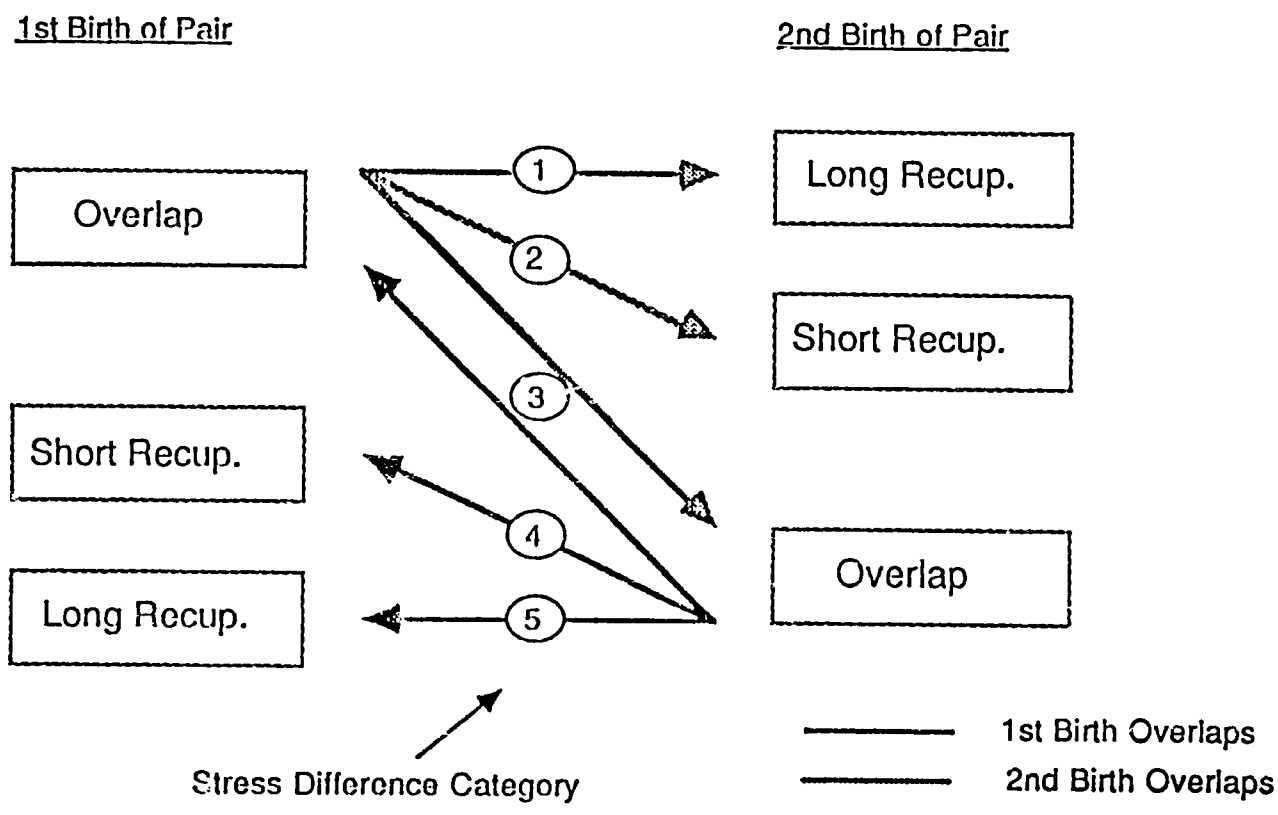
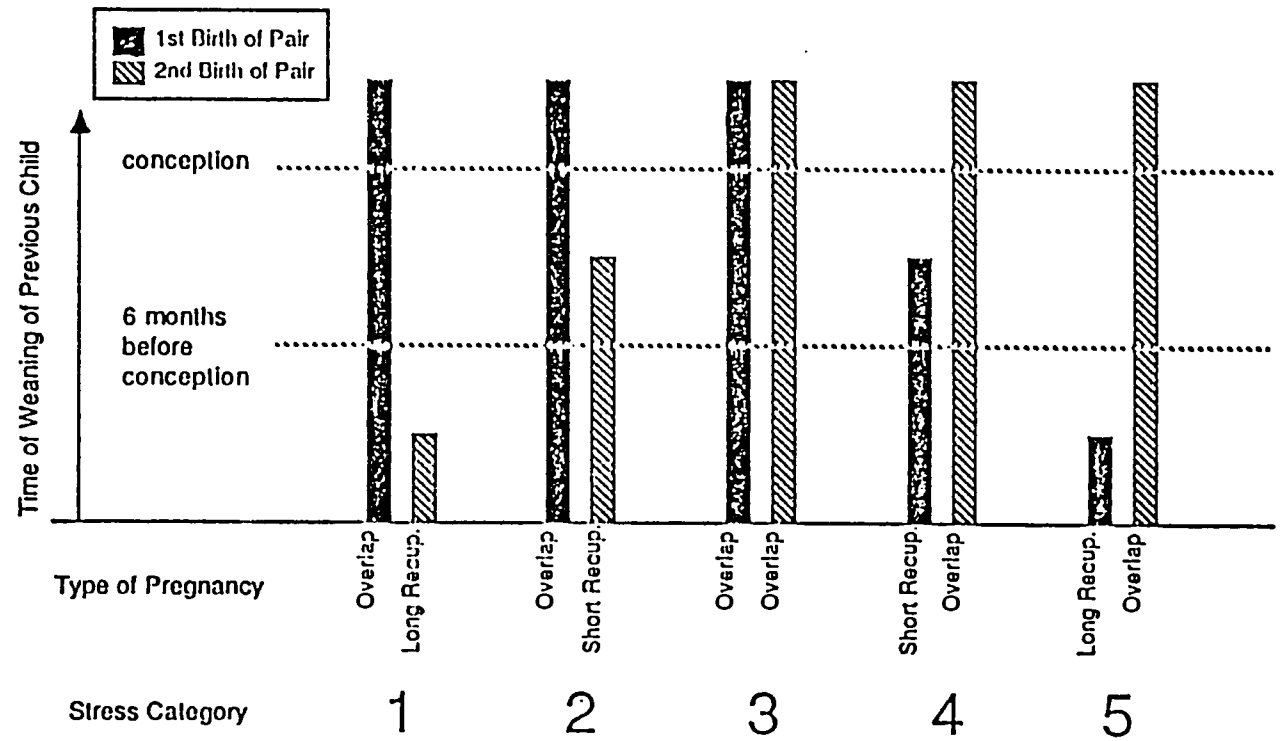


Figure 1: Classification into Stress Difference Categories



Predictions for Differences between Births (2nd Birth - 1st Birth) by Stress Difference Category :

Supplement Intake	−	−	No Change or +	+	+
Thigh Fatfold / Birthweight	+	+	No Change or −	−	−

Figure 2: Postulated energetic stress difference based on time of weaning of previous child for paired consecutive births

APPENDIX B

DISSERTATION

Merchant K. Maternal Nutritional Depletion: Consequences of the Energetic Stress of Frequent Reproductive Cycling on Mother and Fetus. Doctoral Dissertation. Ithaca, NY: Cornell University, Division of Nutritional Sciences. 1989.

PRESENTATIONS AND ABSTRACTS

1. "The Effect of Lactation Concurrent with Pregnancy on Fetal Growth, Maternal Nutritional Status and Dietary Intake in Supplemented Guatemalan Women." (Presented by Kathleen Merchant at the *Maternal Nutrition and Health Care Program; Technical Advisory Group Meeting*, January 24, 1989, Washington, D.C.)

2. "Lactation and Its Effect on Maternal Nutritional Status." (Presented by Tere Gonzalez-Cossio at the Maternal Nutrition and Health Care Program; Technical Advisory Group Meeting, January 24, 1989, Washington, D.C.)

3. Merchant, K and R. Martorell. The Effect of Lactation Concurrent with Pregnancy on Fetal Growth, Maternal Nutritional Status, and Dietary Intake in Supplemented Guatemalan Women. In: *Abstracts of the Federation of American Societies for Experimental Biology*, 3(3):A768. The 73rd Annual FASEB Meeting, New Orleans, Louisiana, March 21, 1989.

5. "Frequent Reproductive Cycling: Does It Lead to Nutritional Depletion of Guatemalan Mothers." (Presented by Kathleen Merchant at the *Field Seminar, Division of Nutritional Sciences*, Cornell University, Ithaca, New York, April 24, 1989.)

6. Merchant, K, Martorell, R and JD Haas. Effects of Overlap of Lactation with Pregnancy, Recuperative Intervals on Mother and Fetus. *The 14th International Congress of Nutrition*, Seoul, Korea, August 1989.

WORK IN PROGRESS

1. "The Effect of Parity on the Body Mass and Composition of Women during Lactation"

2. "Maternal Anthropometry to Predict Lactation Duration"

APPENDIX C

DESCRIPTION OF THE RESEARCH TEAM

Person	Present Employment and Address	Area of Specification	Role in Project
R. Martorell	Professor of Nutrition Food Research Institute Stanford University Stanford, CA 94305	Maternal and Child Health; Nutrition and Birth Weight	Principal Investigator
K. Merchant	Research Associate Food Research Institute Stanford University Stanford, CA 94305 (until December 31, 1989)	Reproductive Stress and Maternal and Fetal Responses	Major analytic and writing responsibilities
M. John	Associate Professor Office of Population Research 21 Prospect Road Princeton University Princeton, NJ 08544	Demography and Reproduction	Advisor on analytical methods
J. Rivera	Crecimiento y Desarrollo Division de Nutrición y Salud INCAP Carretera Roosevelt Zona 11 - Ap. Postal 1188 Guatemala City, Guatemala CENTRAL AMERICA	Maternal Nutrition and Birth Weight	Co-investigator; carried out research at INCAP
T. Gonzalez	Crecimiento y Desarrollo Division de Nutrición y Salud INCAP Carretera Roosevelt Zona 11 - Ap. Postal 1188 Guatemala City, Guatemala CENTRAL AMERICA	Maternal Nutrition and Birth Weight	Co-investigator; carried out research at INCAP

APPENDIX D

EVALUATION OF PARTICIPATION IN THE MATERNAL AND HEALTH CARE PROGRAM

Participation in a structured and coordinated multi-institutional research effort differs from the usual "take-your-money-and-go" administrative arrangement whereby each grantee works in isolation. Participation in ICRW's Maternal and Health Care Program gives one high expectations that the findings of the various investigators, by being integrated into a cohesive framework, will have a greater policy impact than ordinarily expected. We sincerely hope that this will be the case.

On a personal level, ICRW personnel, first Dr. Joanne Leslie and then Dr. Judith Timyan as Project Director and Ms. Laurie Parker as Administrative Assistant, made our job easier. They were always available and provided advise on administrative matters as required on a timely basis. Especially appreciated is the flexibility they have shown in meeting our research needs and in making accommodations to compensate for unforseen circumstances.

The positive aspects far outweigh the negatives. Of the latter, an important one is a sense of frustration at having stopped prematurely, at a point when we had uncovered major issues of importance. We realize that given the nature of the research "beast", analyses can seem to go on forever. However, the time frame of the project was too short; in our case by the time the data files were up and running, there was time to tackle some but not all of the major issues. It would have been a desirable feature of the time to have additional funding available to those research teams deserving assistance.

A second complaint had to do with the meeting held in January of 1989. The aims of this meeting were misunderstood by us, possibly because of poor communication. We thought the conference was to review preliminary research results in order to provide timely suggestions on design, analyses, and interpretation. Our presenters, K. Merchant and T. Gonzalez, felt that

members of ICRW's Advisory Committee expected finished products and that this may have explained the hostile reception to their presentation. Still, there were useful suggestions made in spite of some unpleasantness in the exchange of views. A recommendation for future meetings is to make them as inviting of free exchange as possible within a collegial environment.

The above complaint is minor and our feelings towards the project are very positive.