Short Interpregnancy Interval and the Risk of Low Birthweight

MARK A. KLEBANOFF, MD, MPH

Abstract: The effect of interpregnancy interval on the birthweight of the subsequent child was investigated in a cohort of 5,938 women who registered for two consecutive pregnancies in the Collaborative Perinatal Project. Mean birthweight increased from 3,101 grams for intervals of <3 months to 3,193 grams for intervals of 15–17.9 months and remained stable thereafter (p for trend = 0.006). However, women with shorter intervals were younger, lighter weight, and less educated at the beginning of the first pregnancy than were women with longer intervals; the birthweight of their previous child was lower, and they were of marginally lower socioeconomic status. Adjustment for confounders reduced the maximum difference in mean birthweight by interval length from 92 to 39 grams, and blunted the trend for lower birthweights with shorter intervals (p = 0.45). Similarly, adjustment reduced the increased risk of low birthweight among women with the shortest intervals from 52 per cent to 12 per cent. We conclude that a short interpregnancy interval is primarily a marker for a woman who is otherwise at high risk, and that modification of this interval alone may be unlikely to have a major impact on low birthweight. (*Am J Public Health* 1988; 78:667–670.)

Introduction

Women who become pregnant soon after completing a pregnancy are considered to be at high risk for the delivery of a low birthweight (LBW, <2500 gram) infant. The Institute of Medicine, in its report on the prevention of low birthweight, considered short interpregnancy interval to be a potentially modifiable risk factor for LBW,[1] and at least one obstetrical risk assessment tool considers short intervals as a risk factor for adverse outcome.[2] The presence of confounding and intervening variables may be important, as a woman who gives birth to a LBW child that subsequently dies might want a "replacement" child as soon as possible.[3] Alternatively, women who because of social or behavioral characteristics are at high risk might experience repeated pregnancies in a short time span. In these cases, the interpregnancy interval is only a marker for other factors, and modification of this interval would be unlikely to have a major effect on birthweight.

Studies based on birth certificates[1] and on women registering for prenatal care[4] have shown elevated risks of LBW among women who became pregnant soon after their last delivery. In the Norwegian birth registry, a decreased mean birthweight was noted in pregnancies beginning soon after the last birth, but the authors reported that nearly all of this effect was explained by the birthweight of the prior delivery.[3] The present study is the only one to collect in a prospective manner data on the birthweights of both pregnancies, as well as on other potentially confounding variables such as maternal stature and smoking. The effect of all of these factors on the association between interpregnancy interval and birthweight is the subject of this study.

Methods

The Collaborative Perinatal Project (CPP), a prospective multicenter study of approximately 55,000 pregnancies enrolled from 1959 to 1966, has been previously described.[5] Each center had its own sampling plan (e.g., enrolling every clinic registrant, a random sample of registrants, a systematic sample based on hospital number, or a fixed number of women per month). None of the sampling plans was dependent on parity, nor on the outcome of previous births. However, the very nature of this study resulted in the overrepresentation of women with short interpregnancy intervals, and the truncation of intervals to approximately six years. In order to obtain the most detailed, accurate data regarding both the current and prior pregnancies, this study was restricted to women who registered for two pregnancies in the CPP. There were 43,521 women in the sampling frame whose first pregnancy ended with the delivery of a singleton infant; 7,570 had a second singleton pregnancy in the CPP. The birthweight of the first child was unknown for 176, and 1,324 women had one or more intervening non-enrolled pregnancies between the pregnancies registered in the CPP. There were 42 cases where the interpregnancy interval or duration of the second pregnancy was unknown, primarily because of uncertainty regarding the last menstrual period (LMP), and 90 cases where the birthweight of the second child was unknown, leaving 5,938 women available for analysis.

Interpregnancy interval was defined as the elapsed time from the end of the first pregnancy to the first day of the LMP of the next pregnancy. This interval was grouped in 90-day periods for purposes of analysis. As 90 days is approximately three months, the intervals were considered to be three months long. Only 10.4 per cent of women had intervals of 27 months or longer, and there was no evidence of a trend for increasing or decreasing birthweight with these long intervals. Therefore, women with intervals of 27 months or longer were grouped with those who had intervals of 24–26.9 months.

In the first analysis, the mean birthweight for each time interval was calculated, and the difference was assessed by one-way analysis of variance. Evidence for a trend in birthweight was sought by entering the intervals as a continuous variable in a linear regression, with birthweight as the independent variable. The mean birthweight for each interval was then adjusted, using analysis of covariance, for confounding factors known to be associated with birthweight. When a confounder could change over time, for example maternal weight, education and smoking, the value at the beginning of the first pregnancy was used for adjustment. Although values from the first pregnancy have only an indirect effect on the outcome of the second, they were chosen because they could not possibly be on the casual path from the time interval to the outcome of the subsequent pregnancy. For example, the stress of being pregnant while taking care of a small infant might cause a woman to increase her smoking. In that case, adjustment for smoking during the second pregnancy might not be appropriate, as the short interval caused the increase in smoking.

Address reprint requests to Mark A. Klebanoff, MD, MPH, Epidemiology Branch, National Institutes of Child Health and Human Development, National Institutes of Health, Landow Building, Rm 8A04, Bethesda, MD 20892.
This paper, submitted to the Journal June 26, 1987, was revised and accepted for publication November 10, 1987.

In the next analysis, the fraction of infants that was LBW was determined for each interval; statistical significance was assessed using Armitage's test for trend.[6] Odds ratios for LBW were calculated, with women having the shortest interpregnancy intervals (<3 months) serving as the reference group. Woolf's method[7] was used to calculate 95 per cent confidence intervals, and odds ratios were adjusted for confounders using multiple logistic regression.

Results

The mean and adjusted mean birthweights for each interval are presented in Table 1. Mean birthweight increased by 92 grams as the interval from delivery to LMP increased from <3 months to 15–17.9 months; intervals longer than this did not show further systematic changes in mean birthweight. The overall trend, when tested by simple linear regression, was for an increase in mean birthweight of 8.8 grams per three-month increase in interpregnancy interval (standard error = 3.2); heterogeneity among the specified pregnancy intervals could not be demonstrated by analysis of variance ($F(8,5929) = 1.34$, $p = 0.22$).

Evaluation of other characteristics indicated that maternal age, weight, and education at the beginning of the first pregnancy were all positively associated with interpregnacy interval; women with shorter intervals were younger, lighter weight, and had less education as baseline characteristics. The birthweight of the first child was also positively associated with time interval, and women with shorter intervals were slightly less likely to be White than were women with longer intervals. The mean birthweight was adjusted for these factors, plus smoking and socioeconomic index[8] at registration for the first pregnancy. The beneficial effect of a longer interval diminished from 92 grams to 39 grams, and the trend for increased birthweight with increased interval was blunted ($p = 0.45$) after this adjustment.

Table 2 shows the crude and adjusted odds ratios for the delivery of a LBW infant. The smallest risk of low birthweight was seen among women with interpregnancy intervals of 15–17.9 months. Compared to women who had intervals of <3 months, women with intervals of 15–17.9 months had an odds ratio for LBW of 0.66, which corresponds to a 52 per cent increase in risk (1/0.66) among women with the shortest intervals. After adjustment, the odds ratio increased to 0.89, corresponding to only a 12 per cent increase in risk (1/0.89) of LBW among women with the shortest intervals. Adjustment for confounders similarly reduced the benefits of all intervals compared to the shortest interval. All of the confounding variables in the model presented in Table 2 were associated with LBW in the univariate analyses. After adjustment, all confounders retained their association except for maternal education, which no longer was associated with LBW after controlling for socioeconomic index. There was no trend for increasing or decreasing risk of LBW with increasing time, either before or after adjustment, and there were no interactions involving interpregnancy interval.

The relationship between interpregnancy interval and delivery of a small for gestational age (SGA) infant (weighing less than the 10th percentile for race, sex, and gestational age using California standards[9]) is presented in Table 3. The interval with minimum risk, 18–20.9 months, was associated

TABLE 1—Mean and Adjusted Mean Birthweight by Interpregnancy Interval

Interval (Months)	n	Mean Birthweight (grams)*	Adjusted Mean Birthweight (95% CI)**
<3	623	3101	3161 (3082, 3240)
3–5.9	1,285	3135	3165 (3062, 3238)
6–8.9	1,014	3149	3169 (3094, 3244)
9–11.9	739	3155	3179 (3102, 3256)
12–14.9	535	3185	3200 (3117, 3283)
15–17.9	422	3193	3151 (3065, 3237)
18–20.9	297	3167	3178 (3085, 3271)
21–23.9	237	3163	3159 (3061, 3257)
≥24	786	3186	3186 (3108, 3264)

*$F(8,5929) = 1.34$, $p = 0.22$. p for trend = 0.006

**Adjusted for maternal age, education, socioeconomic index, smoking, and weight at the start of the first pregnancy, birthweight of the last child, and maternal race using analysis of covariance, p for trend = 0.45.

TABLE 2—Fraction of Births Less than 2,500 G by Interpregnancy Interval

Interval (Months)	n	Per Cent LBW	Odds Ratio (95% CI)*	Adjusted Odds Ratio (95% CI)**
<3	623	12.4	1.00	1.00
3–5.9	1,285	12.1	0.98 (0.73, 1.31)	1.14 (0.82, 1.58)
6–8.9	1,014	11.2	0.90 (0.66, 1.22)	1.10 (0.78, 1.56)
9–11.9	739	10.8	0.86 (0.62, 1.20)	0.96 (0.66, 1.40)
12–14.9	535	10.3	0.81 (0.56, 1.17)	0.95 (0.63, 1.43)
15–17.9	422	8.5	0.66 (0.44, 1.00)	0.89 (0.56, 1.43)
18–20.9	297	10.4	0.83 (0.53, 1.29)	0.99 (0.61, 1.60)
21–23.9	237	9.3	0.73 (0.44, 1.20)	0.86 (0.49, 1.49)
≥24	786	11.2	0.89 (0.64, 1.23)	1.06 (0.74, 1.54)

*p for trend = 0.12

**Adjusted for maternal age, education, socioeconomic index, smoking, and weight at the start of the first pregnancy, birthweight of the last child, and maternal race using logistic regression. p for trend = 0.48. Interactions between interpregnancy interval and all of the above main effects were included in a backward-stepping model (p to remove = 0.05). None of the interactions was retained.

TABLE 3—Intrauterine Growth Retardation by Interpregnancy Interval

Interval (Months)	n	Per Cent IUGR	Odds Ratio (95% CI)*	Adjusted Odds Ratio (95% CI)**
<3	543	14.2	1.00	1.00
3–5.9	1,152	12.2	0.85 (0.63, 1.15)	0.96 (0.69, 1.34)
6–8.9	892	11.7	0.80 (0.58, 1.10)	0.88 (0.62, 1.25)
9–11.9	662	11.5	0.78 (0.56, 1.10)	0.85 (0.59, 1.24)
12–14.9	477	11.5	0.79 (0.55, 1.14)	0.91 (0.61, 1.37)
15–17.9	386	10.6	0.72 (0.48, 1.08)	0.95 (0.61, 1.46)
18–20.9	277	10.1	0.68 (0.43, 1.08)	0.81 (0.50, 1.32)
21–23.9	217	12.9	0.90 (0.57, 1.43)	0.88 (0.52, 1.50)
≥24	735	12.4	0.86 (0.62, 1.14)	0.92 (0.64, 1.33)

*p for trend = 0.46

**Adjusted for maternal age, education, socioeconomic index, smoking, and weight at the start of the first pregnancy, birthweight of the last child, and maternal race using logistic regression. p for trend = 0.58.

with an odds ratio for SGA of 0.68, corresponding to a 47 per cent increase in risk among women with intervals of <3 months. After adjustment, the odds ratio increased to 0.81, corresponding to a 23 per cent increase in risk for women with the shortest intervals. Adjustment for confounders therefore reduced by half the increase in risk associated with a short interpregnancy interval.

The possibility that such factors as age, education, and prepregnant weight exert their effect via short intervals was considered. Table 4 lists the cross-classified effects of prepregnant weight (from before the first study pregnancy) and interval. For nearly every interval, maternal prepregnant weight was inversely related to the fraction of infants that were LBW. However, within weight categories the effect of interpregnancy interval was minimal. Similarly, independent effects were seen for maternal race, age, education, and weight at the start of the second study pregnancy; interpregnancy interval had relatively little effect within each of these categories.

Discussion

The results of this study were unexpected. It was initially believed that sociodemographic characteristics such as maternal education and socioeconomic index would exert their adverse effects at least in part through a shortened interpregnancy interval, since from a biologic point of view it is extremely unlikely that these variables are directly responsible for an increased risk of LBW. Instead, it was found that a short interpregnancy interval exerts its effect through the baseline risk profile of the mother. That is, women who became pregnant again soon after completing a pregnancy appeared to be at high risk of giving birth to a LBW infant even before the interval began. This was confirmed when interpregnancy interval and other confounders were evaluated using multivariable techniques. The influence of the "confounders", all of which were determined before the start of the interpregnancy interval, was by and large unchanged but the adverse effect of short intervals was greatly reduced.

The results of this study agree with those of Erickson and Bjerkedal,[3] who noted that the association between interval and birthweight of the earlier born sibling is nearly identical to the association for the later born one. They concluded that the association between interpregnancy interval and birthweight is indirect, and that there were common factors associated with the propensity to have both short intervals and small infants. They also found slight differences in this association depending on whether the pairs were first and second born or second and third born; we found no interactions or significant effects involving maternal parity at the start of the first study pregnancy.

Vital statistics from 49 states and the District of Columbia for 1981 indicated that the relative risk of LBW for intervals of less than six months compared with intervals of 24–35 months was approximately 2.1 for Whites and 1.8 for Blacks.[1] We found a minimum odds ratio for LBW of 0.66, corresponding to a 52 per cent increase in risk of LBW for women in this CPP population (52 per cent White, 45 per cent Black, 3 per cent Puerto Rican). The 95 per cent confidence interval for this odds ratio (0.44, 1.00) includes the level of risk seen in the entire US; however, it is likely that the relative socioeconomic homogeneity of the CPP as compared to the general US population accounts for the diminished risk of short intervals. Birth certificates include the date of termination and outcome of the last pregnancy, but they do not contain data on the last birthweight. This is a major confounder, as the birthweights of successive sibs are correlated,[10] and larger children were followed by a longer interpregnancy interval than were smaller children. It is perhaps noteworthy that the present study and that of Erickson and Bjerkedal,[3] both of which dispute the causal effect of short interpregnancy intervals on the occurrence of LBW, are the only prospective studies of this issue. Both of these studies had at their disposal the birthweight of the earlier-born child of the pair in question, and both noted that LBW infants were followed by a shorter interpregnancy interval than were non-LBW infants. Retrospective studies[1,4] (studies that based their ascertainment on the later-born child of the pair) did not have available detailed data on the birthweight of the earlier-born sib. They therefore did not have available optimal data on the risk status of the mother when the interval began.

Brody and Bracken[4] noted a markedly elevated risk of LBW among women conceiving within one to four months of a previous birth, and a moderately elevated risk among women conceiving within four to eight months compared to women conceiving after nine months. This risk was not diminished after adjustment for confounders, including previous LBW births. There were only 20 women conceiving after one to four months, two of whom had a LBW infant, and 101 conceiving after five to eight months, six of whom had a LBW infant. The point estimates for the relative risks were therefore unstable, with 95% confidence intervals stretching from 0.95 to 14.22.

The present study differs from all others as it was based on consecutive pregnancies rather than consecutive live births. As such, it did not deliberately exclude pregnancies ending in miscarriage or stillbirth. However, birthweight was unknown for the vast majority of miscarriages and only 23 women whose first study pregnancy ended in this manner were included. Elimination of these 23 women had little effect on the results. Pregnancies ending in stillbirth were deliberately included. Prenatal and intrapartum care have undergone great changes since the last CPP pregnancy was enrolled in 1966, and women believed to be at high risk of stillbirth are now likely to receive ante- and intrapartum monitoring using tests that did not exist at the time of the CPP. Modern obstetric and neonatal management might have converted some of the stillbirths into neonatal deaths (who would have had a certificate of live birth), or even into survivors. Stillbirths were therefore included to make these data more relevant to the 1980s. Restriction of these analyses to women having two consecutive live births of at least 500 grams

TABLE 4—Cross-Classified Effects of Interpregnancy Interval and Pre-Pregnancy Weight

Interval (Months)	Prepregnant Weight		
	<53.2 kg	53.2–60.9 kg	>60.9 kg
	number in category (per cent LBW)		
<3	203 (15.3)	199 (10.1)	204 (11.3)
3–5.9	408 (15.2)	449 (12.0)	391 (9.2)
6–8.9	326 (16.0)	344 (9.6)	315 (8.6)
9–11.9	257 (14.8)	219 (10.1)	236 (7.2)
12–14.9	192 (16.1)	172 (10.5)	154 (3.3)
15–17.9	131 (10.7)	137 (11.0)	140 (5.0)
18–20.9	96 (16.7)	92 (8.7)	107 (6.5)
21–23.9	82 (17.1)	65 (7.7)	84 (2.4)
≥24	241 (12.9)	247 (12.8)	269 (9.7)

yielded results similar to those presented. The data for this study are over 20 years old. One major relevant difference between the 1960s and 1980s is the availability of the Special Supplemental Food Program for Women, Infants and Children (WIC), which may be responsible for improvement in birthweight.[11] It is likely that many women in the CPP, had they been pregnant in the 1980s, would have been eligible for WIC during the first study pregnancy. The child from this pregnancy might have been eligible for WIC assistance during the time of the interpregnancy interval, thereby making available more resources to feed the mother and the rest of the family. The mother herself might have been eligible for assistance during the subsequent pregnancy. If there is a nutritional basis for an adverse effect of short interpregnancy intervals, then WIC supplementation might make short intervals even less detrimental than they were at the time of the CPP.

In summary, we found that birthweight decreased with decreasing interpregnancy interval, but also that women with short intervals were at relatively high *a priori* risk of having a small infant. Short interpregnancy interval ceased to be an important risk factor for low birthweight after adjustment for these confounders; modification of the interval alone is unlikely to have a large influence on birthweight. In the CPP, effect of short interpregnancy interval did not vary by maternal race or weight at the start of the first study pregnancy.

Nevertheless, these results may not apply to pregnant women in developing countries, where gross clinical malnutrition is almost certainly more common than among women registered in the CPP. There may be other adverse developmental outcomes associated with closely spaced pregnancies, but it would appear unwise to assume so without documentation which includes careful control of confounders.

REFERENCES

1. Committee to Study the Prevention of Low Birthweight, Division of Health Promotion and Disease Prevention, Institute of Medicine: Preventing Low Birthweight. Washington, DC: National Academy Press, 1985.
2. Creasy RK, Gummer BA, Liggins GC: System for predicting spontaneous preterm birth. Obstet Gynecol 1980; 55:692–695.
3. Erickson JD, Bjerkedal T: Interpregnancy interval: association with birthweight, stillbirth, and neonatal death. J Epidemiol Community Health 1978; 32:124–130.
4. Brody DJ, Bracken MB: Short interpregnancy interval: a risk factor for low birthweight. Am J Perinatol 1987; 4:50–54.
5. Niswander KR, Gordon M (eds): The Women and Their Pregnancies. Philadelphia: W.B. Saunders, 1972.
6. Armitage P: Statistical Methods in Medical Research. Oxford: Blackwell Scientific, 1971; 363–365.
7. Woolf B: On estimating the relation between blood group and disease. Ann Hum Genet 1955; 19:251–253.
8. Myrianthopoulos NC, French KS: An application of the US Bureau of the Census socioeconomic index to a large, diversified patient population. Soc Sci Med 1968; 2:283–299.
9. Williams RL, Creasy RK, Cunningham GC, *et al*: Fetal growth and perinatal viablity in California. Obstet Gynecol 1982; 59:624–632.
10. Morton NE: The inheritance of birthweight. Ann Hum Genet 1955; 20:125–134.
11. Kotelchuck M, Schwartz JB, Anderka MT, Finison KS: WIC participation and pregnancy outcomes: Massachusetts statewide evaluation project. Am J Public Health 1984; 74:1086–1092.

Special Issue of QRB Addresses Problem of Impaired Practitioners

A special April issue of the *Quality Review Bulletin (QRB)* explores solutions to the growing problem of impaired physicians, nurses, pharmacists, and mental health professionals. *QRB* is the monthly refereed journal of quality assurance, published by the Joint Commission on Accreditation of Healthcare Organizations. The April issue features practical expertise of prominent authorities on dealing with impairment, and offers practitioners, managers, and quality assurance professionals an inside view into intervention models, treatment programs, follow-up care methods, and risk management issues.

''Practitioner impairment presents a true threat to the health professions and to the well-being of patients in this country,'' said William Jessee, MD, Joint Commission vice president for education. ''This special-focus *QRB* will heighten health care provider's awareness of these problems and give helpful information to the many impaired practitioner programs that now assist professionals suffering from substance abuse and mental illness.''

Chemical dependence is believed to be a leading occupational hazard for physicians. A critical study for the *New England Journal of Medicine* found that 59 per cent of physicians and 78 per cent of medical students in Massachusetts had used psychoactive drugs at some point in their lives. According to the American Nurses' Association, 6 per cent to 8 per cent of the nation's 1.9 million registered nurses are addicted to drugs or alcohol.

To order the April issue of *QRB*, or to subscribe to the monthly journal, contact the Joint Commission's customer service unit at (312) 642-6061, extension 650, or write to Joint Commission, 875 North Michigan Ave., Chicago, IL 60611.