*A number of earlier studies showed that smoking mothers produced smaller infants and had a higher incidence of premature births than nonsmoking mothers. The data of a Baltimore study reported in 1961 are reexamined by means of multiple regression analysis to investigate the relationship of smoking to birth weight and length of gestation after adjustment for the effects of concomitant variables in the mother and infant. The findings confirm those reported in the original analysis of the Baltimore data. Implications for future research are examined.*

# SMOKING AS AN INDEPENDENT VARIABLE IN A MULTIPLE REGRESSION ANALYSIS UPON BIRTH WEIGHT AND GESTATION

*James R. Abernathy, Ph.D.; Bernard G. Greenberg, Ph.D., F.A.P.H.A.; H. Bradley Wells, Ph.D., F.A.P.H.A.; and Todd M. Frazier, Sc.M.*

DESCRIPTION of the Baltimore Study—The objective of the study conducted in Baltimore by Frazier, et al.,[1] was to determine "whether or not smoking is a significant determinant of prematurity (birth weight of 2,500 grams or less)." Data on 2,736 Negro women seen at the Maternity Interviewing Service Clinic during 1959 who were scheduled for delivery at the Baltimore City Hospital and who received care in prenatal clinics of the Baltimore City Health Department were analyzed. This selection procedure provided an economically and racially homogeneous group whose members had a relatively similar prenatal and delivery experience.

Information for each event was collected from three sources. The first was an interview which consisted of questions concerning smoking history, work history, education, and psychosomatic complaints. The questions used to develop a psychosomatic complaint score were those proposed by Stouffer and associates.[2] The second source of information was the prenatal clinic history from which blood group type, initial hemoglobin values, and data on hypertension and eclampsia were obtained. The third source was the birth or stillbirth certificate.

Results of Baltimore Study Previously Reported—The cited study by Frazier, et al., reported in 1961 that the incidence of premature birth in infants was higher among smoking than nonsmoking mothers. This difference existed even after allowance was made for parity, maternal age, psychosomatic complaint score, work history, education of mother, or gestation. In spite of the high correlation between birth weight and gestation, the average length of gestation for smoking and nonsmoking mothers was found to be essentially the same, 38.4 weeks for women who smoked compared to 38.7 for nonsmokers.

Results of Similar Studies—In a study

of 2,000 women delivered in Birmingham, England, Lowe[3] reported in 1959 that smoking mothers produced smaller infants than nonsmokers. He further reported no substantial difference in length of gestation of smokers and nonsmokers and concluded that, since the effect of smoking on birth weight is not due to a shortening of gestation, it must be attributed to a direct retardation of fetal growth. The effect of smoking on birth weight was unrelated to maternal weight, age, parity, or complications of pregnancy.

Savel and Roth,[4] in a study of 1,400 mothers in a Newark hospital, reported in 1962 that babies born to white mothers who smoked weighed, on the average, 8 ounces less than infants of white nonsmokers. Among Negroes, babies born to smokers averaged 5 ounces less than those born to nonsmokers. Average period of gestation was approximately the same for infants of smokers as nonsmokers.

Herriot, et al.,[5] in a study of 2,700 women in Aberdeen in 1960 reported similar findings. They considered age, parity, height, food intake, and social class of smokers and nonsmokers.

The Surgeon General's Advisory Committee on Smoking and Health,[6] after studying available evidence, concluded that "women who smoke during pregnancy tend to have babies of lower birth weight." No mention was made of gestation. Goldstein, et al.,[7] have prepared an excellent summary of retrospective and prospective studies pertaining to smoking and prematurity covering the period from 1957 to 1963. This summary was based upon a review prepared for the Surgeon General's Advisory Committee.

## Objective of Present Paper

In most of the reports relating to smoking and birth weight, the analysis of data consisted mainly of a comparison of the mean birth weight of infants of smokers and nonsmokers, specific for one or possibly two variables, such as race, maternal age, parity, height, and social class. This is, of course, a valid and acceptable method of analysis. It is not necessarily the most efficient and reliable method of determining the relationship between smoking and birth weight, or between smoking and period of gestation, when many other concomitant variables are associated with the two under study. Multiple regression is a method which permits the simultaneous handling of many variables in order to isolate the effect of each factor adjusted for the presence of the remainder.

The Baltimore Study data have been re-analyzed by using multiple linear regression procedures with birth weight and gestation alternating as response variables. One purpose of the analysis was to determine the relative individual importance of several independent factors in accounting for variations in birth weight and gestation after adjustment for other variables. Primary emphasis would be, of course, upon the smoking variable. Another purpose was to determine the strength of the relationship between the independent variables and the response variable. This is measured by $R^2$, the ratio of the sum of squares for regression to the total sum of squares.

The mathematical model for the regression function may be written

$$Y = \sum_{i=0}^{r} B_i X_i + E$$

and

$$\hat{Y} = \sum_{i=0}^{r} b_i X_i \qquad (1)$$

where

$Y$ = the response variable, birth weight (grams) or gestation (weeks)

$\hat{Y}$ = predicted value of $Y$

$b_i$ = partial regression coefficients computed from the data, estimating $B_i$ in the population

$X_i$ = i-th independent fixed variable considered to be related to Y

r = number of independent variables in the model

E = random error associated with a given Y.

This is simply another way of examining the relationship between smoking and birth weight, or smoking and gestation, at the same time that consideration is given to the relationship of other variables to these responses. Smoking is postulated as one of several "characteristics" of the mother (or variables) which could influence birth weight and/or gestation. This type of analysis permits an estimate of the relative importance of each variable, after adjustment for other variables in the regression function. Consideration of multiple characteristics of the mother simultaneously with regard to their effect on birth weight and gestation is a special feature of this approach. The theory and assumptions underlying the method can be found in most statistical texts and will not be considered here.

There were 15 independent variables used in the birth weight analysis. Several of these variables were subdivided in order to estimate the effect of various contrasts within the variable; for example, mother's hemoglobin was classified as either high, medium, low, or unknown as shown in the footnote to Table 1. These four groupings gave rise to three independent contrasts with one degree of freedom associated with each contrast. The total effect of hemoglobin as a variable was measured by eliminating all components of the variable from the regression function and reanalyzing the data.

The 15 variables and contrasts are shown in Table 1 with their means. The coding used for each of the contrasts (+1 or −1) and a list of the interaction effects are also included.

There were 2,700 live births included in the analyses, 36 having been eliminated due to incomplete data.

## Results and Discussion

Birth Weight Analysis—The full complement of 40 variable/effects listed in Table 1 was included in the first analysis, the primary purpose of which was to test the interaction terms upon birth weight. The data are not shown here but, of the 12 interactions included, only two were significant: sex x parity and sex x maternal age x parity. As indicated by $R^2$, 25 per cent of the variation in birth weight was accounted for or "explained" by the 40 variable/effects. The two effects, gestation and gestation squared, unadjusted for other variables, accounted for 18 per cent of the variation in birth weight. Smoking history alone (unadjusted) accounted for only 1.6 per cent.

The ten nonsignificant interactions were omitted from the function, and the 30 remaining variable/effects were analyzed in order to retest them under this reduced model. In this second stage of analyses, the psychosomatic complaint score was nonsignificant, as was marital status, maternal age squared, work in first trimester, trimester of interview, blood group, and education of mother. It should be emphasized that, for the last three variables mentioned, not only was each separate contrast nonsignificant but the total effect of each variable was tested and also found to be nonsignificant. Sixteen of the 30 variable/effects were significant in this second analysis. They comprised the third and final model, the analysis of which is shown in Table 2.

These 16 variable/effects accounted for 24 per cent of the variation in birth weight, compared with 25 per cent in the full model of 40 variable/effects.

As indicated by the partial regression coefficients, higher average birth weight of infants was associated with the following: male infants, nonsmoking mothers, mothers with low as compared with high hemoglobin, and eclamptics.

Higher average birth weight for infants of eclamptic mothers may have been due to special care and treatment during pregnancy. An increase in birth weight was also associated with an increase in gestation and parity. Some of the effects or contrasts of data involving unknown values were also significant. For exam-

**Table 1—Variable/effects and their means, and interactions used in the analysis of birth weight, and gestation, live births, Baltimore Smoking and Prematurity Study, 1959**

| Variable/Effects | Mean |
|---|---|
| 1. Birth weight (grams) | 3,023.89 |
| 2. a. Gestation (weeks) | 38.09 |
| b. Gestation squared | 1,463.25 |
| 3. a. Maternal age (years) | 24.42 |
| b. Maternal age squared | 631.96 |
| 4. a. Parity (total births) | 3.64 |
| b. Parity squared | 18.41 |
| 5. Smoking history: smoker (+1) vs nonsmoker (−1), (% smokers) | 43.43 |
| 6. *Psychosomatic score: high (−1) vs low (+1), (% high) | 19.48 |
| 7. Work in first trimester: worked (+1) vs not worked (−1), (% worked) | 31.94 |
| 8. Marital status: married (+1) vs unmarried (−1), (% married) | 61.96 |
| 9. a. Blood group I: A (+1) vs AB (−1), (% type A) | 24.89 |
| b. Blood group II: B (+1) vs AB (−1), (% type B) | 18.86 |
| c. Blood group III: O (+1) vs AB (−1), (% type O) | 46.71 |
| d. Blood group IV: unknown (+1) vs AB (−1), (% unknown) | 5.48 |
| 10. †a. Hemoglobin I: medium (+1) vs low (−1), (% medium) | 58.44 |
| b. Hemoglobin II: high (+1) vs low (−1), (% high) | 31.40 |
| c. Hemoglobin III: unknown (+1) vs low (−1), (% unknown) | 7.93 |
| 11. a. Hypertension I: with (+1) vs without (−1), (% with) | 6.69 |
| b. Hypertension II: unknown (+1) vs without (−1), (% unknown) | 10.96 |
| 12. ‡a. Trimester of interview I: 1st (+1) vs 3rd (−1), (% 1st) | 8.00 |
| b. Trimester of interview II: 2nd (+1) vs 3rd (−1), (% 2nd) | 59.61 |
| 13. Sex: male (+1) vs female (−1), (% male) | 49.27 |
| 14. a. Eclampsia I: with (+1) vs without (−1), (% with) | 11.18 |
| b. Eclampsia II: unknown (+1) vs without (−1), (% unknown) | 11.00 |
| 15. a. Mother's education I: 7-9 grade (+1) vs 1-6 (−1), (% 7-9 grade) | 42.18 |
| b. Mother's education II: 10-12 grade (+1) vs 1-6 (−1), (% 10-12 grade) | 44.01 |
| c. Mother's education III: beyond HS (+1) vs 1-6 (−1), (% beyond HS) | 1.32 |
| d. Mother's education IV: nongraded (+1) vs 1-6 (−1), (% nongraded) | 1.50 |
| Interactions: Smoking history x maternal age x parity | |
| Smoking history x parity | |
| Smoking history x maternal age | |
| Maternal age x psychosomatic score x parity | |
| Gestation x psychosomatic score | |
| Maternal age x psychosomatic score | |
| Sex x parity | |
| Sex x parity x maternal age | |
| Sex x maternal age | |
| Psychosomatic score x parity | |
| Maternal age x parity | |
| Smoking history x psychosomatic score | |

* Psychosomatic complaint score: High—5 or more positive responses to 15 questions developed by Stouffer.[2]
Low—less than 5 positive responses to 15 questions developed by Stouffer.

† Hemoglobin: High—11.6 gm or more per 100 cc blood.
Medium— 8.7-11.5 gm per 100 cc blood.
Low—less than 8.7 gm per 100 cc blood.

‡ Trimester of interview: trimester in which prenatal care was begun.

**Table 2—Regression analysis of birth weight, Baltimore Smoking and Prematurity Study, 1959**

| Variable/Effects | b | F |
|---|---|---|
| 1. a. Gestation | 214.32 | 64.52† |
| b. Gestation squared | −2.08 | 31.80† |
| 2. Smoking history | −64.27 | 45.25† |
| 3. Maternal age | 4.15 | 3.73 |
| 4. a. Parity | 56.58 | 14.60† |
| b. Parity squared | −3.68 | 6.94† |
| 5. Sex | 52.68 | 6.40* |
| 6. a. Hemoglobin I | 16.45 | 0.57 |
| b. Hemoglobin II | −45.38 | 3.83 |
| c. Hemoglobin III | −71.77 | 3.89* |
| 7. a. Hypertension I | −77.77 | 2.35 |
| b. Hypertension II | 224.02 | 6.24* |
| 8. a. Eclampsia I | 131.37 | 7.73† |
| b. Eclampsia II | −259.98 | 8.74† |
| Sex x parity | 29.92 | 3.92* |
| Sex x maternal age x parity | −0.84 | 3.81 |
| $R^2$ | 0.2403 | |

* Significant at the 5% level of probability.
† Significant at the 1% level of probability.

ple, higher average birth weight was observed in infants of mothers for whom the presence or absence of hypertension was unknown than in those infants whose mothers were known to be free of hypertension. This may reflect omission of data on blood pressure among mothers who were unquestionably in good health. It would appear that the opposite may be true for mothers with unknown hemoglobin, and mothers unknown as to the presence or absence of eclampsia. Infants of mothers for whom the presence or absence of eclampsia was unknown had a lower average birth weight than infants of mothers without eclampsia. Similarly, infants of mothers with unknown hemoglobin had a lower average birth weight than infants of mothers with low hemoglobin.

After adjustment for the other variables in the regression function, smoking history remained highly significant. Even though significant, the smoking variable accounted for only 1.3 per cent of the total variation in birth weight, compared with 1.6 per cent when concomitant variables were not considered. The magnitude of the smoking effect upon birth weight can be measured in still another way by examining the smoking component of $\hat{Y}$, the predictive equation. The total effect of smoking adjusted under this model is found to be

$$-2(64.27) = -128.54 \text{ grams} \quad .$$

This means that the predicted birth weight of infants of smokers was 129 grams less than infants of nonsmokers. This difference is 144 grams when based upon the regression of birth weight on smoking history alone without considering other variables. In other words, the simultaneous consideration of other variables reduced by about 10 per cent what one would have inferred as the effect of smoking upon birth weight.

The magnitude of the gestation effect, including gestation squared, can be determined in a like manner. For example, as gestation increased from 34 to 35 weeks the predicted birth weight increased 70.8 grams, computed as follows:

$$[214.32(35) - 2.08(35)^2] - [214.32(34) - 2.08(34)^2] = 70.8 \quad .$$

Similar computations for 37 to 38 weeks and 40 to 41 weeks' gestation yielded birth weight increases of 58.3 and 45.8 grams, respectively. Under this model, as gestation increased, the predicted birth weight increased but by gradually decreasing amounts.

The effect of other variables upon birth weight can be determined from the regression coefficients in a similar fashion.

Gestation Analysis—The same variable/effects as used in the first model of the birth weight analysis were used in the gestation analysis with one exception. Since gestation was the response variable, gestation squared, and gestation x psychosomatic complaint score were deleted from the model. Birth weight replaced gestation as an independent variable and this left 38 independent variable/effects.

The first stage test of the 11 interactions produced only one significant effect (sex x parity). The 38 variable/effects in this model accounted for 20.5 per cent of the total variation in length of gestation. Birth weight alone (unadjusted) accounted for 17.1 per cent of the total variation.

The ten nonsignificant interactions were eliminated and the reduced second stage model of 28 effects was analyzed. All but six were nonsignificant. The third and final analysis, the results of which are shown in Table 3, consisted of these six effects and, in addition, trimester of interview II and hemoglobin III. The latter two effects were nonsignificant by themselves but the total effect of trimester of interview and hemoglobin were significant. Therefore, these two contrasts were included in the final analysis for completeness.

These 8 variable/effects accounted for 19.8 per cent of the variation in length of gestation, compared with 20.5 per cent in the full model of 38 variable/effects.

The regression coefficients indicate that after adjustment for other variables in the function, including birth weight, average length of gestation was significantly longer for mothers with a high psychosomatic complaint score, mothers beginning prenatal care in the third trimester as compared with the first, mothers with medium and high hemoglobin levels, and mothers bearing female infants. Mothers beginning prenatal care in the third trimester may have a longer gestation period because of the selectivity factor involved, although the birth weight analysis showed them not to have a different birth weight when adjustment is made for other factors.

Smoking history, a significant factor in accounting for variation in birth weight, was not significant in the analysis of gestation. Parity, hypertension, and eclampsia also affected birth weight but not gestation.

Psychosomatic complaint score and trimester of interview were significant in gestation but not birth weight analysis. The average size of the effect of psychosomatic complaint score on gestation can be computed as

$$-2(0.22) = -0.44 \text{ weeks} .$$

This indicates that the predicted gestation of infants of mothers with a low psychosomatic complaint score was about one-half week less than for infants of mothers with a high score. Similarly, the effect of trimester of interview on gestation was

$$-2(0.66) = -1.32 \text{ weeks} .$$

Thus the difference in predicted gestation of mothers beginning prenatal care in the first and those beginning in the third trimester was well over a week.

The effect of other variables upon gestation can be determined from the regression coefficients. It is apparent that the relationship to birth weight and gestation is not the same for several

**Table 3—Regression analysis of gestation, Baltimore Smoking and Prematurity Study, 1959**

| Variable/Effects | b | F |
|---|---|---|
| 1. Birth weight | 0.003 | 549.70* |
| 2. Sex | −0.268 | 19.60* |
| 3. Psychosomatic complaint score | −0.215 | 7.98* |
| 4. a. Trimester of interview I | −0.490 | 11.00* |
| b. Trimester of interview II | −0.159 | 2.83 |
| 5. a. Hemoglobin I | 0.377 | 8.23* |
| b. Hemoglobin II | 0.671 | 22.57* |
| c. Hemoglobin III | −0.289 | 2.25 |
| $R^2$ | 0.1977 | |

* Significant at the 1% level of probability.

important variables considered, even after adjustment for other characteristics of the mother and infant.

## Summary

Regression analysis was employed in analyzing variation in birth weight and length of gestation in a group of Baltimore Negro women of like socioeconomic class. Several variables were included in the regression function but major emphasis was on smoking history and psychosomatic complaint score.

Variables significant in the regression analysis of birth weight, adjusted for other variables in the model, but not significant in the corresponding analysis of gestation, after adjustment, were smoking history, parity, parity squared, hypertension, and eclampsia.

The total effect of smoking as determined from the predictive equation computed from the data under the present model showed a 129 gram differential in birth weight of offspring of smokers and nonsmokers. The total gestational effect indicated that, as gestation increased, birth weight increased but at a decreasing rate.

Variables significant in the regression analysis of gestation, after adjustment, but not significant in the analysis of birth weight, after adjustment, were psychosomatic complaint score and trimester of interview. There was a significant difference in the mean gestation of infants of mothers with low and high psychosomatic complaint scores, but not in their birth weight. The same can be said concerning infants born to mothers who sought prenatal care in the third as compared with the first trimester. The difference in predicted gestation of infants of mothers with high as compared with low psychosomatic complaint scores was 0.44 weeks. A similar comparison of infants of mothers seeking prenatal care in the first and third trimesters showed a difference in predicted gestation of 1.32 weeks.

These findings confirm those reported in the original analysis of the Baltimore data and in other studies concerning the relation of smoking history to birth weight and gestation. This agreement is singularly important because the present analysis was conducted with due consideration of the multiple characteristics of the mother.

## Implications for Future Research

An explanation for the relationship between smoking and birth weight but not with gestation might be sought in the laboratory because it does not appear to be caused by the concomitant variables of the smoking pregnant woman. The same might be said for parity, hypertension, and eclampsia because they appear to affect birth weight but not the gestation period itself. One aspect common to these is the possible reduced flow of blood across the placenta. It is known that there is an increase in cardiac output during pregnancy to supply the demands of the growing fetus and to insure maternal tissues their customary volume of blood.[8] A reduction in blood flow of smoking mothers, if such exists, could adversely affect the intrauterine growth of the fetus. There have been attempts to study the effects of chronically reducing uterine blood flow in experimental animals by mechanical means. These methods have not been entirely successful, however, and experimentation is continuing.[9] Research is also currently in progress elsewhere to develop a satisfactory method of estimating umbilical blood flow that can be applied in utero with a minimum of disturbance to the fetus and the uterus.[10] When a satisfactory method of measuring uterine blood flow has been perfected, it will be possible to study the effect of smoking on blood flow. Further, when a satisfactory method of chronically reducing blood flow has been produced, the effect of chronic reduction in blood flow on birth weight and gestation of the fetus can be measured.

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The authors are associated with the University of North Carolina School of Public Health, Chapel Hill, N. C. 27515

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# Care of the Premature Infant

In the fall of 1966, the Institutes for Physicians and Nurses in the Care of Premature Infants at the New York Hospital-Cornell Medical Center, under the sponsorship of the New York State Department of Health and the United States Children's Bureau, will begin their eighteenth year of operation. The institutes are designed to meet the needs of physicians and nurses in charge of hospital premature nurseries and special premature centers, and of medical and nursing directors and consultants in state and local premature programs. The attendance at each institute is limited to six physician-nurse teams. The program for physicians is of two weeks' duration and that for nurses, of four weeks' duration. Participants pay no tuition fee and stipends are provided to help cover expenses during attendance at the institute. Institutes for the 1966-1967 fiscal year are scheduled to start on the following dates:

| *Physicians* | *Nurses* |
|---|---|
| September 19-30, 1966 | September 6-September 30, 1966 (Tuesday) |
| November 7-18, 1966 | October 24-November 18, 1966 |
| January 16-27, 1967 | January 3-January 27, 1967 (Tuesday) |
| March 20-31, 1967 | March 6-March 31, 1967 |
| May 8-19, 1967 | April 24-May 19, 1967 |

Early application for these institutes is essential since plans are contingent on the number of applications received.

For additional information write: Box 143, Institute in the Care of Premature Infants, New York Hospital, 525 East 68th Street, New York, N. Y. 10021.