American Journal of Epidemiology
Vol. 108, No. 6
Printed in U.S.A.

CIGARETTE SMOKING DURING PREGNANCY AND THE OCCURRENCE OF SPONTANEOUS ABORTION AND CONGENITAL ABNORMALITY

DAVID U. HIMMELBERGER,[1] BYRON Wm. BROWN, Jr.[2] and ELLIS N. COHEN[3]

Himmelberger, D. U., B. W. Brown, Jr. and E. N. Cohen (Stanford U. School of Medicine, Stanford, CA 94305). Cigarette smoking during pregnancy and the occurrence of spontaneous abortion and congenital abnormality. *Am J Epidemiol* 108:470–479, 1978.

A multiple logistic regression analysis of 12,914 pregnancies and 10,523 live births, based on a mail survey of professional women in medicine, was carried out to determine the relationship between maternal cigarette smoking, and spontaneous abortion and congenital abnormality. After controlling for interfering variables (age, exposure to trace anesthetic gases, pregnancy history, and mailing response), a statistically significant increase in risk associated with maternal cigarette smoking was found for spontaneous abortions and congenital abnormalities. The risk of spontaneous abortion for the heavy smoker is estimated to be as much as 1.7 times that of the nonsmoker in certain risk groups. The risk for congenital abnormality for babies born of smoking mothers is estimated to be as much as 2.3 times that of the nonsmoker, depending on age, pregnancy history, and other factors.

abnormalities; miscarriage; pregnancy; questionnaires; regression analysis; smoking

The present report concerning the influence of maternal cigarette smoking during pregnancy on the risk of spontaneous abortion and congenital abnormality has been developed from data obtained during a two-year study by the American Society of Anesthesiologists Ad Hoc Committee on the Effects of Trace Anesthetic Agents on the Health of Operating Room Personnel.' This study focused on the health experience of anesthesia and operating room personnel in the United States and was reported by Cohen et al. in 1974 (1). Previous studies in Scandinavia and the United States have demonstrated a statistically significant association between maternal cigarette smoking and spontaneous abortion, although in general these studies have not controlled for interfering variables (2–8). On the other hand, few studies on the association of smoking with congenital abnormalities have been reported, and because of the variation in study design, study population, sample size, definition of abnormality, and results, the relationship between maternal cigarette smoking and congenital abnormality remains unclear.

Because of the large number of survey subjects in the Trace Anesthetic Study with available pregnancy histories and other medical and chronologic data, these data presented an opportunity to investigate further the effect of maternal cigarette smoking on the risks of spontaneous abortion and congenital abnormality.

Background

It has been established that women who smoke cigarettes during pregnancy have a

Received for publication March 20, 1978, and in final form May 4, 1978.

[1] Center for Drug Addiction, Department of Pharmacology, Stanford University School of Medicine.

[2] Department of Family, Community and Preventive Medicine, Stanford University School of Medicine, Stanford, CA 94305 (address for reprint requests).

[3] Department of Anesthesia, Stanford University School of Medicine.

Study supported by Contract #HSM 99-73-3, National Institute for Occupational Safety and Health.

greater proportion of infants with lower birth weight than women who do not smoke (2). The relationship between maternal cigarette smoking and perinatal and neonatal mortality has also been studied extensively, and most studies show an excess mortality for offspring of smokers.

In 1971 Kullander and Källen (3) in a prospective study involving 6363 pregnant women found an overall increased risk of spontaneous abortion among smoking women, but this was established to be primarily due to an association between unwanted pregnancy and smoking. After correction was made for the mother's acceptance of pregnancy, the contribution of maternal smoking to spontaneous abortion was only of borderline significance.

Another prospective study of spontaneous abortion in 4312 pregnancies in Sweden, reported in 1971 by Palmgren and Wallander (4), showed that women who smoked heavily throughout pregnancy had a spontaneous abortion rate of 14.5 per cent compared to a rate of 7.8 per cent among nonsmokers. The difference was statistically significant with $p < 0.001$.

Two retrospective studies, one in 1962 by Zabriskie (5) involving 5619 pregnancies, and the other in 1963 by O'Lane (6) with 1914 pregnancies, both found that smokers had a higher incidence of spontaneous abortion than nonsmokers. The rates of spontaneous abortion were an identical 12.6 per cent for the smokers compared to 8.8 and 8.9 per cent among the nonsmokers for Zabriskie and O'Lane, respectively.

In 1965 Underwood et al. (7) reported a slightly increased rate of spontaneous abortion among smokers compared to nonsmokers, but found no difference in the occurrence of major fetal abnormalities. In fact, the rate of major abnormalities was lower among the smokers. A study by Kline et al. (8) in 1977 in which 574 women who aborted spontaneously were matched with 320 control women exhibited an odds ratio of 1.8, significant for the association of smoking with abortion.

There have been fewer studies of the association of smoking during pregnancy and the occurrence of congenital abnormalities in the offspring. The results have been mixed. A study by Bailey (9) in 1971 showed a congenital abnormality rate of 5.4 per cent for the nonsmokers compared to 4.2 per cent for the smokers. In 1976 Alberman et al. (10) found that the proportion of congenital abnormalities tended to fall with the number of cigarettes smoked during pregnancy. However, in 1971 Fedrick et al. (11) reported a large and statistically significant increase in the rate of congenital heart defects among babies born of smoking mothers compared with nonsmoking mothers (7.3 vs. 4.7 per 1000). Their study was based on the 1958 British Perinatal Mortality Survey and the followup National Child Development Study. In 1977 a committee of the American Academy of Pediatrics, chaired by R. W. Miller, concluded that "in the aggregate, studies of the teratogenic effects of cigarette smoking in man have been inconclusive" (12).

METHODS

The data in the present study stem from a survey of 73,496 individuals whose names were supplied by their professional societies (1). There were 49,585 operating room personnel, consisting of members of the American Society of Anesthesiologists, the American Association of Nurse Anesthetists, and the Associations of Operating Room Nurses and of Operating Room Technicians. Also surveyed were 23,911 non-operating room personnel, consisting of members of the American Academy of Pediatrics and the American Nursing Association. For the purposes of this study, we do not distinguish between memberships in the several professional societies.

The questionnaire return rate for the female respondents was 53.2 per cent. The number of pregnancies (therapeutic abortions excluded) was 12,914, and the number of live births was 10,523. Although data were also obtained on the wives of male respondents, the present analysis is confined to the female respondents. The female respondents in this survey were professionals in medicine reporting personally the outcomes of their pregnancy experience, whereas the reports of the male respondents were necessarily second-hand and thus considered more likely to be incomplete and subject to selective reporting.

A questionnaire was mailed to every member of each society, with the exception of the American Nursing Association, where a 10 per cent nationwide sample was used. The forms were individually numbered, and as the responses were received, they were checked off address lists prepared by the societies. The data were edited for inadmissible replies, ambiguities, obvious errors and missing data. Acceptable forms were keypunched and stored in a large campus computer. Photocopies of unacceptable forms were returned to the respondents with indications of deficiencies and a request for correction and return.

The hand-edited and keypunched data, stored in a temporary computer file, were reedited by computer program. Whenever possible, detected discrepancies and deficiencies were rectified.

A second mailing was sent to those individuals who did not respond to the first mailing. Responses to the second mailing were handled in the same manner as first mailing responses, but first- and second-responder data were identified for future analysis.

In the analysis of the data, spontaneous abortion was defined as the loss of the product of conception through the twentieth week of gestation. Pregnancies terminating in therapeutic abortions were ignored. The analysis of congenital abnormalities included only non-skin abnormalities. The questionnaire listed the most common abnormalities in each of six classifications, with "other" as a possible write-in for each group. For those live births in which the "other" category of congenital abnormality was checked, a letter was sent to the mother requesting specific abnormality(ies). This was a further check to insure that an error was not made in filling out the questionnaire. Only abnormalities among live births were analyzed.

To analyze the binary spontaneous abortion and congenital abnormality data, a multiple logistic model was used. This approach provides an estimate of the probability of spontaneous abortion or congenital abnormality adjusted simultaneously for the following variables: maternal age (linear and quadratic terms), pregnancy history, exposure to the operating room environment during the first trimester, smoking, the first order interaction of smoking with the first four variables, and whether the subject had responded to the first or second mailing.

The coding for certain of the variables requires explanation. Smoking refers to cigarette smoking during pregnancy and was coded: 1 = no smoking, 2 = one to 19 cigarettes per day, and 3 = 20 or more cigarettes per day. Pregnancy history (restricted to the 10-year period 1963–1972 immediately preceding the time of survey) was coded in the following manner for spontaneous abortion: 1 = previous pregnancy history with no reported spontaneous abortions, 2 = first reported pregnancy, and 3 = pregnancy history with at least one spontaneous abortion. The coding for congenital abnormalities was as follows: 1 = previous pregnancy history with no reported congenital abnormalities, 2 = first reported pregnancy, 3 = pregnancy history with a spontaneous abortion or still birth, but no live births with congenital abnormalities, and 4 = pregnancy history including one or more live births with congenital abnormality.

Using the logistic model developed by Duncan and Rhodes (13) and Cox (14, 15) and expanded by Walker and Duncan (16), we assume a sample of pregnancies measured or categorized with respect to each of k independent variables. We further assume that the argument is a linear function of the independent variables. In the dicho-

TABLE 1
Total numbers of responses to the first and second mailings

Membership surveyed	Responses					
	First mailing		Second mailing		Total responses	
	No.	%	No.	%	No.	%
52,066	22,417	43.1	5,269	10.1	27,686	53.2

tomous multiple logistic model the observed values of the dependent variables will be one or zero corresponding to occurrence or nonoccurrence of the event, i.e., spontaneous abortion or congenital abnormality, as reported by the subject for a given pregnancy.

The probability, p, of the event is represented as

$$p = 1/(1 + \exp(-X'\beta)) \qquad (1)$$

where X' is the vector of independent variables and β is the vector of unknown coefficients. By an iterative procedure, essentially the Newton-Raphson method, we obtained least squares estimates of β. Tests for the significance of the several regression coefficients for the general regression effect were based on likelihood ratio tests, and asymptotic distribution theory.

RESULTS

Spontaneous abortion

Table 1 shows the number of persons (females) surveyed and the number of responses to the first and second mailings. Table 2 gives the number of pregnancies, excluding therapeutic abortions, and the number of live births reported by the female respondents in the surveys. Table 3 presents crude spontaneous abortion rates where the pregnancies have been categorized by maternal age and whether the mother was smoking or not during pregnancy. The rates are expressed as the number of spontaneous abortions per 100 pregnancies, reported for the 10-year period 1963-1972 preceding the survey (ignoring therapeutic abortions in both the numerator and denominator).

TABLE 2
Number of pregnancies (therapeutic abortions excluded) and number of live births reported by 27,686 female respondents

Events reported	No.
Pregnancies	12,914
Live births	10,523

TABLE 3
Spontaneous abortion rates for smokers and nonsmokers categorized by maternal age

Age at pregnancy	Nonsmokers		Smokers	
	No. of pregnancies	% Spontaneous abortion rate	No. of pregnancies	% Spontaneous abortion rate
<25	2028	15.3	1169	19.0
25–29	3114	13.7	1760	16.5
30–34	2035	15.1	1008	17.0
35–39	943	19.7	438	23.1
40+	300	33.0	119	36.1

Table 3 suggests that both maternal age and smoking are related to the spontaneous abortion rate. In addition to the upward trend with age, we observe that the spontaneous abortion rate is higher for cigarette smokers than for nonsmokers in every age group. However, the rates have not been adjusted for other variables known to be associated with spontaneous abortion, such as past pregnancy problems and operating room exposure.

The multiple logistic regression allows us to investigate the association between maternal cigarette smoking and spontaneous abortion while simultaneously adjusting or controlling for a number of variables. Table 4 defines each of the variables entering into the multiple logistic regression analysis that was carried out (see equation 1 above).

TABLE 4

Summary of variables used in the multiple logistic regression analysis of spontaneous abortions

Variable	Definition
1) Age	Age of mother (in years) at time of pregnancy
2) Age × age	Square of Variable 1
3) Exposure to operating room	Exposure of mother to anesthetic gases in the operating room during first trimester of pregnancy: 0 = no; 1 = yes.
4) Pregnancy history (1963–1972)	*For spontaneous abortion*: 1 = pregnancy history with no spontaneous abortions; 2 = first pregnancy; 3 = pregnancy history with at least one spontaneous abortion.
	For congenital abnormality: 1 = pregnancy history with no congenital abnormalities; 2 = first pregnancy; 3 = pregnancy history with no reported congenital abnormalities but with one or more spontaneous abortions, or still births; 4 = pregnancy history with at least one congenital abnormality.
5) Smoking	Smoking during pregnancy: 1 = no; 2 = 1–19 cigarettes per day; 3 = ≥20 cigarettes per day.
6) Response	Responded to first or second mailing: 1 = first; 2 = second.
7) Smoking × age	Product of Variable 5 with Variable 1.
8) Smoking × age × age	Product of Variable 5 with Variable 2.
9) Smoking × exposure	Product of Variable 5 with Variable 3.
10) Smoking × pregnancy history	Product of Variable 5 with Variable 4.
11) Intercept	

In table 5 we present the maximum likelihood estimates of the regression coefficients (b) and their standard errors (s). In addition to the estimated regression coefficients for spontaneous abortion, table 5 shows the values $t_i = b_i/s_i$, $i = 1, \ldots, k$, the normal test statistics for testing the significance of each regression coefficient against zero, adjusting for the remaining variables, and p_i the significance level attained for each test. From this table we observe that pregnancy history is highly significant as a prediction variable for spontaneous abortion and that exposure to the operating room is also highly significant, as reported earlier (1). The main effect for maternal cigarette smoking during pregnancy, and its interactions with age show rather strong positive relationships to the risk of spontaneous abortion, although these are not significant at the 10 per cent level. We also note that there is a strong negative interaction of smoking with exposure. When the significance of the main effect and the several interaction effects of smoking are tested simultaneously, using the asymptotic chi-squared test, based on the net reduction in likelihood fit, the smoking effect is significant at the 1 per cent level, i.e., $p < 0.01$.

In order to demonstrate the relationship of smoking and the other variables to spontaneous abortion, as disclosed by the logistic analysis, we have used the fitted logistic function to calculate the probability of spontaneous abortion as a function of maternal age for nonsmokers, moderate smokers and heavy smokers, with the other variables fixed to describe a woman who is not exposed to the operating room environment during the first trimester, has had one or more prior pregnancies, none of which resulted in a spontaneous abortion, and who returned her survey form in the first mailing. Figure 1 shows the significant effect of smoking and age on spontaneous abortion for this "typical" female respondent in our study, as calculated from the fitted logistic model.

Table 6 shows the relative risk of spontaneous abortion (heavy smokers vs. nonsmokers), computed from the fitted logistic function, for various fixed values of the interfering variables. For each of the three possible pregnancy history values we have

TABLE 5

Estimated coefficients, standard error coefficients, associated t-values, and p values for spontaneous abortions among female respondents

Variable	Estimate of regression coefficient (b)*	Standard error of estimate (s)	t (b/s)	p
Age at pregnancy	−0.1035	0.0775	−1.34	0.18
Age × age	0.0024	0.0013	1.86	0.06
Exposure to operating room	0.4087	0.1148	3.56	<0.01
Pregnancy history	0.3936	0.0893	4.41	<0.01
Response to mailing	−0.0009	0.0621	−0.01	0.99
Smoking	1.2484	0.8156	1.53	0.13
Smoking × age	−0.0689	0.0541	1.27	0.20
Smoking × age × age	0.0010	0.0009	1.16	0.25
Smoking × exposure	−0.1261	0.0701	−1.80	0.07
Smoking × pregnancy history	0.0298	0.0549	0.54	0.59
Intercept	−1.8158	1.1753	−1.55	
Overall smoking effect		χ^2_5 = 21.7†		<0.01

* The best fitting multiple logistic function is: $p = [1 + \exp - (b_1x_1 + b_2x_2 + \ldots + b_{10}x_{10} + b_{11})]^{-1}$ when the regression coefficients, b, are as given, and the variables, x_i, are as defined in table 4.

† The total "effect" of smoking is measured by comparing the fit with all variables to that obtained when the five variables involving smoking are deleted.

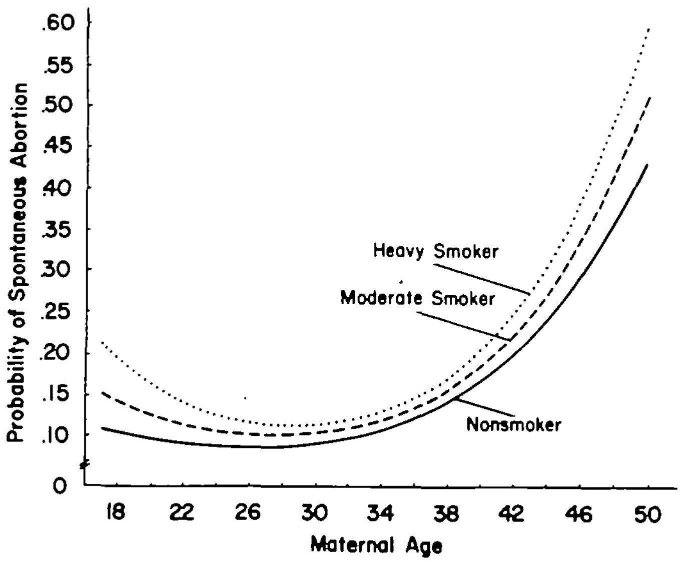

FIGURE 1. Risk of spontaneous abortion according to age and smoking habit. See text for further details.

calculated the relative risk for mothers exposed to the operating room and unexposed, at the two extreme ages of 20 and 40. Relative risk is the ratio of the estimated logistic probability of spontaneous abortion for the woman who is a heavy smoker to the probability of spontaneous abortion for the woman who does not smoke, holding the rest of the interfering variables fixed at specified levels. The mailing response variable has not been included in table 6 because it showed no relationship to spontaneous abortion; it is held fixed at 1, (i.e., first mailing).

TABLE 6

Relative risk of spontaneous abortion for heavy smokers, relative to nonsmokers, for two age levels, three classes of pregnancy history, and two categories of operating room exposure

Pregnancy history	Maternal age	Operating room exposure	
		Unexposed	Exposed
1	20	1.69	1.35
	40	1.22	1.01
2	20	1.70	1.38
	40	1.25	1.04
3	20	1.71	1.39
	40	1.26	1.07

From table 6 and figure 1 it is obvious that the relative risk of spontaneous abortion among female respondents is greater for the young smoking mother than it is for the older mother who smokes. We also observe that the relative risk due to smoking is rather insensitive to changes in pregnancy history. Because a large proportion of our population was exposed to anesthetic gases and subject to an increased risk of spontaneous abortion from that source, it was important to include the exposure variable and its interactions with smoking in our model. Although both smoking and operating room exposure contribute to the risk of spontaneous abortion, the relative risk for smoking is not as large for the exposed mother as for the unexposed mother. The interaction is of borderline statistical significance ($p = 0.07$), as seen in table 5.

The lack of any association of spontaneous abortion rate with first versus second mailing (see table 5) is an indication that the nonresponse bias in this study may not be an important factor.

As a check on the fit of the logistic model to the data, the pregnancies were grouped according to their risk of spontaneous abortion, as calculated from the fitted logistic equation. Actual spontaneous abortion rates were then calculated for the several groups. The results indicated that the calculated rates were very close to those predicted by the logistic model.

TABLE 7

Congenital abnormality rates for smokers and nonsmokers categorized by maternal age

Age at preg-nancy	Nonsmokers		Smokers	
	No. of live births	% Congenital abnormality rates	No. of live births	% Congenital abnormality rates
<25	1680	7.2	931	8.5
25–29	2655	7.6	1435	10.5
30–34	1695	6.7	807	7.2
35–39	734	4.8	322	6.8
40+	194	5.2	70	11.4

Congenital abnormality

Our analysis of the congenital abnormality data follows the same approach as the spontaneous abortion analysis except that now we consider only live births. Table 7 presents congenital abnormality rates for the pregnancies, categorized by maternal age and whether the mother was smoking or not during pregnancy. The rates are expressed as the number of congenital abnormalities per 100 live births reported for the 10-year study period, 1963–1972. Note that there is a consistently higher rate of congenital abnormality among the live births reported by smokers, across all age groups; the smoking versus nonsmoking difference, adjusted for age, is statistically significant at the 1 per cent level, when tested by the usual chi-squared test. However, there is a need to reexamine the smoking effect, adjusting the other variables.

As with spontaneous abortions, we have used the multiple logistic regression model with the variables as defined in table 4. Table 8 gives the maximum likelihood estimates of the regression coefficients (b), the corresponding standard errors (s), the test statistics for the hypotheses that the coefficients are zero ($t = b/s$), and the p values for the tests.

It can be seen from table 8 that both pregnancy history and operating room exposure are highly significant as predictors of congenital abnormality. Though none of the smoking variables is statistically significant alone, the overall smoking effect is significant at the 5 per cent level, as shown on the bottom line of table 8.

The main effect for smoking is positive but its interactions with some of the other variables is negative. In order to show the relationship of smoking and other variables with congenital abnormality, we have plotted in figure 2 the estimated logistic probability of congenital abnormality as a function of maternal age for nonsmokers, moderate smokers and heavy smokers, with all other variables fixed as follows: pregnancy history of one, first questionnaire respondent, and no operating room exposure in the first trimester. For this "typical" female, figure 2 shows the effect of smoking and age on congenital abnormality as calculated from the fitted logistic function. In table 9 we show the risk of congenital abnormality for heavy smokers relative to nonsmokers, conditional on specified values of the sev-

TABLE 8

Estimated coefficients, standard error of coefficients, associated t-values, and p values for congenital abnormalities

Variable	Estimate of regression coefficient (b)*	Standard error of estimate (s)	t (b/s)	p
Age at pregnancy	0.1132	0.1578	0.72	0.47
Age × age	−0.0024	0.0027	−0.90	0.39
Exposure to operating room	0.3898	0.1788	2.18	0.03
Pregnancy history	0.6754	0.1208	5.59	<0.01
Response to mailing	−0.1240	0.1007	−1.23	0.22
Smoking	1.0203	1.4782	0.69	0.49
Smoking × age	−0.0430	0.1018	−0.42	0.68
Smoking × age × age	0.0008	0.0017	0.47	0.64
Smoking × exposure	−0.0699	0.1084	−0.65	0.52
Smoking × pregnancy history	−0.1365	0.0744	−1.83	0.07
Intercept	−5.3610	2.2859	−2.35	
Overall smoking effect		$\chi^2_5 = 11.2$†		<0.05

* The best fitting multiple logistic function is: $p = [1 + \exp - (b_1x_1 + b_2x_2 + \ldots + b_{10}x_{10} + b_{11})]^{-1}$ when the regression coefficients, b, are as given, and the variables, x_i, are as defined in table 4.

† The total "effect" of smoking is measured by comparing the fit with all variables to that obtained when the five variables involving smoking are deleted.

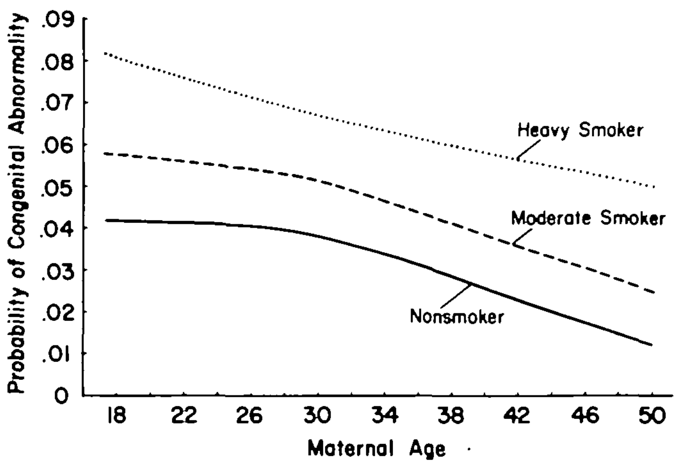

FIGURE 2. Risk of congenital abnormality according to age and smoking habit. See text for further details.

eral interfering variables, as calculated from the fitted logistic function.

Figure 2 and table 9 indicate a relative risk as high as 2.3, the higher smoking risks being observed among women experiencing their first pregnancy or having only trouble-free pregnancies. Among women reporting previous births with congenital abnormalities the relative risk is approximately unity. Although the decreasing age trend shown in figure 2 is not significant, the lack of upward age trend is consistent with the extensive data presented by Hay and Barbano (17). In table 9 it can be seen that women in the operating room show lower relative smoking risk than those women working elsewhere, though, as seen in table 8, this interaction between smoking and operating room exposure is not statistically significant. As with the analysis of the spontaneous abortion data, no association was found between congenital abnormality rate and first or second mailing response, which suggests that non-response bias may not be an important factor in this study.

To check on the goodness of fit of the logistic model to the data, the risk of congenital abnormality was calculated for each live birth based on the fitted logistic model. The live births were grouped according to these risks and the observed rate in each group was compared with the calculated or predicted rate. The results showed very close agreement between observed and predicted rates.

Following the report of Fedrick et al. (11) that congenital heart defects are more numerous among babies of smoking mothers, the defects reported in our study were categorized and the rates compared for smokers and nonsmokers (table 10). It can be seen that the results confirm those of Fedrick et al. and indicate further that abnormalities in each general category are reported more frequently by the smoking mother, many of the differences being at least of borderline significance by statistical comparison of the unadjusted rates.

TABLE 9

Relative risk of congenital abnormality for heavy smokers to nonsmokers, for specified age, operating room exposure and pregnancy history

Pregnancy history	Maternal age	Operating room exposure	
		Unexposed	Exposed
1	20	1.91	1.66
	40	2.34	2.04
2	20	1.46	1.28
	40	1.79	1.55
3	20	1.13	1.01
	40	1.37	1.20
4	20	0.90	0.81
	40	1.06	0.94

CONCLUSIONS

The multiple logistic regression model, with certain interactions, appears to fit the spontaneous abortion and abnormality data well. The model provides an efficient method for adjusting for many variables. Based on this approach we draw the following conclusions.

TABLE 10

Comparison of congenital abnormality rates for babies born of smokers and nonsmokers, by type of abnormality. (Number of congenital abnormalities in parentheses)

Abnormality	Smokers		Nonsmokers		p*
Cardiovascular	19.07†	(68)	13.65	(95)	0.02
Respiratory	15.15	(54)	12.07	(84)	0.10
Musculoskeletal	23.84	(85)	19.69	(137)	0.08
Gastrointestinal	13.46	(48)	9.48	(66)	0.04
Central nervous system	11.50	(41)	10.20	(71)	0.27
Urogenital	21.32	(76)	15.81	(110)	0.02

* One-tail significance level for the test of the difference between two proportions.

† Rate is number of congenital abnormalities per 1000 live births. Rates based upon 3565 live births among the smokers and 6958 live births among the nonsmokers.

Spontaneous abortion. The survey data provide statistically significant indication ($p < 0.01$) that the risk of spontaneous abortion is substantially higher for women who smoke during pregnancy. For the women in this study the risk for the smoking mother is estimated to be 1.2 to 1.7 times that of the nonsmoking mother, for those not working in the operating room, and 1.1 to 1.3 for those working in the operating room.

Congenital abnormality. Analysis of the congenital abnormality data shows a statistically significant risk ($p < 0.05$) associated with maternal smoking. The relative risk ranges from 0.8 to 2.3 times that of the nonsmoker, depending on age, previous pregnancy history, and exposure to the operating room. As with spontaneous abortions, we estimate a relative risk for smokers slightly lower for women working in the operating room.

Keeping in mind that the findings presented here are retrospective survey data, obtained by mail and subject to variation in response due to the experience and background of the participant, this study nonetheless confirms previous reports indicating that smoking is positively correlated with spontaneous abortion and provides evidence of a large increase in the risk of congenital abnormalities for the child born of a mother who smokes.

References

1. Cohen EN, Brown BW Jr, Bruce DL, et al: Occupational disease among operating room personnel. A national study. Anesthesiology 41:321–340, 1974
2. The Health Consequences of Smoking, A Report of the Surgeon General: US Department of Health, Education, and Welfare, 1039(10):123–137, 1973
3. Kullander S, Källen B: A prospective study of smoking and pregnancy. Acta Obstet Gynecol Scan 50:83–94, 1971
4. Palmgren B, Wallander B: Cigarettsokning och abort. Konseketiv prospektiv undersokning av 4312 graviditeter. Lakartidningen 68:2611–2616, 1971
5. Zabriskie JR: Effects of cigarette smoking during pregnancy. Study of 2,000 cases. Obstet Gynecol 21:405–411, 1963
6. O'Lane JM: Some fetal effects of maternal cigarette smoking. Obstet Gynecol 22:181–184, 1963
7. Underwood PB, Hester LL, Lafitte T Jr, et al: The relationship of smoking to the outcome of pregnancy. Am J Obstet Gynecol 91:270–276, 1965
8. Kline J, Stein ZA, Susser M, et al: Smoking: A risk factor for spontaneous abortion. N Engl J Med 297:793–796, 1977
9. Bailey RR: The effect of maternal smoking on the infant birth weight. NZ Med J 71(456):293–294, 1971
10. Alberman E, Creasy M, Elliott M, et al: Maternal factors associated with fetal chromosomal abnormalities in spontaneous abortion. Br J Obstet Gynaecol 83:621–627, 1976
11. Fedrick J, Alberman E, Goldstein H: Possible teratogenic effect of cigarette smoking. Nature 231: 529–530, 1971
12. Miller RW, Brendel WB, Brown AK, et al: Effects of cigarette smoking on the fetus and child. Pediatrics 57:411–413, 1977
13. Duncan DB, Rhodes RD: Multiple regression with a quantal response. (Abstract) Annals of Mathematical Statistics 23:300, 1952
14. Cox DR: The regression analysis of binary sequences. J Royal Statistical Society B 20:215–232, 1958
15. Cox DR: Some procedures connected with the logistic qualitative response curve. Research papers in statistics: Essays in honour of J. Neyman's 70th birthday. (Editor: FN David.) London, Wiley, 1966
16. Walker SH, Duncan DB: Estimation of the probability of an event as a function of several independent variables. Biometrika 54:167–179, 1967
17. Hay S, Barbano H: Independent effects of maternal age and birth order on the incidence of selected congenital malformations. Teratology 6:271–279, 1972