Maternal Cigarette Smoking and Child Psychiatric Morbidity: A Longitudinal Study

Gail M. Williams, PhD*; Michael O'Callaghan, MB, BS‡; Jake M. Najman, PhD§; William Bor, FRANZCP‖; Margaret J. Andersen, AIMS¶; David Richards, PhD#; and Chinlyn U, BSc#

ABSTRACT. *Objective.* **Previous studies have linked maternal smoking during pregnancy with behavioral disturbance in children. However, additional evidence is needed to address the causality of the relationship. The present study analyses result from an Australian cohort of 5342 5-year-old children whose mothers were recruited early in pregnancy.**

Methods. **Smoking history was gathered for prepregnancy, first clinic visit (FCV), late pregnancy, and when the child was 6 months and 5 years of age. Behavior problems at the age of 5 were assessed using a modified Child Behavior Check List (CBCL) shown to have high agreement with the complete CBCL. This resulted in the formation of three scales: internalizing; social, attentional and thought; and externalizing behavior problems, which were then dichotimized at the 90th percentile in each case. Logistic regression was used to model these outcomes as a function of maternal smoking at five time points during which it was assessed. A series of models explored the effect of additional adjustment for confounding. The predictors of attrition (29.5%) throughout the cohort were also identified by multivariate modeling.**

Results. **The final analysis was carried out on a cohort of mother-child pairs for whom data and child behavior outcomes were complete. The mean age of children was 5 years, 6 months with a range from 4 to 6 years. The mean age of mothers at the time of birth of the child was 25 years, with a range from 13 to 47 years. Mothers lost to follow-up were more likely to be younger, single, and less well-educated than those who continued participation, although maternal smoking was not an independent determinant.**

Unadjusted analyses showed strong associations between externalizing child behavior and maternal smoking during pregnancy and at the 5-year follow-up, with relative risks (RRs) up to 2.6 for children of women smoking at least 20 cigarettes per day at the first antenatal clinic visit. A clear dose-response relationship existed in most relationships with higher levels of smoking being associated with higher rates of externalizing behavior problems. Weaker relationships occurred for internalizing behavior and social, attentional and thought behavior problems.

Multivariate analysis of the timing in more detail that the association between maternal smoking and child behavior problems persisted, although the evidence for dose-response diminished. Moreover, it was primarily associated with smoking as determined by questions asked at the FCV (RR = 1.52, 2.03, 2.16) for 1 to 9, 10 to 19, and ≥20 cigarettes per day, respectively, compared with nonsmoking and secondarily by smoking determined at the 5-year follow-up (RR = 1.52, 1.87, 1.29) for 1 to 9, 10 to 19, and ≥20 cigarettes per day respectively, compared with nonsmoking. This association appeared to be independent of a wide range of possible confounders such as maternal age, education, social class, marital status and mental health, gestation at FCV, complications during pregnancy, the child's sex, gestational age at birth, and age at last follow-up. Adjustments were also made for the mother's employment since birth, family structure, and maternal mental health at the time of the CBCL assessment. Associations between externalizing behavior problems and maternal smoking at other times, and those between other behavioral problems examined and maternal smoking were not significant.

Conclusion. **Although previous studies have found evidence for an association between maternal smoking and child behavior problems, the strength of this study lies in its size, its detailed and consistent measurement of maternal smoking, and its ability to control for many social and biological factors linked to maternal smoking and child behavior.**

The statistical evidence for a causal relationship between maternal smoking as measured at the first antenatal clinic visit and the development of externalizing behavior in children is strongly suggestive, because of the specificity of effect and timing, and the adjustment for a comprehensive range of other risk factors. An alternative explanation that mothers who smoke might be inclined to report behavior problems differently was considered unlikely because the effect was specific to externalizing behavior and the major exposure occurred 5 years before the reported behavior. Additionally, the existence of a factor (beyond those already included in the analysis) that might be related to both behavior problems and any propensity to misreport smoking seems sufficiently implausible to rule out misclassification of smoking status as another alternative explanation for the findings.

The timing of the relationship between smoking in pregnancy and externalizing behavior problems, and its independence of small for gestational age status at birth, suggests that placental insufficiency and oxygen deprivation are not important in the pathogenesis. It is possible that nicotine in the fetal brain derived from maternal smoking may alter gene expression and the nature and

From the *Australian Centre for International and Tropical Health and Nutrition and Departments of §Anthropology and Sociology and ¶Obstetrics and Gynecology, University of Queensland, Queensland, Australia; ‡Mater Misericordiae Hospital, South Brisbane, Queensland, Australia; ‖Children's Health Sector, Brisbane North Regional Health Authority, Queensland, Australia; and #Academic Division of Child Health, School of Human Development, University of Nottingham, United Kingdom.

Received for publication Nov 18, 1997; accepted Mar 3, 1998.

Reprint requests to (G.W.) Australian Centre for International and Tropical Health and Nutrition, University of Queensland, Medical School, Herston Rd, Herston, Queensland, Australia, 4006.

function of the nicotine receptors developing in early pregnancy. The presence of a separate, although slightly weaker, association between concurrent maternal smoking and externalizing child behavior suggests both biological and social explanations, including a direct psychopharmacologic effect of nicotine through passive smoking.

Assuming the relationship to be causal, it is estimated that maternal smoking in early pregnancy may account for 25% of externalizing (aggressive) behavior while maternal smoking when the child is 5 years old may account for an additional 16%. These findings provide further support for antismoking programs in pregnancy and in young family settings. ***Pediatrics*** **1998;102(1). URL: http://www.pediatrics.org/cgi/content/full/102/1/e11;** ***smoking, behavior problems, pregnancy, children.***

ABBREVIATIONS. CBCL, Child Behavior Check List; SAT, social, attentional, and thought (problems scale); SGA, small for gestational age; FCV, first clinic visit; OR, odds ratio; RR, relative risk; PAR, population attributable risk; CI, confidence interval.

Maternal smoking during and after pregnancy has been independently associated with behavioral disturbance in several large cohorts of children. A dose–response increase in all behavior problems has been found in children at age 4 to 11 years.[1,2] Parent and teacher reports of conduct disturbance and attentional disorder at 8, 10, and 12 years and increased delinquency in youth also have been reported.[3] Several previous studies link maternal smoking during pregnancy with attentional and mild cognitive difficulties in children.[5,6] Mothers who smoke cigarettes while pregnant have an additional risk of ~40% to 50% of having children with attentional and cognitive difficulties.[2] If this relationship is causal, the contribution of maternal smoking to development of childhood psychiatric morbidity is considerable.

Limitations of previous studies include the measurement, quantification, and timing of cigarette exposure. Although the effect on behavior has been attributed predominantly to smoking during pregnancy rather than to later maternal smoking,[4] no study has collected detailed information on smoking habits prospectively during pregnancy. This is necessary to define the timing of any effect and to eliminate recall bias. Several studies have adjusted for potential confounding factors,[1,2,4] but these have not included specific measures of maternal mood disturbance that are potentially major factors affecting child behavior. Finally, externalizing behaviors including conduct and attentional problems have been the sole measures of behavior in several studies.[3,4] Additional assessment of a broader range of child behavior problems is needed to clarify the specificity of the relationship between cigarette exposure in pregnancy and later childhood behavior disorders.

The present study reassesses the association between maternal smoking and child behavior problems, particularly addresses issues of timing and degree of exposure and type of behavior problem, and establishes whether the association is independent of a range of possible confounding factors such as social background and pregnancy complications as well as maternal anxiety and depression in pregnancy and at age 5 years.

METHODS

The Mater Cohort

The Mater University of Queensland Study of Pregnancy involved 8458 pregnant women enrolled between 1981 and 1984.[6] They were recruited at their first antenatal clinic visit to the Mater Misericordiae Hospital in Brisbane, Australia, which serves a population of approximately one half million people and has a major tertiary obstetric unit.

Extensive information regarding social characteristics of the family and psychological characteristics of the mother was collected at enrollment, 1 or 2 days after birth, 6 months after the birth, and again 5 years after delivery. Biological measures relating to pregnancy, delivery, and the neonatal period were extracted from the medical record. At the 5-year follow-up mothers completed a modified Child Behavior Check List (CBCL), and developmental, behavioral, and health information was obtained on the child.

Initial compliance with the study was very high: of 8556 women approached, only 98 refused. Subsequently, 7689 of these mothers were confined at the Mater Hospital, with pregnancies of at least 20 weeks' gestation. Losses (769) at this stage related to miscarriage or confinement elsewhere. Of those at the Mater Hospital, 112 infants died before discharge, leaving, for the purpose of the present study, a baseline cohort of 7577 infants. Attrition over the following 5 years was 29.5%, resulting in a total contact of 5342 mothers.

Following an approach suggested previously,[7] an analysis was performed to identify those factors, relevant to the present investigation, that predicted attrition from hospital discharge to 5 years of age. This was carried out on the subset of 6989 (of the 7577 discharged infants) for whom information on all variables required measured up to the time of discharge was complete.

The final analysis was performed on the cohort of 4879 mothers and children for whom data on behavioral outcomes and covariables were complete.

TABLE 1. Behavior Scales Derived From the CBCL

Internalizing	SAT	Externalizing
Cronbach's α = 0.76	Cronbach's α = 0.75	Cronbach's α = 0.84
Cries a lot	Acts too young for age	Argues a lot
Feels worthless or inferior	Cannot concentrate, cannot pay attention for long	Demands a lot of attention
Likes to be alone	Cannot get mind off certain thoughts	Destroys own things
Too fearful or anxious	Cannot sit still, restless or hyperactive	Destroys things belonging to others
Nervous, highly strung or tense	Clings to adults or too dependent	Disobedient at home
Feels too guilty	Daydreams or gets lost in thoughts	Gets into many fights
Refuses to talk	Does not get along with other children	Lying or being dishonest
Sulks a lot	Not liked by other children	Screams a lot
Withdrawn; does not get involved with others	Poorly coordinated or clumsy	Sudden changes in mood or feeling
Worrying	Repeats certain acts; has compulsions	Stubborn, sullen, or irritable
		Temper tantrums or hot temper

Measurements

Child Behavior Problems

Child behavior problems were measured using selected items from the CBCL of Achenbach and Edelbrock.[8,9] The CBCL is not a diagnostic test, but is used to derive standardized descriptions of child behaviors. These are behaviors that caregivers of children are likely to see as being of sufficient concern to warrant consulting a clinician. The CBCL is used for the 4- to 18-year age group. In this study, 33 of the 113 items were selected from the CBCL; items excluded were those that occurred infrequently in the 5-year age category. Factor analysis of these 33 items revealed the three broad syndromes identified by Achenbach,[10] collectively involving 31 items. Each of these subscales had a high degree of internal consistency. The internalizing subscale comprised 10 items with a Cronbach α statistic of 0.76; the social, attentional, and thought (SAT) problems scale had 10 items with a Cronbach α statistic of 0.75; and the externalizing scale consisted of 11 items with a Cronbach α statistic of 0.84 and comprised primarily aggressive behaviors (Table 1).

This shortened version of the CBCL was validated by comparison with the full CBCL completed by 76 selected mothers of 5-year-old children. For the externalizing scale, the Pearson correlation coefficient r was 0.94; for the internalizing scale, $r = 0.89$; and for the SAT scale, $r = 0.96$. For these 76 children, the sensitivity of the shortened CBCL for identification of children rated abnormal on the full CBCL was 88%, 60%, and 67%, respectively, for the three scales, with specificity of 96%, 100%, and 100%.

Each behavioral item was graded on three points (often, sometimes, never), and items totaled to produce each of the three subscales. Children scoring at or above the 90th percentile were classified as having behavior problems. This cutoff represents the optimum numbers for allocating individual children to the affected group, based on assessments of the sensitivity and specificity of the CBCL.[9]

Maternal Smoking Status

At the interviews (first clinic visit [FCV], 2 to 4 days after delivery, 6 months after delivery, and at child age 5 years), mothers were asked to quantify their smoking. In the questionnaire administered at the FCV, mothers were asked about their smoking before pregnancy as well as in the past week. In the questionnaire 2 to 4 days after delivery, mothers were asked to recall their smoking level over the last trimester. In the 6-month and 5-year follow-up questionnaires, smoking questions referred to the past week. In all instances, questions referred to the number of cigarettes smoked over a 7-day period. Amount of cigarette smoking was categorized as none, 1 to 9, 10 to 19, and 20 or more cigarettes per day. Mothers were classified according to the extent of self-reported smoking before the pregnancy, at the FCV, in late pregnancy, at 6 months, and at 5 years.

Maternal Anxiety and Depression

Maternal mental health was measured using the Delusions–Symptoms States Inventory of Bedford and Foulds.[11] This measure of mental health was chosen because it assesses symptoms that are not confused easily with those of pregnancy and its consequences. The Delusions–Symptoms States Inventory has been validated extensively, and it has been used in numerous studies.[12–14] Although maternal mental health was assessed at the first survey and all follow-ups, only its assessment at the FCV and at age 5 years was used in this analysis.

Other Characteristics Potentially Associated With Child Behavior Problems and Maternal Smoking

These included:

1. maternal age at the child's birth (in 5-year age groups);
2. maternal education level (special school or primary only; started secondary school; left school at age 15 to 16 years; left school at age 17 to 18 years; college or university);
3. marital status (married, single, living together, other);
4. gestation at FCV, estimated from the dates of the FCV and delivery and gestation at delivery (<16 weeks, 16 to 20 weeks, >20 weeks);
5. social class of the mother and her partner at the FCV;
6. country of birth of the mother and her partner;
7. whether the mother or her partner was indigenous;
8. religiosity of the mother, as measured by frequency of church attendance;
9. number of previous pregnancies and miscarriages of the mother;
10. antenatal admissions to hospital;
11. occurrence of bleeding during pregnancy;
12. gender of the child;
13. gestation (in weeks) at delivery;
14. small for gestational age (SGA) at birth (ie, birth weight below the 10th percentile for gestational age and gender);
15. employment since birth;
16. number of children 0 to 2 years, 3 to 6 years, 7 to 12 years, or 13 to 17 years in the family at the 5-year follow-up; and
17. age of child at last follow-up.

The list above contains a mixture of possibly confounding and intervening variables. They were included to determine whether the smoking effect is independent of other well known or presumed effects, so as to eliminate as many alternative explanations as possible. After such extensive adjustment, the survival of an independent smoking effect would strengthen the evidence for the association between maternal smoking and child behavior problems being truly causal.

Statistical Methods

Multivariate analysis of baseline factors predicting attrition was performed using logistic regression on the cohort of the 6989 mothers for whom complete baseline data were available (588 of the 7577 had missing data for at least one of the measures obtained during pregnancy or soon after delivery). This proceeded in two steps: 1) an initial step to eliminate those variables measured at the FCV that were not predictive of attrition, and 2) a second step that added other variables obtained at delivery.

Preliminary analysis of the consequences of maternal smoking behavior was performed by calculating the percentage of children with behavior problems according to smoking at each of the four times. Relative risks (RRs) estimated by odds ratios (OR) were calculated for each smoking category, with nonsmoking as the reference category. Multivariate logistic regression was used to examine the variation in risk of behavior problems according to maternal smoking, after adjusting for smoking at other time periods, and the various sociodemographic and biological characteristics listed above. Computations were performed using the statistical packages SAS[15] and SPSS.[16]

The burden of behavior problems attributable to maternal smoking was calculated according to the standard formula for obtaining population attributable risk (PAR)[17] involving the prevalence (P) of the risk factor (in this case, maternal smoking) and the RR of the outcome:

$$\mathrm{PAR} = \frac{P(RR - 1)}{1 + P(RR - 1)}$$

This computation was performed within each stratum of cigarette smoking and aggregated over strata to obtain the total PAR for maternal smoking at each phase.

RESULTS

There were 4879 mothers for whom data on smoking and child behavior outcomes were complete. The mean age of these mothers at the time of birth was 25 years, with a range of 13 to 47 years. Children in this cohort were assessed at a mean age of 5 years 6 months, with a range of 4 to 6 years at the last follow-up, owing to difficulties in tracing some children; however, 83.6% of children were 5 years old at follow-up.

Mothers lost to follow-up at 5 years tended to be younger, single, and less educated than those who continued participation (Table 2). They also were more likely to have presented later in their pregnancy, to have been smokers, and to have had higher

TABLE 2. Percent Attrition in Cohort Analyzed by Maternal and Child Characteristics at FCV and After Delivery and Estimated Unadjusted and Adjusted OR, OR_1

Characteristic	*N*	% Loss	OR	OR_1	*P*
	6989	29.5			
Education					
Primary	285	37.9	1	1	
Started secondary	957	34.4	0.86	0.74*	
Left school 15–16 y	3831	29.3	0.68*	0.66*	
Left school 17–18 y	685	33.9	0.84	0.89	
College	1055	24.2	0.52*	0.57	
University	176	35.8	0.91	1.12	<0.0001
Marital status					
Married	3896	25.4	1	1	
Single	423	44.6	2.37*	1.66*	
Living together	465	42.9	2.21*	1.73*	
Other	95	49.2	2.84*	2.27*	<0.0001
Maternal smoking prepregnancy					
None	3514	25.8	1	1	
1–9 Cigarettes/d	859	33.0	1.41*	1.09	
10–19 Cigarettes/d	1227	34.1	1.49*	1.01	
≥20 Cigarettes/d	1389	36.1	1.63*	0.89	0.350
Gestation at FCV					
<16 Wk	2147	23.9	1	1	
16–20 Wk	2370	28.1	1.24	1.21*	
>20 Wk	2472	37.7	1.92	1.71*	<0.0001
Maternal anxiety FCV					
None	2902	26.7	1	1	
Mild	3362	31.2	1.24*	1.08	
Moderate	668	38.8	1.73*	1.17	
Severe	57	47.4	2.47*	1.26	0.135
Maternal depression FCV					
None	4702	27.4	1	1	
Mild	1999	35.3	1.45*	1.13*	
Moderate	256	39.1	1.70*	1.28*	
Severe	32	53.1	3.01*	1.45*	0.039
Maternal smoking FCV					
None	4291	26.5	1	1	
1–9 Cigarettes/d	1170	32.2	1.32*	0.96	
10–19 Cigarettes/d	923	37.5	1.66*	1.20	
≥20 Cigarettes/d	605	41.0	1.92*	1.30	0.152
Maternal smoking late pregnancy					
None	4231	26.3	1	1	
1–9 Cigarettes/d	1010	34.5	1.48*	1.18	
10–19 Cigarettes/d	897	34.6	1.48*	1.13	
≥20 Cigarettes/d	871	39.7	1.85*	1.35	0.228
Maternal age at birth					
<20 Y	1003	43.3	1.71*	1.27*	
20–24 Y	2039	25.2	0.75*	0.83*	
25–29 Y	2670	30.8	1	1	
30–34 Y	947	25.3	0.76*	0.81*	
≥35 Y	330	29.7	0.94	0.99	0.0001
Gender of the child					
Male	3626	29.8	1	1	
Female	3363	30.7	1.04	1.05	0.508
Gestation at birth					
22–35 wks	179	35.2	1.31	1.28	
36–37 wks	529	34.2	1.25*	1.21	
38–39 wks	2424	30.3	1.05	1.10	
≥40 wks	1857	29.3	1	1	0.084
SGA					
No	6252	29.3	1	1	
Yes	737	37.5	1.44*	1.27*	0.005

OR_1 adjusted for all other variables in Table.
Probability obtained from maximum-likelihood test for overall variation among categories, adjusted analysis.
* 95% CI excludes unity.

rates of mental health problems early in pregnancy. Their infants were more likely to have been born of earlier gestation and be of SGA status. However, important from the scope of this paper, multivariate analysis showed that the higher rates of attrition among smokers (prepregnancy and during pregnancy) appear to be a consequence of smokers being younger and less well educated rather than an independent effect of smoking itself. This is evidenced by the reduction to nonsignificance of the association between maternal smoking and attrition.

The percentage of children with behavior problems and estimated RR (compared with nonsmokers) was calculated for each category of maternal smoking on each occasion (Table 3).

This analysis demonstrated that the higher the level of maternal smoking at each of the four times, the greater the risk of behavior problems as assessed by each of the three subscales. The strongest association was between externalizing child behavior at the 5-year follow-up and maternal smoking during pregnancy. A clear dose–response relationship existed in most relationships, with higher levels of smoking being associated with higher rates of child behavior problems.

To determine the relative contribution of maternal smoking at different time periods to child behavior problems at 5 years, three separate logistic regression models were fitted to each of the three scales, with the presence of behavior problems at 5 years as the dependent variable.

Before pregnancy, 46.5% of the cohort were cigarette smokers. This declined to 35.4% at the FCV and 37.3% at the 5-year follow-up. It also was common for women to reduce their consumption levels (as opposed to complete cessation of smoking) at the FCV. Given this amount of changing behavior, analysis can be directed toward differentiating the times when smoking may have a greater or lesser impact on child behavior problems.

RR of child behavior problems by level of maternal smoking was estimated, adjusting for mother's smoking at each other occasion (Table 4). In the first analysis, smoking early in pregnancy was strongly related to later child behavior problems, and this relationship was with externalizing child behaviors rather than with the other scales. There was no statistically significant relationship between smoking later in pregnancy and subsequent child behavior problems (after adjustment for smoking at other times). Behavior problems were related to concurrent maternal smoking at 5 years, although this relationship was weaker than that with smoking at the FCV.

To distinguish the influence of maternal smoking from other factors that may be independent determinants of behavior problems and that may predispose a woman to smoking, a variety of sociodemographic, biological, and maternal mental health variables was added to the analysis as listed earlier. The findings from this analysis were almost identical to the first, indicating that these factors were not further confounding the relationship between either maternal smoking at the FCV or at 5 years and child behavior problems.

The third analysis adds measures of maternal anxiety and depression at the FCV and at 5 years to the model. RRs altered slightly for the phases when mental health was measured, but the levels of statistical significance generally were maintained. In particu-

lar, after all adjustments, the RR associated with the smoking behavior producing highest risk for externalizing behavior problems at age 5 years (smoking at least 20 cigarettes per day in early pregnancy) declined from 2.41 ($P = .01$) to 2.16 ($P = .03$). To test this relationship further, self-reported measures of subjective stress were added to the model for externalizing behavior problems. Risk estimates for maternal smoking factors at phase were virtually unchanged.

Smoking at the FCV and, to a lesser extent, at 5 years therefore is associated with increased externalizing behaviors in the child at 5 years. This relationship is independent of the many additional factors examined in this analysis. Contrary to findings in the unadjusted analysis, there was little evidence of a dose–response relationship between smoking at the FCV and externalizing child behavior.

The PAR percent for maternal smoking in early pregnancy, derived from the adjusted RRs (RR_3) and the prevalence of smoking in each dose category was 7.6%, 10.4%, and 7.4%, giving a total of 25.4% of externalizing problems attributable to smoking in early pregnancy. A similar calculation for smoking at age 5 years yielded a total PAR of 15.5%.

To track the pattern of behavior change and its association with subsequent (5-year) child behavior, the percentage of children with externalizing behavior problems was classified progressively according to maternal smoking status before, during, and after the pregnancy (Figure 1). This has been presented in the form of a tree diagram (Figure). Branches with <100 women and smoking at age 6 months have been excluded for clarity. Of the 2271 prepregnancy smokers, 24.5% reported that they had quit at the FCV, whereas other groups of women stopped smoking late in pregnancy or started smoking after the birth of the child. Nonsmoking mothers at all points of data collection had a low risk of child behavior problems (8.2%), compared with mothers who smoked at all points (14.7%). These observations thus confirm that women who smoke have an increased risk of their child manifesting externalizing behaviors. If they continue to smoke beyond the FCV, however, risk is not increased additionally. Women who had stopped smoking at the FCV and subsequently maintained their nonsmoking status have the risk of child behavior problems reduced to that of continuous nonsmokers (7.9%). Those women who reported prepregnancy smoking, had quit in early pregnancy, but subsequently began smoking had no increased risk of having children with child behavior problems at 5 years of age, except for the group of women ($n = 159$) who had resumed smoking after their infant was born and were smoking at age 5 years. Reduction in smoking some time after the FCV does not reduce the prevalence of later externalizing child behavior problems.

Women who had never smoked until after the birth of their infant and were smoking at age 5 years ($n = 113$) had children with increased rates of externalizing child behavior problems.

No additional statistically significant reduction in behavior problems was observed for those women who continued smoking through pregnancy but were no longer smoking at the 5-year follow up.

DISCUSSION

Results from this study support those reported previously.[1–3] Externalizing behaviors are specifically affected contrary to a previous report,[1] and smoking at the FCV rather than at other times measured is most strongly associated with later behavior problems. Smoking in late pregnancy does not appear to

TABLE 3. Percent With Child Behavior Problems and RR, as Estimated by the OR, by Maternal Smoking Before, During, and After Pregnancy

Cigarettes per day	*N*	Internalizing		SAT		Externalizing	
Prepregnancy		%	RR	%	RR	%	RR
None	2608	10.7	1	11.0	1	8.3	1
1–9	576	9.2	0.84	11.1	1.01	9.7	1.19
10–19	808	12.5	1.19	15.6	1.49*	11.6	1.46*
≥20	887	14.4	1.40*	14.7	1.38*	16.1	2.11*
FCV							
None	3152	10.8	1	10.8	1	8.1	1
1–9	793	10.6	0.98	13.1	1.25	11.5	1.46*
10–19	577	14.6	1.41*	16.5	1.64*	16.1	2.16*
≥20	357	15.1	1.47*	19.6	2.02*	18.8	2.60*
Late pregnancy							
None	3105	10.6	1	10.9	1	8.6	1
1–9	662	10.7	1.02	12.1	1.13	9.5	1.12
10–19	587	13.0	1.26	15.8	1.55*	13.3	1.64*
≥20	525	16.6	1.68*	18.7	1.89*	19.2	2.54*
6 Months							
None	2786	10.6	1	10.7	1	8.3	1
1–9	550	9.0	0.89	10.1	1.02	9.0	1.20
10–19	614	12.0	1.19	15.9	1.59*	12.3	1.51*
≥20	751	15.6	1.49*	16.8	1.65*	16.6	2.15*
5 Years							
None	3056	10.6	1	10.7	1	8.1	1
1–9	408	8.1	0.74	11.8	1.11	12.2	1.59*
10–19	603	12.6	1.22	16.1	1.60*	13.8	1.82*
≥20	812	15.9	1.59*	16.8	1.68*	15.8	2.13*

* 95% CI excludes unity.

TABLE 4. Adjusted Estimated RR of Child Behavior Problems, as Estimated by the OR, by Maternal Smoking Before, During, and After Pregnancy

Cigarettes per day	Internalizing			SAT			Externalizing		
	RR^1	RR^2	RR^3	RR^1	RR^2	RR^3	RR^1	RR^2	RR^3
Prepregnancy									
None	1	1	1	1	1	1	1	1	1
1–9	0.74	0.66	0.61	0.76	0.77	0.73	0.98	0.96	0.93
10–19	0.99	0.90	0.88	0.84	0.74	0.73	0.79	0.76	0.76
≥20	0.96	0.86	0.74	0.62	0.54*	0.47*	1.01	1.00	0.93
FCV									
None	1	1	1	1	1	1	1	1	1
1–9	0.78	0.78	0.71	1.23	1.06	0.96	1.71*	1.66*	1.52
10–19	0.75	0.71	0.62	1.42	1.15	1.03	2.28*	2.20*	2.03*
≥20	0.62	0.63	0.55	1.87*	1.82	1.64	2.37*	2.41*	2.16*
Late pregnancy									
None	1	1	1	1	1	1	1	1	1
1–9	1.35	1.42	1.47	0.97	1.09	1.15	0.65	0.70	0.76
10–19	1.42	1.44	1.47	1.10	1.17	1.19	0.74	0.80	0.77
≥20	1.90	1.86	2.12	1.28	1.43	1.64	0.97	0.98	1.13
6 Months									
None	1	1	1	1	1	1	1	1	1
1–9	0.83	0.77	0.79	0.90	0.68	0.69	0.60	0.54*	0.52*
10–19	0.89	0.88	1.00	1.59*	1.04	1.18	0.79	0.69	0.76
≥20	0.96	0.99	1.04	1.63*	1.01	1.01	0.84	0.76	0.76
5 Years									
None	1	1	1	1	1	1	1	1	1
1–9	0.93	0.86	0.77	1.16	1.22	1.11	1.75*	1.65*	1.52
10–19	1.28	1.20	1.19	1.50*	1.64*	1.63*	1.91*	1.87*	1.87*
≥20	1.42	1.31	1.08	1.40	1.38	1.17	1.60*	1.54*	1.29

Abbreviations: RR_1, adjusted for smoking at other times; RR_2, adjusted for smoking at other times and social and biological factors listed in text; RR_3, adjusted for smoking at other times, social, and biological factors listed in text and maternal mental health at first antenatal visit and at 5 years.
* 95% CI excludes unity.

add to the risk of externalizing behaviors. Externalizing behaviors, in this study and others, also are associated with disturbances in parenting, social disadvantage, and marital difficulties.[22] However, the association between maternal smoking and these behavior problems remains after a wide range of possible social and biological antecedent/intervening and/or confounding variables have been added to the analysis, strengthening the argument that the maternal smoking effect observed is not mediated through them. The evidence that the association that smoking in early pregnancy is causal appears particularly strong because if an unknown confounder, such as personality type, were responsible for this effect, it would have to be independent of all variables already adjusted for, exhibit higher rates within the women who report quitting smoking in early pregnancy, and be associated with externalizing behavior at age 5.

To examine any modification of these effects by gestation at FCV, a separate stratified analysis of gestation at FCV, and externalizing behavior problems (data not shown) provided results that are consistent with the others obtained.

Although Weitzman and colleagues[1] developed their items from the CBCL, they present results separately for six subscales, two of which are broadly comparable with the externalizing scale used in this study. Their study found the largest differences were for antisocial and headstrong behaviors, which corresponded closely to the items in the externalizing scale used in this study. This result also is consistent with the measure of conduct disturbance, attentional disorder, and delinquency reported elsewhere.[2–4] In earlier studies, an increased prevalence of disruptive hyperactivity,[4] hyperactivity and short attention span,[5] and impulsivity with increased level of activity[17] has been reported in association with smoking during pregnancy. Such behaviors overlap with the externalizing and SAT scales in the present study.

Several explanations can be suggested for the association between maternal cigarette smoking and child behavior problems. The timing of the relationship at the FCV and its independence of SGA status at birth suggest that placental insufficiency and oxygen deprivation are not important in the pathogenesis. Acetylcholine is an important neurotransmitter in the brain, with nicotinic receptors developing during early pregnancy.[19] Receptors are mutable during development,[20] and it is possible that nicotine in the fetal brain derived from maternal smoking may alter gene expression and the nature and function of the nicotine receptor. Neurotransmitter levels also influence the development of postsynaptic neurons.[21] A suitable animal model and measurement of nicotinic receptors might allow testing of this hypothesis.

The suggestion that mothers who smoke report the behaviors of their children differently is less likely given that the association is observed for externalizing but not for other behaviors. Specifically, it is unlikely that nicotine effects occurring in early pregnancy would affect a mother's perception of externalizing behaviors, particularly some 5 years later. Similar considerations would apply to a hypothesis that external factors such as psychosocial stress

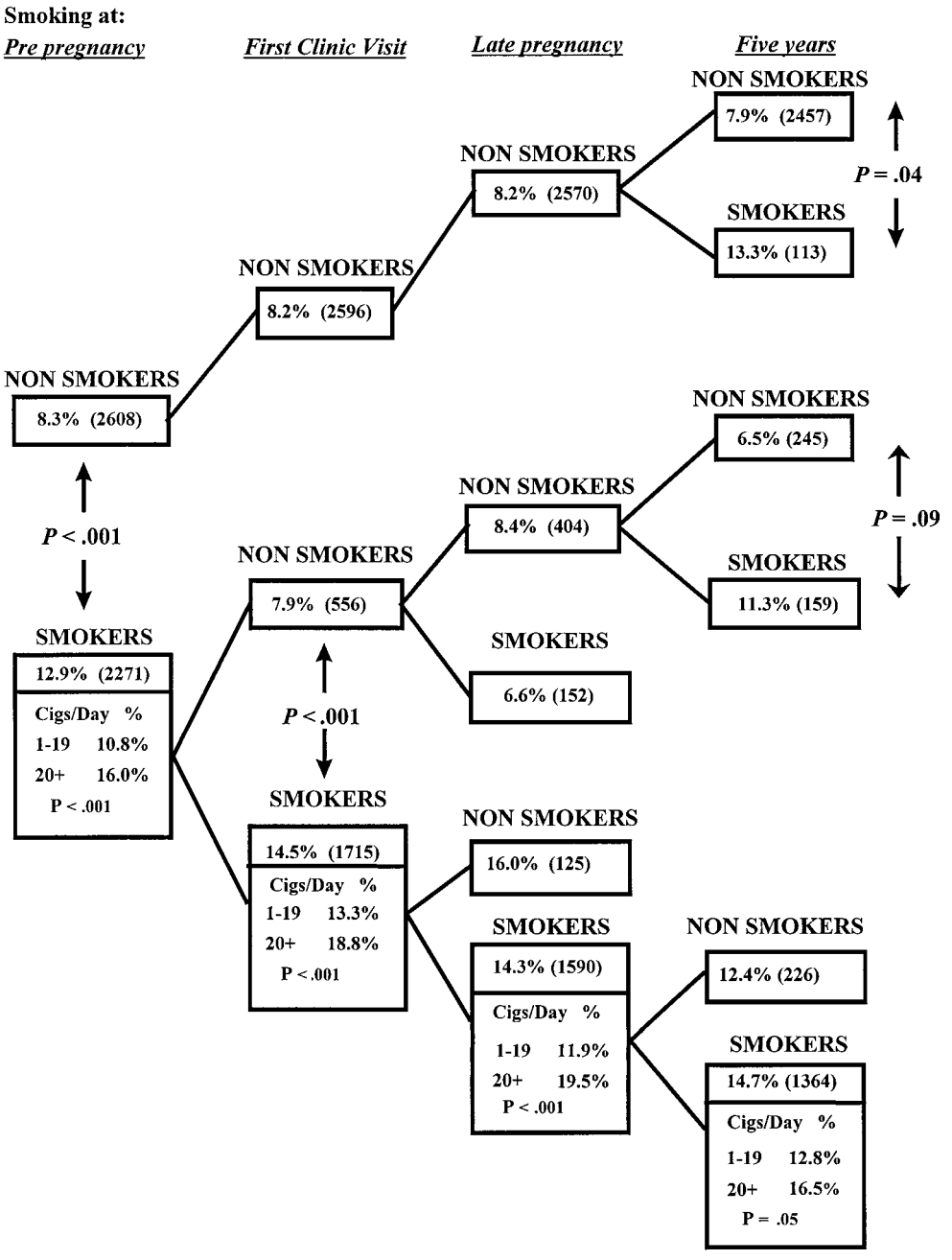

Fig 1. Percentage of children with externalizing behavior problems by maternal smoking before and during pregnancy and at age 5 years (N = 4879).

might simultaneously lead to a woman smoking and influence her perception of her child's behavior.

The presence of a separate although slightly weaker independent association between concurrent maternal smoking and externalizing child behaviors at 5 years again suggests both biological and social explanations, including a direct psychopharmacologic effect of nicotine through passive smoking. Nicotine effects operating as a result of maternal smoking at age 5 years might have such an effect; however, we have no way of discerning this and there is no published literature suggesting this. Although the subgroup of women who began smoking after the birth of their child is a relatively small proportion of the study sample, the finding that their children had higher rates of behavior problems could reflect either biological factors associated with passive cigarette smoking or social learning and/or childbearing processes associated with mothers who smoke cigarettes. This latter possibility is rendered less plausible by the finding that controlling for a wide variety of maternal social variables does not eliminate the associations observed in this study (Table 4).

Based on the rate and level of smoking early in pregnancy and the adjusted RRs presented in Table 4 (and assuming a cause–effect association), it is estimated that up to 25% of behavior problems in children can be attributed to maternal smoking early in pregnancy. A somewhat lesser amount could be attributed to concurrent smoking.

Three methodologic issues could possibly affect

the interpretation of these findings. First, no independent measures of maternal smoking or child behaviors were made to confirm the questionnaire information. Various studies, however, confirm that self-reports of smoking have high reliability and validity.[23–25] Bias in self-reports of smoking would only be misleading if misclassification of smoking was differential with respect to the reporting of child behavior problems. Moreover, if deceptive responses (presumably false- negative) were responsible for the early-pregnancy effect, one would need to posit that the factor actually responsible for the lower rate of externalizing behavior in this group was more frequent in those with a propensity to misreport nonsmoking status in early pregnancy specifically. The existence of such a factor (beyond those already adjusted for) seems implausible. Second, attrition was differential for certain groups, as described previously. This would produce misleading results if there were a systematic association between loss to follow-up and the measurement of child behavior problems. Third, it could be argued that maternal smoking is a marker or is associated with some aspects of maternal child-rearing practices. Perhaps there is some other characteristic of the mother that, on the one hand, is associated with the decision to smoke early in pregnancy or after the child is born and, on the other, influences child-rearing practices. If this were so, it would be difficult to explain why smoking at the first trimester is a more important predictor variable than smoking at the 5-year follow-up. The association between maternal smoking during early pregnancy is strong, and there is some evidence that it is dose-related; it involves specific behaviors and is independent of measured confounding.

The attributable risk is large and, although additional investigation is required, these findings provide further support for antismoking programs in pregnancy and in young family settings.

ACKNOWLEDGMENT

The Mater–University Study of Pregnancy was supported by the National Health and Medical Research Council of Australia.

REFERENCES

1. Weitzman M, Gortmaker S, Sobol A. Maternal smoking and behavior problems of children. *Pediatrics.* 1992;90:342–349
2. Fergusson DM, Horwood LJ, Lynskey MT. Maternal smoking before and after pregnancy. Effects on behavioral outcomes in middle childhood. *Pediatrics.* 1993;:92:815–822
3. Rantakallio P, Laara E, Isohanni M, Moilanen R. Maternal smoking during pregnancy and delinquency of the offspring: an association without causation? *Int J Epidemiol.* 1992;21:1106–1113
4. Denson R, Nanson JL, McWatters MA. Hyperkinesis and maternal smoking. *Can Psychiatr Assoc J.* 1975;20:183–187
5. Naeye RL, Peters EC. Mental development of children whose mothers smoked during pregnancy. *Obstet Gynecol.* 1984;64:601–607
6. Keeping JD, Najman JM, Morrison J, Western JS, Andersen MJ, Williams GM. A prospective longitudinal study of social, psychological and obstetric factors in pregnancy: response rates and demographic characteristics of the 8556 respondents. *Br J Obstet Gynaecol.* 1989;96:289–297
7. Berk RA. An introduction to sample selection bias in sociological data. *Am Soc Rev.* 1983;48:386–398
8. Achenbach TM, Edelbrock C. Behavioral problems and competencies reported by parents of normal and disturbed children aged four through sixteen. *Monogr Soc Res Child Dev.* 1981;46:1–82
9. Achenbach TM, Edelbrock C. *Manual for the Child Behavior Checklist and Revised Child Behavior Profile.* Burlington, VT: University of Vermont Department of Psychiatry; 1983
10. Achenbach TM. *Manual for the Child Behavior Checklist/4–18 and 1991 Profile*. Burlington, VT: University of Vermont Department of Psychiatry; 1991
11. Bedford A, Foulds G. Manual of the delusions–symptoms–states inventory (DSSI). Windsor, UK: NFER; 1978
12. Bagshaw VE. A replication study of Foulds and Bedford's hierarchical model of depression. *Br J Psychiatry.* 1977;151:53–55
13. Foulds GA, Bedford A, Csapo KG. Class change in the personal illness hierarchy. *Br J Psychiatry.* 1975;127:316–319
14. McPherson FM, Antram MC, Bagshaw UE, Carmichael SK. A test of the hierarchical model of personal illness. *Br J Psychiatry.* 1977;131:56–60
15. SAS Institute, Inc. *SAS User's Guide: Basics*. Version 5 ed. Cary, NC: SAS Institute, Inc; 1985
16. Statistical Package for the Social Sciences Version 7.0
17. Kahn HA, Sempos CT. *Statistical Methods in Epidemiology.* Oxford, UK: Oxford University Press; 1989:74–75
18. Kristjansson EA, Fried PA, Watkinson B. Maternal smoking during pregnancy affects children's vigilance performance. *Drug Alcohol Depend.* 1989;4:11–19
19. Cole PV, Hawkins LH, Roberts D. Smoking during pregnancy and its effects on the fetus. *J Obstet Gynaecol Br Commonw.* 1972;79:782–787
20. Laurie DJ, Wisden W, Seeburg PH. The distribution of 13 GABA subunit receptor subunits mRNAs in the rat brain. III. Embryonic and post natal development. *J Neurosci.* 1992;12:4151–4172
21. Trescher WH, Johnson MV. In: Miller C, Ramer JC, eds. *Neurobiology of Static Encephalopathics. Static Encephalopathies of Infancy and Childhood.* New York, NY: Raven Press; 1992:228–229
22. Offord DR, Waters BGH. In: Levine MD, Carey WB, Crocker AC, Gross RT, eds. *Socialization and Its Failure. Developmental—Behavioral Pediatrics.* Philadelphia, PA: WB Saunders Co; 1983:650–681
23. Haziandreu EJ, et al. The reliability of self-reported cigarette consumption in the United States. *Am J Public Health.* 1989;79:1020–1023
24. Slattery ML, et al. Validity of cigarette smoking habits in three epidemiologic studies in Utah. *Prev Med.* 1989;18:11–19
25. Strecher VJ, et al. Using patients' descriptions of alcohol consumption, diet, medication compliance and cigarette smoking. *J Gen Intern Med.* 1989;4:160–166

Maternal Cigarette Smoking and Child Psychiatric Morbidity: A Longitudinal Study

Gail M. Williams, Michael O'Callaghan, Jake M. Najman, William Bor, FRANZCP?; Margaret J. Andersen, AIMS¶; David Richards and Chinlyn U, BSc

Pediatrics 1998;102;e11
DOI: 10.1542/peds.102.1.e11

PEDIATRICS®
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Maternal Cigarette Smoking and Child Psychiatric Morbidity: A Longitudinal Study

Gail M. Williams, Michael O'Callaghan, Jake M. Najman, William Bor, FRANZCP?; Margaret J. Andersen, AIMS¶; David Richards and Chinlyn U, BSc

Pediatrics 1998;102;e11
DOI: 10.1542/peds.102.1.e11