Gestational Exposure to Cigarette Smoke Imperils the Long-Term Physical and Mental Health of Offspring

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BACKGROUND: In this study, we sought to understand whether prenatal exposure to cigarette smoke would be associated with increased offspring hospitalization through age 22 years for various physical and mental health diagnoses. **METHODS:** We used multivariate logistic regression to investigate the relationship between gestational exposure to cigarette smoke and offspring hospitalization for physical and mental health conditions based on International Classification of Diseases (ICD; World Health Organization) diagnoses. **RESULTS:** When controlling for parental psychiatric status, maternal somatic health, socioeconomic status, parity, and maternal age, youth born to mothers who smoked six or more cigarettes per day were more likely to have experienced hospitalization for neuroses (OR, 1.97), diseases of the nervous system (i.e., neurological disorders) (OR, 1.47), respiratory infections (OR, 1.28), accidents (OR, 1.44), infections (OR, 1.54), undiagnosed symptoms (OR, 1.65), and total admissions (OR, 1.48). Female offspring prenatally exposed were more likely to have experienced hospitalization for obstetric complications (OR, 2.94). No association was found for the remaining categories analyzed: blood disorders, skin diseases, psychoses, metabolic/endocrine disease, circulatory disease, digestive disease, disease of the skeletal/muscular system, physical anomalies, neoplasms, and genital/urinary disease. **CONCLUSIONS:** This is the first study to investigate the impact of gestational exposure to cigarette smoke on global measures of somatic and physical health in offspring. This study adds to the literature by demonstrating that smoking during pregnancy increases offspring risk for additional health outcomes not previously recognized in the literature, and that the effect of smoking during pregnancy persists throughout the developmental period. The possibility that these findings are related to lifestyle markers or smoke exposure during childhood should also be considered. *Birth Defects Research (Part A) 73:170–176, 2005.* © 2005 Wiley-Liss, Inc.

Key words: smoking; pregnancy; child health; hospitalization

INTRODUCTION

Prior to the thalidomide tragedy of the late 1950s, there was little research on prenatal environmental effects on fetal development. It was believed that the fetus occupied a privileged site within the uterus, protected from environmental insult (Jones, 1989). Since that infamous tragedy, a wide variety of environmental agents have been implicated in adversely impacting fetal development. One such factor is gestational exposure to cigarette smoke. Cigarettes contain many chemical compounds and a significant proportion of these compounds cross the placental barrier. Some of the chemicals in cigarettes (e.g., lead, cadmium, carbon monoxide, arsenic, cyanide, and nicotine) are known to have toxic effects if consumed in sufficient quantities (Astrup et al, 1972; Stevens et al., 1988). While it is generally understood that smoking during pregnancy has a deleterious effect on the developing fetus, the quantity of research on adverse effects of smoking during pregnancy is far less than that on alcohol and other drugs such as cocaine (Nugent et al., 1996). Thus, the mechanisms and the extent of the adverse affects have not been fully explicated.

Much of the gestational smoking research has focused on directly observable characteristics in the prenatal or neonatal time period. It has been established that pregnancies among women who smoke are marked by an in-

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creased risk for adverse prenatal and perinatal outcomes (Kallen, 2001; Adams, 2003). This literature provides evidence that children of women who smoke during pregnancy have babies who are born prematurely with greater frequency and with lower birth weights than women who do not smoke (Floyd et al., 1993; Ojima et al., 2004). There also is evidence for increased risk of placenta previa and spontaneous abortion. Of these prenatal and perinatal outcomes, birth weight is most clearly linked to maternal smoking. Epidemiological studies since the 1950s have consistently shown that mothers who smoke during pregnancy have infants born 150–250 gm lighter than nonsmoking controls (Hardy and Mellitis, 1972; Floyd et al., 1993; Magee et al., 2004). The U.S. Department of Health and Human Services (1980) indicates that smoking doubles the risk of having an infant born weighing less than 2500 grams. These lower birth weights result from intrauterine growth retardation that continue to be evident at all gestational ages (Floyd et al., 1993). The critical number of cigarettes necessary to result in intrauterine growth deficiency has not been established (Jones, 1989). However, research indicates that regular smoking of five or more cigarettes per day throughout pregnancy was associated with decreased birth weight. Several studies demonstrate that the most severe effects on birth weight are associated with the heaviest maternal smokers (Jones, 1989).

Researchers have investigated the impact of gestational exposure on a diverse range of infant, child, and adolescent development. A number of research teams have found associations in infancy with delayed gross and fine motor coordination (Fried et al., 1987), increased colic (Shenassa and Brown, 2004), increased activity level (Batstra et al., 2003), and a higher prevalence of sudden infant death syndrome (SIDS) (Sundell, 2004). Other studies have identified gestational smoking as a risk factor for physical health outcomes. The most widely documented health outcome is an association with respiratory tract illness (Martinez et al., 1992; Chilmoncyzk et al., 1993; Aligne and Stoddard, 1997; Gilliland et al., 2001). Such exposure has been related to decreased size of lungs and production of less elastin in children (Hanrahan et al., 1992). Some researchers believe that children exposed during the prenatal period may have congenital damage to the developing respiratory system in the bronchial tree of the immune system that predisposes these children to respiratory problems later in development (Cunningham et al., 1994). Additional effects may be the result of the connection between smoking and low birth weight, which has been associated with adverse prenatal lung development.

Prenatal exposure to cigarettes is also associated with physical stature. Children exposed to prenatal smoke are known to be shorter than children from nonsmoking mothers. Butler and Goldstein (1973) found in a large English sample that the seven-year-old children of smokers were on average 1 cm shorter than the children of nonsmokers. At age 11, the difference was 1.6 cm. In addition, several recent studies have linked gestational smoke exposure with an increased likelihood of obesity among offspring (Vik et al., 1996; Fried et al., 1999; Wideroe et al., 2003), a serious public health concern, particularly if the condition persists into adulthood.

There also is evidence that prenatal exposure to cigarette smoke can result in a variety of sensory, cognitive, and behavioral deficits. A number of researchers have found that maternal smoking during pregnancy resulted in auditory processing defects (Fried and Watkinson, 1988, 1990; Sexton et al., 1990; McCartney and Fried, 1993; McCartney et al., 1994; Fried et al., 2003). Numerous studies have documented a relationship between gestational exposure and cognitive and academic deficits (Butler and Goldstein, 1973; Fogelman and Manor, 1988; Sexton et al., 1990; Bauman et al., 1991; Olds et al., 1994). There also is evidence that children born to mothers who smoked during pregnancy are at higher risk for behavioral and psychological pathology such as hyperactive behavior, conduct disorder, and antisocial disorder (Denson et al., 1975; Streissguth et al., 1984; Kristjansson et al., 1989; Fried et al., 1992; Fergusson et al., 1993; Milberger et al., 1996; Wakschlag et al., 1997; Fergusson et al., 1998; Naeye and Peters, 1984; Rantakallio and Koiranen, 1987; Sexton et al., 1990; Silberg et al., 2003). Of these behaviors, the association with increased activity level has been the most frequently studied.

Generally speaking, the gestational smoking studies focus on a narrow range of psychological, behavioral, or health outcomes and have difficulty controlling for confounding variables (e.g., maternal age, maternal socioeconomic status (SES), parental psychiatric status) that may have contributed to the reported outcomes. The primary purpose of this article is to report the results of a research effort designed to augment the understanding of the long-term effects of maternal gestational smoking on offspring's physical and mental health well-being. This study was able to control for the above-noted factors and simultaneously investigate a larger array of mental and physical health outcomes that have not been previously studied.

MATERIALS AND METHODS

Participants

Participant data were obtained from the Helsinki Longitudinal Project, a prospective study of the antecedents and sequelae of youth physical and mental health outcomes. The total sample consisted of all children (n = 6,401) born between July 1, 1975 and June 30, 1976 in Helsinki, Finland and the adjacent suburbs of Vantaa and Espo. The cohort size was adjusted by eliminating data for one twin of each twin pair. This adjustment resulted in a final cohort of 6,388 children.

There are two features of this study that are noteworthy. First, the region from which the cohort was obtained is exceptionally homogeneous with regard to ethnicity: 90% are ethnic Finns; 7% are ethnic Swedes; and 2% are from other Nordic countries; only 1% are from non-Nordic countries. Second, the region also was homogeneous with regard to most indicators of social class. During the 1970s Finland provided a strong social and economic support system for its citizens, including free health care and education. For example, Wrede et al. (1980) report that during the 1970s, 95% of mothers took part in prenatal care provided at government-supported clinics. Thus, the SES stratification that is common among many other industrialized countries was less evident in Finland during that time period.

Within this study, expectant mothers at each prenatal visit to a government prenatal clinic were asked to complete a questionnaire describing their somatic and psychological health during the past month of pregnancy. Mothers were informed that participation was voluntary and was for research purposes. About 55% of the mothers

Table 1
Comparison of Entire Cohort and That Portion of the Cohort for Whom Mothers Completed Symptom Questionnaires during Pregnancy

Characteristic	Cohort	Sub-sample with pregnancy data
Gender	52.7% male	53.0% male
Maternal parity	56.7% primipara	57.7% primipara
	43.3% multipara	42.3% multipara
Mean maternal age	27.26 years (s.d. = 4.51)	27.33 (4.30)
Mean paternal age	29.28 years (s.d. = 5.33)	29.17 (4.92)
Mean number of older siblings	0.74 (s.d. = .92)	0.68 (.84)
Mean socioeconomic status	2.77 (s.d. = 1.41)	2.78 (s.d. = 1.39)

chose to participate in the pregnancy questionnaire portion of the study. This amounts to 3,489 of the initial cohort of 6,388.

Hospital discharge registry. The Finnish government maintains a registry of every hospitalization in the country. Since few Finns migrate out of the country, and since very few persons from other countries migrate into Finland, this database captures the hospitalization history of the vast majority of citizens of the country. Information used in this research was obtained from this registry and includes a record of each admission, the number of days of patient hospitalization, and the primary, secondary, and tertiary diagnoses at the time of hospitalization. These records were available for both parents of the cohort youth and for the youth. Hospitalization data were available for cohort youth through their 22nd birthday. Of the 3,247 offspring for whom hospitalization data are available, 88.3% also included pregnancy questionnaire data, resulting in a final sample size of 2,867.

Pregnancy questionnaire. At each prenatal visit, expectant mothers completed a 15-item questionnaire that asked about their somatic and mental health symptoms during the past month of pregnancy. The questionnaire included lists of symptoms of upper respiratory infection (fever, cough, rhinitis, sore throat) and more general symptoms that might be related to pregnancy or other illnesses (nausea, diarrhea, fatigue, sleep problems, muscle pain, headache). The questionnaire also contained lists of symptoms related to maternal mental health (anxiety/depression and mood lability). In addition, the smoking behavior of the mother was included on this questionnaire. Mothers were asked to indicate how much they smoked per day on average for the past month. Response options were none, one to five cigarettes per day, and six or more cigarettes per day.

Methods

In order to determine whether maternal smoking is related to offspring hospitalization, multivariate logistic regression was employed. Variables controlled for in the analysis included parental psychiatric status, maternal somatic health, socioeconomic status, parity, and maternal age. The first of three of these variables were obtained from the hospital discharge registry and the latter two from self-report of mothers. Hospitalization diagnoses (International Classification of Diseases [ICD]-8 or -9; World Health Organization) of offspring across 17 categories of mental and physical health were compiled and analyzed: obstetric complications, neuroses, nervous system disorders, respiratory infection, accidents, infectious disease, undiagnosed symptoms, blood disorders, skin diseases, psychoses, metabolic/endocrine disease, circulatory disease, digestive disease, disease of the skeletal/muscular system, physical anomalies, neoplasms, and genital/urinary disease. Total number of hospital admissions and number of days hospitalized were also compiled and analyzed.

RESULTS

Because only about 55% of the cohort mothers provided pregnancy questionnaire data, there was a chance that those who completed the pregnancy questionnaires were different from those who did not. Data in Table 1 provides an analysis of the demographic and family variables that were available in this study, comparing the frequencies and mean levels of the entire cohort to those women who provided pregnancy questionnaire data. These data indicate that the responders to the pregnancy questionnaire were not different from those in the cohort, at least with regard to the variables studied: gender distribution, maternal parity, SES of mother (an occupation-based measure obtained from medical records), percentage of children who were only children, and mean number of older siblings. Similarly, an investigation of hospitalization rates during pregnancy between pregnancy questionnaire responders and nonresponders did not reveal any significant difference.

Data presented in Table 2 include results concerning the central thesis of this study. When controlling for parental psychiatric status, maternal somatic health, socioeconomic status, parity, and maternal age, a number of associations between maternal smoking and child hospitalization were observed. Children born to mothers who smoked six or more cigarettes per day were more likely to have experienced hospitalization for neuroses (OR, 1.97), diseases of the nervous system (OR, 1.47), respiratory infections (OR, 1.28), accidents (OR, 1.44), infections (OR, 1.54), undiagnosed symptoms (OR, 1.65), and total admissions (OR, 1.48). The data allowed for an investigation of obstetric complications among female offspring. Data were unavailable for male offspring in relation to obstetric complications. The results indicated an increased likelihood of obstetric complication hospitalization (OR, 2.94) following gestational smoke exposure. As shown in Table 2, female prenatally exposed offspring experienced an ever greater likelihood of hospitalization across all categories except nervous system disease (i.e., neurological disorders). The

Table 2
Relationship between Smoking during Pregnancy and Offspring Hospitalization*

Primary diagnosis	No smoke		Smoke exposure		Odds ratio	Chi-square
	n	%	*n*	%		
Neuroses[b]						
Total	95	4.29[a]	53	8.10[a]	1.97 (1.39–2.7995%CI)	14.98[i]
Male	74	6.30	40	11.11	1.86 (1.24–2.7595%CI)	9.29[g]
Female	21	2.02	13	4.42	2.24 (1.11–4.5395%CI)	5.30[e]
Nervous system disease[b]						
Total	204	7.12	85	2.96	1.47 (1.13–1.9395%CI)	7.95[g]
Male	129	10.98	56	15.56	1.49 (1.07–2.1095%CI)	5.45[f]
Female	75	7.23	29	9.86	1.40 (0.90–2.2095%CI)	2.22[j]
Respiratory infections						
Total	774	34.98	266	41.67	1.28 (1.07–1.5295%CI)	7.09[g]
Male	560	47.66	191	53.06	1.24 (0.98–1.5795%CI)	3.21[e]
Female	214	15.32	62	21.09	1.32 (0.98–1.7895%CI)	3.23[e]
Accidents						
Total	443	20.02	173	26.45	1.44 (1.17–1.7695%CI)	12.39[h]
Male	284	24.17	111	30.83	1.40 (1.08–1.8295%CI)	6.41[f]
Female	159	15.32	62	21.09	1.48 (1.07–2.0595%CI)	5.51[f]
Infections						
Total	269	12.16	115	17.58	1.54 (1.22–1.9695%CI)	12.83[h]
Male	211	17.86	80	22.22	1.31 (0.98–1.7495%CI)	3.26[e]
Female	58	5.59	35	11.90	2.28 (1.47–3.5595%CI)	14.08[i]
Undiagnosed symptoms[c]						
Total	198	8.95	91	13.91	1.65 (1.26–2.1495%CI)	13.74[h]
Male	117	9.96	47	13.06	1.36 (0.95–1.9595%CI)	2.77[e]
Female	81	7.80	44	14.97	2.07 (1.40–3.0895%CI)	13.82[h]
Obstetric complications[d]						
Female	98	9.44	69	23.47	2.94 (2.09–4.1495%CI)	41.12[i]
Total admissions						
Total	1465	66.20	486	74.31	1.48 (1.21–1.7995%CI)	15.27[i]
Male	920	78.30	301	83.61	1.41 (1.04–1.9395%CI)	4.78[e]
Female	545	52.50	185	62.93	1.54 (1.18–2.0095%CI)	10.04[h]

*Total sample size = 2867 (no smoke exposure = 2213); smoke exposure (≥6 per day) = 654. Male sample size = 1535 (no smoke exposure = 1175); smoke exposure (≥6 per day) = 360. Female sample size = 1332 (no smoke exposure = 1038); smoke exposure (≥6 per day) = 294.

[a]Each row in the above table furnishes number of hospitalizations according to smoke exposure (yes/no). Each row represents 1/2 of a 2×2 matrix for three different samples (total, male, and female) {Hospitalization (yes/no) by Smoking Exposure (yes/no). Neurosis (total) example: The sample for neurosis hospitalization (yes) by smoking (yes) is 53 while the sample for hospitalization (yes) by smoking (no) is 95. The remaining half of the matrix {Neurosis hospitalization (no) by smoking (yes/no)} may be calculated by referring to the sample size presented below for each row. In this case, neurosis hospitalization (no) by smoking (no) is 2118 while neurosis hospitalization (no) by smoking exposure (yes) is 601.

[b]Indicators of mental health outcomes.

[c]Possible indicator of mental health outcomes. Diagnosis may have been deferred to avoid stigma at youthful age.

[d]Only obstetric complication data for females are available.

[e]Significant at $p < 0.10$.

[f]Significant at $p < 0.05$.

[g]Significant at $p < 0.01$.

[h]Significant at $p < 0.001$.

[i]Significant at $p < 0.0001$.

[j]Nonsignificant.

results were not significant for the remaining hospitalization categories analyzed: blood disorders, skin diseases, psychoses, metabolic/endocrine disease, circulatory disease, digestive disease, disease of the skeletal/muscular system, physical anomalies, neoplasms, and genital/urinary disease. Furthermore, children born to expectant mothers who smoked between one and five cigarettes per day did not experience any elevation in hospitalization rate. The data for age at hospitalization is unavailable. In all these analyses, the first admission through age 22 years was analyzed. This means that whether a patient was hospitalized one time or four times, the patient was coded positive for having been admitted to a hospital for a particular diagnostic category. An analysis of the median number of days hospitalized is presented in Table 3. This analysis included all days hospitalized through age 22 years. As shown, the number of days hospitalized is higher for all the gestationally exposed groups (i.e., combined, female only, and male only) that were studied.

DISCUSSION

This study is one of the first to examine a wide array of long-term mental and physical health outcomes among offspring exposed to gestational cigarette smoke. This study furnishes information on health outcomes via an

Table 3
Number of Days Hospitalized

	No smoke exposure			Smoke exposure				
	Average[a]	Median	Interquartile range (25–75%)	Average[a]	Median	Interquartile range (25–75%)	Z-value	Significance[b]
Total	12.31	3	0–10	18.99	6	1–14	6.17	$p < 0.0001$
Male	16.86	6	1–13	19.86	7	2.5–15	3.45	$p < 0.001$
Female	7.15	1	0–6	17.90	4	0–10	5.30	$p < 0.0001$

[a]Included for descriptive purposes.
[b]Based on Wilcoxon Rank Sums analysis.

examination and coding of diagnostic information at hospitalization discharge. ICD diagnoses were categorized in 17 physical and mental health outcomes. A global measure of health (total hospital admissions) was also categorized.

The results of this study indicate that prenatal exposure to cigarette smoke is associated with significantly increased offspring hospitalization on a number of important health variables. Across all diagnostic categories, except neurological disorders, the results highlight the increased vulnerability of female offspring. This finding raises important questions about the potential contribution of gestational smoking to the understanding of hospitalization outcomes among offspring. Because this is a unique finding that has been rarely reported in the literature, it warrants further investigation.

In relation to specific diagnostic categories, one of the more compelling findings was with obstetric complications. Obstetric complications subsume a range of adverse outcomes, including prematurity and low birth weight. Female children born to mothers who smoked six or more cigarettes per day experienced hospitalizations for obstetric complications at a rate nearly two times (194%) that of female children born to mothers who did not smoke (OR, 1.94). This finding is consistent with the literature, which reports increased risk of prematurity and low birth weight following gestational exposure to cigarette smoke (Jones, 1989; Magee et al., 2004; Ojima et al., 2004). Our findings confirm and quantify this risk. Moreover, the experience of obstetric complications may have implications for later development. A literature base exists that suggests that obstetric complications might be directly or indirectly associated with later adverse neuropsychiatric outcomes such as cognitive deficits, learning delays, and behavioral outcomes (Hack and Fanaroff, 1999).

The results of this study also show that prenatal exposure to cigarette smoke approximately doubles the risk of hospitalization for neuroses (e.g., mood disorders, anxiety and depression) (total OR, 1.97; male OR, 1.84; female OR, 2.24). There also is an increased risk of hospitalization for nervous system disease (e.g., neurological disorders) (total OR, 1.47; male OR, 1.49; female OR, 1.40). The gestational smoking literature has scant information on psychiatric conditions that may be considered internalizing disorders such as neuroses. What is available generally focuses on the relationship with externalizing conditions such as attention-deficit/hyperactivity disorder (ADHD), conduct disorder (CD), and antisocial behavior (Denson et al., 1975; Naeye and Peters, 1984; Streissguth et al., 1984; Rantakallio and Koiranen, 1987; Kristjansson et al., 1989; Sexton et al., 1990; Fried et al., 1992; Fergusson et al., 1993, 1998; Milberger et al., 1996; Wakschlag et al., 1997; Silberg et al., 2003). Thus, our findings provide compelling evidence for an association with internalizing conditions and provide data that extend the risk of gestational smoking to a broader range of psychiatric outcomes (e.g., neurotic disorders such as anxiety, depression, and mood lability). Also, the significant finding with respect to undiagnosed symptoms may provide evidence for increased risk for psychiatric outcomes. Many patients present with vague symptoms or with symptom complexes that do not readily fit standard diagnostic categories. Some portion of these is related to the psychological and psychiatric health of the patient. Further, the diagnosing physician may have deferred a suspected mental health diagnosis in such cases until further psychiatric or medical information becomes available.

Our finding with respect to increased hospitalization for accidents (total OR, 1.44; male OR, 1.40; female OR, 1.48) may be supportive of the literature that provides evidence for externalizing psychiatric conditions such as hyperactivity or ADHD (Thapar et al., 2003). Accident-prone individuals generally display a clustering of traits (e.g., high impulsivity, poor judgment, aggression) that may predispose them to risk for accidents (Poole et al., 1997; Marusic et al., 2001)

There also is research available that provides evidence for an association between maternal prenatal smoking and neurological conditions such as learning disabilities and cognitive deficits (Batstra et al., 2003). Our significant findings with respect to increased hospitalization for nervous system disorders (i.e., neurological difficulties) are consistent with this literature although the ICD category of nervous system disorders includes a wide range of neurological pathologies.

The results of our study indicate an increase in hospitalizations for respiratory conditions among offspring who were prenatally exposed to by-products of cigarette smoke (total OR, 1.28; male OR, 1.24; female OR, 1.32). This finding is consistent with research that links gestational cigarette exposure to later respiratory conditions such as asthma and respiratory tract illness (Gilliland et al., 2001). It is acknowledged that there is an alternative hypothesis for our findings. Health consequences resulting in increased hospitalization for respiratory dysfunction may be related to postnatal second-hand smoke exposure. Women who smoked during pregnancy are likely to maintain this habit after their pregnancy, and exposure to second-hand smoke has been associated with increased risk for respiratory conditions (Lelong et al., 2001).

Regarding the remaining two outcomes of increased hospitalization for infections and total hospitalizations, there is less available supporting literature. It is possible

that gestational exposure to cigarette smoking may lead to increased hospitalization for infectious disease via the mechanism of reduced immunity. There is some research that suggests that smoking during pregnancy can alter fetal immune system functioning via an alteration to the neonatal cytokine response (Noakes et al., 2003). This alteration may increase susceptibility to hospitalization for infectious disease. Another pathogenic mechanism should be considered. Epidemiological data (e.g., Curns et al., 2002; Jensen-Fangel et al., 2004) suggest that otitis media poses a major infection risk for younger children and can often lead to hospitalization. One important contribution to this infection is second-hand smoke. Additional research is needed in relation to generalized susceptibility to infection following gestational cigarette exposure.

The higher level of hospitalization for offspring of mothers who smoked during pregnancy in the current study is a manifestation of the wide array of specific disease categories in which these children had higher hospitalization rates. We found that maternal smoking during pregnancy was associated with hospitalization for obstetric complications, neuroses, diseases of the nervous system, respiratory infections, accidents, infections, and undiagnosed symptoms. These categories include some of the most frequent reasons to hospitalize individuals in the developmental period. Therefore, the association with total number of hospitalizations was not surprising. This finding indicates that gestational exposure to the by-products of cigarette smoke has a generalized negative affect on health, resulting in an increased likelihood of not only hospitalization, but also number of days hospitalized.

There are two perspectives from which the outcomes of this study might be viewed. First, smoking during pregnancy is a marker for lifestyle (Eysenck, 1991). Smoking during pregnancy is associated with younger mothers, mothers who experience greater psychiatric distress, mothers who are more impulsive and engage in high-risk behaviors, and greater poverty (Cherry and Kiernan, 1976; Rantakallio, 1979; Eysenck, 1991; Graham, 1995). There are a wide range of prenatal and postnatal exposures and experiences that are associated with this lifestyle marker. Many of these exposures may have deleterious effects on fetal development (e.g., maternal cocaine use during pregnancy) and be associated with experiences that are less than optimal for development in the postnatal period (e.g., the adverse affects of maternal depression on child development). This research was designed to control for these lifestyle variables by controlling for socioeconomic status, parental psychiatric status, maternal age, and parity. However, it is acknowledged that many factors could not be controlled that may relate to important lifestyle factors. To mention one, it is possible that subclinical levels of maternal depression or stress that would not result in hospitalization might be related to offspring outcomes (Martin et al., 1999). Another caveat must be acknowledged in order to fully interpret these data. No data were available on maternal smoking after pregnancy. Several studies have shown that the prevalence of smoking after pregnancy for mothers who smoke during pregnancy is high; even for those that smoked prior to pregnancy and stopped during pregnancy, 70% resume after childbirth (Fingerhut et al., 1990; Isohanni et al., 1995; Lelong et al., 2001). Therefore, it might be safe to deduce that a significant portion of mothers who smoked during pregnancy continued to smoke postnatally. There also is the possibility that youth's own smoking behavior contributed to some of these outcomes. However, information on smoking behavior among offspring was not available in this study. Thus, some of the effects observed for maternal smoking could result from direct exposure to cigarette smoke or to second-hand smoke during the developmental period because the mothers who smoked during pregnancy likely also smoked postnatally.

The second perspective for viewing these results is that gestational exposure to cigarette smoke has a direct and adverse physiological impact on the developing fetus. Cigarettes have between 3000 and 4000 different compounds, and it is possible that the chemical agents in these compounds are teratogenic. Further research is needed to uncover the specific effects of each of these compounds.

Although this article does not furnish a critical threshold of teratogenicity, it does present some interesting findings. Although smoking less than six cigarettes did not produce any significant effects, smoking six or more cigarettes was strongly and significantly associated with increased hospitalization risk among offspring. Future research should focus on determining the existence of a threshold of teratogenicity.

Overall, the smoking behavior of mothers during pregnancy is significantly associated with global measures of physical and mental health. These results were obtained despite controlling for maternal SES, parity, age, parental psychiatric status, and maternal somatic health problems during pregnancy. The findings of this study indicate that the deleterious effect of smoking during pregnancy persists throughout the developmental period. Consistent with the position held by the Public Affairs Committee of the Teratology Society (Adams, 2003), these findings support the urgent need to implement smoking cessation programs among women in their reproductive period.

REFERENCES

Adams J. 2003. Statement of the Public Affairs Committee of the Teratology Society on the importance of smoking cessation during pregnancy. Birth Defects Research Part A Clin Mol Teratol 67:895–899.

Aligne C, Stoddard J. 1997. Tobacco and children. Arch Pediatr Adolesc Med 151:648–653.

Astrup P, Olson HM, Trolle D, Kjeldsen K. 1972. Effects of carbon monoxide exposure on foetal development. Lancet 2:1220–1222.

Batstra L, Hadders-Algra M, Neeleman J. 2003. Effect of antenatal exposure to maternal smoking on behavioural problems and academic achievement in childhood: prospective evidence from a Dutch birth cohort. Early Hum Dev 75:21–33.

Bauman K, Flewelling R, LaPrelle, J. 1991. Parental cigarette smoking and cognitive performance of children. Health Psychol 10:282–288.

Butler NR, Goldstein H. 1973. Smoking in pregnancy and subsequent child development. Br Med J 4:573–575.

Cherry N, Kiernan K. 1976. Personality scores and smoking behavior—a longitudinal study. Br J Prev Soc Med 30:123–121.

Chilmoncyzk B, Salmun L, Megathlin K, et al. 1993. Association between exposure to environmental tobacco smoke and exacerbations of asthma in children. N Engl J Med 328:1665–1669.

Cunningham J, Dockery D, Speizer F. 1994. Maternal smoking during pregnancy as a predictor of lung function in children. Am J Epidemiol 139:1139–1152.

Curns AT, Holman RC, Shay DK, et al. 2002. Outpatient and hospital visits associated with otitis media among American Indian and Alaska native children younger than 5 years. Pediatrics 190:41.

Denson R, Nanson JL, McWatters MA. 1975. Hyperkinesis and maternal smoking. Can Psychiatr Assoc J 20:183–187.

Eysenck H. 1991. Smoking, personality, and stress. New York: Springer-Verlag. 130 p.

Fergusson D, Horwood J, Lynskey M. 1993. Maternal smoking before and after pregnancy: effects of behavioral outcomes in middle childhood. Pediatrics 92:815–822.

Fergusson DM, Woodward L J, Horwood JL. 1998. Maternal smoking during pregnancy and psychiatric adjustment in late adolescence. Arch Gen Psychiatry 55:721–727.
Fingerhut LA, Kleinman JC, Kendrick JS. 1990. Smoking before, during, and after pregnancy. Am J Public Health 80:541–544.
Floyd RL, Rimer BK, Giovino GA, et al. 1993. A review of smoking in pregnancy: effects on pregnancy outcomes and cessation efforts. Annu Rev Public Health 14:379–411.
Fogelman KR, Manor O. 1988. Smoking in pregnancy and development into early adulthood. BMJ 297:1233–1236.
Fried PA, Watkinson B, Dillon RF, Dulberg CS. 1987. Neonatal neurological status in a low-risk population after prenatal exposure to cigarettes, marijuana, and alcohol. J Dev Behav Pediatr 8:318–326.
Fried PA, Watkinson B. 1988. 12- and 24-month neurobehavioral follow-up of children prenatally exposed to marijuana, cigarettes, and alcohol: cognitive and language assessment. Neurotoxicol Teratol 16:305–313.
Fried PA, Watkinson B. 1990. 36- and 48-month neurobehavioral follow-up of children prenatally exposed to marijuana, cigarettes, and alcohol. J Dev Behav Pediatr 11:49–58.
Fried PA, Watkinson B, Gray R. 1992. A follow-up study of attentional behavior in six-year-old children exposed prenatally to marijuana, cigarettes and alcohol. Neurotoxicol Teratol 14:299–311.
Fried PA, Watkinson B, Gray R. 1999. Growth from birth to early adolescence in offspring prenatally exposed to cigarettes and marijuana. Neurotoxicol Teratol 21:513–525.
Fried PA, Watkinson B, Gray R. 2003. Differential effects on cognitive functioning in 13- to 16-year-olds prenatally exposed to cigarettes and marihuana. Neurotoxicol Teratol 25:427–439.
Gilliland FD, Li YF, Peters JM. 2001. Effects of maternal smoking during pregnancy and environmental tobacco smoke on asthma and wheezing in children. Am J Respir Crit Care Med 163:429–436.
Graham H. 1995. Women, smoking and disadvantage. In: Slama K, editor. Tobacco and Health, proceedings of the 9th World Conference on Tobacco and Health, Plenum Press. New York: Plenum Press. pp. 695–697.
Hack M, Fanaroff AA. 1999. Outcomes of children of extremely low birthweight and gestational age in the 1990's. Early Hum Dev 3:193–218.
Hardy JB, Mellitis DD. 1972. Does maternal smoking during pregnancy have a long-term effect on the child? Lancet 2:1332.
Hanrahan J, Tager I, Segal M, et al. 1992. The effect of maternal smoking during pregnancy on early infant lung function. Am Rev Respir Dis 145:1129–1135.
Isohanni M, Oja H, Moilanen I, et al. 1995. Smoking or quitting during pregnancy: associations with background and future social factors. Scand J Soc Med 23:32–38.
Jensen-Fangel S, Mohey R, Johnsen SP, et al. 2004. Gender differences in hospitalization rates for respiratory tract infections in Danish youth. Scand J Infect Dis 36:31–36.
Jones KL. 1989. Effects of chemical and environmental agents. In: Creasy RK, Resnik R, editors. Maternal-fetal medicine: principles and practice. 2nd ed. Philadelphia: Saunders. pp. 180–192.
Kallen K. 2001. The impact of maternal smoking during pregnancy on delivery outcome. Eur J Public Health 11:329–333.
Kristjansson EA, Fried PA, Watkinson B. 1989. Maternal smoking during pregnancy affects children's vigilance performance. Drug Alcohol Depend 24:11–19.
Lelong N, Kaminski M, Saurel-Cubizolles MJ, Bouvier-Colle MH. 2001. Postpartum return to smoking among usual smokers who quit during pregnancy. Eur J Public Health 11:334–339.
Magee BD, Hattis D, Kivel NM. 2004. Role of smoking in low birth weight. J Reprod Med 49:23–27.
Martin RP, Noyes J, Wisenbaker J, Huttunen MO. 1999. Prediction of early childhood negative emotionality and inhibition from maternal distress during pregnancy. Merrill-Palmer Q 45:370–391.
Martinez F, Cline M, Burrows B. 1992. Increased incidence of asthma in children of smoking mothers. Pediatrics 89:21–26.
Marusic A, Musek J, Gudjonsson G. 2001. Injury proneness and personality. Nord J Psychiatry 55:157–161.
McCartney JS, Fried PA. 1993. Prenatal cigarette exposure and central auditory processing abilities in 6-11 year old children. Teratology 47: 456–457.
McCartney JS, Fried PA, Watkinson B. 1994. Central auditory processing in school age children prenatally exposed to cigarette smoke. Neurotoxicol Teratol 16:267–276.
Milberger S, Bieberman J, Farone SV, et al. 1996. Is maternal smoking during pregnancy a risk factor for attention deficit hyperactivity disorder in children? Am J Psychiatry 153:1138–1142.
Naeye RL, Peters EC. 1984. Mental development of children whose mothers smoked during pregnancy. Obstet Gynecol 64:601–609.
Noakes PS, Holt PG, Prescott SL. 2003. Maternal smoking in pregnancy alters neonatal cytokine responses. Allergy 58:1053–1058.
Nugent JK, Lester BM, Greene SM, et al. 1996. The effects of maternal alcohol consumption and cigarette smoking during pregnancy on acoustic cry analysis. Child Dev 67:1806–1816.
Ojima T, Uehara R, Watanabe M, et al. 2004. Population attributable fraction of smoking to low birth weight in Japan. Pediatr Int 46:264–267.
Olds D, Henderson C, Tatalbaum R. 1994. Intellectual impairment in children of women who smoke cigarettes during pregnancy. Pediatrics 93:221–227.
Poole GV, Lewis JL, Devidas M, et al. 1997. Psychopathologic risk factors for intentional and nonintentional injury. J Trauma 42:711–715.
Rantakallio P. 1979. Social background of mothers who smoke during pregnancy and influence of these factors on the offspring. Soc Sci Med 13:423–429.
Rantakallio PA, Koiranen M. 1987. Neurological handicaps among children whose mothers smoked during pregnancy. Prev Med 16:597–606.
Sexton M, Fox NL, Hebel JR. 1990. Prenatal exposure to tobacco. II. Effects on cognitive functioning at age 3. Int J Epidemiol 72–77.
Shenassa ED, Brown MJ. 2004. Maternal smoking and infantile gastrointestinal dysregulation: the case of colic. Pediatrics 114:497–505.
Silberg JL, Parr T, Neale MC, et al. 2003. Maternal smoking during pregnancy and risk to boys' conduct disturbance: an examination of the causal hypothesis. Biol Psychiatry 53:130–135.
Stevens RJ, Becker RC, Krumpos GL, et al. 1988. Postnatal sequelae of parental smoking during and after pregnancy. J Reprod Infant Psychol 6:61–81.
Streissguth AP, Martin DC, Barr HM, et al. 1984. Intrauterine alcohol and nicotine exposure: attention and reaction time in 4-year-old children. Dev Psychol 20:533–541.
Sundell HW. 2004. SIDS prevention—good progress, but now we need to focus on avoiding nicotine. Acta Paediatr 93:450–452.
Thapar A, Fowler T, Rice F, et al. 2003. Maternal smoking during pregnancy and attention deficit hyperactivity disorder symptoms in offspring. Am J Psychiatry 160:1985–1989.
U.S. Department of Health and Human Services. 1980. The health consequences of smoking for women: a report of the surgeon general. Washington DC: U.S. Department of Health and Human Services. pp. 26–50.
Vik T, Jacobsen G, Vatten L, Bakketeig LS. 1996. Pre- and post-natal growth in children of women who smoked in pregnancy. Early Hum Dev 45:245–255.
Wakschlag LS, Lahey BB, Loeber R, et al. 1997. Maternal smoking during pregnancy and the risk of conduct disorder in boys. Arch Gen Psychiatry 54:670–676.
Wideroe M, Vik T, Jacobsen G, Bakketeig LS. 2003. Does maternal smoking during pregnancy cause childhood overweight? Paediatr Perinat Epidemiol 17:171–179.
Wrede G, Mednick SA, Huttunen MO, Nilsson CG. 1980. Pregnancy and delivery complications in the births of an unselected series of Finnish children with schizophrenic mothers. Acta Psychiatr Scand 62:369–381.