Fetal Growth and Length of Gestation in Relation to Prenatal Exposure to Environmental Tobacco Smoke Assessed by Hair Nicotine Concentration

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We assessed the effects of prenatal exposure to environmental tobacco smoke on fetal growth and length of gestation. The study population consisted of 389 nonsmoking women who were selected from a population-based study in southeast Finland on the basis of questionnaire information after delivery (response rate 94%). The final exposure assessment was based on nicotine concentration of maternal hair sampled after the delivery, which measures exposure during the past 2 months (i.e., the third trimester). The exposure categories were defined *a priori* as high (nicotine concentration ≥ 4.00 µg/g; n = 52), medium (0.75 to < 4.00 µg/g; n = 186), and low as the reference category (< 0.75 µg/g; n = 151). In logistic regression analysis, controlling for confounding, the risk of preterm delivery (< 37 weeks) was higher in the high [adjusted odds ratio (OR) = 6.12; 95% confidence interval (CI), 1.31–28.7] and medium exposure categories (adjusted OR = 1.30; 95% CI, 0.30–5.58) compared with the reference category, and there was a 1.22 (95% CI, 1.07–1.39) increase in adjusted OR with a 1 µg/g increase in hair nicotine concentration. The corresponding adjusted OR was 1.06 (95% CI, 0.96–1.17) for low birth weight and 1.04 (95% CI, 0.92–1.19) for small-for-gestational-age. *Key words:* biomarkers, birth weight, hair nicotine, preterm delivery, small for gestational age, tobacco smoke pollution. *Environ Health Perspect* 109:557–561 (2001). [Online 21 May 2001]
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The adverse effects of maternal smoking during pregnancy on fetal growth (*1,2*), as well as on the risk of preterm delivery (*3*) are well established. People exposed to environmental tobacco smoke (ETS) encounter mainly the same compounds as in the mainstream smoke inhaled directly by the smoker, although the concentrations and time patterns differ (*2,4*). Although individual studies have often been inconclusive (*5–31*), a recent meta-analysis by Windham and colleagues (*32*) suggests that exposure to ETS during pregnancy has a small effect on birth weight and the risk of term low birth weight. The effects on the length of gestation and risk of preterm delivery have been studied less (*10,19,23,25*), and the evidence of any effect is weak.

Assessment of exposure during a relevant time period and control of confounding are the most critical issues of validity in studies of the effects of ETS on pregnancy outcomes (*32,33*). In the first reports, exposure assessment was based only on information on the spouse's smoking (*5–7,9,11–13,15–17,21, 22,24,26*). Later studies collected information on multiple sources, such as other family members and work exposure or on quantity measured as daily duration of exposure or number of cigarettes smoked indoors (*10,18–20,25,31*). Questionnaire or interview information on sources of exposure is sensitive to information bias, especially if carried out after the delivery and if the accuracy of the smoking information is compromised due to inaccurate recall and variation of environmental conditions such as air change, area, and volume of the space. Few studies have used biomarkers of exposure such as serum cotinine (*14,28,30*) and saliva cotinine (*29*) measured during pregnancy or after delivery. Both of these biomarkers share a common feature of having a short half-life (*4*), and therefore they measure exposure only during a couple of days before sampling. Hair nicotine is a new promising biomarker; the method is noninvasive, and a sample of 0–2 cm from the proximal hair gives a good estimate of the exposure during the past 2 months (*34,35*). Taking into account the time frame, a hair sample at birth would describe exposure during the last trimester, which is considered the most important period for fetal growth. In a recent case–control study by Nafstad and colleagues (*36*), the risk of small-for-gestational-age births was related to the hair nicotine concentration of newborns and of their nonsmoking mothers after the delivery. We further studied the relation between exposure to ETS measured as maternal hair nicotine concentration after delivery and the risk of being small for gestational age. With the present study design, we were also able to study the effects on birth weight and the risks of low birth weight and preterm delivery. We also assessed the relations between hair nicotine concentration and reported exposure to ETS.

Methods

Study population. The Finnish Prenatal Environment and Health Study focused on a source population that included all the 2,751 children born from 1 May 1996 to 30 April 1997 in two geographically defined hospital districts in southeast Finland (Kymi and Porvoo Hospital Districts). All mothers were asked after delivery to complete a self-administered questionnaire (response rate 94.2%). The respondents, 2,591 mothers, had 2,568 singletons and 23 twin pairs. A total of 1,621 (62.3%) women were nonsmokers. They were used as a framework for selecting 472 nonsmoking women for the present study: 189 women reported exposure to ETS either at home or outside the home, and 283 women reported no exposure to environmental tobacco smoke. The latter group was selected randomly from the unexposed with a one-to-one balance according to the spouse's current smoking, so that in 141 women the spouse was a current smoker, and in 142 women the spouse was a never smoker or quit smoking more than 12 months ago. Out of the 472 hair samples, we excluded 43 samples with weight less than 2 mg, 38 samples with a concentration below detection limit (0.05 µg/g), and 2 samples from a twin pregnancy. The present study focused on 389 singleton newborns of women whose hair sample provided a hair nicotine measurement above detection limit. The characteristics of the study population are presented in Table 1.

Data collection. The Environment and Pregnancy questionnaire administered at the birth clinic inquired about maternal health in general and during pregnancy; parents' education, profession, and behavioral factors such as smoking and exercise; and details of the home and other environments. We requested records for the women in this study from the maternity health clinics in the two areas and received 97% of the records. Additional information on the child's birth weight, gestational age, and maternal smoking habits during

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pregnancy were obtained from the Finnish Medical Birth Registry established in 1987 and run by the Ministry of Social Affairs and Health. The study protocol was approved by the Ethical Committees of the Department of Public Health, University of Helsinki, three participating hospitals, and the Ministry of Social Affairs and Health.

Health outcomes. The primary health outcomes were fetal growth and preterm delivery. We used three different measures of fetal growth: birth weight in grams, low birth weight (< 3,000 g), and small for gestational age (SGA). A higher than traditional cut point for low birth weight, 3000 g, was chosen to increase the number of cases from 7 to 46. Small for gestational age was defined as birth weight in the lowest 10th percentile according to the week of gestation, which was calculated from the present source population of nonsmoking women. Preterm delivery was defined as length of gestation less than 37 weeks. We retrieved information on gestational age from maternity health clinic records. Gestational age was practically always verified by ultrasound examination during the 18th week of gestation.

Exposure assessment. The determinant of interest was prenatal exposure to ETS. Exposure assessment was based on the nicotine concentration of hair taken after delivery (*34*). We also used maternity clinic medical records, the questionnaire at the birth clinic, and birth registry data as additional sources of information.

Hair nicotine concentration. The proximal 0–2 cm segment of maternal hair was analyzed for nicotine using gas chromatography/mass spectrometry (*34*). The detection limit was 0.05 µg nicotine/g hair when the sample was at least 15 mg. Nicotine concentration in hair samples < 1.5 mg was not reported due to uncertainty in the estimated concentrations.

Maternity clinic medical records. According to nationwide instructions, during the first prenatal visit health care personnel are advised to record information about the smoking habits of the mother and her spouse on a standard form.

Questionnaire information. We requested information about smoking habits of the parents and other family members in general and during pregnancy. We also asked about the number of cigarettes smoked daily indoors by the spouse and other family members and the amount of time exposed to tobacco smoke outside home. The quantitative information was missing for a large proportion of subjects and was not used in the main analyses.

Birth registry information. The birth registry information provided categorical information on the mother's smoking during pregnancy (no, yes, smoked after the first trimester, quit during the first trimester, no information).

Covariates. We used the following potential confounders as covariates in the analyses: sex, birth order, maternal age, body mass index before pregnancy, marital status, a combined index of maternal and paternal education as an indicator of socioeconomic status (low: neither parent with vocational education; medium: either one or both parents with vocational school as highest education; high: either one or both parents with college or university education as a reference category), alcohol consumption during pregnancy, and employment during pregnancy.

Statistical methods. We estimated the prevalences (percent) of the reproductive outcomes with 95% confidence intervals (CIs) based on the binomial distribution and the mean of birth weight with confidence intervals based on the *t* distribution. First, we compared the mean birth weight and the risks of low birth weight, small for gestational age, and preterm delivery in the different categories of exposure defined by the hair nicotine concentration and questionnaire information. The relations between birth weight and the determinants of interest were estimated in linear regression analysis controlling for potential confounding. For the three dichotomous outcomes, odds ratio (OR) was the measure of effect. We used logistic regression analysis to estimate adjusted ORs. We adjusted for all the potential determinants of the outcomes listed above.

Results

Characteristics of the study population. The characteristics of the study population were compared according to the three exposure categories, high, medium and low (reference), that were defined by the hair nicotine concentration (Table 1). The three groups were similar in most of the factors that were possible determinants of the pregnancy outcomes. Alcohol consumption during pregnancy was slightly more common among the

Table 1. Characteristics of the study population, 389 mothers and newborns, the Finnish Prenatal Environment and Health Study, 1996–1997.

	Exposure category (µg/g)							
	Low < 0.75		Medium 0.75 to < 4.00		High ≥ 4.00		Total	
Characteristic	No.	%	No.	%	No.	%	No.	%
Total	151		186		52		389	
Sex								
Male	86	57.0	96	51.6	30	57.7	212	54.5
Female	65	43.0	90	48.4	22	42.3	177	45.5
Maternal age (years)								
< 25	28	18.5	47	25.3	9	17.3	84	21.6
26–30	56	37.1	72	38.7	23	44.2	151	38.8
31–35	50	33.1	48	25.8	14	26.9	112	28.8
≥ 36	17	11.3	19	10.2	6	11.6	42	10.8
Maternal body mass index								
<20	21	14.1	22	12.0	7	13.5	50	13.0
20 to < 25	90	60.4	97	52.7	32	61.5	219	56.9
25 to < 30	28	18.8	49	26.6	5	9.6	82	21.3
≥ 30	10	6.7	16	8.7	8	15.4	34	8.8
Parity								
Nulliparous	54	35.8	78	41.9	19	36.5	151	38.8
1	56	37.1	65	35.0	19	36.5	140	36.0
≥ 2	41	27.1	43	23.1	14	27.0	98	25.2
Marital status								
Married or cohabiting	146	96.7	181	97.3	50	98.0	377	97.2
Single	5	3.3	5	2.7	1	2.0	11	2.8
Combined parental education[a]								
Low	22	15.0	36	19.8	12	24.0	70	18.5
Medium	75	51.0	105	57.7	26	52.0	206	54.3
High	50	34.0	41	22.5	12	24.0	103	27.2
Alcohol consumption during pregnancy								
No	108	72.0	127	68.7	33	64.7	268	69.4
Yes	42	28.0	58	31.3	18	35.3	118	30.6
Worked during pregnancy								
No	55	36.9	63	34.2	17	33.3	234	64.8
Yes	94	63.1	121	65.8	34	66.7	155	35.2
Maternity leave (weeks)								
< 34	97	64.2	107	57.5	30	57.7	234	60.2
34 to <36	45	29.8	64	34.4	19	36.5	138	32.9
≥ 36	9	6.0	15	8.1	3	5.8	27	6.9

Number of subjects with missing information: maternal body mass index, 4; marital status, 1; parental education, 10; alcohol consumption, 3; and work during pregnancy, 5. Low exposure is the reference category.
[a]Low: neither parent with vocational education; medium: either one or both parents with vocational school as highest education; high: either one or both parents with college or university education.

high exposure group (35.3%) than in the reference group (28.0%).

Exposure to environmental tobacco smoke. The mean and median hair nicotine concentrations were related to the reported exposure to environmental tobacco smoke both at home and at work, as shown in Table 2. In women who reported no exposure either at home or work, the hair nicotine concentration was substantially higher if the spouse was a current smoker (medians: 1.32 vs. 0.61 μg/g). We also asked about the number of cigarettes per day smoked indoors during each trimester. This seemed to be a difficult question, because only 29% of women reporting exposure estimated quantity. Among those reporting quantity, the mean concentration (± SD) was higher the higher the number of cigarettes reported (1–9 cigarettes/day, 2.68 ± 1.99 μg/g; 10–19 cigarettes/day, 3.14 ± 2.40 μg/g; ≥ 20 cigarettes/day, 5.17 ± 7.24 μg/g).

Exposure to environmental tobacco smoke and pregnancy outcomes. The mean birth weight (± SD) in the study population was 3,555 ± 512 g, which corresponds well with the average birth weight of Finnish children (3,550 ± 582 g) (*37*). Only seven of the newborns (1.8%) were low birth weight children, according to the traditional definition of below 2,500 g (Table 3). We decided to apply a higher cut point, 3,000 g, which maintains the original idea of indicating a possible fetal growth disturbance. The cut point of 2,500 g was defined during a time when the average birth weight was substantially lower due to maternal nutrition and other factors. There were 46 children (11.8%) who were considered low birth weight children by this criterion. A total of 35 newborns were considered small for gestational age (9.1%), and there were 16 preterm deliveries (4.1%).

Table 3 shows that the mean birth weight was lower and the prevalences of adverse pregnancy outcomes were in general higher the higher the exposure, defined either by the hair nicotine concentration or questionnaire information on exposure at home and work.

In linear regression analysis adjusting for confounding, the mean birth weight was slightly but not significantly (17g, 95% CI, −178–145) lower in the high exposure category than in the reference category. We also fitted continuous nicotine concentration in the model, but there was no clear association (−0.9 g birth weight per microgram per gram nicotine; 95% CI, −20–18). Birth weight was not significantly related to either reported exposure at home (yes vs. no exposure: −99 g, 95% CI, −273–75) or work (yes vs. no exposure: −101 g, 95% CI, −258–56).

The risk of low birth weight was related to maternal hair nicotine with an exposure–response pattern, although the lower 95% confidence limits were < 1.00 (Table 4). The adjusted OR contrasting the medium exposure to the reference category was 1.28 (95% CI, 0.59–2.60), the high exposure 1.55 (95% CI, 0.55–4.43), and 1.06 (95% CI, 0.96–1.17) for a unit increase in hair nicotine. A corresponding pattern was found when using questionnaire information as a measure of exposure. The risk was related to work exposure and combined home and work exposure, which corresponded well with the hair nicotine concentration distribution in the questionnaire information-based exposure categories.

The relations between exposure and small for gestational age were in general weaker, although indicating an exposure–response pattern.

The risk of preterm delivery was related to exposure assessed both by hair nicotine concentration and questionnaire information. We estimated an adjusted OR of 1.22 (95% CI, 1.07–1.39) for a unit increase in hair nicotine concentration. The risk of preterm delivery was increased in the presence of work exposure alone (2.35; 95% CI, 0.50–11.1) and especially with both work and home exposure (8.89; 95% CI, 1.05–75.3), but not with home exposure only (0.65; 95% CI, 0.06–6.81).

Table 2. Maternal hair nicotine concentration after delivery by reported exposure to environmental tobacco smoke during pregnancy, the Finnish Prenatal Environment and Health Study, 1996–1997.

			Hair nicotine concentration (μg/g)			
	No.	%	Mean ± SD	25%	Median	75%
Total	389	100.0	1.96 ± 2.64	0.46	1.07	2.56
Home exposure[a]						
No	319	82.0	1.67 ± 2.01	0.45	0.86	2.22
Yes	70	18.0	3.30 ± 4.27	1.27	2.03	4.22
Work exposure[a]						
No	299	78.1	1.79 ± 2.56	0.45	0.92	2.26
Yes	84	21.9	2.57 ± 2.84	0.61	1.85	3.31
Combined reported exposure						
No, spouse nonsmoker	128	32.9	0.87 ± 1.02	0.25	0.61	1.00
No, spouse smoker	126	32.4	2.27 ± 2.46	0.63	1.32	3.14
Home yes, work no	51	13.1	2.93 ± 4.23	0.90	1.89	3.83
Home no, work yes	65	16.7	2.07 ± 2.01	0.57	1.51	2.71
Home yes, work yes	19	4.9	4.29 ± 4.34	1.58	2.89	5.10

[a]Any exposure during pregnancy.

Discussion

The present results are consistent with adverse effects of exposure to ETS on fetal growth. The results also suggest an increase in the risk of preterm delivery. The strength of the present study lies in the use of maternal hair nicotine concentration as a measure of exposure during the third trimester and use of objectively measured health outcomes.

Validity of results. The use of hair nicotine concentration provided an objective exposure assessment with comparable information for newborns with and without normal pregnancy. This approach minimized

Table 3. Mean birth weight and the prevalence of low birth weight (LBW), small for gestational age (SGA), and preterm delivery (< 37 weeks) according to maternal hair nicotine concentration (μg/g) and reported exposure to ETS during pregnancy, the Finnish Prenatal Environment and Health Study, 1996–1997.

	Total		Birth weight (g)	LBW (< 2,500 g)		LBW (< 3,000 g)		SGA[a]		Preterm[a]	
Exposure category	No.	%	(mean ± SD)	No.	%	No.	%	No.	%	No.	%
Total	389	100.0	3,555 ± 512	7	1.8	46	11.8	35	9.1	16	4.1
Hair nicotine concentration (μg/g)											
< 0.75	151	38.8	3,559 ± 472	1	0.7	15	9.9	12	8.0	4	2.7
0.75 to < 4.00	186	47.8	3,554 ± 534	5	2.7	23	12.4	18	9.7	7	3.8
≥ 4.00	52	13.4	3,547 ± 547	1	1.9	8	15.4	5	9.8	5	9.6
Reported exposure											
No, spouse nonsmoker	128	32.9	3,590 ± 464	1	0.8	12	9.4	10	7.8	5	3.9
No, spouse smoker	126	32.4	3,587 ± 502	2	1.6	16	12.7	11	0.7	3	2.4
Home yes, work no	51	13.1	3,488 ± 458	1	2.0	5	9.8	5	9.8	2	3.9
Home no, work yes	65	16.7	3,459 ± 538	2	3.1	9	13.9	6	9.4	4	6.2
Home yes, work yes	19	4.9	3,616 ± 833	1	5.3	4	21.1	3	17.7	2	10.5

[a]Three newborns with gestational age < 35 weeks were excluded.

the problems of random and systematic error in the exposure assessment, which could be introduced in a retrospective questionnaire. However, the nicotine levels corresponded well to the reported exposure information given that several uncontrolled intervening factors, such as air change and volume in environmental spaces, could influence the relation between source strength and exposure. We used *a priori* criteria for defining exposure categories on the basis of a previous Norwegian case–control study (*36*). All of the outcomes were based on objective measurements that were made independently from the exposure assessment.

The high participation rate in the study, 94%, minimized the influence of any hypothesized selection bias. The hair nicotine concentration was not available to some mothers due to a too-small hair sample, but there is no reason to believe that the availability would be related to either exposure or studied outcomes.

Use of medical records and questionnaire information allowed us to take into account an extensive number of potential confounders. The exposed and unexposed were relatively similar with respect to measured determinants of the outcomes. The effect of work exposure on preterm delivery was stronger compared with the effect of home exposure, although the concentrations of hair nicotine due to reported home and work exposure were similar. This could be explained by confounding by unknown working conditions. Another explanation is that pregnant women can influence the home exposure more than work exposure, and thus they could better avoid exposures perceived disturbing at home than at work. The proportion of women employed during pregnancy was similar among exposed and unexposed subjects, and we adjusted for employment in all the models, including those assessing the relations between hair nicotine concentration and pregnancy outcomes.

The total eligible study population consisted of 1,621 nonsmoking women, but the cost of hair nicotine analysis was the limiting economic factor. To optimize the power and the cost of the study, we selected the study subjects on the basis of questionnaire information on exposure to ETS and spouse's current smoking.

Synthesis with previous knowledge. There are several suggested mechanisms for the effects of tobacco smoke on fetal growth (*38*). Most of these studies have been carried out on active smokers. Because sidestream smoke contains the same compounds as mainstream smoke, it is likely that the mechanisms are similar both in active and passive smoking. Inhaled carbon monoxide and nicotine increase fetal carboxyhemoglobin and reduce placental blood flow, resulting in low fetal tissue oxygenation. Structural changes in the placenta of smoking mothers have been observed as additional evidence of a plausible biologic mechanism (*39*). Smoking during pregnancy increases metabolites of tobacco in the fetus that may have toxic effects (*40*). Maternal smoking has also been attributed to fetal zinc deficiency (*41*). Zinc is considered an essential trace element for many aspects of growth and development (*42*).

The present results of a small effect of prenatal exposure to ETS on fetal growth are consistent with the previous studies. Windham and colleagues (*32*) carried out a meta-analysis of their own and 22 previous studies from 1966–1995 and reported a pooled effect estimate of 25 g (95% CI, 16–41). Combining all eight studies that examined low birth weight gave a pooled OR of 1.00 (95% CI, 0.90–1.10). In the present study, the adjusted OR for low birth weight was 1.55 when contrasting high exposure to the reference, but the 95% CI was wide (0.55–4.43). The corresponding estimate from 11 studies of small-for-gestational-age births or term low birth weight was 1.19 (1.08–1.32), which is similar to the results of the present study.

Only a few previous studies have used a biomarker in the assessment of exposure (*14, 28,30,36*). In a study of 1,231 women, Haddow et al. (*14*) found an effect of 104 g (95% CI, 35–173) in exposed nonsmoking women defined by serum cotinine from 1 to 10 ng/mL compared with unexposed (< 0.5 ng/mL). Their effect estimate was not adjusted for gestational age, and therefore it incorporates the effects of reducing gestation length, as well as reducing intrauterine growth rate. Eskenazi et al. (*28*) reported a small reduction of 45 g (95% CI, −36–126) related to exposure assessed by serum cotinine (2–10 ng/mL vs. <2 ng/mL) around 27 weeks of gestation. There was no effect on the risk of preterm delivery, and the effect on the risk of low birth weight was weak (1.35; 95% CI, 0.60–3.30). Peacock et al. (*30*) reported a 0.2% (95% CI, −2.4–2.8) reduction in birth weight in newborns of women whose serum cotinine during pregnancy was in the upper quintile compared with newborns of women in the lowest quintile. In the case–control study by Nafstad et al. (*36*), the risk of small-for-gestational-age births

Table 4. Crude and adjusted odds ratios for low birth weight (LBW), small for gestational age (SGA), and preterm delivery according to maternal hair nicotine concentration (µg/g) and reported exposure to environmental tobacco smoke during pregnancy, the Finnish Prenatal Environment and Health Study, 1996–1997.

	LBW (< 3000 g)		SGA[a]		Preterm (< 37 weeks)[a]	
Exposure category	Crude OR	Adjusted OR[b]	Crude OR	Adjusted OR[b]	Crude OR	Adjusted OR[b]
Nicotine concentration (µg/g)						
< 0.75 (reference category)	1.00	1.00	1.00	1.00	1.00	1.00
0.75 to < 4.00	1.28	1.28	1.24	1.05	1.47	1.30
	(0.64–2.55)	(0.59–2.60)	(0.58–2.66)	(0.44–2.49)	(0.41–5.01)	(0.30–5.58)
≥ 4.00	1.65	1.55	1.25	1.18	3.91	6.12
	(0.66–4.15)	(0.55–4.43)	(0.42–3.74)	(0.34–4.19)	(1.01–15.2)	(1.31–28.7)
per µg/g	1.06	1.06	1.04	1.04	1.12	1.22
	(0.97–1.17)	(0.96–1.17)	(0.92–1.17)	(0.92–1.19)	(1.01–1.25)	(1.07–1.39)
Reported exposure						
No exposure, spouse nonsmoker (reference category)	1.00	1.00	1.00	1.00	1.00	1.00
No exposure, spouse smoker	1.52	1.92	1.11	1.41	0.59	1.00
	(0.68–3.42)	(0.79–4.70)	(0.45–2.72)	(0.52–3.82)	(0.14–2.52)	(0.20–5.07)
Home yes, work no	1.18	1.13	1.31	1.06	1.02	0.65
	(0.39–3.58)	(0.34–3.78)	(0.42–4.04)	(0.30–3.73)	(0.19–5.45)	(0.06–6.81)
Home no, work yes	1.67	1.43	1.19	1.02	1.58	2.35
	(0.65–4.25)	(0.50–4.12)	(0.41–3.43)	(0.31–3.31)	(0.41–6.07)	(0.50–11.1)
Home yes, work yes	2.76	2.08	2.46	1.47	2.82	8.89
	(0.78–9.79)	(0.44–9.73)	(0.61–10.0)	(0.23–9.32)	(0.51–15.7)	(1.05–75.3)

Values shown in parentheses are 95% CI.
[a]Three newborns with gestational age < 35 weeks were excluded. [b]Logistic regression analysis: adjusted for sex, birth order, maternal age, body mass index before pregnancy, marital status, index of socioeconomic status, alcohol consumption during pregnancy, and employment during pregnancy.

was related to maternal hair nicotine concentration both in nonsmoking and smoking mothers. The adjusted OR for the medium exposure category (0.75–4.00 µg/g) was 3.4 (95% CI, 1.3–8.6) and 2.1 (95% CI, 0.4–10.1) for the high exposure category (> 4.00 µg/g) compared with the reference category (<0.75 µg/g).

The possible effect of prenatal exposure to ETS on the length of gestation and the risk of preterm delivery has received less attention, and the results of the previous studies are inconsistent. Martin and Bracken (*10*) conducted a prospective cohort study of 3,891 women in New Haven, Connecticut, and found no effect of passive smoking during pregnancy on gestational age. In a cohort study of 4,687 Swedish pregnant women by Ahlborg and Bodin (*19*), the adjusted risk ratio for preterm delivery was 0.49 (95% CI, 0.23–1.06) in women exposed in the home only and 1.27 (95% CI, 0.70–2.31) in the workplace. In a study of 4,644 Canadian women by Fortier and colleagues (*25*), the adjusted OR in women exposed in the home only was 0.93 (95% CI, 0.64–1.31) and 0.92 (95% CI, 0.58–1.51) in those exposed in the workplace only. None of the previous studies using biomarkers reported the relation between exposure and risk of preterm delivery. The present study shows for the first time an exposure-related increase in the risk of preterm delivery related to exposure to ETS.

Concluding remarks. The present results based on objective assessment of exposure during a period most relevant for fetal growth provide further evidence of the adverse effects of tobacco smoke exposure. The results suggest that prenatal exposure may also increase the risk of preterm delivery.

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