



# Archives of Environmental Health: An International Journal

ISSN: 0003-9896 (Print) (Online) Journal homepage: <https://www.tandfonline.com/loi/vzeh20>

## Parental Exposure to Organic Solvents and Reduced Birth Weight

Eunhee Ha , Sung-Il Cho , Dafang Chen , Changzhong Chen , Louise Ryan , Thomas J. Smith , Xiping Xu & David C. Christiani

To cite this article: Eunhee Ha , Sung-Il Cho , Dafang Chen , Changzhong Chen , Louise Ryan , Thomas J. Smith , Xiping Xu & David C. Christiani (2002) Parental Exposure to Organic Solvents and Reduced Birth Weight, Archives of Environmental Health: An International Journal, 57:3, 207-214, DOI: [10.1080/00039890209602938](https://doi.org/10.1080/00039890209602938)

To link to this article: <https://doi.org/10.1080/00039890209602938>



Published online: 05 Apr 2010.



Submit your article to this journal [↗](#)



Article views: 46



Citing articles: 16 [View citing articles](#) [↗](#)

# Parental Exposure to Organic Solvents and Reduced Birth Weight

**EUNHEE HA**

Department of Preventive Medicine  
Ewha Woman's Medical University  
Seoul, South Korea

and

Department of Environmental Health  
Harvard School of Public Health  
Boston, Massachusetts

**SUNG-IL CHO**

Department of Environmental Health  
Harvard School of Public Health  
Boston, Massachusetts

**DAFANG CHEN**

Center for Ecogenetics  
Beijing Medical University  
Beijing, China

**CHANGZHONG CHEN**

Department of Environmental Health  
Harvard School of Public Health  
Boston, Massachusetts

**LOUISE RYAN**

Department of Biostatistics  
Harvard School of Public Health  
and

Dana-Farber Cancer Institute  
Harvard Medical School  
Boston, Massachusetts

**THOMAS J. SMITH**

Department of Environmental Health  
Harvard School of Public Health  
Boston, Massachusetts

**XIPING XU**

Department of Environmental Health  
Harvard School of Public Health  
Boston, Massachusetts

and

Channing Laboratory  
Brigham and Women's Hospital  
Harvard Medical School  
Boston, Massachusetts

**DAVID C. CHRISTIANI**

Department of Environmental Health  
Harvard School of Public Health  
Boston, Massachusetts

and

Massachusetts General Hospital  
Harvard Medical School  
Boston, Massachusetts

**ABSTRACT.** The authors investigated the association of birth weight with maternal and paternal exposure to organic solvents in 1,222 couples employed in a large petrochemical corporation in Beijing, China, during the period between 1994 and 1998. A trained interviewer assessed parental exposures to organic solvents. The authors used generalized additive models to examine the association between birth weight and parental exposure to organic solvents. After the authors adjusted for potential confounders, maternal exposure to solvents was significantly associated with reduced birth weight ( $-81.7$  gm, 95% confidence interval =  $-106.3, -3.1$ ), and reduced birth weights of female babies and of younger mothers' babies were statistically significant. Maternal exposure to organic solvents was associated with reduced birth weight in this population, but paternal exposure to organic solvents was not similarly associated.

<Key words: organic solvents, parental exposure, reduced birth weight>

ORGANIC SOLVENTS are ubiquitous in industrialized society, both at work and at home.<sup>1</sup> Many women of childbearing age are exposed occupationally to organic solvents.<sup>2</sup> Fuels such as petroleum<sup>3</sup> are mixtures

of various hydrocarbons,<sup>4</sup> and may contain benzene, toluene, xylene, and styrene, and other components. Many organic solvents are teratogenic,<sup>5</sup> embryotoxic,<sup>6</sup> and genotoxic<sup>7,8</sup> in laboratory animals.

The effects of maternal exposure to organic solvents on spontaneous abortion have been observed frequently,<sup>9-11</sup> although some studies have not supported these findings.<sup>12</sup> In addition, several epidemiologic studies have provided evidence that exposure to organic solvents during pregnancy increased congenital anomaly,<sup>13,14</sup> increased stillbirth,<sup>15</sup> reduced fertility,<sup>16,17</sup> and increased small-for-gestational-age births.<sup>18</sup>

The relationship between a mother's organic solvent exposure and reduced birth weight has been studied previously in hairdressers,<sup>19</sup> laboratory workers,<sup>11</sup> dry cleaning employees,<sup>20</sup> and laundry workers.<sup>21</sup> The odds ratios in these studies were increased, in the range of 1.5 to 1.7, but were not statistically significant at the 5% level. A recent Canadian study showed statistically significant reduced birth weights among individuals who experienced a longer period of organic solvent exposure.<sup>13</sup> The study of national natality and fetal mortality showed a greater proportion of employed mothers who gave birth to low-birth-weight infants,<sup>22</sup> and a substantial excess of low birth weight in food and beverage and service employees (observed/expected = 1.42). In addition, water pollution was associated significantly with incidence of low birth weight.<sup>23</sup> The weight of mouse fetuses was reduced significantly when exposure to the vapor of organic solvents from a synthetic adhesive<sup>24</sup> occurred. In some studies, however, these findings have not been supported,<sup>25</sup> or higher birth weights were evident among solvent-exposed babies than unexposed infants.<sup>12</sup>

The results of several studies have suggested an association between paternal solvent exposure and certain adverse reproductive outcomes, such as reduced fertility,<sup>17</sup> spontaneous abortion,<sup>14,26</sup> and congenital anomalies.<sup>27,28</sup> In one study, the authors found that paternal exposure to benzene was associated with a 1.5-fold increase in risk of having an infant who was small for his or her gestational age.<sup>15</sup> In a study of paternal occupational exposure, spray painters with frequent exposure to solvents fathered babies with lower birth weights, compared with babies fathered by electronic workers.<sup>29</sup> The risk of low birth weight also increased among infants born to male workers exposed to solvents in autobody shops, compared with a control group.<sup>30</sup> In contrast to the suggestive associations observed sporadically, a more recent (i.e., 1997) study in which investigators used prospectively collected occupational histories and more detailed demographic and behavioral variables failed to find a significant effect of paternal occupational exposure on birth weight.<sup>31</sup>

Such inconsistent results raise the need for further study of the effects of parental solvent exposure on birth weight. In the current study, therefore, we investigated the association between birth weight and maternal and paternal exposures to organic solvents among couples, of which both members were employed in a large petrochemical corporation in Beijing, China.

## Method

**Study site.** This study was conducted at the Beijing Yanshan Petrochemical Corporation (BYPC), which is

located in a suburban area of Beijing, China. The BYPC, which has been operational since 1986, employs more than 47,000 individuals and comprises 17 major production plants and institutes for petroleum and chemical processing. The major occupational exposures are to aromatic solvents, including benzene, toluene, styrene, and xylene. The levels of these solvents are all maintained lower than 1 ppm as an 8-hr time-weighted average.<sup>32</sup> Approximately 80% of local residents are employed at the BYPC. In general, pregnant employees stop work at about 28 wk of gestation. The BYPC staff hospital is the only regional hospital that serves the local community and the employees of the BYPC. All of the BYPC workers are entitled to free medical care, including routine health examinations, family-planning counseling, prenatal care, delivery care, and neonatal care.

**Study population and procedure.** Eligible women were current employees at the BYPC who had had a live birth at the BYPC staff hospital between May 1996 and December 1998. The women had various job titles, including machine operator, quality-assurance laboratory technician, electrician, instrument personnel, assistant engineer, and maintenance worker. Among the 1,426 potential subjects, those who had multiple gestations ( $n = 28$ ) or births with major congenital defects ( $n = 12$ ) were excluded. We also restricted the study population to the women who had spouses employed at the BYPC.

After obtaining informed consent, trained interviewers administered a questionnaire to women and men separately to obtain information on demographic variables, active and passive smoking, alcohol consumption, physical activity, occupational exposures, and medical and reproductive histories. Maternal clinical data, including prepregnancy weight and height, the first day of the last menstrual period, and birth outcomes (including the infant's gender, gestational age, and birth weight) were recorded by a trained nurse. Given that few women smoke in China, those who had smoked during or before their pregnancies were excluded ( $n = 15$ ). Of the remaining 1,371 pregnancies, 149 (10.8%) pregnancy outcomes were not recorded completely; therefore, birth weights, adjusted for gestational age, could not be calculated. Finally, 1,222 mother-father-infant triads remained for data analysis. The study protocol was approved by the institutional review boards of the Harvard School of Public Health and Beijing Medical University.

**Occupational exposure data collection.** Exposure assessment was based on a questionnaire administered by a trained interviewer. A detailed checklist of 42 chemical and physical reproductive hazards present in the industry was developed on the basis of a toxicological literature review and information regarding petrochemical production processes. The interviewer asked both the mother and father, separately, to indicate on the checklist 3 major hazards that they contacted in their daily work. If any of the 4 aromatic solvents (i.e., benzene, toluene, xylene, or styrene) were reported, the participant was rated as "exposed to organic solvents."

**Statistical analysis.** Birth weight represents one outcome of pregnancy. Reduced birth weight can result from preterm delivery, intrauterine growth retardation, or both. This study specifically focused on adverse effects of parental organic solvent exposures on intrauterine growth; therefore, all regression models were adjusted for gestational age. To appropriately adjust for gestational age, we examined its functional relationship with birth weight using a generalized additive model (GAM).<sup>33</sup> The GAM provides a flexible method for the identification of nonlinear covariate effects in a variety of modeling situations, and it can be used in a data-analytic fashion for understanding the effects of covariates.<sup>33,34</sup> There was a significant departure from linearity; therefore, birth weight was adjusted for with locally weighted smoother (LOESS) function for all subsequent analyses in S-PLUS.<sup>35</sup>

We used GAMs to examine the associations of birth weight with maternal exposures to solvents and other covariates. All exposure variables were treated as binary or dummy variables. We examined the association between birth weight and maternal, paternal, and infant variables. Infant gender, maternal prepregnancy body mass index (BMI) and age, and paternal height and education were strong predictors for birth weight ( $p < .001$ ), so we entered these variables in the final model.

Gestational age suggested a nonlinear relationship; therefore, we adjusted it with LOESS function. For all

analyses, we used SAS Unix version 6.08 and S-PLUS (i.e., S-PLUS 2000). In S-PLUS, we started with the original model and then attempted to improve the model fit by several model selections. First, we estimated the effects of organic solvents on infant birth weight by 2 and then by 4 categories, as well as the interactions of parental exposure with a chi-square test,  $t$  test, and simple regression models. Second, we adjusted crude effects for parental age, education, BMI, height, and weight. Finally, in the analyses of low birth weight, the effects of organic solvents were also adjusted for gestational age.

## Results

The characteristics of the study population, such as parental age, BMI, weight, height, education, infant gender, alcohol consumption, and passive smoking, by parental organic solvent exposure status, are shown in Table 1. A total of 1,222 female workers and their husbands were surveyed for exposure to organic solvents. This sample was generally a low-risk group. The majority of women were at their optimal reproductive ages, and most women were nonsmokers who were at ideal weights for their respective heights. The mothers and fathers in the exposed and nonexposed groups were similar with respect to age distribution, parental weight and height, parity, and infant gender. However, most of the

**Table 1.—Characteristics of the Study Population**

Variable	Maternal group				Paternal group			
	No exposure (n = 1,111)		Exposure (n = 111)		No exposure (n = 1,096)		Exposure (n = 126)	
	$\bar{x}^*$	SD	$\bar{x}^*$	SD	$\bar{x}^*$	SD	$\bar{x}^*$	SD
Age (yr)	26.8	2.4	26.9	2.3	28.4	3.1	28.9	2.8
BMI (kg/m <sup>2</sup> )†	22.4	3.5	22.8	4.1	23.5	3.0	23.5	2.8
Weight (kg)	58.3	9.3	59.1	10.9	70.5	10.0	70.0	8.9
Height (cm)	161.2	5.1	160.9	4.3	173.2	5.2	172.3	4.7
Infant birth weight (gm)	3,424.0	436.0	3,347.0	396.0	3,418.0	458.0	3,408.0	389.0
Gestational age (wk)	39.9	1.3	39.9	1.5	39.9	1.3	39.9	1.4
Variable	Number‡	Percentage	Number‡	Percentage	Number‡	Percentage	Number‡	Percentage
Infant sex (female)	533	48.1	56	50.9	530	48.5	59	46.7
Parity (first baby)	1,060	90.9	51	89.5	1,045	95.3	120	96.0
Education								
Middle school or lower	173	15.6	12	10.8	223	20.3	24	19.0
High school	791	71.2	92	82.9	617	56.4	80	63.4
College or graduate level	147	13.2	7	6.3	257	23.3	21	16.6
Alcohol consumption (yes)	21	1.9	2	1.9	505	46.0	59	47.6
Active smoking (yes)					638	58.2	75	60.0
Passive smoking (yes)	673	60.6	59	53.2	662	60.5	70	56.0

Note:  $\bar{x}$  = mean, and SD = standard deviation.

\*Tested by  $t$  test, but there were no statistically significant differences between exposure and no-exposure groups, except with respect to paternal education.

†BMI = body mass index.

‡Tested by  $\chi^2$  test, but there were no statistically significant differences between exposure and no-exposure groups, except with respect to paternal education.

**Table 2.—Infant Birth Weight, by Characteristics of Study Population**

Variable	Maternal				Paternal			
	No exposure (n = 1,111)		Exposure (n = 111)		No exposure (n = 1,059)		Exposure (n = 126)	
	$\bar{x}$	<i>SD</i>	$\bar{x}$	<i>SD</i>	$\bar{x}$	<i>SD</i>	$\bar{x}$	<i>SD</i>
Age (yr)								
< 25	3,369	456	3,247	300	3,358	461	3,400	407
25–29	3,434	424	3,371	410	3,421	432	3,416	410
≥ 30	3,475	483	3,325	452	3,422	448	3,387	340
BMI (kg/m <sup>2</sup> )*								
< 25	3,353	387	3,319	463	3,403	429	3,458	366
25–29	3,438	447	3,356	423	3,460	462	3,285	427
≥ 30	3,486	476	3,406	375	3,426	434	3,175	459
Infant gender								
Male	3,470	435	3,429	397	3,465	438	3,473	359
Female	3,373	431	3,268	386	3,367	449	3,325	397
Parity								
First baby	3,422	435	3,357	393	3,417	437	3,403	388
Second and over	3,472	452	3,166	446	3,433	462	3,510	449
Education								
Middle school or lower	3,371	418	3,204	337	3,357	452	3,522	343
High school	3,429	449	3,358	406	3,426	443	3,350	372
College or above	3,459	379	3,442	330	3,452	408	3,495	468
Alcohol consumption								
Yes	3,288	340	3,276	330	3,418	471	3,330	384
No	3,426	437	3,356	385	3,418	407	3,476	386
Passive smoking								
Yes	3,447	422	3,371	339	3,439	399	3,383	382
No	3,409	445	3,325	442	3,439	417	3,405	451

Notes:  $\bar{x}$  = mean, and *SD* = standard deviation. There were some differences in infant birth weight between exposure and no-exposure groups, but they were not statistically significant.

\*BMI = body mass index.

mothers in the exposed group did not have a college education, but most fathers in the exposed group were college educated. The overall mean birth weight for the sample was 3,427 gm (standard deviation [*SD*] = 433 gm). Gestational age had a near-normal distribution (mean = 39.9 wk [*SD* = 1.3 wk {range = 33–44 wk}]).

Infant birth weights, by parental organic solvent exposure, and with adjustment for gestational age, are shown in Table 2. The mean birth weight for mothers in the organic-solvents-exposed group was 77.1 gm lower ( $p = .054$ ) than for those in the nonexposed group. The weight difference for fathers between these groups was 10.3 gm ( $p = .781$ ), which reflected the same trend observed for the mothers.

We, therefore, examined the relationship between parental organic solvent exposures and low birth weight by constructing several exposure models. Table 3 reveals marginally significant risks of low birth weight resulting from maternal organic solvent exposure in the basic GAM, in which gestational age—but not paternal organic solvent exposure—was adjusted for.

The aforementioned associations were evaluated further by multivariate analysis. The GAM included parental organic solvent exposure, infant gender, parity, mother's prepregnancy BMI, age, alcohol consumption, father's height, and father's education (Table 4). Although the organic solvent exposure level was low in

our population, it was associated significantly with reduced birth weight (–81.7 gm; 95% confidence interval [CI] = –106.3, –3.1). The association between reduced birth weight of female babies and of younger mothers' babies and exposure was statistically significant, but higher maternal BMI, paternal height, and paternal education were protective against low birth weight. Maternal passive smoking, alcohol consumption, and "first" baby were not statistically significant predictors of reduced birth weight. We also explored the association between parental organic solvent exposure and prematurity, but there were no differences between exposed and nonexposed individuals.

## Discussion

We found that maternal exposure to organic solvents was associated with reduced birth weight in our population, but no such association was found for paternal exposure to solvents.

This is one of the few studies in which researchers examined self-reported organic solvent exposure relative to birth weight. The study was based on a large number of female workers from a modern petrochemical plant, where epidemiologic and clinical data were collected with a validated questionnaire. Consistent methods were used by trained research staff, and occupational

**Table 3.—Adjusted Association of Birth Weight with Parental Exposure to Organic Solvents, by 4 Different Models**

Models of organic solvent exposure*†	n	Estimated change in birth weight	95% CI	p
<b>Model 1</b>				
No maternal exposure	1,111	Referent		
Maternal exposure	111	-79.0	-156.0, -1.9	.0447
<b>Model 2</b>				
No paternal exposure	1,059	Referent		
Paternal exposure	126	-3.3	-76.3, 70.1	.930
<b>Model 3</b>				
No exposure	1,019	Referent		
Maternal exposure only	78	-36.6	-68.8, -4.2	.027
Paternal exposure only	92	-9.9	-52.1, 42.2	.645
Maternal and paternal exposures	33	14.2	-20.9, 49.3	.428
<b>Model 4</b>				
No exposure	1,111	Referent		
Maternal exposure	111	-81.7	-106.3, -3.1	.042
Paternal exposure	126	12.6	-62.0, 87.2	.740

Note: CI = confidence interval.

\*If any of the 4 aromatic solvents (i.e., benzene, toluene, xylene, or styrene) were reported, the participant was rated as "exposed to organic solvents."

†All estimates were derived from generalized additive models (GAMs), including infant gender, paternal education, parental height, maternal body mass index, age, passive smoking, and GAM smoothing of gestational age.

exposure was determined with objective exposure assessment.<sup>32</sup>

The results of this study support previous epidemiologic and animal studies in which organic solvents, as reproductive toxins,<sup>15,36-38</sup> were associated with low birth weight.<sup>14</sup> The relationship between occupational exposure and low birth weight has been studied for chemicals such as organic solvents,<sup>30</sup> lead,<sup>39,40</sup> and organic solvents in combination with lead.<sup>41</sup> The aforementioned studies have shown that the relationship between maternal exposure and low birth weight is positive. No effects, however, were found from paternal exposure to organic solvents.<sup>25</sup> In the evaluation of a relationship between spontaneous abortion and benzene exposure, paternal exposure did not increase risk.<sup>42</sup> Multivariate analysis that adjusted for confounders showed that autobody painters fathered babies who were 82 gm lighter on average than babies in a control group.

The results of studies of the relationship between occupational parental exposure to organic solvents and adverse pregnancy outcomes have often been conflicting. In a recent case-referent study in which self-administered questionnaires were used, hairdressers were more likely to give birth to small-for-gestational-age infants, and they had an increased risk of having low-birth-weight infants, but these findings were not statistically significant.<sup>19</sup> In a prospective controlled study,<sup>13</sup> investigators found an increased frequency of birth defects among the group exposed to solvents and, as a secondary result, birth weight was also significantly lower among the exposed group. There have been

**Table 4.—Association of Birth Weight with Organic Solvent Exposures, after Adjustment for Covariates**

Variable	Estimated	p	95% CI
Organic solvent exposure* (mother)	-81.7	.042	-106.3, -3.1
Organic solvent exposure* (father)	12.6	.740	-62.0, 87.2
Infant gender (female)	-124.3	.0001	-168.4, -80.2
Parity	-27.4	.616	-134.6, 79.8
Age (mother)	-12.8	.012	-22.8, -2.8
BMI† (mother)	11.5	.0001	5.3, 17.7
Height (father)	14.6	.0001	10.3, 18.9
Passive smoking	-37.1	.111	8.4, -82.6
Alcohol consumption	-30.4	.719	-196.4, 135.6
Education (father)	70.3	.022	6.3, 144.3

Note: CI = confidence interval.

\*All estimates were derived from generalized additive models (GAMs), including infant gender, paternal education, parental height, maternal body mass index, age, passive smoking, and GAM smoothing of gestational age.

†BMI = body mass index.

strong indications of a relationship between maternal organic solvent exposure and low birth weight. The results of our study are consistent with previous studies with respect to parental exposure to organic solvents, and the effect was most distinct for maternal exposure.

We used regression models to examine the association between birth weight and maternal exposure to solvents. We adjusted for potential confounders, after which maternal exposure to solvents was significantly associated with reduced birth weight (−81.7 gm; 95% CI = −106.3, −3.1); paternal exposure, however, did not show a significant association. When we included both maternal and paternal exposure in a generalized additive model, maternal organic solvent exposure retained its statistically significant relationship with birth weight. GAMs do not require the assumption of covariate-response relation,<sup>43</sup> and they are very useful for characterizing effects of nonlinear covariates.<sup>34,44</sup>

The father's college education was associated significantly with higher birth weight in our population, and it may reflect some confounders that were not measured directly. We have examined other occupational factors and information on lifestyle factors, and none of them explained the effect of father's education. Although we did not have information on other measures of socioeconomic status, which might have been associated with the father's education, we assumed that such socioeconomic factors were not sufficiently associated with maternal solvent exposure to explain the effects of solvent exposure on birth weight. Our results showed that only maternal exposure, not paternal exposure, was associated with birth weight. Our results suggest that the association of maternal exposure likely reflects true effects, rather than spurious results confounded by socioeconomic status. It is likely, therefore, that socioeconomic status would have been associated with both paternal and maternal exposure to a similar degree.

Comparison of self-reported data with other sources has indicated underreporting of solvent exposure.<sup>45,46</sup> This underreporting tends to dilute the effects, or, if it is related to the outcome, it introduces a bias that can overestimate or underestimate an effect.<sup>37</sup> Some supportive results from a recent study of the comparison of self-assessed solvent exposure and occupational hygienist-assessed exposure showed that there was fair agreement between workers' self-reports and measurement or professional assessment.<sup>47</sup>

When the results of this study are interpreted, several methodological limitations should be taken into account. The major occupational exposures in this study population were benzene, toluene, xylene, and styrene. We studied a low-risk population with low-level organic solvent exposure as the major occupational exposure. Thus, the generalizability of our findings to women in other populations—and to other occupational exposures—is limited. A dose-response relationship between organic solvent exposure and birth weight could not be examined given the lack of data on individual cumulative exposure.

The misclassification of exposure and pregnancy outcome is an important source of bias in studies of these variables. Random error in the classification of exposure status (i.e., nondifferential misclassification) may have diluted the effects of exposures and may explain the absence of association.<sup>26</sup> None of the factors sub-

stantially changed the effect of parental exposure by inclusion in or exclusion from the model, or by changing the exposure variables, which were either 2 categories or 4 categories.

In the biological mechanism involving maternal organic solvent exposure on birth weight, benzene produces several toxic metabolites that affect rapidly growing cells (e.g., bone marrow), cause oxidative damage in the cells, and suppress cell growth.<sup>5,48</sup> Exposure to benzene can cause embryotoxicity and reduced fetal weight;<sup>49</sup> and benzene and some of its metabolites (i.e., toluene and xylene) cross the placenta in pregnant mice.<sup>50,51</sup> Embryo-fetal toxic effects of toluene were apparent in female rats exposed to toluene before pregnancy and during its early stages.<sup>52</sup> Investigators evaluated the embryotoxicity of toluene, xylene, benzene, styrene (and its metabolite, styrene oxide) by using the *in vitro* culture of postimplantation rat embryos. The results of this study showed that toluene, xylene, benzene, and styrene all have a concentration-dependent embryotoxic effect on the developing rat embryo *in vitro*.<sup>53</sup>

The mechanisms that involve paternal organic solvent exposure and embryotoxicity are unknown. Investigators have speculated, however, that the etiologic pathway might involve male-mediated exposure of mothers or actual toxicity to paternal reproductive function that predisposes abnormal development of the fetus.<sup>54</sup> In this study, we saw no paternal effect. This absence may have been caused by low exposure and potential exposure misclassification. Given that we used the same method of exposure assessment for both parents, our results demonstrated the relative importance between maternal and paternal contribution, with maternal exposure showing a stronger association with fetal maldevelopment.

Our study findings have several implications. First, given that organic solvent exposure is prevalent in the general population, even a small amount of shift in the mean birth weight distribution curve toward the left among those exposed may translate into a significantly increased number of low-birth-weight infants. This would contribute to a significant etiologic fraction of low birth weight. Second, in our examination of simultaneous exposure, we found that maternal organic solvent exposures are more important than paternal ones.

\* \* \* \* \*

This study was supported in part by grants HD32505 from the National Institute of Child Health and Human Development; ES08337 and ES00002 from the National Institute of Environmental Health Science; OH03027 from the National Institute of Occupational Safety and Health; G73B1382 from the U.S. Environmental Protection Agency; and 20-FY98-0701 from the March of Dimes Birth Defects Foundation.

Submitted for publication August 21, 2000; revised; accepted for publication April 2, 2001.

Requests for reprints should be sent to Eunhee Ha, M.D., Ph.D., Department of Preventive Medicine, Ewha Woman's University College of Medicine, 911-1 Mok-6-Dong Yangchun-Gu, Seoul, South Korea.

E-mail: eunheeha@mm.ewha.ac.kr

\* \* \* \* \*

## References

- Ashley DLB, Bonin MA, Cardinali FL, et al. Blood concentrations of volatile organic compounds in a nonoccupationally exposed U.S. population and in groups with suspected exposure. *Clin Chem* 1994; 40(7):1401-04.
- Tikkanen J, Heinonen OP. Cardiovascular malformations and organic solvent exposure during pregnancy in Finland. *Am J Ind Med* 1988; 14(1):1-8.
- Carpenter CPG, Geary DL Jr, Ryers RC, et al. Petroleum hydrocarbon toxicity studies. XVI. Animal response to vapors of "naphthenic aromatic solvent." *Toxicol Appl Pharmacol* 1977; 41(2):261-70.
- McMartin KI, Chu M, Kopecky E, et al. Pregnancy outcome following maternal organic solvent exposure: a meta-analysis of epidemiologic studies. *Am J Ind Med* 1998; 34(3):288-92.
- Laskin JD, Rao NR, Punjabi CJ, et al. Distinct actions of benzene and its metabolites on nitric oxide production by bone marrow leukocytes. *J Leukoc Biol* 1995; 57(3):422-26.
- Ungvary G, Tatrai E. On the embryotoxic effects of benzene and its alkyl derivatives in mice, rats and rabbits. *Arch Toxicol Suppl* 1985; 8:425-30.
- Janik-Spiechowicz E, Wyszynska K. Genotoxicity evaluation of tetramethylbenzenes. *Mutat Res* 1999; 439(1):69-75.
- Karacic V, Skender L, Bosner-Cucancic B, et al. Possible genotoxicity in low level benzene exposure. *Am J Ind Med* 1995; 27(3):379-88.
- Agnesi RV, Valentini F, Mastrangelo G. Risk of spontaneous abortion and maternal exposure to organic solvents in the shoe industry. *Int Arch Occup Environ Health* 1997; 69(5):311-16.
- Doyle PR, Roman E, Beral V, et al. Spontaneous abortion in dry cleaning workers potentially exposed to perchloroethylene. *Occup Environ Med* 1997; 54(12):848-53.
- Taskinen H, Kyyronen P, Hemminki K, et al. Laboratory work and pregnancy outcome. *J Occup Med* 1994; 36(3):311-19.
- Ahlborg G Jr, Hogstedt C, Bodin L, et al. Pregnancy outcome among working women. *Scand J Work Environ Health* 1989; 15(3):227-33.
- Khattak SK, Moghtader G, McMartin K, et al. Pregnancy outcome following gestational exposure to organic solvents: a prospective controlled study. *JAMA* 1999; 281(12):1106-09.
- Taskinen H, Anttila A, Lindbohm ML, et al. Spontaneous abortions and congenital malformations among the wives of men occupationally exposed to organic solvents. *Scand J Work Environ Health* 1989; 15(5):345-52.
- Savitz DA, Whelan EA, Kleckner RC. Effects of parents' occupational exposures on risk of stillbirth, preterm delivery, and small-for-gestational-age infants. *Am J Epidemiol* 1989; 129(6):1201-18.
- Plenge-Bonig A, Karmaus W. Exposure to toluene in the printing industry is associated with subfecundity in women but not in men. *Occup Environ Med* 1999; 56(7):443-48.
- Sallmen M, Lindbohm ML, Kyyronen P, et al. Time to pregnancy among the wives of men exposed to organic solvents. *Occup Environ Med* 1998; 55(1):24-30.
- Seidler A, Raum E, Arabin B, et al. Maternal occupational exposure to chemical substances and the risk of infants small-for-gestational-age. *Am J Ind Med* 1999; 36(1):213-22.
- Kersemakers WM, Roeleveld N, Zielhuis GA. Reproductive disorders among hairdressers. *Epidemiology* 1997; 8(4):396-401.
- Olsen J, Hemminki K, Ahlborg G, et al. Low birthweight, congenital malformations, and spontaneous abortions among dry-cleaning workers in Scandinavia. *Scand J Work Environ Health* 1990; 16(3):163-68.
- Ahlborg G Jr. Pregnancy outcome among women working in laundries and dry-cleaning shops using tetrachloroethylene. *Am J Ind Med* 1990; 17(5):567-75.
- McDonald AD, McDonald JC, Armstrong B, et al. Prematurity and work in pregnancy. *Br J Ind Med* 1988; 45(1):56-62.
- Witkowski KM, Johnson NE. Organic-solvent water pollution and low birth weight in Michigan. *Soc Biol* 1992; 39(1-2):45-54.
- Tachi N, Shimotori S, Fujise H, et al. Fetotoxic effects of exposure to the vapor of organic solvents from a synthetic adhesive in mice. *Bull Environ Contam Toxicol* 1994; 53(3):471-78.
- Olsen J, Rachootin P. Organic solvents as possible risk factors of low birthweight [letter]. *J Occup Med* 1983; 25(12):854-55.
- Lindbohm ML, Hemminki K, Bonhomme MG, et al. Effects of paternal occupational exposure on spontaneous abortions. *Am J Public Health* 1991; 81(8):1029-33.
- Brender JDS, Suarez L. Paternal occupation and anencephaly. *Am J Epidemiol* 1990; 131(3):517-21.
- Olshan AF, Teschke K, Baird PA. Paternal occupation and congenital anomalies in offspring. *Am J Ind Med* 1991; 20(4):447-75.
- Hoglund GVI, Iselius EL, Knave BG. Children of male spray painters: weight and length at birth. *Br J Ind Med* 1992; 49(4):249-53.
- Daniell WEV, Vaughan TL. Paternal employment in solvent-related occupations and adverse pregnancy outcomes. *Br J Ind Med* 1988; 45(3):193-97.
- Shea KM, Farrow A, Little R. An investigation of the effect of paternal occupation group at conception on birth weight and gestational age. ALSPAC Study Team of Pregnancy and Childhood. *Am J Ind Med* 1977; 31(6):738-43.
- Chen D, Cho SI, Chen C, et al. Benzene exposure, occupational stress, and reduced birth weight. *Occup Environ Med* 2000; 57(10):661-67.
- Hastie T, Tibshirani R. *Generalized Additive Models*. Boca Raton, FL: Chapman and Hall/CRC Press, 1990.
- Hastie T, Tibshirani R. Generalized additive models for medical research (see comments section). *Stat Methods Med Res* 1995; 4(3):187-96.
- Venables WN, Ripley BD. *Modern Applied Statistics with S-PLUS*. New York: Springer-Verlag, 1999; 3rd ed.
- Xu X, Cho SI, Sammel M. Association of petrochemical exposure with spontaneous abortions. *Occup Environ Med* 1998; 55:31-36.
- Lindbohm ML. Effects of parental exposure to solvents on pregnancy outcome. *J Occup Environ Med* 1995; 37(8):908-14.
- Sallmen M, Lindbohm ML, Kyyronen P, et al. Reduced fertility among women exposed to organic solvents. *Am J Ind Med* 1995; 27(5):699-713.
- Min YI, Vorrea-Villasenor A, Stewart PA. Parental occupational lead exposure and low birth weight (see comments section). *Am J Ind Med* 1996; 30(5):569-78.
- Irgens A, Kruger K, Skorve AH, et al. Reproductive outcome in offspring of parents occupationally exposed to lead in Norway. *Am J Ind Med* 1998; 34(5):431-37.
- Kristensen P, Irgens LM, Daltveit AK, et al. Perinatal outcome among children of men exposed to lead and organic solvents in the printing industry. *Am J Epidemiol* 1993; 137(2):134-44.
- Strucker I, Mandereau L, Aubert-Berleur MP, et al. Occupational paternal exposure to benzene and risk of spontaneous abortion. *Occup Environ Med* 1994; 51(7):475-78.
- Hin LY, Lau TK, Rogers MS, et al. Dichotomization of continuous measurement using generalized additive modeling application in predicting intrapartum caesarean delivery. *Stat Med* 1999; 18:1101-10.
- Hastie T, Tibshirani R. Generalized additive models. Some applications. *J Am Stat Assoc* 1987; 82(398):371-86.
- Lindbohm ML, Taskinen H, Sallmen M, et al. Spontaneous abortions among women exposed to organic solvents. *Am J Ind Med* 1990; 17(4):449-63.
- Cordier SH, Ayme S, Goujard J. Maternal occupational exposure and congenital malformations. *Scand J Work Environ Health* 1992; 18(1):11-17.
- Hu YA, Smith TJ, Xu X, et al. Comparison of self-assessment of solvent exposure with measurement and professional assessment. *Am J Ind Med* 2000; 41(6):483-89.
- Rao NR, Snyder R. Oxidative modifications produced in HL-60 cells on exposure to benzene metabolites. *J Appl Toxicol* 1995; 15(5):403-09.
- Maronpot RR. Ovarian toxicity and carcinogenicity in eight recent National Toxicology Program studies. *Environ Health Perspect* 1987; 73:125-30.
- Ghantous H, Danielsson BR. Placental transfer and distribution of toluene, xylene and benzene, and their metabolites during gestation in mice. *Biol Res Pregnancy Perinatol* 1986; 7(3):98-105.
- Donald JMH, Hooper K, Hopenhayn-Rich C. Reproductive and

developmental toxicity of toluene: a review. *Environ Health Perspect* 1991; 94:237-44.

52. Ono A, Sekita K, Ogawa Y, et al. Reproductive and developmental toxicity studies of toluene. II. Effects of inhalation exposure on fertility in rats. *J Environ Pathol Toxicol Oncol* 1996; 15(1):9-20.
53. Brown-Woodman PD, Webster WS, Picker K, et al. In vitro as-

essment of individual and interactive effects of aromatic hydrocarbons on embryonic development of the rat. *Reprod Toxicol* 1994; 8(2):121-35.

54. Anttila AS, Sallmen M. Effects of parental occupational exposure to lead and other metals on spontaneous abortion. *J Occup Environ Med* 1995; 37(8):915-21.

# OUR ARCHIVES

now available online.

Powerful keyword search.  
Easy to use.  
Find articles quickly.

[www.heldref.org](http://www.heldref.org)

*Archives of Environmental Health* is published by Heldref Publications, a division of the nonprofit Helen Dwight Reid Educational Foundation

