

RESPIRATORY DISEASES

Prenatal ambient air exposure to polycyclic aromatic hydrocarbons and the occurrence of respiratory symptoms over the first year of life

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Abstract. The purpose of the study was to test the hypothesis that infants with higher levels of prenatal exposure to polycyclic aromatic hydrocarbons (PAHs) from fossil fuel combustion may be at greater risk of developing respiratory symptoms. The study was carried out in a cohort of 333 newborns in Krakow, Poland, followed over the first year of life, for whom data from prenatal personal air monitoring of mothers in the second trimester of pregnancy were available. The relative risks of respiratory symptoms due to prenatal PAHs exposure were adjusted for potential confounders (gender of child, birth weight, maternal atopy, maternal education as a proxy for the socio-economic status, exposure to postnatal environmental tobacco smoke, and moulds in households) in the Poisson regression models. Increased risk related to prenatal PAH exposure was observed for various respiratory symptoms such as barking cough (RR=4.80; 95% CI: 2.73–8.44), wheezing without cold (RR=3.83; 95% CI: 1.18–12.43), sore throat (RR=1.96; 95% CI: 1.38–2.78),

ear infection (RR=1.82; 95% CI: 1.03–3.23), cough irrespective of respiratory infections (RR=1.27; 95% CI: 1.07–1.52), and cough without cold (RR=1.72; 95% CI: 1.02–2.92). The exposure to PAHs also had impact on the duration of respiratory symptoms. The effect of PAHs exposure on the occurrence of such symptoms as runny nose or cough was partly modified by the simultaneous exposure to postnatal passive smoking. The analysis performed for the duration of respiratory symptoms confirmed significant interaction between PAHs exposure and postnatal ETS for runny or stuffy nose (RR=1.82; 95% CI: 1.57–2.10), cough (RR=1.18; 95% CI: 0.99–1.40), difficulty in breathing (RR=1.39; 95% CI: 1.01–1.92) and sore throat (RR=1.74; 1.26–2.39). Obtained results support the hypothesis that prenatal exposure to immunotoxic PAHs may impair the immune function of the fetus and subsequently may be responsible for an increased susceptibility of newborns and young infants to respiratory infections.

Key words: Infants, Polycyclic aromatic hydrocarbons, Prenatal exposure, Respiratory symptoms

Introduction

Polycyclic aromatic hydrocarbons (PAHs) such as benzo(a)pyrene contaminate the indoor environment in which infants spend most of their time. Major sources of PAHs compounds in indoor air include emissions from residential heating (e.g., coal or wood stoves, fireplaces, kerosene heaters), unvented gas appliances, environmental tobacco smoke (ETS), and fumes from cooking, grilling, and frying [1–4]. In addition, major outdoor sources of PAHs emissions, such as car fumes and power plants, increase PAHs concentrations in outdoor air, and affect their levels indoors.

PAHs represent an important class of environmental immunosuppressive contaminants, which may be linked to altered production and function of T and

B lymphocytes and impairment of monocyte differentiation pathways in various animal models and in human cells [5–9]. It may be assumed that prenatal exposure to immunotoxic PAHs may impair the immune function of the fetus and subsequently be responsible for an increased susceptibility of newborns and young infants to respiratory infections.

Presumably, frequent episodes of chest infections in early life may lead to persistent lung damage and a long-standing susceptibility to all forms of lung disease in adulthood. In fact, the association between chest illness in childhood and both chronic respiratory morbidity and impaired ventilatory lung function in later life has been observed by several investigators, who postulated that lower respiratory illness in the first year of life is associated with later cough, phlegm, and impaired ventilatory function,

independent of smoking habit and social class [10–19]. These findings, together with ecological correlation have been interpreted as evidence of persistent lung damage from chest infections in infancy.

The majority of studies conducted so far have investigated the effect of indoors particulate matter and ETS on the occurrence of respiratory symptoms in very early life, however, no attempts have been made to measure prenatal exposure to PAHs. As the relationship between prenatal exposure to environmental hazards and infant's health is still poorly understood, the purpose of the study was to test the hypothesis that infants with higher levels of prenatal exposure to PAHs may be at greater risk of developing respiratory symptoms.

Materials and methods

The study uses data collected for the birth cohort of children from Krakow being the part of the collaborative study with Columbia University in New York. The research gained approval from the Ethics Committee of the Jagiellonian University. Between November 2000 and August 2002, a total of 341 healthy pregnant women in the first and second trimester of pregnancy were recruited from ambulatory prenatal clinics and enrolled in the study. Response rate was 93% among those approached and eight subjects were lost from the follow-up. An overall number of 333 women took part in the 1-year follow-up of infants. Only non-smoking women with singleton pregnancies, aged 18–35, without illicit drug use and HIV infection, free from chronic diseases such as diabetes or hypertension, and residents of Krakow for at least 1 year prior to pregnancy were eligible. All women were interviewed and expressed their informed consent to participate in the project. They completed a detailed questionnaire on the demographic data, house characteristics, medical and reproductive history, occupational hazards, and smoking practices of others household residents.

After delivery, newborns were followed-up every 3 months over 1 year and mothers of infants were interviewed at each visit. Trained interviewers collected information by the standardized questionnaires on infants' health and household characteristics. The respiratory outcomes were analyzed for the following symptoms: (1) runny or stuffy nose, (2) ear infections (otitis media), (3) sore throat, (4) cough with or without cold, (5) barking cough, (6) difficult (puffed) breathing, (7) wheezing or whistling in the chest irrespective of respiratory infection, (8) wheezing without cold. For each of the symptoms the number of episodes and duration in days over a given period were recorded. An episode of respiratory symptom was defined as the occurrence of a specific symptom over at least 1 day. Subsequently, the number of episodes and duration of respiratory symptoms in each 3-month

period was summarized and the total number of respiratory episodes and their duration over 1-year follow-up was calculated.

Environmental tobacco smoke after delivery and the presence of moulds in the household were determinants of the postnatal indoor air quality. Postnatal ETS was defined as any reported ETS at home from any household members at 3, 6, 9 and 12 months of the infant's age. The presence of moulds in the household was identified by the answers to questions about moisture stains and visible mould growth on the walls in the household. Maternal atopy was confirmed if the mother reported allergic skin disorders or allergy-related respiratory diseases.

Personal monitoring of PAH exposure over pregnancy

Monitoring of personal PAH inhalation was carried out in all pregnant women for over a 48-hour period during the second trimester of pregnancy. In the subsample of 87 women the measurements of PAHs were available from the third trimester of pregnancy.

The women were instructed how to use personal monitor by the trained staff member and asked to wear the monitoring device during the daytime hours for two consecutive days and to place it near the bed at night. On the second day the air monitoring staff assistant and interviewer visited the woman's home to change the battery-pack and to complete the questionnaire on the household characteristics. They checked faultless operating of the monitoring device or exchanged it in case of the evident failure.

In our field study we used a sampling pump to draw air through a polyurethane (PUF) sampler for the measurement of PAH. The single pump/two impactors sampling method has been developed at Harvard School of Public Health and applied to particles and gases. Its capacity allows to draw air at a constant flow rate of 4 liters per minute (LPM). Flow rates were calibrated (with filters in place) prior to the monitoring, and checked again after changing the battery-pack on the second day and at the conclusion of the monitoring. After sampling, the field samplers were frozen and shipped to South-West Research Institute in Texas on dry ice. Determination of the total PAH (benzo(a)anthracene, benzo(b)fluoranthene, benzo(k)fluoranthene, benzo(g,h,i)perylene, benzo(a)pyrene, chrysene/iso-chrysene, dibenzo(a,h)anthracene, indeno(1,2,3-c,d)pyrene, and pyrene) in extracts was performed. Chemical procedures in the analysis of the collected samples were described elsewhere [20].

Statistical analysis

The main purpose of the statistical analysis was to correlate the prenatal PAHs exposure with the outcome variables (respiratory symptoms) over the first year of life. To identify potential confounders,

associations between population characteristics and outcome variables were investigated. Differences between subgroups with lower and higher PAHs exposure were tested by χ^2 -statistics (categorical variables) or by *t*-test (numerical variables). Poisson multivariate regression models were used to analyze the association between prenatal PAHs or recent postnatal ETS and the occurrence of individual respiratory symptoms (number of episodes) and their total duration (in days) recorded over the follow-up. Dependent variables were represented as observed counts of episodes or reported total number of days a given symptom was present in the follow-up period. In addition to the main effects of PAHs exposure and postnatal ETS, a set of potential confounders such as child gender, birth weight, season of birth, maternal education, maternal atopy, and moulds in the household were included in the statistical models as independent variables. The PAH variable was introduced in the models as numeric data after transformation to logarithmic values, which normalized the distribution. The interaction effect of PAH and postnatal ETS on individual symptoms also was tested using multiple Poisson regression models. The effect of prenatal exposure to PAHs was initially examined in a series of univariate analyses as binary 'lower and higher exposed' indicator variables (based on median) and then as numeric variables. Statistical analyses were performed with STATA software for Windows [21].

Results

Personal measurements of prenatal exposure to PAHs were within a wide range of 3.3–316.4 ng/m³ with the geometric mean of 26.1 ng/m³ (95% CI: 22.9–29.7). All subjects had detectable inhalation PAH levels.

PAH levels were significantly higher during the heating season (GM = 58.9, 95% CI: 54.9–66.8) than in the non-heating season (GM = 9.6, 95% CI: 8.6–10.8). Relatively small proportion of mothers (12%) confirmed postnatal ETS exposure of the infants over the first year of life. Although gestational age was not different between groups with various exposure levels, weight, length, and head circumference at birth were significantly smaller in infants from the higher than from the lower exposure group. Reported postnatal ETS, presence of moulds in the households, occurrence of parental atopy, and season of birth did not differentiate the groups in terms of higher and lower PAH exposure (Table 1).

Table 2 presents the number of episodes of respiratory symptoms and their duration over the 1-year follow-up period in the total group and in the exposure subgroups. The symptoms reported over the follow-up period occurred with the following frequencies: runny or stuffy nose (87.7%), cough (67.6%), episodes of puffy breathing (31.2%), sore throat (30.9%), wheezing with or without cold (18.3%), ear infections (13.5%), cough without cold

Table 1. Characteristic of study subjects (n = 333)

	Total (n = 333)	PAH level (ng/m ³)		<i>p</i>
		Low (< 24.93)	High (≥ 24.93)	
Gender (n, % of boys)	168 (50.5%)	85 (51.5%)	82 (49.4%)	0.700
Pregnancy duration in weeks (mean, SD)	39.36 (1.62)	39.45 (1.48)	39.28 (1.75)	0.385
Birth length in cm (mean, SD)	54.47 (2.90)	54.83 (2.80)	54.12 (2.97)	0.017
Birth weight in grams (mean, SD)	3410.3 (493.2)	3461.5 (468.36)	3365.6 (512.46)	0.033
Birth head circumference in cm (mean, SD)	33.86 (1.50)	34.02 (1.34)	33.70 (1.63)	0.033
Mother's allergy (n, %)	81 (24.3%)	40 (24.2%)	41 (24.7%)	0.923
Allergy in mother's family ^a (n, %)	114 (34.2%)	60 (36.6%)	54 (32.5%)	0.439
Father's allergy ^b (n, %)	65 (19.9%)	33 (20.3%)	31 (19.0%)	0.780
Allergy in father's family ^c (n, %)	70 (23.9%)	34 (23.8%)	36 (24.2%)	0.939
ETS ^d (n, %)				
> 0–5	25 (7.8%)	12 (7.6%)	13 (8.2%)	0.454
> 5–10	7 (2.2%)	5 (3.1%)	2 (1.3%)	
> 10	7 (2.2%)	2 (1.3%)	5 (3.2%)	
PAH total ^e in ng/m ³ Geometric mean, (95% CI)	26.1 (22.9–29.7)	9.3 (8.5–10.1)	73.1 (66.1–80.7)	0.000
Moulds at home (n, %)	32 (9.6%)	13 (7.9%)	18 (10.8%)	0.355
Season of the birth (n, %)				
Spring/summer	175 (52.9%)	81 (49.1%)	94 (56.6%)	0.170
Autumn/winter	156 (47.1%)	84 (50.9%)	72 (43.4%)	

^aData were available for 332 cases.

^bData were available for 327 cases.

^cData were available for 293 cases.

^dData were available for 319 cases.

^eData were available for 331 cases.

ETS – the average number of cigarettes smoked in the presence of child/day during 1 year postnatal.

Table 2. The occurrence of respiratory symptoms among children during their first year of life

	Total number of children with a given symptom (%)	Occurrence of respiratory symptom				
		Episodes			Days	
		Total	Mean	Sum	Mean duration per child with the symptom	Mean duration per episode
Runny or stuffy nose	292 (87.7%)	957	3.3	7309	25.0	7.6
Ear infection	45 (13.5%)	56	1.2	483	10.7	8.6
Cough	225 (67.6%)	557	2.5	4050	18.0	7.3
Cough without cold	33 (9.9%)	60	1.8	675	20.5	11.3
Barking cough	32 (9.6%)	73	2.3	414	12.9	5.7
Difficult breathing	104 (31.2%)	175	1.7	1521	14.6	8.7
Wheezing in the chest	61 (18.3%)	104	1.7	966	15.8	9.3
Wheezing without cold	7 (2.1%)	12	1.7	245	35.0	20.4
Sore throat	103 (30.9%)	149	1.4	1004	9.7	6.7

(9.9%), barking cough (9.6%), and wheezing without cold (2.1%).

The frequency of respiratory episodes during 1 year observation period was highest for runny or stuffy nose (mean 3.3), cough (2.5) and barking cough (2.3), lowest for puffy breathing (1.7), both wheezing and wheezing without cold (1.7), and ear infections (1.2). Mean duration of a given symptom per episode was longest for wheezing without cold (20.4 days), cough without cold (11.3 days), puffy breathing (8.7 days), ear infections (8.6 days), runny or stuffy nose (7.6 days), followed by cough (7.3 days), and barking cough (5.7 days). The number of episodes and their duration was markedly higher in those children who lived with mothers exposed to higher levels of PAHs exposure during pregnancy (Table 3).

The crude and adjusted relative risks of respiratory symptoms for the PAHs exposure concentrations were estimated using the Poisson regression models (Table 4). The highest adjusted risk was observed for barking cough (RR = 4.80; 95% CI: 2.73–8.44) and wheezing without cold (RR = 3.83; 95% CI: 1.18–12.43) while lower risks were found for sore throat

(RR = 1.96; 95% CI: 1.38–2.78), ear infection (RR = 1.82; 95% CI: 1.03–3.23), and cough (RR = 1.27; 95% CI: 1.07–1.52). The analysis of the duration of a given symptom over the 1-year showed its significant relationship with the PAH exposure level. The adjusted relative risks ranged from 1.99 (95% CI: 1.59–2.50) for barking cough to 1.10 (95% CI: 1.05–1.15) for runny or stuffy nose. Other estimates were in the intermediate range and they also – except of cough without cold – reached the level of significance. The risk estimates for episodes of respiratory symptoms and their duration due to PAHs exposure levels dichotomized by median values were consistent with the estimates derived from the statistical models where the PAHs exposure was treated as continuous variable (Table 5).

As mentioned earlier, all risk regression estimates for the number of episodes and duration of symptoms over the follow-up period were adjusted for potential confounders such as gender of child, season at birth, postnatal ETS, moulds at home, maternal atopy and maternal education. Out of all confounders considered gender of child, maternal atopy and postnatal ETS had significant effects.

Table 3. The occurrence of respiratory symptoms among children during their first year of life by level of prenatal PAH exposure (in ng/m³)

	Total number of children with a given symptom (%)	No. of episodes (mean)		Duration in days (mean)	
		Low PAH (< 24.93)	High PAH (≥ 24.93)	Low PAH (< 24.93)	High PAH (≥ 24.93)
		Runny or stuffy nose	292 (87.7%)	2.99	3.55
Ear infection	45 (13.5%)	1.14	1.30	9.79	11.30
Cough	225 (67.6%)	2.08	2.82	16.04	19.75
Cough without cold	33 (9.9%)	1.47	2.11	27.67	14.44
Barking cough	32 (9.6%)	1.58	2.70	9.25	15.15
Difficult breathing	104 (31.2%)	1.75	1.64	12.43	16.00
Wheezing in the chest	61 (18.3%)	1.70	1.71	13.04	18.06
Wheezing without cold	7 (2.1%)	2.00	1.60	14.50	43.20
Sore throat	103 (30.9%)	1.30	1.55	9.25	10.06

Table 4. Relative risk for number of respiratory episodes and their duration due to prenatal exposure (per log unit of PAH concentration in ng/m³) over the 1-year follow-up estimated from the multiple Poisson regression model

Respiratory symptoms	RR	95% CI	RR adjusted*	95% CI
<i>Number of respiratory episodes over the 1-year period</i>				
Runny or stuffy nose	1.16	1.02–1.31	1.11	0.97–1.27
Ear infection	1.97	1.18–3.30	1.82	1.03–3.23
Cough	1.44	1.23–1.69	1.27	1.07–1.52
Cough without cold	1.68	1.03–2.73	1.72	1.02–2.92
Barking cough	4.50	2.75–7.37	4.80	2.73–8.44
Difficult breathing	1.38	1.04–1.84	1.12	0.82–1.55
Wheezing in the chest	1.44	0.99–2.09	1.23	0.83–1.84
Wheezing without cold	3.55	1.10–11.49	3.83	1.18–12.43
Sore throat	1.84	1.34–2.51	1.96	1.38–2.78
<i>Duration of respiratory symptoms over the 1-year period</i>				
Runny or stuffy nose	1.18	1.13–1.23	1.10	1.05–1.15
Ear infection	1.72	1.44–2.04	1.64	1.34–2.00
Cough	1.35	1.27–1.44	1.18	1.10–1.26
Cough without cold	0.80	0.69–0.92	0.78	0.67–0.91
Barking cough	2.57	2.12–3.11	1.99	1.59–2.50
Difficult breathing	1.98	1.79–2.18	1.84	1.65–2.05
Wheezing in the chest	2.09	1.85–2.37	1.77	1.55–2.02
Sore throat	1.82	1.61–2.05	1.79	1.56–2.06

RR – relative risk.

CI – confidence interval.

*Adjusted for gender of child, child's birth weight, season of birth, ETS in postnatal period, mother's allergy, mother's education level, moulds at home.

Significant increased risks are bolded.

Table 5. Relative risk for number of respiratory episodes and their duration over the 1-year follow-up due to PAH prenatal exposure (dichotomized by median values of PAH distribution) estimated from the multiple Poisson regression model

Respiratory symptoms	RR	95% CI	RR adjusted*	95% CI
<i>Number of respiratory episodes over the 1-year period</i>				
Runny or stuffy nose	1.22	1.08–1.39	1.15	1.00–1.31
Ear infection	2.45	1.37–4.39	2.00	1.09–3.65
Cough	1.54	1.30–1.82	1.34	1.12–1.61
Cough without cold	1.74	1.03–2.94	1.71	1.00–2.93
Barking cough	2.86	1.70–4.82	2.34	1.36–4.03
Difficult breathing	1.51	1.12–2.04	1.19	0.87–1.64
Wheezing in the chest	1.27	0.86–1.87	1.05	0.70–1.58
Wheezing without cold	2.01	0.61–6.68	2.33	0.69–7.90
Sore throat	1.86	1.33–2.60	1.76	1.23–2.52
<i>Duration of respiratory symptoms over the 1-year period</i>				
Runny or stuffy nose	1.14	1.09–1.20	1.04	0.99–1.09
Ear infection	2.49	2.04–3.04	2.05	1.66–2.52
Cough	1.39	1.31–1.48	1.19	1.11–1.27
Cough without cold	0.63	0.54–0.74	0.62	0.53–0.72
Barking cough	2.75	2.21–3.41	1.82	1.45–2.30
Difficult breathing	2.07	1.86–2.31	1.71	1.52–1.91
Wheezing in the chest	1.75	1.54–2.00	1.38	1.21–1.59
Sore throat	1.70	1.49–1.93	1.44	1.26–1.65

RR – relative risk.

CI – confidence interval.

*Adjusted for gender of child, child's birth weight, season of birth, ETS in postnatal period, mother's allergy, mother's education level, moulds at home.

Significantly increased risks are bolded.

In the final stage of the statistical analysis, the interaction terms between PAH concentrations (dichotomized by median values) and the presence of

postnatal ETS were tested. The interaction terms were only significant for the episodes of runny or stuffy nose (RR = 1.96; 95% CI: 1.34–2.87), and cough

(RR = 1.70; 95% CI: 1.04–2.78). The analysis performed for duration of respiratory symptoms confirmed significant interaction for runny or stuffy nose (RR = 1.82; 95% CI: 1.57–2.10), cough (RR = 1.18; 95% CI: 0.99–1.40), difficulty breathing (RR = 1.39; 95% CI: 1.01–1.92) and sore throat (RR = 1.74; 95% CI: 1.26–2.39).

Discussion

The analysis of prenatal exposure of the infants enrolled in the Krakow study showed that PAHs exposures were within a very wide range of 3.3–316.4 ng/m³ with the geometric mean of 26.1 ng/m³ (95% CI: 22.9–29.7). These are high levels compared with the respective data coming from other urban populations. Similar study carried out in New York city – where the same sampling design and the same chemical analysis techniques for environmental monitoring were used – showed personal exposure several times lower than in Krakow [22].

The results of our study have demonstrated a significant association between prenatal exposure to PAHs measured by personal monitoring of exposure in the second trimester of pregnancy and the occurrence of respiratory outcomes observed in infants over the first year of life. The number of episodes of ear infections, cough, barking cough, and throat infections was significantly related to the exposure in question. Moreover, the duration of the respiratory episodes was significantly longer among infants who were prenatally exposed to higher PAHs exposure levels. The highest risks of respiratory episodes related to the PAHs exposure were noted for barking cough (RR = 4.80; 95% CI: 2.73–8.44) and wheezing without cold (RR = 3.83; 95% CI: 1.18–12.43). Besides, wheezing and barking cough, and other respiratory symptoms occurred more frequently and lasted longer in infants with higher prenatal PAHs exposure than among those exposed to the lower PAHs concentrations.

Our findings confirm earlier observations that higher exposure to PAHs over pregnancy is associated with clear biological effects in terms of reduced birthweight, body length and head circumference (Choi H et al. manuscript in preparation). Potential confounders such as socioeconomic status, gender of child, parity or duration of gestational age did not justify these effects. Infants with reduced body size are more likely to have diminished lung function soon after birth while infants with small airways may be susceptible to respiratory symptoms [23].

However, our investigation did not allow us to clearly distinguish the effect of the prenatal from the postnatal PAHs exposure as the postnatal indoors PAHs concentrations were not available. However, postnatal ETS reflects to some degree indoor air quality over early infancy. Nevertheless, we are not quite certain whether our findings represent delayed

effects of prenatal PAHs exposure on infants, or more immediate effects of postnatal PAHs exposure over the first year of life. The increased risk for respiratory problems after early exposure to PAHs seems to appear very early and the hypothesis about the effect of prenatal PAHs exposure on the occurrence of respiratory symptoms in early life is plausible.

The most important potential confounders of the relationship between prenatal ambient risk factors and the respiratory outcomes of infants such as chronic diseases or active tobacco smoking by mothers or prenatal ETS have been removed through entry criteria. Other risk factors that are thought to affect the probability of respiratory diseases in infants are birth weight, maternal allergy, indoor air quality (postnatal ETS, presence of moulds in the households), socioeconomic status, and season of birth. All these potential confounders have been taken into consideration and the estimates of main effects were adjusted for them.

An important feature of our study is the personal monitoring of ambient PAHs exposure, which is a highly relevant measure of individual exposure. However, the extent to which the measurements made during the second trimester reflect the exposure level in the first or the third trimesters of pregnancy is not known. The extrapolation from a short term to a long term period is always difficult as the exposure to environmental hazards is not only a function of lifestyle and mobility of pregnant woman but also of changes in weather and meteorological patterns. For instance, in wintertime, outdoor and indoor air pollution may greatly increase due to household heating and therefore the misclassification of exposure in other pregnancy periods cannot be excluded. However, additional comparative analysis of the measurements from the second trimester with a subsample of 87 subjects taken during the third trimester has shown a good correlation between measured concentrations in both periods ($r = 0.50$, $p < 0.000$).

Over the last decades there has been growing concern over the health effects associated with air pollution. The studies concentrated mainly on the morbidity patterns from respiratory diseases, occurrence of respiratory symptoms, pulmonary function, and physician office visits in infants and young children. The air pollution surveys very seldom considered chemical components of air pollutants. Until now, none of the studies investigated the effects of personal exposure to PAHs over the pregnancy on health of infants in the first year of life.

Earlier studies have attempted to quantify the concentrations of outdoor air pollutants in the residence area, mainly TSP, PM₁₀, SO₂ or CO, and assign exposure values to the study subjects or use the area-based exposures to approximate individual exposures. In some studies, residential proximity to industry was the proxy for exposure to industrial pollution from local industries. Estimating individual average

exposures during specific gestational months by relying on the ambient air monitoring station even close to the maternal residence may result in exposure misclassification. Networks of air pollution stations are usually located far away from the residences and may provide the least accurate surrogate measures for personal exposure. Moreover, the ecological studies conducted, failed to consider important confounding factors such as maternal atopy or postnatal ETS exposure.

The biological mechanisms whereby PAHs might cause adverse health effects in infants have not been yet established. Inhibited production of immunocompetent cells is likely to be one of the mechanisms contributing to the immunosuppression due to PAHs. Indeed, exposure to PAHs inhibits the differentiation of human monocytes [24, 25] and macrophages and induces apoptosis of both pre-T cells in the thymus and pre-B cells in the bone marrow, which may account for thymic atrophy and decreased cell recovery from the spleen, lymph nodes, and bone marrow in PAHs exposed experimental animals [26–29]. Mature differentiated immune cells also constitute targets for PAHs. These environmental contaminants diminish T-cell related cytokine production and B-cell mediated Ab secretion, impair some functional properties of differentiated macrophages such as cellular adhesion and cytokine production [9].

The experimental data support the hypothesis that higher incidence of respiratory symptoms all over the world may result from immunotoxic effects of prenatal PAHs exposure on developing fetus or in early infancy. This might explain the fact that allergic respiratory diseases such as hay fever and bronchial asthma have indeed become more common in the last decades in all industrialized countries, especially in young children. In this context, the dramatic increase of traffic and traffic related diesel exhaust pollution is of great importance. It is plausible that the exposure to PAH compounds may play a role, not only in the onset and increasing frequency of respiratory infections, but may also be associated with asthma aggravation [30–33]. Therefore, prevention measures should be much more focused on controlling sources of air pollution, which contain PAH compounds.

Summing up, the results of our study suggest that prenatal exposure to PAHs had an effect on the occurrence of many respiratory symptoms during early infancy and that this was independent from the effects of postnatal environmental tobacco smoke. However, the impact of prenatal PAHs exposure on the occurrence of certain symptoms such as runny nose and cough might partly be modified by simultaneous exposure to postnatal passive smoking.

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