Benefits of Reducing Prenatal Exposure to Coal-Burning Pollutants to Children’s Neurodevelopment in China

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BACKGROUND: Coal burning provides 70% of the energy for China’s industry and power, but releases large quantities of polycyclic aromatic hydrocarbons (PAHs) and other pollutants. PAHs are reproductive and developmental toxicants, mutagens, and carcinogens.

OBJECTIVE: We evaluated the benefit to neurobehavioral development from the closure of a coal-fired power plant that was the major local source of ambient PAHs.

METHODS: The research was conducted in Tongliang, Chongqing, China, where a coal-fired power plant operated seasonally before it was shut down in May 2004. Two identical prospective cohort studies enrolled nonsmoking women and their newborns in 2002 (before shutdown) and 2005 (after shutdown). Prenatal PAH exposure was measured by PAH–DNA adducts (benzo[a]pyrene–DNA) in umbilical cord blood. Child development was assessed by the Gesell Developmental Schedules at 2 years of prenatal exposure to other neurotoxicants and potential confounders (including lead, mercury, and environmental tobacco smoke) was measured. We compared the cohorts regarding the association between PAH–DNA adduct levels and neurodevelopmental outcomes.

RESULTS: Significant associations previously seen in 2002 between elevated adducts and decreased motor area developmental quotient (DQ) (p = 0.043) and average DQ (p = 0.047) were not observed in the 2005 cohort (p = 0.546 and p = 0.146). However, the direction of the relationship did not change.

CONCLUSION: The findings indicate that neurobehavioral development in Tongliang children benefitted by elimination of PAH exposure from the coal-burning plant, consistent with the significant reduction in PAH–DNA adducts in cord blood of children in the 2005 cohort. The results have implications for children’s environmental health in China and elsewhere.

KEY WORDS: China, coal burning, lead, neurobehavioral development, PAH–DNA adducts, prenatal. Environ Health Perspect 116:1396–1400 (2008). doi:10.1289/ehp.11480 available via http://dx.doi.org/ [Online 14 July 2008]

China’s vast industrial network and power plant system rely on coal for approximately 70–75% of their energy needs (Economy 2003; Zhang et al. 2002). Coal burning in China is the major source of ambient polycyclic aromatic hydrocarbons (PAHs). PAHs are also present in tobacco smoke and charred foods. Molecular and epidemiologic studies show that fetuses and infants are more susceptible than adults to environmental toxicants including PAHs (Perera et al. 2005), lead (Agency for Toxic Substances and Disease Registry (ATSDR) 2005), and mercury (ATSDR 1999). Experimentally, benzo[a]pyrene (BaP), a representative PAH, is a reproductive toxicant (Archibong et al. 2002), producing neurodevelopmental effects including decreased motor activity, neuro-muscular, physiologic and autonomic abnormalities, and decreased responsiveness to sensory stimuli (Saunders et al. 2002, 2003; Wormald et al. 2004). In studies in Europe, the United States, and China, prenatal exposure to PAHs has been associated with reduced fetal growth (Choi et al. 2006; Perera et al. 1998, 2003; Särmä et al. 2005; Tang et al. 2006) and developmental deficits (Perera et al. 2006). In addition, PAHs are mutagenic and carcinogenic, including via transplacental exposure (Bostrom et al. 2002; Bulay and Wattenberg 1971). PAH–DNA adducts reflect individual variation in exposure, absorption, metabolic activation, and DNA repair; they therefore provide an informative biologic dosimeter that has been associated with risk of cancer and developmental impairment (Bartsch et al. 1983; Perera et al. 2007; Tang et al. 2001). Here we use adducts as a measure of exposure rather than as a mechanistic marker. PAH–DNA adduct concentrations in cord blood have been shown to increase across a gradient of ambient PAH exposure, albeit with substantial interindividual variation (Perera et al. 2005; Whyatt et al. 1998). Cord blood adducts in the 2002 Tongliang cohort (mean, 0.32 per 10⁸) were significantly higher than those in cohorts of newborns in the United States and Poland (Perera et al. 2005). As previously reported, in the 2002 Tongliang, Chongqing, China cohort, PAH–DNA adducts in cord blood were associated with reduced birth head circumference (Tang et al. 2006) and reduced developmental quotients (DQs) at 2 years of age (Tang et al. 2008). As in the present sample, comparison of all cord bloods showed a significant decrease in adduct levels in 2005 (unpublished data).

Lead and mercury are also released by coal burning (Guo et al. 2002; Wang et al. 2006; Zhang et al. 2003) as well as other sources. Both metals are developmental neurotoxicants even at low levels (ATSDR 1999, 2005; Canfield et al. 2003; Needleman et al. 1996) and are potential confounders of associations between PAH–DNA adducts and developmental outcomes.

We tested the hypothesis that comparison of the two cohorts of newborns in Tongliang both followed through 2 years of age would show that elimination of prenatal exposure to coal-burning emissions from the power plant resulted in improved developmental outcomes and in failure to observe the significant effects of PAH–DNA adducts on 2-year development seen in the first cohort, consistent with decreased levels of PAH–DNA adducts in cord blood of children in the second cohort.

Methods

Study design. Two identical prospective cohort studies were carried out (pre-and postplant shutdown, respectively). Nonsmoking mothers and their newborns were enrolled at delivery as described (Tang et al. 2008). The newborns were followed through their second birthdays,

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at which time their intellectual and behavioral development was assessed using the Gesell Developmental Schedules (GDS). Levels of PAH–DNA adducts (specifically BaP–DNA adducts) were measured in umbilical cord blood. Exposure to known neurotoxicants [lead, mercury and environmental tobacco smoke (ETS)] and other potential confounders was assessed by biomarkers or questionnaire.

**Setting.** Tongliang, a county in Chongqing Municipality, has a population of around 810,000 and is situated in a basin approximately 3 km in diameter. Before 31 May 2004, a coal-fired power plant located just south of the town center operated every year during the dry season from 1 December to 31 May to compensate for insufficient hydroelectric power during that period (Chow et al. 2006; Tang et al. 2006). The plant was not equipped with modern pollution reduction technology and combusted about 25,000 tons of coal during each 6-month period of operation. In 2002, nearly all domestic heating and cooking units had been converted to natural gas, and motor vehicles were limited in number. Air monitoring analysis carried out as part of the study showed that PAHs of medium molecular weight (168–266) increased by up to 3.5 times during the operational period of the Tongliang power plant (Chow et al. 2006). After the government-mandated shutdown of the plant in May 2004, mean ambient levels of the same PAHs declined significantly (for BaP, \( p = 0.01 \)), as did adducts in cord blood (unpublished data).

**Participants.** Subjects were children born to women who gave birth at any one of three major Tongliang County Hospitals located in the Town of Bachuan (informally known as Tongliang City) (representing about 95% of the Chinese population (Beijing Mental Health Cooperative Group 1985). Each child is assigned a DQ in each of the four areas: motor, adaptive, language, and social. The standardized mean (± SD) of the DQ is 100 ± 15; a score < 85 indicates developmental delay (Hudson et al. 1998). A study by Jin et al. (2007), which also used the GDS, showed means in the same range as those in our study. Testing was conducted by physicians in the same group who were certified in the GDS to maximize reliable assessment and valid interpretation. Therefore, both interexaminer and intraexaminer variability were minimal.

Research workers abstracted relevant information on covariates from maternal and infant medical records after delivery such as date of delivery, gestational age, and sex of newborn. Other covariates were derived from questionnaire data on socioeconomic status and environmental exposures.

**Statistical analysis.** The statistical methods have been previously described with respect to analysis of the 2002 cohort (Tang et al. 2008) and are briefly summarized here. Analysis of the 2005 cohort followed the same procedures. The main exposure of interest was PAH–DNA adducts in cord blood. As before (Tang et al. 2008), adducts were treated as a continuous variable, with nondetectable samples assigned a value of 0.125 per 10\(^8\) (midway between 0 and the detection limit of 0.25). Lead and mercury values were dichotomized at the median to minimize the influence of outliers. In multiple regression analyses, age-adjusted DQs in the motor area, adaptive area, language area, social area, and the average of these four DQs served as the outcome variables. In logistic regression, the outcomes were developmental delays in the respective areas. As in our prior analyses, we included as covariates sex, gestational age, maternal education, ETS (hours of exposure/day), and lead. Mercury and exposure to chemicals during pregnancy were not included, because neither was a contributor to DQ at the level of \( p ≤ 0.1 \) (Tang et al. 2008). We did not have direct measures of postnatal PAH–DNA adducts or lead but were able to adjust for postnatal ETS exposure.

We first compared the two cohorts with respect to developmental outcomes (mean DQ scores and frequency of developmental delay) by performing unadjusted analyses using \( t \)-test or Fisher’s exact test as appropriate. Multiple linear regression and logistic regression were used to test whether the DQ means or odds ratios (ORs) for developmental delay differed significantly between the two cohorts after adjustment for relevant covariates (prenatal ETS, mother’s education, gestational age, and sex) and further including cohort as a covariate. The associations between adducts and developmental outcomes were examined by multiple linear regression and logistic regression as
except for language were reduced in 2005.

Covariates of developmental delay in all DQ areas are intercorrelated (OR = 1.91; 95% CI, 1.22 to 2.97, p = 0.004), this association was not seen in 2005 (OR = 1.91; 95% CI, 1.22 to 2.97, p = 0.004). In 2005, cord adducts were associated with average DQ adjusted (β = −14.58; 95% CI, −28.77 to −0.37, p = 0.047). In contrast, in the 2005 cohort, cord adducts were not significantly associated with any of the DQs before or after adjusting for the same covariates (for motor area DQ, adjusted β = −5.90; 95% CI, −24.96 to 13.17; p = 0.546) and average DQ (β = −12.38; 95% CI, −28.95 to 4.21; p = 0.146). However, in 2005, associations for all DQs remained inverse, albeit not statistically significantly. Whereas in the 2002 cohort, by logistic regression analysis, a 0.1-unit increase (0.1 adduct/10⁸ nucleotides) in cord adducts was associated with increased odds of being developmentally delayed in the motor area (OR = 1.91; 95% CI, 1.22 to 2.97, p = 0.004), this association was not seen in 2005 (OR = 2.06; CI, 0.62 to 6.84, p = 0.240), nor were significant associations seen in 2005 between PAH–DNA adducts and developmental delay in the other DQ areas (Table 5). However, the interaction term (PAH × cohort) was not significant in multiple or logistic regression models, which may be attributable to small sample size.

Further controlling for postnatal ETS, in multivariate regression the associations between adducts and DQ in the motor area and average DQ remained significant in the 2002 cohort: β = −16.89; 95% CI, −31.76 to −2.01, p = 0.026 and β = −16.56; 95% CI, −31.21 to −1.92, p = 0.027, respectively. Also by logistic regression, the OR for adducts and motor area delay remained significant: OR = 2.18; 95% CI, 1.31 to 3.61; p = 0.003. Inclusion of postnatal ETS in the 2005 models did not affect the results.

Discussion

As hypothesized, comparison of the two cohorts of newborns in Tongliang, China, both followed through 2 years of age, has provided evidence that elimination of prenatal exposure to coal-burning emissions resulted in measurable benefits to children’s development. In contrast to the 2002 cohort, in the 2005 cohort we did not observe a significant effect of PAH–DNA adducts on 2-year developmental scores. Consistent with prior analyses of adducts among all newborns (unpublished data), in the present subset the average adduct concentration and the frequency of detectable adducts in cord blood were reduced in the 2005 cohort by 38% and 36%, respectively. The mean cord adduct level in the 2002 cohort (0.32 adducts/10⁸ nucleotides) was significantly higher than in New York City (0.21 adducts/10⁸ nucleotides) or Krakow, Poland (0.28 adducts/10⁸ nucleotides), consistent with the higher ambient PAH exposure in Tongliang (Perera et al. 2005). After the power plant shutdown, the adduct levels in Tongliang in 2005 (0.20/10⁸ nucleotides) were similar to those in New York City (0.21/10⁸).

Whereas PAH–DNA adducts in cord blood were significantly associated with DQ decrements in the motor area and in the average DQ among children who were in utero during the power plant operation, these significant associations were not seen among children who were in utero after the power plant had been shut down. In the 2002 cohort, adducts were associated with an approximate 2-fold increased odds of developmental delay in the motor area; again, that effect was not seen in the 2005 cohort. However, the observation in the 2005 cohort of inverse, albeit non–statistically significant, associations between adducts and all DQs except for the average DQ suggests that even greater benefits will accrue in the future. PAHs are lipid-soluble compounds (Nickerson 2006), and it is reasonable to expect that the concentrations of PAHs stored in mothers’ adipose tissue and transferrable to the fetus will be reduced over time. In 2007, we enrolled a third

**Table 1.** Enrollment and retention of the cohorts.

| Characteristic        | 2002 (n = 110[^a]) | Mean ± SD (range) or % | 2005 (n = 107) | Mean ± SD (range) or % |
|-----------------------|-------------------|------------------------|----------------|------------------------|
| Maternal age (years)  |                    | 25.18 ± 3.15 (20.34–34.28) | 27.91 ± 4.59 (20.45–37.80) |
| Maternal education (%)|                   | 43.6                  | 55.1           |
|                     |                   | 50.9                  | 44.9           |
| Sex of newborn (%)   |                   | 55.4                  | 44.9           |
| Gestational age (days)|                   | 277.35 ± 11.27 (242–294) | 276.69 ± 9.19 (250–300) |
| Cord lead (mg/dL)    |                   | 3.60 ± 1.59 (0.82–12.93) | 3.74 ± 1.50 (1.49–10.82) |
| Cord mercury (ppb)   |                   | 6.97 ± 4.43 (2.28–39.72) | 6.61 ± 2.77 (1.72–14.23) |
| Prenatal ETS exposure (hr/day) | | 0.29 ± 0.58 (0–5.00) | 0.30 ± 0.54 (0–3.00) |

[^a]Number of subjects with each type of data varies due to missing data. *p < 0.05; comparisons of continuous variables by Mann–Whitney test, and binary variables by chi-square test.
in improving developmental outcomes among children living in Tongliang, Chongqing. Because coal-fired power plants currently produce 75% of China’s electricity and most new plants in China are being built to burn coal, albeit with modern pollution control, the results from the Tongliang study are relevant to the development of other children living in China and have implications for policies concerning energy and public health.

Table 3. Comparison of Gesell scores in the two prospective cohorts.a

| DQ area | 2002 Cohort | 2005 Cohort |
|---------|-------------|-------------|
| n = 110 | n = 107     |             |
| Motor area | Mean ± SD (range) | 97.53 ± 11.47 (65–135) | 97.83 ± 7.82 (74–116) |
| Normal (n [%]) | 95 (86.4) | 102 (95.3) |
| Developmental delay (n [%]) | 15 (13.6) | 5 (4.7) |
| Adaptive area | Mean ± SD (range) | 98.71 ± 14.90 (50–124) | 101.18 ± 10.96 (76–129) |
| Normal (n [%]) | 96 (87.7) | 96 (89.7) |
| Developmental delay (n [%]) | 14 (12.7) | 11 (10.3) |
| Language area | Mean ± SD (range) | 102.10 ± 12.83 (56–122) | 100.47 ± 9.78 (74–127) |
| Normal (n [%]) | 99 (90.0) | 96 (89.7) |
| Developmental delay (n [%]) | 11 (10.0) | 11 (10.3) |
| Social area | Mean ± SD (range) | 99.40 ± 11.79 (57–121) | 101.83 ± 6.81 (76–117) |
| Normal (n [%]) | 100 (90.9) | 104 (97.2) |
| Developmental delay (n [%]) | 10 (9.1) | 3 (2.8) |
| Average | Mean ± SD (range) | 99.42 ± 10.74 (57–120) | 100.30 ± 7.16 (76–117) |
| Normal (n [%]) | 100 (90.9) | 104 (97.2) |
| Developmental delay (n [%]) | 7 (6.4) | 2 (1.9) |

aUnadjusted comparisons of DQs between cohorts by t-test, percent delay by Fisher’s exact test; adjusted analyses by regression as described. bThis material appears as originally published in Tang et al. (2008). cUnadjusted, p = 0.3; adjusted, p = 0.017. dUnadjusted, p = 0.064; adjusted, p = 0.033. eUnadjusted NS (not significant); it is not appropriate to use logistic regression due to small cell count.

Table 4. Results of multiple regression analyses of Gesell scores at 2 years of age and PAH–DNA adducts.a

| DQ area | 2002 Cohort | 2005 Cohort |
|---------|-------------|-------------|
| Motor area | β (95% CI), p-value | −16.01 (−31.30 to −0.72), p = 0.043 | −5.90 (−24.98 to 13.17), p = 0.546 |
| Adaptive area | −15.51 (−35.63 to 4.61), p = 0.134 | −22.06 (−47.70 to 3.58), p = 0.095 |
| Language area | −16.64 (−33.73 to 0.46), p = 0.059 | −20.39 (−42.62 to 1.85), p = 0.075 |
| Social area | −9.29 (−25.28 to 6.70), p = 0.294 | −1.50 (−17.62 to 14.61), p = 0.85 |
| Average | −14.58 (−28.77 to −0.37), p = 0.047 | −12.38 (−29.85 to 4.20), p = 0.146 |

aModel included cord lead level, sex, gestational age, maternal education, lead, and ETS as covariates.

Table 5. Results of logistic regression analyses of developmental delay at 2 years of age and PAH–DNA adducts.a

| DQ area | 2002 Cohort | 2005 Cohort |
|---------|-------------|-------------|
| Motor area | OR (95% CI), p-value | 1.91 (1.22 to 2.97), p = 0.043 | 2.06 (0.62 to 6.84), p = 0.240 |
| Adaptive area | 1.16 (0.78 to 1.76), p = 0.500 | 1.78 (0.79 to 4.00), p = 0.161 |
| Language area | 1.31 (0.84 to 2.05), p = 0.234 | 2.34 (0.96 to 5.71), p = 0.081 |
| Social area | 1.52 (0.93 to 2.50), p = 0.095 | 3.38 (0.59 to 19.35), p = 0.171 |
| Average | 1.67 (0.93 to 3.00), p = 0.088 | NA |

aModel included cord lead level, sex, gestational age, maternal education, and ETS as covariates. bThe ORs for cord adducts presented in this table represent the effect of a 1-unit (0.1 adduct/10^6 nucleotides) increment in cord adducts. cSPSS statistical software (SPSS Inc, Chicago, IL, USA) failed to provide accurate estimates.

Conclusion

In conclusion, these results indicate that an intervention to eliminate emissions from a polluting coal-burning power plant was effective in improving developmental outcomes among children living in Tongliang, Chongqing. Because coal-fired power plants currently produce 75% of China’s electricity and most new plants in China are being built to burn coal, albeit with modern pollution control, the results from the Tongliang study are relevant to the development of other children living in China and have implications for policies concerning energy and public health.
Hudon L, Moise KJ Jr, Hegemier SE, Hill RM, Moise AA, Smith ED, et al. 1998. Long-term neurodevelopmental outcome after intrauterine transfusion for the treatment of fetal hemolytic disease. Am J Obstet Gynecol 178:859–863.

Schröder RJ, Binková B, Dejmek J, Bobak M. 2005. Ambient air pol- lutants on birth outcomes in a multi-ethnic population. Environ Health Perspect 111:201–205.

Perera FP, Santella RM, Tsai WY, Kinney P, Camann D, Barr D, et al. 2007. Relationship between polycyclic aromatic hydrocar- bon–DNA adducts, environmental tobacco smoke, and child development in the World Trade Center cohort. Environ Health Perspect 115:1497–1502.

Perera FP, Santella RM, Rauh V, Tsai WY, Tung D, Diaz D, et al. 2006. Effect of prenatal exposure to airborne polycyclic aromatic hydrocarbons on neurodevelopment in the first 3 years of life among inner-city children. Environ Health Perspect 114:1297–1299.

Ke DH, Su D, Zhang YX, Gao X. 2004. Effect of active medical intervention on the physique and neuropsychological development of full-term infants: follow-up effect evaluation [in Chinese]. Chinese J Clin Rehabil 8:506

Needleman HL, Riess JA, Tobin MJ, Biesecker GE, Greenhouse JB. 1996. Bone lead levels and delinquent behavior. JAMA 275:363–369.

Bartsch H. 1994. Validation of a new fluorometric assay for benzo[a]pyrene-DNA adducts in mothers and newborns from Northern Manhattan, the World Trade Center Area, Poland, and China. Cancer Epidemiol Biomarkers Prev 14:709–714.

Perera FP, Rauh V, Tsai WY, Kimney P, Damann D, Barr D, et al. 2003. Effects of transplacental exposure to environmental pollutants on birth outcomes in a multi-ethnic population. Environ Health Perspect 111:201–205.

Rojas M, Alexandrov K, van Schooten FJ, Hillebrand M, Kriek E, Bartsch H. 1983. Quantitative com- parisons of carcinogenicity, mutagenicity and elec- trophilicity of 10 direct-acting alkylating agents and the initial 6-alkylguanine ratio in DNA with carcinogenic potency in rodents. Mutat Res 110:181–219.

Archibong AE, Inyang F, Ramesh A, Greenwood M, Nayyar T, Kopsombut P, et al. 2002. Alteration of pregnancy related hormones and fetal survival in F-344 rats exposed by inhalation to benzo[a]pyrene. Reprod Toxicol 16:381–409.

Bartsch H, Terracini B, Malaveille C. 1983. Initial 06-alkylguanine ratio in DNA with carcinogenic potency in rodents. Mutat Res 110:181–219.

Zhou X, Luo Y, Liang J, Chen T, Zhang N, Cheng S, et al. 2004. Follow-up study of mental developments in high-risk chil- dren [in Chinese]. Zhejiang Da Xue Xue Bao Yi Xue Ban 33:449–451.

Zhou X, Zhao Z, Jiang J, Liang L, Wang J, Moe HQ, et al. 2005. Multifactorial analysis of effects of mothers’ autoim- mune thyroid disease on their infants’ intellectual develop- ment [in Chinese]. Zhonghua Er Ke Za Zhi 43:340–344.

Bostrom CE, Gerde P, Hanberg A, Jerström B, Johansson C, Kyrklund T, et al. 2002. Cancer risk assessment, indicators, and guidelines for polycyclic aromatic hydrocarbons in the ambient air. Environ Health Perspect 110:451–488.

ATSDR. 2005. Toxicological Profile for Mercury. Atlanta, GA:Agency for Toxic Substances and Disease Registry.

ATSDR. 2004. A Critical Link, Interventions for Physical Growth and Psychological Development. Geneva:World Health Organization, Department of Child and Adolescent Health and Development.

World Health Organization. 2004. The Importance of Caregiver-Child Interactions for the Survival and Healthy Development of Young Children. Geneva:World Health Organization, Department of Child and Adolescent Health and Development.

Wormley DD, Chiuva S, Nayyar T, Wu J, Johnson S, Brown LA, et al. 2004a. Inhaled benzo[a]pyrene impairs long-term potentiation in the F1 generation rat dentate gyrus. Cell Mol Biol (Noisy-le-grand) 50:715–721.

Wormley DD, Ramesh A, Hood DB. 2004b. Environmental contam- inant-mixture effects on CNS development, plasticity, and behavior. Toxicol Appl Pharmacol 197:49–65.

Zhang J, Li TY, Liu JJ, Chen YH, Qu L, Perera FP. 2006. PAH-DNA adducts in cord blood and fetal and child develop- ment in a Chinese cohort. Environ Health Perspect 114:1297–1300.

Zhang D, Li TY, Liu JJ, Zhou JJ, Yuan T, Chen YH, et al. 2004. Effects of prenatal exposure to coal-burning pollutants on children’s development in China. Environ Health Perspect 116:674–679.

Zhang D, Phillips DH, Stumper M, Mooney LA, Hsu Y, Cha S, et al. 2001. Association between carcinogen-DNA adducts in white blood cells and lung cancer risk in the physicians’ health study. Cancer Res 61:6708–6712.

Wang D, He L, Wei S, Feng X. 2006. Estimation of mercury emission from different sources to atmosphere in Chongqing, China. Sci Total Environ 366:722–728.

Wang HY, Santella RM, Jedyrchowski W, Garte SJ, Bell DA, Ottman R, et al. 1998. Relationship between ambient air pollution and procarcinogenic DNA damage in Polish mothers and newborns. Environ Health Perspect 106:821–826.

World Health Organization. 1999. A Critical Link, Interventions for Physical Growth and Psychological Development. Geneva:World Health Organization, Department of Child and Adolescent Health and Development.

World Health Organization. 2004. The Importance of Caregiver-Child Interactions for the Survival and Healthy Development of Young Children. Geneva:World Health Organization, Department of Child and Adolescent Health and Development.

Archibong AE, Inyang F, Ramesh A, Greenwood M, Nayyar T, Kopsombut P, et al. 2002. Alteration of pregnancy related hormones and fetal survival in F-344 rats exposed by inhalation to benzo[a]pyrene. Reprod Toxicol 16:381–409.

Bartsch H, Terracini B, Malaveille C. 1983. Quantitative com- parisons of carcinogenicity, mutagenicity and elec- trophilicity of 10 direct-acting alkylating agents and the initial 6-alkylguanine ratio in DNA with carcinogenic potency in rodents. Mutat Res 110:181–219.

Beijing Mental Development Cooperative Group. 1985. Gesell Developmental Diagnosis Scale. Beijing, China:Beijing Mental Development Cooperative Group.

Boström CE, Gerde P, Hanberg A, Jerström B, Johansson C, Kyrklund T, et al. 2002. Cancer risk assessment, indicators, and guidelines for polycyclic aromatic hydrocarbons in the ambient air. Environ Health Perspect 110:451–488.

Buly GM, Wattenberg LW. 1971. Carcinogenic effects of polycyclic hydrocarbon carcinogens administered to mice during pregnancy on the progeny. J Natl Cancer Inst 46:397–402.

Canfield RL, Henderson CR, Cory-Slechta DA, Cox C, Josko TA, Lanphear BP. 2003. Intellectual impairment in children with blood lead concentrations below 10 µg per deciliter. N Engl J Med 348:1517–1521.

Chai H, Jedyrchowski W, Spengler J, Camann DE, Whytht RM, Rauh V, et al. 2006. International studies of prenatal exposure to polycyclic aromatic hydrocarbons and fetal growth. Environ Health Perspect 114:1744–1750.

Chow JC, Watson JD, Chen LW, Karacan D, Zielenska B, Tang D, et al. 2006. Exposure to PM2.5 and PAHs from the Tongliang, China, epidemiological study. J Environ Sci Health A-Tox Hazard Subst Environ Eng 41:517–542.

Cui H, Hou J, Ma G. 2001. Influences of rearing style on the development of full-term infants: follow-up effect evaluation [in Chinese]. Chinese J Clin Rehabil 8:506

Deng RW, Zhang MQ, Zhu YC. 2002. Evaluation of mercury pollution and procarcinogenic DNA damage in Polish mothers and newborns. Environ Health Perspect 106:821–826.

Wormley DD, Chiuva S, Nayyar T, Wu J, Johnson S, Brown LA, et al. 2004a. Inhaled benzo[a]pyrene impairs long-term potentiation in the F1 generation rat dentate gyrus. Cell Mol Biol (Noisy-le-grand) 50:715–721.

Wormley DD, Ramesh A, Hood DB. 2004b. Environmental contam- inant-mixture effects on CNS development, plasticity, and behavior. Toxicol Appl Pharmacol 197:49–65.

Zhang J, Han C-L, Xu Y-G. 2003. The release of the hazardous elements from coal in the initial stage of combustion process. Fuel Process Technol 84:121–133.

Zhang MQ, Zhu YC, Deng RW. 2002. Evaluation of mercury emissions to the atmosphere from coal combustion, China. Ambio 31:482–484.

Zhang X, Li J. 1994. The revise of Gesell Developmental Scale on 3/12 —6 years of age in Beijing [in Chinese]. CJCP 2:148–150.

Zhou L, Luo Y, Liang J, Chen T, Zhang N, Zheng S, et al. 2004. Follow-up study of mental developments in high-risk chil- dren [in Chinese]. Zhejiang Da Xue Xue Bao Yi Xue Ban 33:449–451.

Zhu H, Zhao ZY, Jiang YJ, Liang L, Wang JY, Mao HQ, et al. 2006. PAH-DNA adducts in cord blood and fetal and child develop- ment in a Chinese cohort. Environ Health Perspect 114:1297–1300.

Tang D, Li TY, Liu JJ, Zhou JJ, Yuan T, Chen YH, et al. 2004. Effects of prenatal exposure to coal-burning pollutants on children’s development in China. Environ Health Perspect 116:674–679.