EFFECTS OF PERINATAL EXPOSURE TO ENVIRONMENTALLY PERSISTENT ORGANIC POLLUTANTS AND HEAVY METALS ON NEUROBEHAVIORAL DEVELOPMENT IN JAPANESE CHILDREN: II. PROTOCOL AND DESCRIPTION OF STUDY COHORT

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Introduction

Several longitudinal prospective cohort studies on the effects of perinatal exposures to polychlorinated biphenyls (PCBs) and dioxins on growth of children have demonstrated that the transplacental and lactational exposures to PCBs significantly relate to the delay in the neurodevelopment (reviewed in ref 1). Dioxins and PCBs are highly lipophilic and chemically stable compounds that accumulate in the food chain. Therefore, the main sources of environmental exposure to those toxic compounds are dairy products, meat and fish; especially seafood eating might be most responsible. Since Japanese likes seafood eating, the health hazard problems in relation to these environmentally contaminated compounds should be important. In addition to these halogenated pollutants, methylmercury has been also shown to be a potent neurotoxicant to the developing fetal brain. Since the main source of this compound is also seafood, the combined effects of these compounds must be clarified in Japan. The final destination of this study is to examine the effects of perinatal exposures to environmentally persistent organic pollutants and heavy metals on neurobehavioral development in Japanese children. This study will show the protocol and description of the study cohort which has been in progress in the Tohoku area in Japan since 2001.

Methods and Materials

The details of the registration and the biological samples collection protocols had been reported in our previous report[2]. Briefly, we have started to recruit the healthy pregnant mothers with informed consent at two large hospitals from December 2000. To establish an optimal study population, only infants born at term (36 to 42 week of gestation) without congenital anomalies or diseases were included. Pregnancy and delivery had to be completed without overt signs of serious illness or complications. A blood sample was taken from the mothers at 28 week of their pregnancy. The umbilical cord was also taken after the delivery. The tissues from placenta and cord were collected and stored. Two days after the delivery, hair samples were taken from the mothers and the questionnaire including food frequency were performed. The mothers were finally asked to give us a sample of breast milk a month after the delivery.

The neurobehavioral development was examined with Brazelton Neonatal Behavioral Assessment Score (NBAS) when the infants were three days old. The development of the infants at 7 months old were evaluated with Bayley Scales for Infant Development, Kyoto Scale of Psychological

Development (KSPD) and Fagan Test of Infant Intelligence (FTII). The home environment and the socio-economical status are also measured.

The study protocol was approved by the Medical Ethics Committee of the Tohoku University School of Medicine.

Results and Discussion

Registration has been performed at the two major hospitals in Sendai. We already explained our cohort to 823 mothers from January 2001 to March 2002, and the informed consent was obtained from 354 mothers, indicating the rate of consent obtained was approximately 43%. This value was gradually increased. W e already performed NBAS to 216 health infants. We expect to recruit finally more than 400 mother-infant pairs.

The concentrations of PCBs and dioxin in blood and breast milk samples are not yet determined. We will measure the major PCBs in blood samples and TEQ values in the breast milk samples, considering the chemical measurement protocols used in a Dutch cohort[3]. Essential elements and heavy metals including selenium and mercury will be measured in blood, cord and placenta samples.

The most PCB cohort studies have used BSID as the psychodevelopmental test. Since BSID is not yet standardized in Japan, no Japanese age-norms are available. Therefore, the raw scores were used for the analysis. In addition, KSPD is a established standard neuropsychological test in Japan. We decided to perform BSID and KSPD at the same time, and to compare the results from both tests. FTII is a visual recognition memory test based on the infant's ability to recognize facial pictures, and has been reported to be associated with prenatal PCB levels in a PCB cohort[4]. This test is suggested to be able to predict the later intelligence ability of children. In our protocol, BSID and KSPD will be used when the children are at 18 months old, and a test battery including an intelligence test such as the Kaufman Assessment Battery for Children will be used when they are at 42 months old.

Although our cohort study is not yet completed, the sample size will be more than 400 mother-infant pairs. This study will be the first longitudinal prospective cohort designed to clarify the effects of the perinatal PCBs and dioxin exposures to the neurodevelopment of Japanese children. We will welcome any suggestion and comment to our study protocol.

Acknowledgments

We thank all families who participated in this study. We also thank the medical staffs for their support to perform the informed consent and cord blood collections. This research was funded by the Health Sciences Research Grants on Environmental Health from Japanese Ministry of Health, Labour and Welfare.

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