

Preliminary results on prenatal and lactational exposure to PCBs and DDE and pubertal growth and development

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Perinatal exposure to certain chemicals can have profound impacts on later development of the reproductive system; the classic example is diethylstilbestrol. Whether exposure to low levels of ubiquitous environmental contaminants would have similar effects is not known.

We have been following since birth a cohort of approximately 900 children born between 1978 and 1982 in three sites in the state of North Carolina, USA, to determine effects of prenatal and lactational exposure to PCBs and DDE ¹⁻⁶. These children are from the general population and have no special exposure.

There are suggestions that perinatal exposures to PCBs and DDE could affect pubertal development. Members of the DDT family have been shown to have estrogenic and anti-androgenic properties ⁷⁻⁸. In animal studies, perinatal exposure to PCBs ⁹⁻¹⁰ or structurally related compounds (PBBs ¹¹, dioxins ¹²⁻¹⁵) has permanent effects on various aspects of pubertal development and hormonal status. Shortened penis length has been reported in boys exposed transplacentally to heat-degraded PCBs in the Yucheng poisoning in Taiwan ¹⁶. We are examining pubertal growth and development in the NC cohort to see whether low-level exposures have discernible effects.

Samples of breast milk were collected throughout lactation, as were maternal blood at birth and six weeks, cord blood, and placenta. These samples were analyzed for total PCBs and DDE. Questionnaire information on lactation was collected repeatedly throughout lactation. This allows estimation of both transplacental exposure and exposure through lactation.

Starting in 1993, families have been sent annual questionnaires asking the child's height, weight, and onset of menstruation (if female). We also ask about Tanner stages of pubertal development;

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we use a modification of the Tanner scale in which line drawings of secondary sexual characteristics appear as an ordered progression. Either the parents, the child, or both may send information. Children are followed until they reach the final stage on both Tanner scales and, if female, have begun menstruation.

We have information on 600 children. The study is ongoing; 180 children are still being followed in the study as of March 1996. Preliminary analysis of female pubertal stage in relation to prenatal PCB exposure reveals no dose-related patterns. Other preliminary results will be presented at the meeting.

References:

- 1) Rogan W.J., B.C. Gladen, J.D. McKinney, N. Carreras, P. Hardy, J. Thullen, J. Tingelstad and M. Tully (1986): Polychlorinated biphenyls (PCBs) and dichlorodiphenyl dichloroethene (DDE) in human milk: Effects of maternal factors and previous lactation. *American Journal of Public Health* 76, 172-177.
- 2) Rogan W.J., B.C. Gladen, J.D. McKinney, N. Carreras, P. Hardy, J. Thullen, J. Tingelstad and M. Tully (1986): Neonatal effects of transplacental exposure to PCBs and DDE. *Journal of Pediatrics* 109, 335-341.
- 3) Rogan W.J., B.C. Gladen, J.D. McKinney, N. Carreras, P. Hardy, J. Thullen, J. Tingelstad and M. Tully (1987): Polychlorinated biphenyls (PCBs) and dichlorodiphenyl dichloroethene (DDE) in human milk: Effects on growth, morbidity, and duration of lactation. *American Journal of Public Health* 77, 1294-1297.
- 4) Gladen B.C., W.J. Rogan, P. Hardy, J. Thullen, J. Tingelstad and M. Tully (1988): Development after exposure to polychlorinated biphenyls and dichlorodiphenyl dichloroethene transplacentally and through human milk. *Journal of Pediatrics* 113, 991-995.
- 5) Rogan W.J. and B.C. Gladen (1991): PCBs, DDE, and child development at 18 and 24 months. *Annals of Epidemiology* 1, 407-413.
- 6) Gladen B.C. and W.J. Rogan (1991): Effects of perinatal polychlorinated biphenyls and dichlorodiphenyl dichloroethene on later development. *Journal of Pediatrics* 119, 58-63.
- 7) Kupfer D. and W.H. Bulger (1980): Estrogenic properties of DDT and its analogs. In: McLachlan J., ed. *Estrogens in the Environment*. Elsevier North Holland, 239-263.
- 8) Kelce W.R., C.R. Stone, S.C. Laws, L.E. Gray, J.A. Kemppainen and E.M. Wilson (1995): Persistent DDT metabolite p,p'-DDE is a potent androgen receptor antagonist. *Nature*; 375, 581-585.
- 9) Gellert R.J (1978): Uterotrophic activity of polychlorinated biphenyls (PCB) and induction of precocious reproductive aging in neonatally treated female rats. *Environmental Research*

16,123-130.

10) Sager D.B. and D.M. Girard (1994): Long-term effects on reproductive parameters in female rats after translactational exposure to PCBs. *Environmental Research* 66, 52-76.

11) McCormack K.M., W.E. Braselton, Jr., V.L. Sanger and J.B. Hook (1980): Residual effects of polybrominated biphenyls following perinatal exposure in rats. *Toxicology and Applied Pharmacology* 53, 108-115.

12) Mably, T.A., R.W. Moore and R.E. Peterson (1992): In utero and lactational exposure of male rats to 2,3,7,8-tetrachlorodibenzo-p-dioxin: 1. Effects on androgenic status. *Toxicology and Applied Pharmacology* 114, 97-107.

13) Mably T.A., R.W. Moore, R.W. Goy and R.E. Peterson (1992): In utero and lactational exposure of male rats to 2,3,7,8-tetrachlorodibenzo-p-dioxin: 2. Effects on sexual behavior and the regulation of luteinizing hormone secretion in adulthood. *Toxicology and Applied Pharmacology* 114, 108-117.

14) Mably T.A., D.L. Bjerke, R.W. Moore, A. Gendron-Fitzpatrick and R.E. Peterson (1992): In utero and lactational exposure of male rats to 2,3,7,8-tetrachlorodibenzo-p-dioxin: 3. Effects on spermatogenesis and reproductive capability. *Toxicology and Applied Pharmacology* 114, 118-126.

15) Gray L.E. Jr., W.R. Kelce, E. Monosson, J.S. Ostby, L.S. Birnbaum (1995): Exposure to TCDD during development permanently alters reproductive function in male Long Evans rats and hamsters: reduced ejaculated and epididymal sperm numbers and sex accessory gland weights in offspring with normal androgenic status. *Toxicology and Applied Pharmacology* 131, 108-118.

16) Guo Y.L., T.J. Lai, S.H. Ju, Y.C. Chen, C.C. Hsu (1993): Sexual developments and biological findings in Yucheng children. In: Fielder H., H. Frank, O. Hutzinger, W. Parzefall, A. Riss and S. Safe, eds. *Organohalogen Compounds*. Vienna: Federal Environmental Agency, 14, 253-238.