MILK TRANSFER OF COPLANAR PCB CONGENERS IN MICE

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Polychlorinated biphenyls (PCBs) are widespread environmental contaminants that give rise to harmful effects on several environmental levels. In man, PCBs have caused several cases of toxicity, *e.g.* by ingestion of PCB-contaminated rice oil in Japan 1968 and in Taiwan 1979. At both these occations, children to exposed women exhibited a number of symptoms including small birth weight, and skin and CNS disorders. The PCB effects on the developing nervous system have recently been reviewed by Tilson and coworkers[1] .

PCBs cross the placenta, and are detected in 90% of human milk samples in industrialized countries[2]; thus both the fetus and nursing infants are exposed[3]. It is generally concidered that the major part of the PCB transfer during the perinatal period is an effect of lactation, both in humans[4], and in experimental animals[5]. In mice, lactating mothers essentially eliminated their body burden of 2,2,4,4',5,5'-hexachlorobiphenyl during a lactation period[6]. Recent studies suggest however that the effects of transplacentally transferred PCBs, at least on the development of CNS, are more severe than upon breast milk transfer, in spite of a much higher PCB accumulation in the latter case[7,8].

In an ongoing project, the toxic Ah-receptor-binding PCB congeners 3,3'.4,4'-tetra-, 3,3',4,4',5-penta-, and 3,3',4,4',5,5'-hexachlorobiphenyl (I-77, I-126, I-169) are studied with regard to the situation during pregnancy and lactation. Of these congeners, I-77 has become of special interest because of its fetal accumulation properties[9]. In the present study the comparative breast milk transfer and accumulation in the offspring, of the congeners I-77 and I-126 are studied in C57BL and NMRI mice.

Methods

^{14}C-labelled 3,3',4,4'-tetra-(I-77), and 3,3',4,4',5-pentachlorobiphenyl (I-126) were given by Dr Åke Bergman, Wallenberg Laboratory, University of Stockholm, Sweden. NMRI and C57BL mice were purchased from Alab (Sollentuna, Sweden). The animals were kept at 22 °C, 12 hr light/12 hr dark and were given commercial pelleted food and tap water *ad libitum*.

The labelled I-77 and I-126 were dissolved in DMSO and injected i.v. [2.05 μmol (20-50μCi)/kg body wt.] as a single dose at day 11 postpartum. One day later the maternal blood was collected (orbital plexsus) in heparinized capillary tubes and the milk were collected by a milking device[10]. The pups were separated from the dams for 2 hr before milking to allow milk to accumulate in the glands. Dams were anesthetized with sodium pentobarbital (Mebumal) (15 mg/kg body wt.) and treated with oxytocin a few minutes before milking to allow milk secretion. Milk was collected again 4 days after injection (day 15 postpartum).There after dams and pups were sacrificed: whole blood, liver and adipose tissue were obtained from the dams and whole blood, liver and stomach from the pups. About 60-100 mg of organ tissues and 50-100 μl of serum and milk were dissolved in 1ml Soluene-350 (Packard) and radioactivity was measured by liquid scintillation.

Results and discussion

This study shows that I-77 and I-126 equivalents are transferred to neonatal mice *via* maternal milk during lactation. Regarding I-77, the highest concentration detected was found in neonatal serum, having higher level at 4 days after adminstration than had maternal serum at 1 or 4 days. Also in the liver, offspring had higher concentrations of I-77 equivalents than had the mother (Fig. 1A). The high serum offspring/mother ratio may be a result of repeated exposure by nursing and accumulation in the neonatal liver and/or lower rates of neonatal metabolism and excretion of I-77 equivalents. A lower tissue concentration in maternal and neonatal NMRI mice than in C57BL mice (data not shown) could be explained by the hypothesis that NMRI mothers have comparably higher metabolism and excretion capacity of I-77 equivalents (unpublished observation). This observation may also explain that fetal uptake was higher in C57BL than in NMRI mice (see abstract: Darnerud et al.). Milk fat content may also play a role for differences in the neonatal accumulation of PCBs (Jennes, 1974).

The other PCB congener, I-126, gave rise to very high concentration in maternal and neonatal liver, but also to a certain extent in maternal adipose tissue (Fig. 1B). The high lipophilicity of I-126 could explain the storage in adipose tissue and milk, whereas the high concentration in the liver could be related to induction of new I-126 binding sites *via* Ah-receptor mediated induction of cytchrome P-450[11,12]. The liver and adipose tissue accumulation could be the reason for the comparably high levels of I-126 in human milk[13] .

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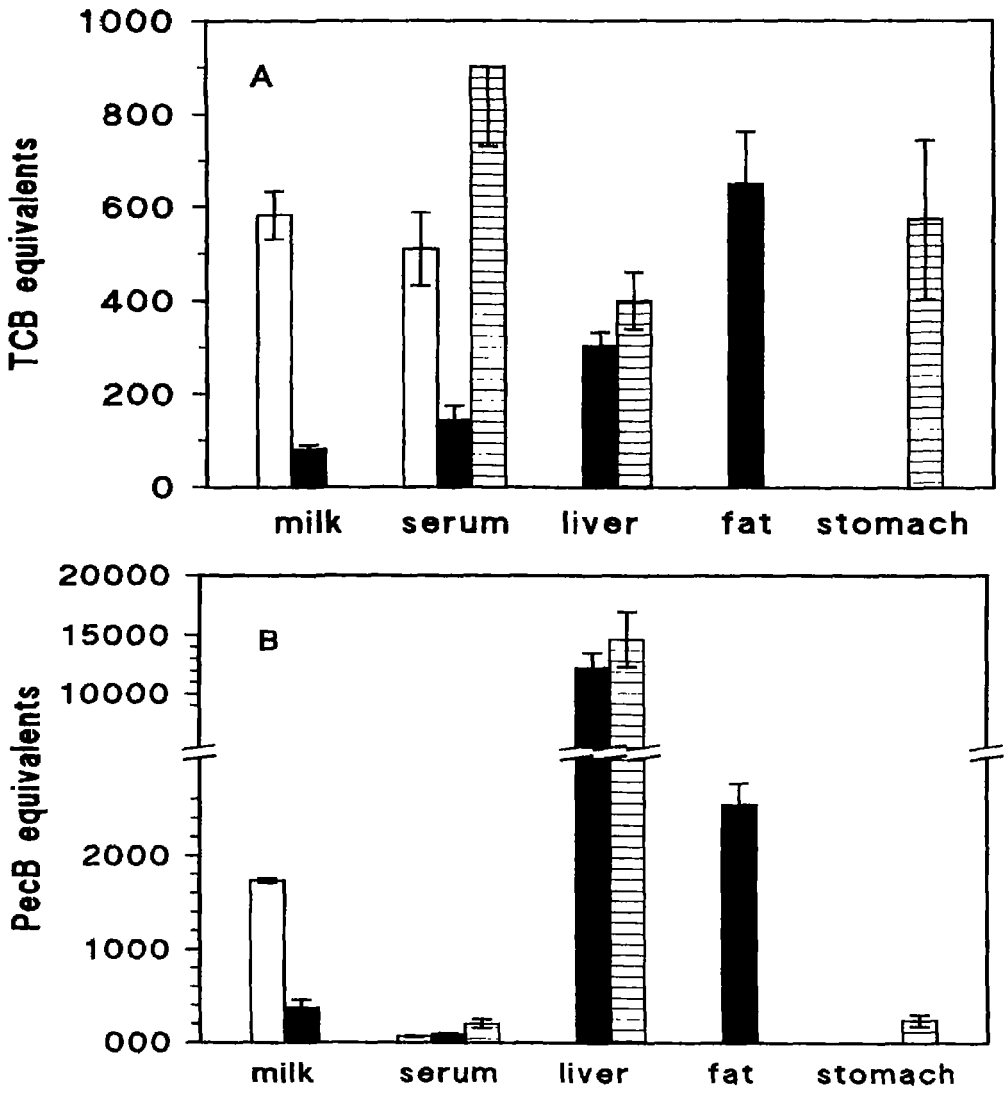
Fig.1 :Distribution of ^{14}C-I-77 (=TCB) (A) and ^{14}C-I-126 (=PeCB) ((B) equivalents in breast and certain tissues of maternal and neonatal C57BL mice.



dose = 2.05 umol/kg body wt.

Empty bars = Dams at day 12 postpartum , 1 day after ^{14}C-injection, n = 4.

Filled bars = Dams at day 15 postpartum , 4 days after ^{14}C-injection, n = 4.

Hatch bars = Pups at day 15 of age, n = 15-16.

PCB congener equivalents expressed as pmol/ml (milk; serum) or g (tissue).