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Teratogen Update: Polychlorinated Biphenyls

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Polychlorinated biphenyls, synthetic hydrocarbon compounds once used as hydraulic fluids and lubricants in electrical transformers and capacitors, are among the most ubiquitous and persistent environmental contaminants. Although banned in most Western nations since the 1970s, substantial residues of these compounds persist in air, water, soil, and sediment world wide (Swain, '83) and can be detected in biological tissue in most residents of industrialized countries (Jensen, '87). Because they are hydrophobic and lipophilic, PCBs become increasingly concentrated as they are transferred through the aquatic food chain. Consumption of fatty sports fish from contaminated bodies of water, such as Lake Michigan, provides a major source of human exposure. Transplacental passage has been documented in humans (Kodama and Ota, '77; J. Jacobson et al., '84a), although relatively small quantities reach the fetus. Much larger quantities are transferred postnatally via maternal milk due to its high lipid content (Masuda et al., '78; J. Jacobson et al., '89). Polychlorinated dibenzofurans (PCDFs) and dibenzo-p-dioxins (PCDDs) are highly toxic by-products in the manufacture and combustion of PCBs that accumulate in biological tissue and the environment in a manner similar to the parent compounds, albeit at considerably lower levels (Kubiak et al., '89).

The PCBs used for industrial purposes were complex mixtures of various congeners, each with its own unique molecular structure and potentially different toxicological effects. The non-*ortho* coplanar PCB congeners, which are structural analogs of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD; "dioxin"), are known to be highly toxic in several organ systems (Safe, '90), but little is known about the relative neurotoxicity of the PCB congeners. Two dioxin-like congeners (Nos. 77 and 126) have been shown to be neurotoxic in experiments with laboratory animals (Tilson et al., '79; Eriksson et al., '91; Holene et al., '95). However, certain di-*ortho*-substituted congeners, such as No. 17, lead to reduced dopamine levels in the caudate nucleus, hypothalamus, and substantia nigra in laboratory monkeys (Seegal et al., '90), suggesting that neurodevelopmental disruption may also be caused by nondioxin-like congeners.

STUDIES OF TERATOGENIC EFFECTS

Initial evidence of acute PCB toxicity came from two industrial incidents—one in Japan in 1968; the other in Taiwan in 1979—in which cooking oil (*Yusho* in Japanese; *Yu-cheng* in Taiwanese) was accidentally contaminated with large quantities of PCBs and PCDFs. Adults who ingested the contaminated oil developed chloracne, dark brown pigmentation of the skin and lips, swollen eyelids, and swelling and pain in the joints (Higuchi, '76; Hsu et al., '85). Liver disease and peripheral nervous system neuropathy were also reported (Rogan and Gladen, '92). Infants born to women who had ingested large quantities of the contaminated rice oil exhibited dark brown pigmentation of the skin and nails, early eruption of teeth, and swollen eyelids and gums (Higuchi, '76; Wong and Hwang, '81) (Fig. 1). In Taiwan, one-fifth of the infants with hyperpigmentation died (Hsu et al., '85). In a clinical follow-up study, exposed Japanese children were described as dull, apathetic, and hypotonic, with IQs in the mental retardation range (Harada, '76). The toxic effects of both the *Yusho* and *Yu-cheng* exposures are believed to be attributable primarily to PCDF congeners, which were present at unusually high levels in the contaminated oil and are structurally and toxicologically similar to the coplanar PCBs.

Effects of chronic prenatal PCB exposure from environmental sources have been examined most extensively in two prospective longitudinal studies of children recruited at birth at the beginning of the 1980s. The Michigan cohort was selected to overrepresent the offspring of women who had eaten relatively large quantities of PCB-contaminated Lake Michigan fish (S. Jacobson et al., '83; J. Jacobson et al., '84b); the North Carolina cohort was drawn from the general population (Rogan et al., '86a). Additional infant data have recently become available from prospective studies initiated during the early 1990s of Lake Ontario fish-eating families in Oswego, New York, (Lonky et al., '96) and the general population in two cities in the Netherlands (Huisman et al., '95a). Prospective longitudinal data have also been collected in two case-control studies of *Yu-cheng*-exposed children in Taiwan (Rogan et al., '88; Ko et al., '94). Because subjects cannot be randomly assigned to predetermined levels of exposure in human studies, a large number of control variables are assessed and controlled statistically by multivariate analysis. These control variables include socioeconomic status, parental education, prenatal exposure to alcohol and smoking, perinatal medical complications, and quality of intellectual stimulation provided by the parents. The assessment of control variables is often as

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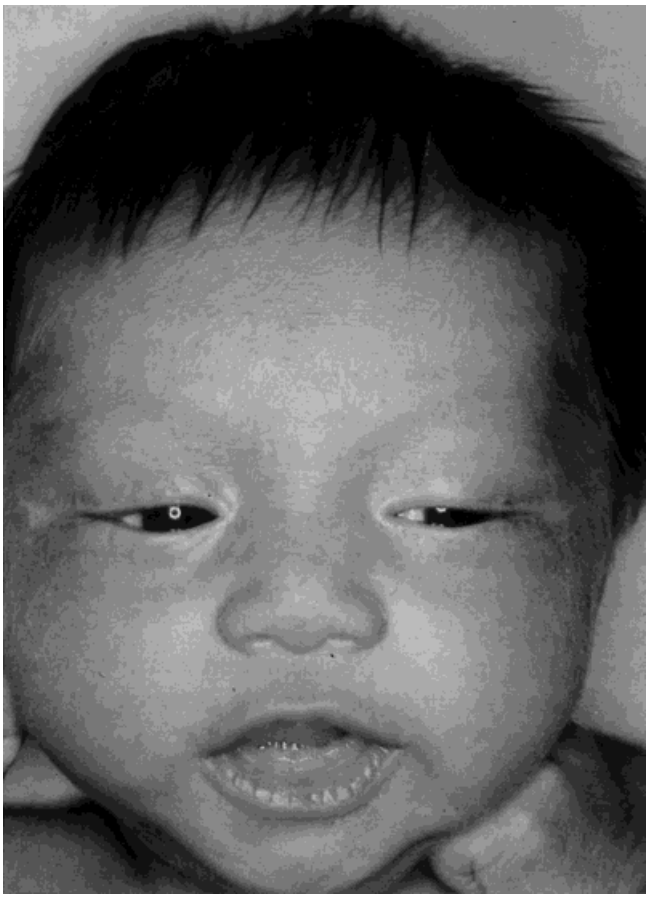

Fig. 1. Hyperpigmentation and acne form eruptions on the face of a *Yu-cheng*-exposed infant. From Wong and Hwang, '81.

time intensive in these studies as the evaluation of exposure and outcome. For example, the assessment of parental intellectual stimulation may involve administration of a 20-min parental vocabulary or nonverbal IQ test as well as the HOME Inventory (Caldwell and Bradley, '79), a 20-min semistructured interview that also entails informal observation of parent–child interaction.

Umbilical cord serum and maternal serum and milk samples were collected in all four studies of chronic, environmental exposure. Because of the long half-life of these compounds in biological tissue, cord serum samples provide a biological record of exposure in utero. In Michigan and North Carolina, the biological samples were analyzed by packed column gas chromatography based on the Webb and McCall ('73) method. Although Webb-McCall was state-of-the-art at the time, it provides no information regarding levels of individual PCB congeners. In more recent studies, analyses have been based on capillary column gas chromatography.

In the three studies that have reported biological levels to date, cord serum PCB levels were generally low (J. Jacobson et al., '84a; Rogan et al., '86a; Koopman-Esseboom et al., '94a), which is not surprising given that PCBs are lipophilic and cord blood is lean. In Michigan, two-thirds of the cord serum samples were below the laboratory detection limit of 3 ng/ml, which rendered the reliability of many of the reported values uncertain. From a statistical point of view, the limited number of reliable cord serum values increased the risk of Type II error, making it more difficult to detect effects in the data. By contrast, none of the maternal milk PCB levels were below the laboratory detection limit. In North Carolina, where 88% of the cord serum samples were below the laboratory detection limit, prenatal exposure was estimated on the basis of two maternal serum samples and series of maternal milk samples obtained periodically while the infant was being breastfed (McKinney et al., '84). Since PCBs are in equilibrium in fat deposits throughout the body, maternal serum and milk PCB levels indicate maternal body burden, which determines the level of PCBs transmitted prenatally across placenta. Although maternal serum and milk provide a less direct measure of fetal exposure than cord serum, PCB accumulation is higher and, therefore, easier to detect.

PHYSICAL GROWTH

Prenatal exposure to PCBs was associated with reduced birthweight in the Michigan cohort (Fein et al., '84), in offspring of occupationally exposed women in the United States (Taylor et al., '84) and Japan (Hara, '85) and in female infants from the general Japanese population (Yamashita and Hayashi, '85). Reduced birthweight has also been reported in laboratory studies with rhesus monkeys (Allen et al., '80), rats (Overmann et al., '87; Bernhoft et al., '94), and mice (Chou et al., '79). The birthweight deficit reported in Michigan was small (200–250 g) and similar in magnitude to that associated with smoking during pregnancy (U.S. Public Health Service, '79). However, whereas the offspring of smokers tend to catch up during the early postpartum months (Russell et al., '68; J. Jacobson et al., '94), intrauterine PCB exposure continued to be associated with smaller size at 5 months (Jacobson and Jacobson, '88) and slightly lower weight at 4 years of age (Jacobson et al., '90b). Persistent growth deficits have also been reported in laboratory studies of rat pups (Brezner et al., '84; Bernhoft et al., '94), in the *Yu-cheng*-exposed children (Rogan et al., '88), and in the female Japanese children noted above to have been smaller at birth (Yamashita and Hayashi, '85).

NEONATAL BEHAVIORAL FUNCTION

Neonatal behavioral deficits have been reported in all four studies of chronic environmental PCB exposure. In Michigan and Oswego, New York, higher levels of maternal PCB-contaminated fish consumption were associated with poorer autonomic regulation, more abnormally weak reflexes, and decreased responsiveness to external stimulation (J. Jacobson et al., '84b;

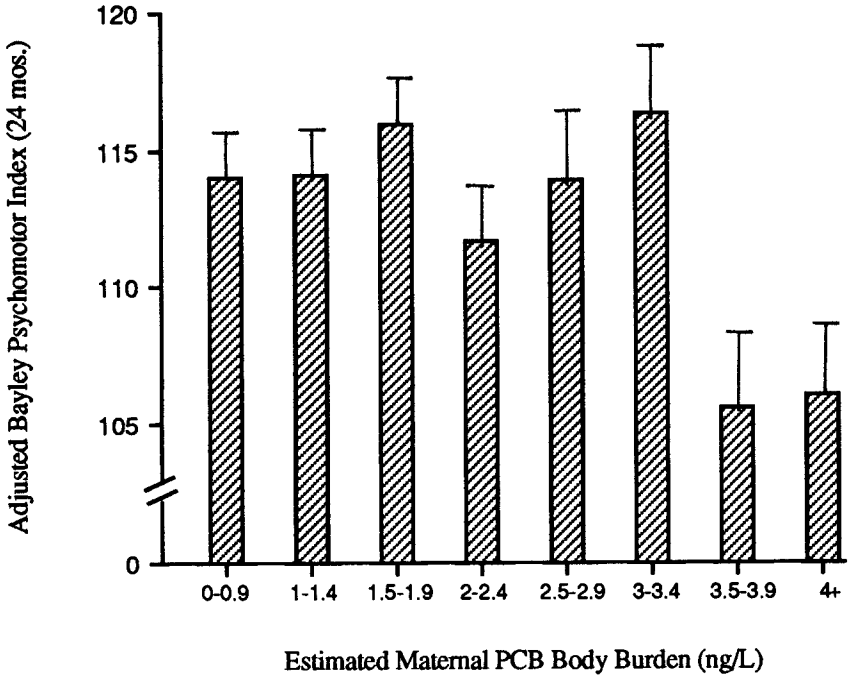

Fig. 2. Relation of prenatal PCB exposure (estimated from maternal body burden) to Bayley Psychomotor Scale scores at 24 months (adjusted for gender, race, number of older siblings, age at examination, examiner, and maternal age, education, occupational status, smoking, and usual level of alcohol consumption) from the North Carolina study (Rogan and Gladen, '91). Error bars indicate standard errors. The two highest exposed groups differed from the others in the sample at $P < 0.05$ based on analysis of variance for heteogeneity of groups.

Lonky et al., '96). In North Carolina, prenatal PCB exposure was related to abnormally weak reflexes and depressed tonicity and activity level (Rogan et al., '86b). In the Netherlands (Huisman et al., '95a) prenatal and early lactational exposure to PCBs was associated with hypotonia and reduced neurological optimality (Touwen et al., '80) at 2 weeks postpartum.

COGNITIVE AND MOTOR DEVELOPMENT DURING INFANCY AND EARLY CHILDHOOD

In North Carolina, prenatal PCB exposure was associated with poorer gross motor function on the Bayley Scales, the most widely used standardized test of infant development, at 6, 12, and 24 months (Gladen et al., '88; Rogan and Gladen, '91). Dose-response analyses indicated that these deficits were seen only in the highest exposed children—those whose mothers' milk PCB levels exceeded 1.75 µg/g (on a lipid basis, adjusted by dividing by 2 as recommended by Jensen, '87) (Fig. 2). Prenatal PCB exposure was also linked to poorer gross motor function in a neurological assessment in the Netherlands at 18 months (Huisman et al., '95b). No effects were seen on the Bayley Scales in Michigan, possibly because they were administered at 5 months, before the emergence of the independent sitting, standing, and walking assessed at the later ages (Jacobson and Jacobson, '96b). Developmental delay was seen on both the Mental and Psychomotor Development Indices of the Bayley at the higher levels of exposure in Taiwan (Yu et al., '91).

In Michigan higher cord serum PCB level was associated with poorer performance on the Fagan Test of Infant Intelligence (FTII; S. Jacobson et al., '85). In the FTII (Fagan and Singer, '83), the infant is initially shown two identical target photos, one of which is then presented together with a novel stimulus. If the infant spends more time looking at the novel target, it can be inferred that certain fundamental aspects of cognitive processing are intact, that is, that s/he has been able to encode the original stimulus, retrieve it from memory, and discriminate it from the new one. In contrast to the Bayley, whose predictive validity for childhood cognitive functioning is poor probably because it confounds sensorimotor and cognitive function, the FTII, which focuses more narrowly on memory and attention, is moderately predictive of childhood IQ (McCall and Carriger, '93). Cord serum PCB level was related to poorer FTII score in a dose-dependent fashion, with the highest exposed infants showing essentially no preference for the novel stimulus (S. Jacobson et al., '85) (Fig. 3). In the early 1990s, Ko et al. ('94) recruited a new cohort of *Yu-cheng*-exposed infants and matched controls. Their study provided the first confirmation of the association between prenatal exposure and poorer recognition memory on the FTII (S. Jacobson et al., '94).

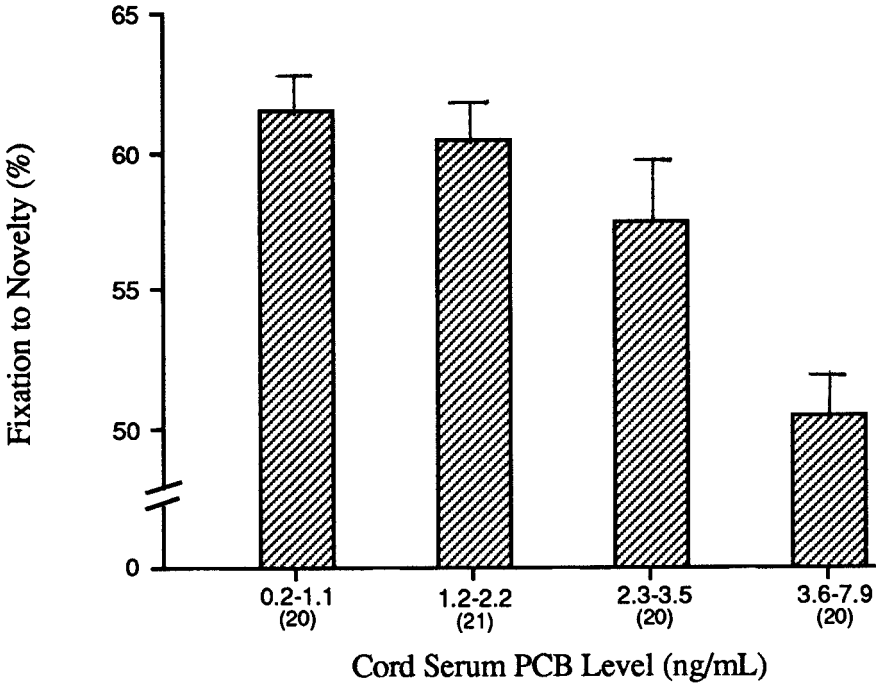

Fig. 3. Relation of cord serum PCB level to fixation to novelty on the Fagan Test of Infant Intelligence (adjusted for socioeconomic status, maternal age, and parity) from the Michigan study (S. Jacobson et al., '85). Error bars indicate standard errors. The highest exposed group differed from each of the two lowest exposed groups at $P < 0.05$, one tail, based on Duncan's multiple range test. Number of children in each group is given in parentheses.

At age 4 years in Michigan, higher cord serum PCB level was associated with poorer performance on the Verbal and Memory Scales from the McCarthy Scales of Children's Abilities, an IQ-type test for preschool age children (J. Jacobson et al., '90a). The higher exposed Michigan children also made more errors on a computer test of memory for pictures and processed information more slowly on a timed test of visual discrimination (J. Jacobson et al., '92). Dose-response analyses indicated that cognitive impairment was seen most consistently in the most highly exposed children; that is, those whose mothers' milk PCB levels exceeded 1.25 μg/g (Jacobson and Jacobson, '96b). The *Yu-cheng*-exposed children studied by Rogan et al. ('88) also performed more poorly on standardized tests of intellectual function at ages 4–7 years (Chen et al., '92).

Not all the effects seen in the Michigan and Taiwan children were confirmed in the general population samples studied in North Carolina and the Netherlands. Although PCB exposure was associated with decreased neurological optimality in the Netherlands at the two ages tested, the Dutch researchers failed to detect deficits on the 7-month Bayley Scales or the FTII (Koopman-Esseboom, '95), and the 4-year short-term memory deficits found in Michigan were not seen in North Carolina (Gladen and Rogan, '91). The exposure levels in the general population North Carolina and Netherlands samples may have been lower than in the fish-eating Michigan mothers; comparison is difficult due to between-study differences in analytic methodologies. Differences in the effects observed may also be attributable to local differences in the relative proportions of specific PCB congeners, which vary considerably in toxicity but could not be assessed individually by the analytic methodologies available during the early 1980's.

In addition, infants of fish-eating mothers may be exposed to heavier doses of PCBs in utero. Whereas most mothers in the general population in the United States and the Netherlands accumulate these contaminants in small daily increments from dairy and other food products, Humphrey ('88) has shown that a single contaminated Lake Michigan fishmeal can cause a transient increase in PCB serum level ranging from 230% to 500% (Fig. 4). This increase peaks within 10 hr and declines gradually over a 7-day period as the PCBs are partitioned into body fat. Experimental research on prenatal exposure to alcohol has demonstrated that a given quantity of alcohol ingested over a period of a few hours causes markedly higher blood alcohol concentrations and greater neuronal and behavioral impairment than the same quantity ingested gradually over several days (Bronthius and West, '90; Goodlett et al., '87). Thus, a fetus exposed to a series of contaminated fish meals may be subjected to much heavier doses than an infant with a comparable cord serum PCB level whose mother has ingested PCBs gradually over a period of several years.

The persistent effects on cognitive function seen in Michigan and Taiwan are consistent with learning deficits found in PCB-exposed laboratory animals. Com-

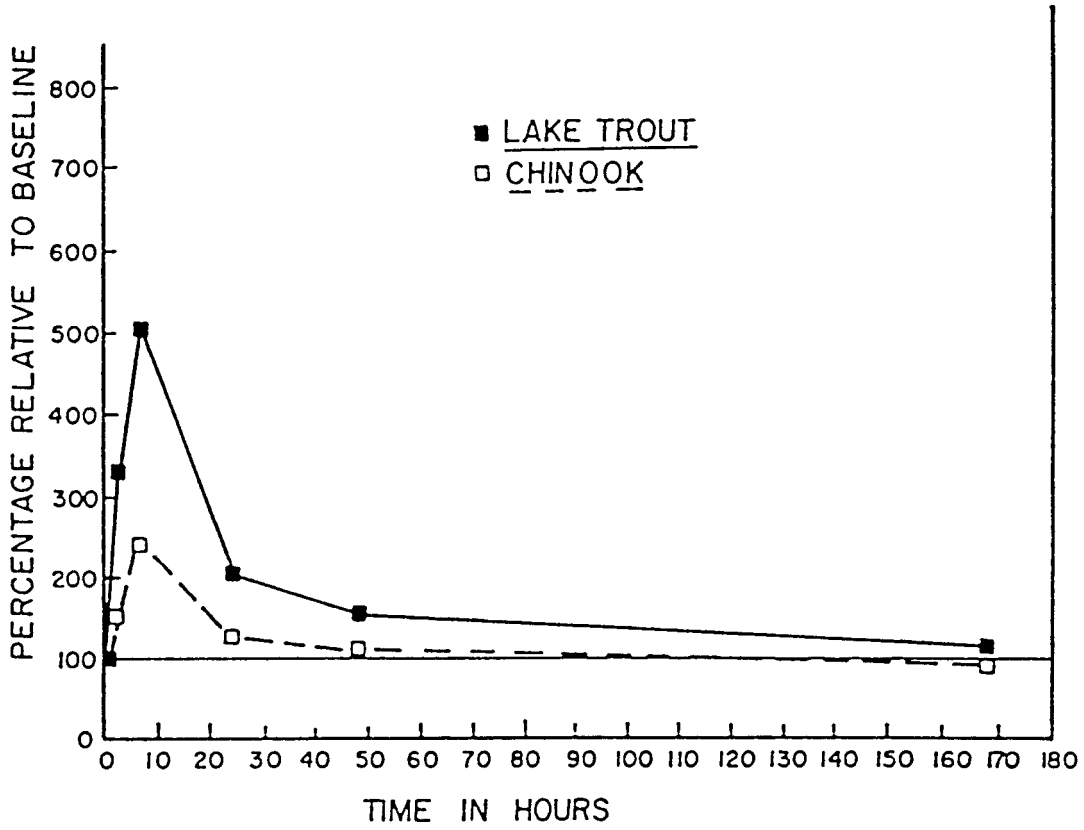

Fig. 4. Median concentration of the chromatographic elution peaks of PCBs in human serum as a function of time since ingestion of a PCB-contaminated fish meal. (From Humphrey, '88.)

bined pre- and postnatal exposure to industrial PCB mixtures has been found to impair discrimination reversal learning in monkeys (Bowman et al., '78; Schantz et al., '89), active avoidance learning in mice (Strom et al., '81) and rats (Pantaleoni et al., '88), and maze learning in rats (Shiota, '76). In studies of specific congeners, prenatal exposure to No. 77, a non-*ortho* congener, led to poorer active avoidance learning in mice (Tilson et al., '79), and perinatal exposure to either No. 126, a non-*ortho*, or No. 118, a mono-*ortho* congener, led to impaired visual discrimination learning in rats (Holene et al., '95). When tested in a delayed spatial alternation paradigm, monkeys exposed to Aroclor 1254, a PCB mixture, showed a pattern of perseverative attentional errors characteristic of monkeys with lesions in the dorsolateral prefrontal cortex (Levin et al., '88, '92). The frontal lobes and their associated subcortical structures are believed to be critically important for executive function, the component of attention involving the ability to organize and plan complex behavioral responses and modify them in response to feedback (Pennington et al., '95).

ACTIVITY LEVEL

In utero PCB exposure was associated with increased motor activity during open field testing in mice (Tilson et al., '79; Storm et al., '81), male rats (Shiota, '76; Holene et al., '95), and rhesus monkeys (Bowman et al., '81). However, one group of monkeys hyperactive at 12 months of age was found to be hypoactive relative to controls at 44 months (Bowman and Heironimus, '81). Hypoactivity was also reported in two studies of rat pups receiving only postnatal exposure (Koja et al., '79; Pantaleoni et al., '88) and in one study of prenatally exposed rats in which testing was performed just prior to weaning (Pantaleoni et al., '88). Thus, prenatally exposed animals are hyperactive relative to controls, whereas postnatal PCB exposure appears to be associated with a reduction in activity level.

North Carolina infants exposed prenatally were hypoactive and hypotonic during newborn behavioral testing (Rogan et al., '86b); exposed Michigan newborns were less readily aroused by the testing procedure (Jacobson et al., '84b). Higher serum PCB levels during childhood were associated with reduced activity level in the Michigan fisheater cohort (J. Jacobson et al., '90b) and in a sample of 6- to 12-year-old children from Michigan families who had lived on PCB- and polybrominated biphenyl-contaminated farms (Schantz et al., '90). Although statistically significant, the magnitude of the childhood activity deficit was small. Because breastfeeding was the principal determinant of childhood

PCB body burden in both cohorts (J. Jacobson et al., '89; Schantz et al., '94), lactation exposure appears likely to be responsible for this effect. *Yu-cheng*-exposed children, who were generally not breast-fed and, therefore, received little postnatal exposure, were rated more active than matched controls by parents and teachers (Chen et al., '94), whereas *Yusho*-exposed children, whose breast-feeding history was not documented, were described clinically as hypoactive (Harada, '76). The data are, therefore, consistent with the hypothesis that postnatal PCB exposure is associated with reduced activity level in both animals and humans.

TIMING OF EXPOSURE

Much larger quantities of PCBs are transferred postnatally via lactation than *in utero*. In the Michigan study, for example, many children who breast-fed for 1 year or longer accumulated PCB body burdens equivalent to those of their mothers (J. Jacobson et al., '89). Nevertheless, except for the small reduction in activity level seen in the Michigan studies (Jacobson et al., '90b; Schantz et al., '90), there is little evidence of impairment as a consequence of breast-feeding exposure. All the deficits in physical growth and cognitive and motor function reported to date were seen only in relation to transplacental PCB exposure (S. Jacobson et al., '85; Gladen et al., '88; J. Jacobson et al., '90a, '90b, '92; Rogan and Gladen, '91; Ko et al., '94). Although early lactation exposure did appear to contribute to greater 2-week neurological nonoptimality in the Netherlands study (Huisman et al., '95a), even in that study nonoptimality later in infancy was related only to prenatal exposure (Huisman et al., '95b). In the sole animal study to use cross-fostering to attempt to discriminate the effects of pre- versus postnatal exposure, Lilienthal and Winneke ('91) found poorer active avoidance learning and visual discrimination retention in rats exposed to PCBs prenatally but not in those lacking prenatal exposure who were nursed by PCB-exposed dams.

COGNITIVE FUNCTION AT SCHOOL AGE

To date only the Michigan study has assessed cognitive function in school age children known to be exposed prenatally to PCBs at environmental levels (Jacobson and Jacobson, '96a). To improve reliability and sensitivity in the assessment of fetal PCB exposure, a new composite measure was constructed, similar to the one used in the North Carolina study (Rogan et al., '86a). This composite measure is based on the premise that the average of three moderately reliable interrelated measures of fetal exposure is likely to be more reliable and, therefore, more sensitive than any single measure examined alone (Nunnally, '78). Cord serum and maternal serum and milk values were averaged together (after conversion to *z*-scores); serum values were included only if they exceeded the detection limit (Jacobson and Jacobson, in press). The validity of the new composite measure was supported by the finding that it correlated more strongly than any of its components with maternal PCB-contaminated fish consumption. The greater sensitivity of this new measure was indicated in a reanalysis of the 4-year McCarthy Scale data, which showed that, whereas cord serum PCB level related significantly only to the Verbal and Memory Scales, the new composite was also associated with lower scores on the Quantitative Scale and GCI, the McCarthy Scales equivalent to overall IQ.

Prenatal PCB exposure was associated with significantly lower Full Scale and Verbal IQ scores at age 11 years (Jacobson and Jacobson, '96a). This effect was seen primarily in the most highly exposed children (Fig. 5), that is, those with prenatal exposures equivalent to at least 1.25 μg/g in maternal milk, 4.7 ng/ml in cord serum, or 9.7 ng/ml in maternal serum. The children exposed above this threshold averaged 6.2 points lower on Full-Scale IQ, after adjustment for potential confounding variables, and were more than three times as likely to perform poorly (>1 standard deviation below the mean) than the other children in the sample. The strongest effects were seen on IQ subtests relating to short-term memory, planning or executive function, verbal concept formation, and long-term memory. On an academic achievement test battery, prenatal exposure was associated primarily with poorer reading word comprehension. Expressed in terms of age-equivalent norms, the more highly exposed children lagged behind their peers on word comprehension by an average of 7.2 months. These findings are consistent with recent reports of reduced 11-year IQ scores and poorer school achievement in the *Yu-cheng*-exposed children (Guo, '95). As with the infant and preschool measures, postnatal PCB exposure was not related to poorer school-age cognitive outcome (Jacobson and Jacobson, '96a).

MECHANISMS OF ACTION

The mechanisms of action responsible for the effects of prenatal PCB exposure on early central nervous system (CNS) development are not well understood. A protein known as the aryl hydrocarbon (Ah) receptor has been identified in vitro as a mediator in the production of toxic compounds following exposure to TCDD and the structurally similar non-*ortho* coplanar PCBs (Safe, '90), but the role of the Ah receptor in PCB neurotoxicity has not been studied. Recently, considerable attention has been focused on the potential of PCBs to disrupt endocrine function. Several studies have provided evidence of endocrine disruption by PCBs and organochlorine pesticide contaminants in wildlife (Guillette et al., '94; Giesy et al., '94). Much of this research has focused on the estrogenic properties of these compounds, although other hormones can be affected as well. With regard to the CNS deficits associated with prenatal PCB exposure, thyroid hormone seems the most likely candidate. Thyroid hormone is necessary to stimulate neuronal and glial proliferation and differentiation during the late gestation and early postnatal periods (Porterfield and Hen-

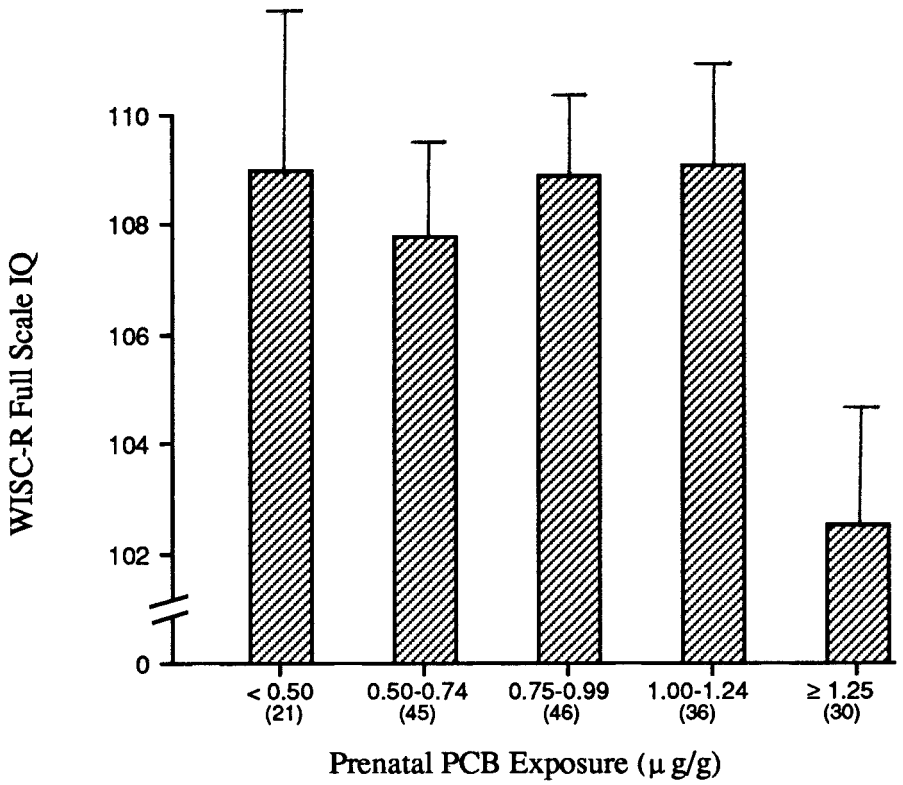

Fig. 5. Relation of prenatal PCB exposure (based the average of the cord serum and maternal serum and milk values) to 11-year IQ score (adjusted for socioeconomic status, maternal education and vocabulary score, and the HOME Inventory) from the Michigan study (Jacobson and Jacobson, '96a). Error bars indicate standard errors. The highest exposed group differed from each of the other four groups at $P < 0.05$, one tail, based on Duncan's multiple range test. Number of children in each group is given in parentheses.

TABLE 1. Evidence of effects of prenatal exposure to PCBs and related contaminants on fetal development

Compound	Human	Animal	Selected/references
Polychlorinated biphenyl (PCB) mixtures	+	+	Allen et al., '80 Bernhof et al., '84 Huisman et al., '95a; '95b J. Jacobson et al., '90a; '96 S. Jacobson et al., '85 S. Levin et al., '88 Pantaleoni et al., '88 Rogan et al., '86b
Nonplanar PCG congeners	0	+	Eriksson et al., '91 Holene et al., '95 Tilson et al., '79
Polychlorinated dibenzofurans (PCDFs)[1]	+	0	Chen et al., '92 Ko et al., '96 Rogan et al., '88
Polychlorinated dibenzodioxins (PCDDs)	0	0	

+, effects observed; 0, not tested.
[1]Effects of the Yucheng exposure are listed under PCDFs because it is generally assumed that the usually high levels of PCDFs in this exposure were the predominant source of neurotoxicity (Masuda et al., '82).

drich, '93), and a thyroid hormone deficiency during this period causes spasticity and mental retardation (Frost, '86). In utero PCB exposure has been linked to reduced fetal brain concentrations of thyroid hormones in prenatally exposed Dutch infants (Koopman-Esseboom et al., '94b), but these reductions are small relative to those found in cognitively impaired, thyroid deficient infants. Given the vulnerability of the developing brain, there are numerous alternative mechanisms through which prenatal PCB exposure may disrupt

fetal CNS development as well. Migratory cells and cells undergoing mitosis are particularly sensitive to toxic insult (Annau and Eccles, '86), the fetal blood–brain barrier is incomplete (Woodbury, '74), and the fetus lacks important drug-metabolizing detoxification capacities that are found postnatally (Dvorchek, '81).

CONCLUSIONS

Evidence of the teratogenicity of PCBs and related compounds is summarized in Table 1. The data reported to date are consistent with the hypothesis that prenatal exposure to these compounds can cause persistent changes in the developing brain that adversely affect cognitive function, at least through school age. It is important to emphasize, however, that none of the prospective studies has found an increased frequency of mental retardation. In the Michigan study, for example, only one child performed in the mentally retarded range, and none was in the mildly retarded ("borderline") range (Jacobson and Jacobson, '96a). Nevertheless, prenatal PCB exposure was associated with a substantial increase in the proportion of children at the lower end of the normal range, who would be expected to function more poorly in school. Since random assignment to exposure level is not possible in human studies, extensive efforts have been made to control for a broad range of potential confounding influences. Because it is never possible to control for all conceivable confounders, the animal experiments provide important corroborative evidence of a causal link between in utero exposure and neurobehavioral deficit, although the doses administered to the laboratory animals are several orders of magnitude greater than contemporary human environmental exposure (Tilson et al., '90).

In light of the evidence of PCB teratogenicity, many states routinely test sports fish for PCB concentrations and advise anglers that women of child-bearing age and children limit their consumption of certain fish species obtained from specified rivers and lakes. Because these compounds may also be present in other foods (e.g., fatty meats and dairy products) that are not routinely tested, however, it is not possible for an individual to restrict his/her PCB intake completely. Moreover, given the long half-life of these compounds in body tissue, restriction of intake during pregnancy may not be adequate to protect the fetus. Pregnant women can be reassured, however, that there is no evidence that exposure from breast-feeding poses any appreciable risk to the infant when the mother has been exposed at contemporary environmental levels.

It is important to emphasize that the developmental deficits associated with prenatal PCB exposure were generally limited to children with exposure levels in the top 3–5% of those measured in the general population sample studied in North Carolina (Rogan et al., '86b; Gladen and Rogan, '88) and the top 10–15% of the presumably more heavily exposed fisheater sample in Michigan (Jacobson and Jacobson, '96a, '96b). In light of the general decline in PCB levels in environmental samples since the early 1980s, future studies are not likely to detect similar deficits unless extensive efforts are made to include sufficient numbers of more heavily exposed children. Nevertheless, continued vigilance regarding these contaminants is warranted because the amount in use in older electrical equipment and in landfills exceeds the total quantity that has escaped into the environment to date (Tanabe, '88).

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