

REVIEW

Position Paper of the American Council on Science and Health: Public Health Concerns about Environmental Polychlorinated Biphenyls (PCBs)^{1,2}

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Polychlorinated biphenyls, or PCBs, were widely used in various industrial applications for their insulating and fire retardant properties. In the 1960s, PCBs were found in soil and water, and research confirmed that some PCB congeners degrade very slowly in the environment and can build up in the food chain. Two widespread poisoning episodes in Japan and Taiwan were initially attributed to the consumption of rice bran oil contaminated with PCBs. Although subsequent analysis suggested that toxic thermal degradation products of PCBs in the oil, rather than the PCBs, were responsible for the observed health effects, commercial production of PCBs in the United States was discontinued in 1979. Several regulatory and advisory agencies have categorized PCBs as animal carcinogens; however, studies of workers exposed to high doses of PCBs over long periods of time have not demonstrated an increased cancer risk. In fact, the only health effects that could be attributed to PCBs were skin and eye irritation. Recent studies of the possible effects of prenatal exposure to PCBs on neurodevelopment in infants and children have been criticized for methodological deficiencies. There is no conclusive evidence that PCB levels in the general population are causing intellectual deterioration in children exposed *in utero*. Some investigators have also suggested that PCBs and other chemicals in the environment can interfere with the body's endocrine system, leading to infertility, certain types of cancer, and other hormone-related disorders. Evidence for estrogenic effects of environmental PCBs remains weak and circumstantial. The following actions are recommended: development of innovative, cost-effective remediation techniques, particularly for sites that are difficult to remediate (e.g., river sediments); and scientifically based improvements to risk assessment, to reduce the considerable uncertainty associated with PCB exposure and health effects in humans. © 1997 Academic Press

EXECUTIVE SUMMARY

Polychlorinated biphenyls, or PCBs, are a family of more than 200 chemical compounds (congeners), each of which consists of two benzene rings and 1 to 10 chlorine atoms. They were widely used in a variety of industrial applications due to their insulating and fire retardant properties. Concern about the presence of PCBs in the environment began in the 1960s, when PCBs were found in soil and water. Research confirmed that some PCB congeners degrade very slowly in the environment and can build up in the food chain. In 1968, a widespread human poisoning episode in Western Japan (called "Yusho," or "oil disease") was at first attributed to the consumption of rice bran oil contaminated with PCBs. Although subsequent analysis indicated the presence of toxic thermal degradation products in the oil, which are now believed to have been responsible for the observed health effects, the Yusho incident and a similar incident in Taiwan ("Yu-Cheng") increased concern over the safety of PCBs. In the 1970s, commercial production of PCBs in the United States was restricted and ended in 1979.

PCBs do not cause acute health effects in animals, except at extremely high doses. However, they have been found to cause tumors in animals. Several regulatory and advisory agencies, including the U.S. Environmental Protection Agency (EPA) have determined that there is sufficient evidence to consider PCBs to be animal carcinogens. However, studies of workers exposed by inhalation and skin contact to high doses of PCBs over long periods of time have not demonstrated an increased risk of cancer. In fact, skin and eye irritation were the only health effects in the workers that could be attributed to PCBs.

In the Japan and Taiwan episodes mentioned above, consumption of PCB-contaminated rice bran oil resulted in a severe form of acne called chloracne, fatigue, nausea, and liver disorders. There was also an increase in liver cancer mortality in the Yusho incident and an increase in mortality from other liver diseases in the Yu-Cheng incident. The levels of PCB in the blood of workers exposed to PCBs exceeded those of the Yusho and Yu-Cheng victims, yet the extent of toxicity was far greater in the Yusho and Yu-Cheng victims. This is believed to be due to the presence in the rice bran oil of substances generated from the thermal breakdown of PCBs. These substances, furans (similar to dioxins) and quaterphenyls, are far more toxic than PCBs.

Studies of people who ate PCB-contaminated fish found that, while the quantity of fish consumed was correlated with PCB blood levels, there were no significant health differences between those who consumed a lot of fish and those with lower exposures. A 1996 study suggested that prenatal exposure to PCBs from maternal ingestion of contaminated fish is associated with neurodevelopmental effects in infants and children. However, this is inconsistent with studies that have found no relationship between maternal PCB exposure and infant birth weight or head circumference. Problems with study methodology, specifically, exposure assessment and selection of the control (comparison) group, further limit the interpretation of the 1996 study results. Furthermore, as the concentrations of PCBs in the maternal blood were only slightly greater than in the blood of subjects who did not report eating fish (and were within the range of PCB blood concentrations for North America), we should be witnessing a widespread phenomenon throughout North America if PCBs could indeed cause intellectual impairment in children. There is no evidence of widespread intellectual impairment among children; thus, warning parents is not warranted at this time.

It has been suggested that chemicals such as PCBs in the environment can mimic the body's natural hormones (e.g., estrogen) and that this "endocrine (hormone) disruption" can lead to infertility, certain types of cancer, and other hormone-related disorders. However, the evidence for the estrogenic effects of environmental PCBs—on either wildlife or humans—remains weak and circumstantial, and premature conclusions have been drawn based upon inadequate and incomplete evidence. Numerous researchers have characterized the

hypothesis that environmental estrogens cause increased breast cancer or male reproductive problems as unproven and implausible.

In summary, there is no conclusive evidence that background PCB levels in the general population, or even the very high levels to which some occupational groups were exposed, have resulted in acute effects, increased cancer risk, "endocrine disruption," or widespread intellectual deterioration in children exposed to PCBs *in utero*. In fact, even those effects noted in PCB-exposed populations, e.g., chloracne, cannot be definitively linked to PCBs because of simultaneous exposure to other, known toxic agents, such as furans and quaterphenyls.

It is important to recognize that commercial and environmental PCBs consist of mixtures of individual PCB congeners. These congeners vary in their degree of toxicity, and the toxicity of any mixture is dependent upon the toxicity of the individual congeners. Laboratory studies of PCBs are, for the most part, conducted on the commercial product; however, environmentally degraded PCBs to which people may be exposed can differ in their composition and toxicity from the original commercial PCB mixture. Regulatory agencies are beginning to acknowledge this as an important factor in evaluating risk from exposure to PCBs in the environment.

Because of the ban on PCB production, decreasing use of PCBs, and efforts to remediate contaminated sites, general population exposure to PCBs in fish and other foods has been significantly reduced, and PCB levels in human blood are also decreasing. Industry and government should focus on the development of novel and cost-effective remediation and disposal techniques as well as on scientifically improved health risk analysis to reduce the uncertainty associated with PCB exposure and health effects in humans.

1. INTRODUCTION

Polychlorinated biphenyls, or PCBs, are a family of more than 200 structurally related chemical compounds (congeners), consisting of two benzene rings and 1 to 10 chlorine atoms (Fig. 1). They range from light, oily fluids to heavier, greasy or waxy substances. They were widely used in a variety of in-

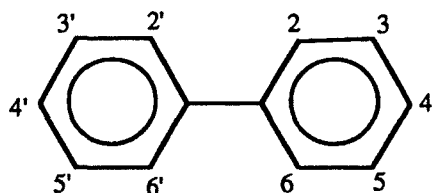


FIG. 1. Basic chemical structure of PCBs. The numbers 2–6 and 2'–6' represent possible chlorine positions on each benzene ring. There are 209 specific PCB family members (congeners). Each PCB congener is unique with respect to chlorine position. For example, a PCB with four chlorine atoms is a tetrachlorobiphenyl ("biphenyl" refers to the two benzene or "phenyl" rings); a more specific name, e.g., 3,3',4,4'-tetrachlorobiphenyl, would indicate the exact positions of the four chlorines on the benzene ring.

dustrial applications, until concern over possible adverse effects on health and the environment resulted in a ban on PCB manufacture. This article is written to explain the history and toxicity of PCBs and regulatory actions that have been taken, with the aim of providing a balanced and scientifically founded perspective.

PCBs were discovered over 100 years ago; their production and commercial use began in 1929. Because of their remarkable insulating capacity and their flame retardant nature, they soon gained widespread use as coolants and lubricants in transformers and other electrical equipment where these properties are essential. PCBs replaced combustible insulating fluids and thereby reduced the risk of fires in office buildings, hospitals, factories, and schools. In fact, some city codes banned the mineral oil variety of insulation and required that all capacitors and transformers be of the PCB type. Not only did PCBs make capacitors flame resistant, they also allowed capacitors to be made smaller, thus lowering equipment costs. Insurance companies required PCB equipment in many locations.

For several decades, PCBs were also routinely used in the manufacture of a wide variety of common products such as plastics, adhesives, paints and varnishes, pesticides, carbonless copying paper, newsprint, fluorescent light ballasts, and caulking compounds. It is estimated that between 1929 and 1977, about 1.1 billion pounds of PCBs were produced in the United States. Monsanto was the sole United States producer.

Even though United States production of these chemicals has ceased, PCBs have been identified in at least 387 of the nation's 1416 Superfund hazardous waste sites (ATSDR, 1996). PCBs persist in the environment and thus continue to be detected long after manufacturing has ceased. Moreover, potential sources of PCB release still exist due to past disposal practices.

2. HOW DID PCBs GET INTO THE ENVIRONMENT?

In the past, discharges of PCB-laden wastes into rivers, streams, and open landfills were considered acceptable, legal, and hazard-free practices. PCBs were also sometimes intentionally released into the environment—for example, to reduce dust emissions from dirt roads or as extenders in some agricultural pesticide formulations. In retrospect, these practices were inappropriate and potentially harmful.

There have also been accidental releases of PCB and associated contaminants into the environment via leaking of sealed PCB fluid compartments during commercial use of transformers and capacitors and as a result of improper disposal of PCB-containing equipment or chemical products. The contamination of food for animal and human consumption has also occurred from PCBs leaking or leaching from malfunctioning heating coils into foods during manufacturing. PCBs can also enter the food chain through the ingestion of contaminated fish from PCB-contaminated water.

Finally, transformer and capacitor (electrical) fires have led

to the environmental release of PCBs and thermal degradation products such as polychlorinated dibenzo-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs), and quaterphenyls (PCQs). These incomplete combustion products are considered to be far more toxic than PCBs, as discussed below.

3. HISTORICAL CONCERN OVER PCBs

Concern about the presence of PCBs in our environment began around 1966 when research in Sweden revealed the presence of PCBs in environmental samples (soil and water) being screened for DDT (Jensen, 1966). Further study confirmed suspicions that the rate of biodegradation (natural breakdown) was very slow for some of the PCB congeners (Jensen, 1972).

In 1968, a widespread human poisoning episode in Western Japan was attributed to the consumption of rice bran oil that became contaminated with PCBs during processing. World-wide concern grew over the potential health effects of PCBs. This concern was spurred on by another human poisoning episode in 1978, involving PCB-contaminated rice bran oil in Taiwan.

In 1971, Monsanto Chemical Company voluntarily limited the types of PCB mixtures (each with the trade name Aroclor) produced to those containing less than 60% chlorine substitution (by weight) and reformulated one of its Aroclors to reduce the percentage of higher-chlorinated PCBs. A series of U.S. government decisions led to the regulation of PCBs under the Toxic Substances Control Act in 1976. A 1974 rule was issued to restrict the use of PCBs to closed-system applications (mainly transformers and capacitors). The decision to ban U.S. commercial production of all PCBs was reached in 1976, although U.S. production did not actually end until 1979. There is no commercial PCB production in Europe; world production figures are not known.

PCBs are now regarded as ubiquitous environmental contaminants (Atlas and Giam, 1981; Bacon *et al.*, 1992; Ballschmitter, 1991; Wasserman *et al.*, 1979; Wolff *et al.*, 1982). These chemicals bioaccumulate (build up) in the food chain; because of their relative insolubility in water and high solubility in fats, PCBs are stored in body fat. However, environmental persistence does not necessarily imply that they threaten public health.

Animal experiments involving PCB exposure have raised questions about possible health hazards in humans. PCBs have only been found to cause acute life-threatening effects in animals at extremely high doses. However, as discussed in the following section, PCBs have been shown to cause tumors in animals.

4. DO PCBs CAUSE CANCER AND OTHER SERIOUS HEALTH PROBLEMS IN ANIMALS?

The weight of the experimental evidence supports the conclusion that PCBs can cause cancers in animals. Extensive

reviews by the International Agency for Research on Cancer (IARC, 1987), the National Toxicology Program (NTP, 1989), the American Conference of Governmental Industrial Hygienists (ACGIH, 1996), and the U.S. Environmental Protection Agency (EPA, 1996a,b) have all determined that sufficient evidence exists to consider PCBs to be animal carcinogens. Chlorine content was previously regarded as an important factor in the degree of carcinogenicity of particular PCB mixtures. However, recent studies (Brunner *et al.*, 1996) suggest that the *position* of the chlorines in the PCB molecule is also a key determinant of carcinogenicity. This issue will be important in future EPA dose-response assessments (EPA, 1996b).

Effects (other than cancer) on the liver, blood, immune system, nervous system, reproductive system, and other organ systems have been observed in various animal studies of PCBs (ATSDR, 1996; WHO, 1993). Systemic toxicity more frequently results from ingestion rather than absorption through the skin.

Recent concerns have been raised about the degradation of PCBs into PCDFs and PCDDs during combustion of fluids in electrical equipment fires or under inadequate incineration conditions (Hutzinger *et al.*, 1985). Studies of these breakdown products in animals have found toxic effects at much lower dose levels of PCDDs or PCDFs than of PCBs (Bandiera *et al.*, 1984). This is significant, since analysis of the contaminated rice bran oil in Japan and Taiwan revealed that the PCB fluid was partially heat degraded and contained high levels of PCDFs and PCDDs.

The EPA's current policy is to consider chemicals that cause cancer in animals to be potential human carcinogens. However, when interpreting results from animal toxicity studies, one must take the following into account:

- interspecies differences between the laboratory animals used in animal testing and humans;
- variation within the human population, depending on age, sex, and individual susceptibility; and
- the very large doses of the agent administered to animals in experiments. These doses greatly exceed the level of human exposures. Effects observed at these very high doses may be irrelevant to humans exposed at much lower doses.

In summary, present scientific evidence indicates that PCBs are carcinogens and toxicants to animals under conditions of chronic exposure. Knowledge of the possible role of quaterphenyls, dioxins, and furans in the Yusho incident came after the American public was already alarmed about PCB exposure. The issue of chemical contamination of PCBs in Japan and Taiwan continues to complicate the interpretation of animal and human data on the acute and carcinogenic effects of PCBs in the United States.

5. DO PCBs CAUSE HEALTH EFFECTS IN HUMANS?

Health effects are traditionally classified as acute or chronic. With respect to PCB exposure, acute effects are considered to be physiologic responses that occur shortly after exposure.

Chloracne and, possibly, peripheral neuropathy (adverse effects on peripheral nerves associated with muscles, skin, and joints) have been associated with short-term PCB exposures, although, as previously discussed, PCB degradation products rather than PCBs may have been the actual culprit. Contact dermatitis has been reported in PCB-exposed workers who were, however, also exposed to epoxy compounds, known skin sensitizers.

Chronic effects mainly refer to responses occurring after prolonged exposure, including the development of cancer. However, more recently other effects such as those relating to reproduction and endocrine disruption have also been investigated with regard to PCB exposure (Falck *et al.*, 1992; Krishnan and Safe, 1993). In general, most effects other than cancer associated with chemical exposures have a specific threshold exposure dose (i.e., a dose below which adverse effects will not occur). The EPA relies on this concept in establishing "reference doses" (RfDs), doses to which even the most sensitive members of the population can be exposed over a lifetime without experiencing adverse effects. The EPA has established RfDs for two specific mixtures of PCBs: Aroclor 1254 (0.02 $\mu\text{m}/\text{kg}$ body wt/day) and Aroclor 1016 (0.07 $\mu\text{m}/\text{kg}/\text{day}$) (EPA, 1996a).

Epidemiologists have attempted to identify increases in the incidence of acute and chronic effects among groups exposed to PCBs (Brown, 1987; Brown and Jones, 1981; Bertazzi *et al.*, 1987; Gustavsson *et al.*, 1986; Shalat *et al.*, 1989; NIOSH, 1977; Davidorf and Knupp, 1979; Yassi *et al.*, 1994). In these types of studies, health effects in heavily exposed groups are compared with effects in controls, individuals who have received no PCB exposure other than background levels. These types of studies may examine routine and accidental exposures in occupational or other settings.

5.1. Occupational Studies

Over 50 years have passed since workers were first heavily exposed to PCBs, a period which should be sufficient to detect even disease such as cancer, which have a long latency period of 10 to 30 years (the period of time between initial exposure and development of the disease). The most extensive occupational studies of long-term exposure to PCBs have focused on workers employed in the manufacture of electrical equipment. These individuals had daily skin contact with PCBs for many years, inhaled relatively high levels of the chemical, and probably ingested some while eating near their work stations. Aside from skin and eye irritation, and perhaps liver enzyme induction (a sign of increased metabolic activity in the liver), no other acute or chronic health effects can be definitively attributed to PCBs from occupational studies. Despite high serum and fat concentrations of PCBs in these workers, the severe form of chloracne and other effects seen in the Yusho victims has not occurred (Rosenman, 1992).

Four occupational studies are particularly important:

- NIOSH (the National Institute for Occupational Safety

and Health) studied maintenance workers exposed to PCBs at two utility companies (Smith *et al.*, 1981a). Blood PCB concentrations were much higher among the workers than the national background level [12 to 298 parts per billion (ppb) vs 10 to 20 ppb]. The workers did not exhibit any health effects, not even chloracne.

- NIOSH studied 224 workers exposed to PCBs at an electrical equipment manufacturing plant and found PCB blood concentrations ranging from 15 to 3580 ppb. Despite such high levels, no adverse effects were noted (Smith *et al.*, 1981b).

- Lawton *et al.* (1985) studied the health of 194 workers heavily exposed to PCBs for an average of 15 years, some for as long as 35 years. The first report, of workers followed through 1976 indicated no adverse effects. A 1979 reevaluation again did not produce evidence of health effects among these workers.

- The most comprehensive study of long-term health effects of PCB exposure involved more than 2500 workers employed at two separate capacitor manufacturing plants (Brown and Jones, 1981). The NIOSH researchers did not identify any statistically significant excesses of individual cancers among workers, more than half of whom had spent at least 20 years on the job. NIOSH reported that the total cancer mortality for this occupationally exposed population was slightly lower than that of the general U.S. population. Thirty-nine cancers were observed, although more than 43 would have been expected in a population with a demographic profile (e.g., similar age/sex/race distribution) similar to that of the 2500 workers. Also, there was no clear dose-response relationship between length of employment in PCB-exposed jobs and risk of mortality due to cancer.

These studies found no correlation between exposure level and effect and therefore provide no evidence that PCB exposure increases cancer risk in humans (ATSDR, 1996). Given the small number of cases in these studies, the possibility remains that highly exposed workers may eventually develop PCB-related disease and increased mortality. It is clear, however, that serious health problems (acute and chronic) such as those seen in victims of the incidents in Japan and Taiwan, have not been observed as a result of occupational PCB exposure (Rosenman, 1992).

5.2. The Yusho and Yu-Cheng Incidents

In 1968 some 1300 people in Fukuoka, Nagasaki, and other areas of Western Japan, became ill from consuming rice bran oil contaminated with 2000–3000 parts per million (ppm) of a Japanese brand of a PCB heat-transfer agent (Kunita *et al.*, 1984; Kuratsune, 1989). The victims developed a very severe and persistent form of acne called chlorine acne or chloracne. The disease symptoms soon progressed to include fatigue, nausea, and swelling of the arms and legs; some people developed liver disorders. Neurological manifestations (primarily subjective in nature) also were reported. Some newborns of exposed mothers exhibited small size, discoloration of skin and nails,

and premature eruption of teeth (Kuratsune *et al.*, 1972). Within 5 years of the Japan poisoning, about 1200 cases of "Yusho" ("oil disease") had been reported and by 1977, 1665 cases had been recognized. During the 11 years following exposure, 51 Yusho patients died. The cause of death was determined in 31 cases, and 11 of these (or 35%) were due to cancer. In a similar unexposed population only 21% of deaths would have been expected to result from cancer. Ikeda *et al.* (1985) examined deaths among 1761 Yusho patients through 1983. Excess mortality from liver cancer was observed in both males and females, but was statistically significant only in males. However, the geographic distribution of liver cancer deaths was markedly uneven, occurring mostly in Fukuoka, while no such excess was observed in Nagasaki.

A similar poisoning episode occurred in Taiwan in 1978 and was reported as "Yu-Cheng" disease. Once again, rice bran oil was contaminated by heat-degraded PCBs and subsequently ingested by over 2000 people. Effects were observed among the Yu-Cheng victims similar to those in the Yusho victims. Offspring of Yu-Cheng mothers exhibited symptoms of acute toxicity as well (Rogan, 1989; Rogan *et al.*, 1988). Elevated mortality from liver diseases other than cancer was observed within 3 years after the poisoning outbreak (Hsu *et al.*, 1985; Hsieh *et al.*, 1996).

In the years following the Japan and Taiwan poisoning incidents, additional evidence indicated that PCBs might not be the sole cause of the symptoms associated with illness. Analysis revealed that the heat-transfer fluid that contaminated the rice bran oil consisted of only 50% PCBs (by volume) (Kashimoto *et al.*, 1981). Furthermore, due to mechanical problems in the heat exchanger which was the original source of the oil, approximately one-half of the original PCB fluid had been converted into chlorinated quaterphenyls. After heating, the contaminated oil mixture contained significant levels of PCDFs and PCDDs (Buser *et al.*, 1978; Chen *et al.*, 1981; Miyata *et al.*, 1985, 1977).

Levels of PCBs in the blood of Japanese and Taiwanese capacitor workers were greater than in the Yusho and Yu-Cheng victims (Kashimoto and Miyata, 1986), yet health problems were greater in the Yusho and Yu-Cheng patients. These findings, and those of feeding experiments in which monkeys experienced skin effects only when PCDFs were added to doses of PCBs or PCQs, suggest that the effects seen in the Yusho and Yu-Cheng victims were not the result of exposures to "pure" PCBs or commercially produced mixtures but rather were the consequence of other contaminants present along with the PCBs, i.e., PCQs, PCDDs, and, most importantly, PCDFs (Kunita *et al.*, 1984; Kashimoto *et al.*, 1981; Kashimoto and Miyata, 1986).

Children of the Yusho and Yu-Cheng poisoning victims have been followed in several studies. Developmental effects (nail abnormalities, musculoskeletal changes, behavioral problems, and cognitive deficits) were observed and are thought to be the result of high exposure to a contaminant mixture con-

taining PCDFs, PCQs, and PCDDs, involving maternal levels up to 200 times those seen in "background" environmental exposures (Rogan, 1989; Rogan *et al.*, 1988; Feeley, 1996; Chen *et al.*, 1992; Yu *et al.*, 1991).

5.3. Recent Studies of the Effects of Low-Level PCB Exposure

Investigators have continued to study the reproductive and developmental effects of low-level exposure to PCBs and other related contaminants. Epidemiological studies have been conducted in Michigan, the Netherlands, and North Carolina.

Some of these studies examined infants born to mothers who consumed fish with high levels of PCBs before and during pregnancy. Other studies examined infants born to women with no known exposure other than to background levels of PCBs. These are extensive ongoing studies that have followed the children throughout childhood. In all studies, the mothers exhibited no signs of PCB toxicity. In order to correlate possible reproductive effects with maternal exposure levels, samples of umbilical cord serum, breast milk, and maternal blood were collected.

Lower birth weight was reported in some of the infants born to mothers who consumed contaminated fish, but was not correlated with maternal exposure levels (Fein *et al.*, 1984). There have been reports of prenatal PCB exposure-related neurodevelopmental deficits among the most highly exposed subgroup of a North Carolina cohort of infants. Among these were motor deficits at birth (Fein *et al.*, 1984; Rogan *et al.*, 1986; Gladen and Rogan, 1991), deficits in motor skills at the end of the first year (Gladen *et al.*, 1988), impaired visual recognition memory at 7 months of age (Jacobson *et al.*, 1985), and significantly lower psychomotor scores (on the Bayley Scale of Infant Development) at 18 and 24 months, as well as deficits in short-term memory at 4 years of age. A more recent report indicated that some deficits observed at earlier ages were no longer apparent at ages 3, 4, or 5 years (Gladen and Rogan, 1991).

In a recent report in the *New England Journal of Medicine*, Jacobson and Jacobson (1996) claim that fetal exposure to PCBs from mothers eating contaminated Great Lakes fish during pregnancy was associated with effects on nervous system development and deficits in intellectual performance in infants and young children, effects that may persist later into childhood. These effects were correlated with prenatal exposures (Jacobson and Jacobson, 1996), but not with postbirth exposure via breast milk (Jacobson *et al.*, 1990a,b). The *NEJM* findings are inconsistent with studies that found no relationship between maternal PCB exposure and infant birth weight or head circumference (Fein *et al.*, 1984; Rogan *et al.*, 1986). The concentrations of PCBs in blood of the mothers in the Jacobsons' study (1996) were only slightly greater than the blood levels of mothers who did not eat contaminated fish and were within the range of PCB blood levels reported for the entire North American population. If such trace levels could indeed affect intellectual development in infants and children, there should be

evidence of widespread intellectual deficits among North American children. Clearly, there is no evidence of such a phenomenon.

Several methodological problems raise questions about the validity of the Jacobson study findings. For example, the exposure assessment of the mothers was based on maternal estimates of fish consumption over the previous 6 years, a notoriously unreliable method (as demonstrated in this case by the low correlation between fish consumption estimates and fetal cord serum PCBs) (Paneth, 1991; Seegal, 1996). PCB levels in umbilical cord serum samples were below detection limits in over half of the samples obtained; the method used to "assign" PCB levels to these children is unclear. This casts doubt upon statements by the investigators of a dose-dependent relationship between fetal cord serum PCBs and behavioral endpoints (Seegal, 1996).

Although the Jacobsons claim to have controlled for various factors that influence intellectual development, they did not control for all possible environmental, social, economic, and genetic factors that can influence intellectual development. Critics of the study have also claimed that the small number of control subjects may have limited the ability of the statistical methods to control for potential confounders, such as maternal alcohol consumption and prepregnancy body weight (Seegal, 1996; Schantz, 1996). Alcohol consumption and maternal body weight are both determinants of birth weight, independent of PCB exposure, and alcohol consumption is also associated with cognitive outcomes in the child (Schantz, 1996).

In all the studies of consumption of contaminated fish, there have been significant confounding factors, such as the presence of methyl mercury, PCDFs, PCDDs, DDT, and other organochlorine pesticides (Foster, 1995).³ Many of these chemicals are reproductive and developmental toxicants and therefore the adverse effects reported in these studies cannot be specifically attributed to PCB exposure. In fact, the Jacobsons have themselves stated: "it is possible that the behavioral deficits associated with fish consumption are due to the presence of toxins other than PCBs in the same contaminated fish" (Jacobson *et al.*, 1984).

In addition, the investigators did not find a significant association between PCBs in breast milk (which were hundreds of times greater than PCB concentrations in maternal blood) and intellectual impairment. While the Jacobsons explain this anomaly by suggesting that the developing fetal brain is uniquely sensitive to PCB effects, in fact brain development continues for many years; some areas of the brain are relatively mature at birth, whereas others undergo considerable development after birth (Schantz, 1996). Certainly breast milk containing trace levels of PCBs could represent a potentially much greater exposure to infants than transplacental exposure.

While animal studies in several species have found that maternal PCB exposure can lead to adverse reproductive and neurodevelopmental effects (ATSDR, 1996; Gray *et al.*, 1993; Arnold *et al.*, 1990, 1993a,b; Kihlstrom *et al.*, 1992; Meserve *et al.*, 1992), further investigation is needed to determine that PCBs act alone or as a cofactor to cause developmental impairment in humans.

5.4. Do PCBs Disrupt the Human Endocrine System?

Endocrine (hormone) disruption as a measurable indicator of toxicity is a relatively new issue that is receiving much attention. Some scientists have hypothesized that hormonally related health problems occur because of disruptive effects of trace chemical pollutants on the endocrine system. This was widely publicized as a general principle in 1996 with the release of *Our Stolen Future* (Colburn *et al.*, 1996). The authors suggest that some chemicals, acting as hormonal disrupters, may lead to infertility, some cancers (e.g., cancers involving the breast, prostate, testes, ovaries, and uterus), and other hormonally induced disorders.

Estrogens are produced in both males and females, but at higher levels among females. In males, estrogen is produced from testosterone and is thought to be involved in the formation of sperm. In females, estrogen production is primarily responsible for the development of reproductive and other related tissues. Estrogen production ceases after menopause. Estrogens are also found naturally in plants (phytoestrogens) and are consequently consumed in the diet. Lignins (a family of phytoestrogens) can be estrogenic or antiestrogenic in nature, depending on the hormonal environment and specific target tissue. Some phytoestrogens are under investigation as anticarcinogenic agents (Aldercreutz *et al.*, 1995).

The evidence of the effects of environmental estrogens on wildlife remains weak and circumstantial. For example, *Our Stolen Future* suggests that chemicals in the environment acting as endocrine disrupters may be responsible for the production of female animals from eggs containing male embryos. However, it has been found that the same sex change can occur in turtles when eggs containing male embryos are incubated at 2°C higher than normal (Crews *et al.*, 1994). Thus, it is clear that some effects have been prematurely attributed to "endocrine disruption" based on incomplete evidence. The "hormonal activity" described in *Our Stolen Future* has been frequently attributed to estrogen-enhancing (estrogenic) or estrogen-blocking (antiestrogenic) activity. However, "endocrine disruption" is not a toxic endpoint per se, but may be used to describe a mechanism through which toxicity may occur and should be used in this capacity.

Dr. Stephen Safe, a widely recognized expert in the toxicology of organochlorine compounds, believes that PCBs are not estrogenic but that their metabolites have weak estrogenic activity (Safe, 1995). Indeed PCB mixtures can exhibit both estrogenic as well as antiestrogenic activity. Dr. Safe has estimated that the estrogenic activity in the average diet is about 40

³ While some of these chemicals, specifically the PCDDs, may occur as breakdown products of PCBs under conditions of high heat, they are also present in the environment from sources unrelated to PCB use.

million times greater than that of environmental estrogens. He has characterized the hypothesis that environmental estrogens cause increased rates of breast cancer or male reproductive problems as both unproven and implausible.

Several studies have observed high levels of organochlorines (PCBs and other chlorinated compounds) in fat and milk of breast cancer patients. The totality of the evidence on organochlorines suggests no correlation between these chemicals and breast cancer. Key and Reeves (1995) analyzed six studies of the relationship between PCBs (as well as DDT) and breast cancer. The review found no difference in body levels of either substance between cancer patients and cancer-free controls. Another review of the available data also did not support the hypothesis that DDT or PCBs cause an increased risk of breast cancer (Ahlborg *et al.*, 1995).

The complexity of PCB mixtures and their thermal breakdown products has made this group of chemicals difficult to characterize in terms of toxicity. It is important to recognize that toxicity of PCB mixtures is dependent on the toxicity of the individual PCB congeners present within the mixture and, of course, on the presence of other more potent contaminants (Safe, 1994; DeVoogt and Brinkman, 1989). There is no scientific basis to assume that all PCB mixtures will have the same toxicity; this is now beginning to be recognized by regulatory agencies such as the EPA. Some PCBs and their thermal degradation products are much more toxic than others. Moreover, thermally or environmentally degraded PCB mixtures significantly deviate in composition and consequent toxicity from the original commercial PCB mixture (McFarland and Clarke, 1989; Safe, 1990; Borlakoglu *et al.*, 1990a,b,c; Brown *et al.*, 1987). In addition, studies conducted to assess human health risks have been complicated by the presence of other, known toxic agents, such as methyl mercury and pesticides. Therefore, the careful examination of specific contaminant mixtures is evolving as an important tool in gauging health risk (Safe, 1994; EPA, 1991a).

5.5. PCBs in Fish and Other Foods

PCBs discharged into rivers tend to concentrate in sediments and may be taken up by fish. As fish eat other fish or bottom-dwelling organisms, they take on the body burden of PCBs present in their prey. Fish are able to metabolize some PCBs; those that are not metabolized or excreted accumulate in fatty tissues. The result is bioaccumulation of PCBs. Humans who consume fish will also bioaccumulate PCBs. For these reasons, fish are monitored for PCB concentration in contaminated bodies of water. The FDA has also established a PCB tolerance limit of 2 ppm for fish fillets sold for retail, above which it will take action. There is a National Fish Consumption Advisory Database to keep consumers informed of monitored contaminant levels in fish (Nowell and Resck, 1994; FDA, 1988).

Two studies of fish eaters have not demonstrated direct adverse health effects from PCBs. The Michigan Department of Public Health, under the sponsorship of the FDA, measured

potential health effects of higher-than-normal exposure to PCBs due to consumption of fish. The study involved 182 adults, 105 of whom consumed over 26 lb of Great Lakes fish per year. A significant correlation between blood PCB levels and the quantity of fish consumed was observed. An evaluation of health histories and current medical problems of the study subjects, however, did not reveal any significant differences between the heavy fish-consuming group and those with lower exposure to PCB-contaminated fish (Michigan Department of Public Health, 1975; Humphrey, 1980).

In another study, the Connecticut Department of Health Services conducted an analysis of blood samples and reviewed medical histories of persons who reported eating fish from the Housatonic River. Again there was a significant correlation between the amount of fish consumed and the levels of PCBs in the blood, but no link could be made between clinical observations and PCB levels (Beck, 1981).

Studies conducted since 1980 have found that PCB levels in freshwater fish have been decreasing. Mean levels ranged from 0.5 to 1.9 ppm (ATSDR, 1996). In a 1986–1989 EPA national assessment, fish from 97% of sites contained 10 ppm PCB or less, while one study demonstrated that fish from 74% of sites contained 1 ppm or less (Keuhl *et al.*, 1994). Fish near some heavily contaminated industrial sites, however, contain much higher levels of PCBs.

According to FDA studies, the amount of PCBs consumed in the diet has decreased steadily (from almost 7 mg/day in 1971 to less than 0.1 mg/day in 1988) (Shank, 1991), and the primary source of PCBs has shifted from fish to meat (ATSDR, 1996). The following FDA allowable tolerance limits for foods marketed commercially are currently in effect:

- 2 ppm in fish fillets (FDA, 1988);
- 1.5 ppm in milk fat (*Fed. Reg.*, 1979);
- 1.5 ppm in the fat portion of manufactured dairy products (*Fed. Reg.*, 1979);
- 3 ppm in poultry (*Fed. Reg.*, 1979); and
- 0.3 ppm in eggs (*Fed. Reg.*, 1979).

Measured levels in most of the products mentioned above are well below the allowable tolerances. In 1992, FDA set an action level for manufactured foods (most pertinent to red meat) at 3 ppm of PCBs detectable in fat.

6. PCB RISK ASSESSMENT

Based on animal studies, EPA, ACGIH, IARC, and NTP have all classified PCBs as potential human carcinogens ("probable human carcinogens" under EPA's weight of evidence scheme). There is no conclusive evidence implicating PCBs as human carcinogens. The toxicity criteria (RfDs and numerical estimates of cancer potency) published by EPA, used to quantify cancer and noncancer risks to humans, are derived solely from animal studies.

There is significant uncertainty underlying these criteria; more scientific research is needed to improve prediction of

human health risk. In 1996, a joint team of scientists from EPA, ATSDR, and NTP was organized to evaluate specific information that would reduce or eliminate uncertainty in human health assessments for PCBs (ATSDR, 1996). Rather than simply basing risk values on effects on animals, and assuming that all PCB mixtures are equally toxic and carcinogenic, this panel has acknowledged that determining the toxicity of specific PCBs will be important in reducing uncertainty in epidemiological studies and subsequently making scientifically based risk decisions (Shannon, 1996). Unfortunately, measures of specific PCB concentrations are seldom obtained from analyses of environmental samples (soil, etc.), making it difficult to assess risk from exposures to particular PCBs.

The EPA has recently attempted to address another major source of uncertainty in PCB risk assessment. Commercial PCB mixtures differ from the mixtures present in the environment, both in composition and in toxicity. The EPA is now using toxicity criteria specific to the medium of exposure (e.g., soil, air, food) (EPA, 1996b), to account for the differences in the PCB mixtures present in these different environmental media. Also notable is the recent lowering of EPA's published estimates of PCB cancer potency by 4- to 20-fold, reflecting the use of new scientific data and revised risk assessment methodology (EPA, 1996b). Previously developed "dioxin-like toxic equivalency factors"⁴ will also be incorporated into risk evaluations, when PCB-specific concentrations are available. These developments in PCB risk assessment are based on updated scientific information in areas highlighted by the joint committee.

7. PCB REGULATIONS

There are several federal regulations that address PCBs. The Toxic Substances Control Act (TSCA) of 1976 banned the manufacture, processing, distribution, and use of PCBs in all products that were not totally enclosed. Originally, PCB regulation was the focus of TSCA. Since then, the scope of TSCA has grown to provide guidance for toxicity testing and release of other chemicals; however, PCBs are the only chemical family fully regulated under any government act. This includes the regulation of any release of PCBs into the environment, including accidental leaks or spills; specific actions are required depending upon the concentration of PCBs in soil resulting from spills. The PCB Spill Cleanup Policy issued under TSCA is the source of risk-based PCB "cleanup levels" for unrestricted versus restricted areas (i.e., areas that are easily accessible by the general public versus sites that are remote or difficult to access) that have been applied to the remediation of contaminated sites under other federal programs, such as Superfund (EPA, 1987).

EPA regulations required that capacitors in areas where public exposure might occur (such as utility poles in backyards) be

removed from service by 1988 (*Fed. Reg.*, 1982a,b, 1985). Use of capacitors in protected environments—such as fenced utility company grounds—was permitted until the end of their useful life. Under TSCA, owners and operators of these facilities are required to report regularly on safety, use, and disposal. EPA added additional restrictions (*Fed. Reg.*, 1985) on the use of PCB-containing transformers (500 ppm or greater PCB in dielectric fluid) to deal with the possible hazards from fires in electrical equipment.

After 1990, most regulations have focused on PCB waste tracking and disposal (EPA, 1991b, 1992a,b). In 1991, the EPA established a Maximum Contaminant Level for drinking water of 0.004 ppm for adult and 0.001 ppm for children; many individual states have also established more stringent drinking water standards and guidelines (EPA, 1994).

In April 1996, President Clinton partially lifted the ban on PCB imports, enabling PCB waste to be shipped to the United States for incineration (McTague, 1996). Canada responded in November 1996 with an extension of an export ban to prevent the export of PCB waste from Canada, reflecting the evolving competition for hazardous waste business.

8. THE ALTERNATIVES TO PCBs

PCBs were important industrially due primarily to their flame-resistant characteristics. There are various chemical alternatives to PCBs (including silicone fluids, fluorocarbons, high molecular weight hydrocarbons, low molecular weight chlorinated hydrocarbons, and high boiling oils and esters) which will work in electrical equipment. However, a transformer constructed for use with PCB fluid may not operate at the same power load with a substitute chemical, i.e., it must be "derated," (*Fed. Reg.*, 1985). Such a transformer becomes less efficient, resulting in a higher operating cost as well as added risk of fire. Precautionary measures must be implemented to ensure fire safety and proper disposal of waste. Clearly, shifting from PCBs to alternatives has involved tradeoffs, not the *elimination*, of health and safety risks.

9. WHAT ARE WE DOING TO CLEAN UP PCBs? SOME EXAMPLES

There are efforts under way to clean up PCBs in the environment. Most sites have been cleaned up by soil excavation and disposal in EPA-approved landfills, although soil incineration has also been used. These efforts, along with the ban on PCB manufacture, ensure that exposure to PCBs in the U.S. will continue to decline. EPA is currently overseeing several Superfund sites containing significant levels of PCBs, where complete remediation has been delayed by various factors, including lack of suitable technology (a particular problem for sediments) and local opposition to landfills or incinerators. Before actual remediation can occur, remedial investigation and feasibility studies (including cost analysis) must be performed.

⁴ Criteria that account for similarities in structure and toxicity between certain individual PCBs and dioxins.

Such a process is underway for the Hudson River, heavily contaminated because of industrial discharges. From 1947 to 1977, over 500,000 lb of PCBs were discharged, under permit, into the Hudson River from two General Electric (GE) capacitor manufacturing plants at Fort Edward and Hudson Falls, New York. The New York State Department of Environmental Conservation has spent well in excess of three million dollars to investigate the extent of PCB contamination in the river. This study identified 40 hot spots in the upper Hudson River (a "hot spot" is defined as sediment containing 50 ppm or more PCBs). In 1992, EPA's Phase I report of the remedial investigation revealed PCB oil droplets in the fractured bedrock (deep beneath the river) which act as an additional source of PCBs leaching into the river. The concentration of PCBs measured at these spots has been as high as 44,000 ppm.

It was initially suggested (and is maintained by GE) that leaving contaminated rivers and waterbeds alone would allow for natural restoration and remediation of PCB-laden waters. Bacterial dechlorination of PCBs in buried sediments in the upper Hudson River has occurred (Brown *et al.*, 1987), but currently there is no practical means to accelerate this process. The time frames for "natural" remediation were estimated as being 20–30 years longer than for active remediation, but it was argued that natural remediation would be far cheaper and less disruptive to the ecosystem than remedial measures such as dredging. However, any remediation that does not address the continued seepage of PCB oil droplets from the fractured bedrock beneath the dredgable portion of the Hudson River will not be effective in the long term.

While active remediation was deemed necessary, alternatives to dredging are being investigated. GE has built a water treatment plant at the Hudson Falls site to reduce PCB concentrations to 65 parts per trillion (ppt) before release into the main trunk of the river. At the present time, EPA is completing Phase II of the remedial investigation; reports are expected to be released by the spring of 1997. This will be followed by the final Phase II report(s) that will include a proposed method for remediation, alternate approaches, and a cost analysis. Until this is completed, there will be no regulated remediation of the Hudson River.

In Massachusetts, studies are under way concerning the removal of PCBs from the New Bedford harbor. A wastewater treatment facility has been built, and some dredging of the river harbor sediment hot spots has occurred. However, remedial design and construction is still taking place.

In Lake Michigan's Waukegan Harbor, where PCBs were discharged from several sources, over one million pounds of contaminated sediment have been dredged from the harbor. The EPA and citizen advisory groups are now working together to plan further action, including an assessment of the effectiveness of the dredging and restoration of the harbor's impaired uses. Alternatives to dredging are also under investigation due to concern over recontamination of the water by

stirred-up sediments and public concern over the disposal and incineration of dredged materials. In fact, the one million pounds of sediments dredged from Waukegan Harbor are currently in isolated storage. Six million dollars has been allocated over a 6-year period for continuing cleanup of Waukegan Harbor.

Remediation techniques and disposal technologies continue to evolve. Many approaches have been tested but none has emerged as a technically and economically viable solution for the myriad of environmental situations encountered. A useful method for cleaning water will probably not be effective in treating soil. Highly chlorinated PCBs will not be as readily decomposed as less-chlorinated PCBs. These types of factors contribute to the challenges of effective and cost-efficient remediation of PCB-contaminated sites. Bacterial degradation or biodegradation of PCBs in soil and sediment is a potentially useful technology that is receiving much attention (Shannon, 1996; Brenner *et al.*, 1994; Furukawa, 1994; Abramowicz, 1994; Anonymous, 1997). Preliminary results on the biodegradation of soil samples, including those taken from the Hudson River, are promising. A "thermal blanket" approach, in which soil is heated from the surface downward and volatilized PCBs are removed under vacuum, is also under investigation.

10. WHAT IS ALL THIS COSTING US?

Replacing, monitoring, and disposing of PCBs has cost a substantial sum of money (estimates provided in 1982 and 1985 *Federal Register* notices totaled almost \$970 million), relating to the following activities (*Fed. Reg.*, 1982a, 1985):

- inspection of transformers (other than those in food and feed facilities);
- removing selected capacitors by 1988;
- replacing PCB electrical equipment in food and feed facilities by 1985;
- providing enhanced electrical protection;
- labeling and registration of PCB transformers; and
- removing higher voltage transformers and providing electrical protection for other remaining transformers (*Fed. Reg.*, 1985).

There have been other costs as well. For instance, the Cleveland Electric Illuminating Company expects an incremental cost of \$8 million to be passed on to the public due to the required early replacement of all PCB-containing power capacitors in its system. Public pressure in San Francisco caused the Pacific Gas & Electric Company to agree to early capacitor replacement, at a cost of about \$12 million.

Obviously, these inspection and replacement costs for electric utilities turn up in the consumer utility bill. The cost to private industry of inspecting its equipment and replacing capacitors and transformers contributes to higher prices for goods. However, equipment replacement and maintenance costs pale in comparison to cleanup costs for PCB spills and

dump sites. In the 1990s and beyond, the majority of costs will go toward the remediation of severely contaminated PCB sites such as the Hudson River, New Bedford, Massachusetts, and Lake Michigan. The EPA has recently estimated the total quantity of PCB wastes remaining to be remediated at 525 million tons (Agarwal, 1994); assuming an average cost of \$250 per ton for landfilling, and \$500 per ton for incineration, the cost of disposal of this quantity of waste is an astounding \$131 to \$263 billion.

Several factors will influence the cost of such cleanups, including the location of PCBs (in water, soil, sediment, bedrock, etc.); aerobic (exposed to air) versus anaerobic conditions; specific PCBs present (highly chlorinated PCBs are generally more difficult to degrade than less-chlorinated PCBs); and specific methods of treatment, including developments in bioremediation (bacterial degradation) and other novel remediation techniques.

11. SUMMARY AND RECOMMENDATIONS

Although PCBs are persistent in the environment and are stored in body fat, PCB levels in fish, other foods, and human blood are decreasing (ATSDR, 1996). No conclusive evidence exists that background levels in the general population, or even the very high levels that occurred among some occupational groups, resulted in acute or carcinogenic effects. In humans, the only adverse health effects that are strongly associated with PCB exposures are skin and eye problems (chloracne, changes in skin pigmentation, and chronic skin and eye irritation). These effects have only been reported following exposures to unusually high levels of PCBs, along with other chemicals. None of these effects have been observed in populations exposed through the consumption of fish. Cancer has not been correlated with levels of PCB exposure and, therefore, cannot be attributed to PCB exposure.

PCBs have been detected in body tissues; even so, the presence of a chemical in tissue does not necessarily indicate a health hazard. Recent reports suggesting a correlation between exposure to PCBs *in utero* (from maternal consumption of contaminated fish) and impaired intellectual development are not supported by other studies of prenatal exposure and are limited by deficiencies in exposure assessment and control of confounding variables. Nor is there evidence of a nationwide deterioration in the intellectual development of children, even though the maternal blood levels at which these effects allegedly occurred are only slightly higher than levels in blood of women who did not consume contaminated fish and are within the range of PCB blood levels for North America.

Decreasing use of PCBs, a production ban, and cleanup efforts have been successful in significantly reducing general population exposure. Any potential health risks from PCB exposure should follow a similar trend. ACSH recommends the following actions:

- Industry and government should focus on the development of novel and cost-effective remediation and disposal techniques, particularly for difficult-to-clean sites, such as riverbeds;
- Continue scientific research that can be used to improve health risk analysis—for example, additional elaboration of the toxicity of specific PCBs and PCB mixtures *found in the environment* is needed to reduce the uncertainty associated with PCB exposure and health effects in humans.

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