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Polychlorinated Biphenyls In Israel: a Risk Assessment

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THE HISTORY OF POLYCHLORINATED BIPHENYLS (PCBs) represents a unique example of a common industrial chemical which became a universal contaminant. During the years of widespread occurrence in the environment, the chemical and physical characteristics and chronic toxicity of PCBs have raised great concern about possible health hazards, especially in the industrialized countries (*1*).

PCBs, a mixture of synthetic aromatic halogenated biphenyl compounds, have been commercially available for more than 50 years. Beginning in the 1950s, because of their typical properties of an excellent dielectric constant, high electric resistance, thermal and chemical stability, and high lipophylicity, PCBs achieved practical importance which make them very useful in many industrial applications. The cumulative world production of PCBs through the years was estimated at around 1 million tons.

In 1966 PCBs were detected in dead fish in the Archipelago of Stockholm (*2*), and further evidence emerged each succeeding year of the presence of this industrial compound in the environment, in food, and in human beings. Many factors, such as areawide contamination by dumping or incineration of waste products containing PCBs, and serious accidental poisonings in man have shown that these contaminants have become a controversial health hazard.

Starting in 1970, huge efforts have been made by regulatory agencies to introduce severe restrictions on or even ban production and use of PCBs. Parallel methods and techniques, followed by monitoring programs, have been developed for surveillance of PCBs' residues in the environment, in foods, and in humans in an attempt to elucidate the toxicological significance to man and provide the epidemiologic tools needed to correlate adverse health parameters to exposure and body burden (*3*).

PCBs in Israel

PCBs are not produced locally in Israel, but are imported as technical substances under their various trademarks, and no statistical information is available on the national consumption. Polychlorinated biphenyls found in Israel have the same versatile industrial applications as in other countries; however, following restrictions imposed on the international level, PCBs were replaced by alternative substances or limited to closed systems. The stringent scheme imposed on the uses, disposal, and distribution helps to assure that no further significant quantities of PCBs are introduced into the environment.

Nevertheless, PCBs already present in ecosystems cannot be eliminated rapidly. This occurs only by processes of slow excretion and degradation. Prudent public health policy dictated the need for an adequate assessment of the possible health risk of PCBs in order to consider if actions are required for the protection of human health. The process of evaluation combines consideration of exposure, sources of contamination, residues, toxicological data, and epidemiologic investigation. The status of this evaluation is reviewed in this paper.

Exposure and Residues

The presence of PCBs in the environment has been studied in Israel since 1975, and residues were found in liver and egg samples of wild birds and hens and in the aquatic system. In air quality biomonitoring, the presence of PCBs was evaluated by measuring their accumulation in the lichen *Ramalina duriaei* (*4*). The highest values in the lichen were obtained at busy road intersections with heavy traffic, while lower amounts were detected at sites in more isolated agricultural areas removed from traffic.

Beginning in 1977, the Ministry of Health's Institute for the Control and Standardization of Drugs has evaluated human exposures to PCBs by monitoring residues in foods, commodities, and human milk. For protection of the general public, foods are presumed to be the main source of contamination, since PCBs are efficiently absorbed from the gastrointestinal tract, bioaccumulated, and stored in the adipose and other lipid-containing tissues. A large number of foodstuffs such as milk, dairy products, meat, poultry, eggs, fish, grains, animal feeds, or their components were analyzed. Residues were detected only in fish samples; however, these PCB residues were relatively low (less than 1 ppm). In Israel, the aquatic ecosystem can be regarded as a main potential source of PCB contamination with a per capita fish consumption of 24.4 grams per day. Samples of food materials were found free of PCBs, and no cases of industrial incidents, direct leakage, contact with foods, or irregular waste disposal have been reported.

Human Milk

Because human beings are at the top of most food chains, it was not surprising that human adipose tissues accumulate significant levels of persistent organochlorine compounds. Studies have proven that the levels of PCBs in the milk fat fraction, like those for DDT or DDE, reflect concentrations in the adipose tissues (*5*). Since milk secretion provides, by a noninvasive method, repeatable large volumes, this biological specimen has been recognized as a practical monitoring tool for measuring the body burden of xenobiotics in the general population.

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Percentage of breast milk samples from 100 mothers in the Jerusalem area with polychlorinated biphenyl contamination[1]

Residue level	Mean value	Percent
	Level in mg per kg fat	
Less than 0.5 ppm	0.25	63
Less than 1.0 ppm	0.71	25
Less than 1.5 ppm	1.20	7
Less than 2.1 ppm	....	1
More than 2.0 ppm	2.56	4
	Level in µg per kg of whole milk	
Less than 10 ppb	5.36	40
Less than 20 ppb	15	34
Less than 30 ppb	23.61	15
Less than 40 ppb	34.52	6
More than 40 ppb	73.78	5

[1] Fat: percentage mean value 3.36 (± 1.80); PCBs: mean value 0.54 (± 0.55) mg per kg milk fat.

In view of the fact that human milk can be the main food source for infants for many months, it was deemed to be important to study the residues of PCB in milk. One hundred samples of milk collected from mothers residing in the Jerusalem area, 2 weeks to 3 months after parturition, were analyzed. The mean PCB value was 540 ppb on a fat basis or 16.50 ppb on a whole milk basis. The table gives the percentage distribution of PCB levels in breast milk on fat and on a whole milk basis. The levels found were about two-thirds of the values reported in Canada (*6*) and three times less than the values reported in the Michigan survey (*7*).

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The majority of the milk samples come from mothers born in Israel. However, a small number of samples were from mothers born outside Israel, and a certain trend has been observed. The PCB level in milk from mothers born in Sweden, Poland, the U.S.S.R., and the United States was around 1–2 ppm; in samples from mothers born in Africa and Asian countries, the residues were lower than the mean value of 0.54 ppm.

Effects in Man

The main sources of information on the effects of PCBs in man stem from incidents of occupational exposure and the outbreaks of Yusho disease, which was caused by the ingestion of rice oil contaminated with PCBs, polychlorinated quaterphenyls (PCQs), and polychlorinated dibenzofurans (PCDFs), that occurred in Japan and Taiwan. In the Japanese incident, 1,200 persons were affected, and in Taiwan 2,000 cases were reported. The concentration of the contaminants in the Taiwan rice oil was lower than in the outbreak in Japan; however, the clinical symptoms were similar. Growth disturbances seen in Yusho babies tended to disappear a few years after exposure (*8*), and the total concentration of PCBs in blood approached the levels seen in normal persons. Eleven years after exposure, in patients still having active symptoms, the amount of PCDFs in the blood was very high compared with that of the normal population, while concentrations of PCQs were quite similar to those of PCBs (9–11). Another interesting fact was that the total blood concentration of PCBs in the Yusho victims was much lower than the levels found in workers occupationally exposed to PCBs, but that the chloracne was more persistent in Yusho patients. The preceding results indicate that PCBs might not be the only direct causative agent in Yusho victims and that PCQs, and especially the highly toxic PCDPs, can be important factors.

Nine of 22 deaths among Yusho victims that occurred after the exposure were attributed to malignant neoplasms in the stomach, liver, lungs, or breast and malignant lymphomas. In a group of 51 workers heavily exposed to PCBs and possibly other chemicals, a total of three malignant melanomas and two pancreatic carcinomas were diagnosed. In a group of 2,567 workers in two plants where PCBs were used, the total cancer mortality was lower than expected: 39 observed deaths versus 43.8 expected deaths (*12*).

Animal Toxicity

Symptoms of poisoning vary from species to species, and a relationship of dose versus time has been observed. Since PCBs have a high persistence, it appears that when the exposure was extended for a longer period of time a lesser total amount of PCBs was needed to produce a toxic effect in the animals. Treated animals developed a high induction of mixed function oxidase enzymes, thymic atrophy, and porphyria. Carcinogenic effects were reported in both mice and rats, and these data were used to support the conclusion that for "practical purposes polychlorinated biphenyls should be regarded as if they were carcinogenic to humans" (*13*).

Assessment of the Risk

According to the available epidemiologic data, no cases of adverse effects attributable to PCBs were reported outside of workers engaged in the production of PCBs, cases of Yusho victims, or high environmental exposure. Various actions were proposed subsequently to set allowable residue levels for PCBs in various foods and place restrictions or bans on production and uses. Despite these precautions, human beings are likely to remain contaminated with PCBs for a few decades due to their accumulation in adipose tissues.

Therefore, in the last several years the public health significance of contamination by PCBs and their excretion in human milk has become a problem of increasing concern for health officials and pediatricians (*14*).

Newborns are generally more sensitive to the toxicological effects of xenobiotics. Consequently, PCBs can circulate throughout the body for long periods of time and pass into the brain. This has been validated in the Yusho infant victims, where functional cerebral disorders have been observed. Although increased concern has arisen about possible health implications due to PCB residues in human milk, public health authorities, given the well-known benefits of human milk, have encouraged the practice of breast feeding. Two guidance levels on accepted PCB levels in human milk have been proposed:

one based on the adverse effects observed in Yusho disease (*15*) proposed as an "acceptable intake," 0.001 mg/kg/body weight daily, and the second by the Wisconsin State Health Department as an "advisory level" of 2.5 ppm (fat basis) when pediatricians are asked to check the mother's history and the records of the child's birth and development (*16*).

Conclusion and Recommendations

Faced with the gap in current knowledge, it is not possible at this stage to make a reliable assessment on possible public health effects of PCBs, especially in breast fed infants. New validated experimental data in animals and epidemiologic investigations in breast fed children are required in the process of health decisions; however, breast feeding must be further encouraged. In order to obtain more scientific data, a comprehensive surveillance of PCBs in human milk in the framework of a well-designed epidemiologic investigation is proposed in Israel, to evaluate the possible relationship of PCBs intake during nursing and subtle adverse effects in infants. The study must be performed on a selected cohort starting from pregnancy and include birth data and followup of the infants for a period of 2 or 3 years. Such an epidemiologic investigation will try to fill present information gaps on placental transfer of PCBs, immunotoxic effects, mixed function oxidase (MFO) induction, and identification of PCBs isomer or impurities present in blood or milk. Since induction of MFO represents an important biochemical parameter, it is recommended that a validated, noninvasive method of sampling, useful in field trials, such as tests of saliva, be developed to study the enzyme induction in man. Further problems such as carcinogenicity risk for man inter alia via breast milk, possible effects on reproduction, and whether newborns are more susceptible than adults must also be investigated. Efforts should also be made to obtain information on the carcinogenic effect, not only from confirmatory experimental tests, but by epidemiologic evidence—in particular, continuing followup of survivors of the Yusho episodes in Japan and Taiwan.

These kinds of studies require sophisticated methodology and involve commitment of staff and resources. Since our society recognizes that there are finite resources—not just money but also qualified teams of experts—it is imperative to develop collaborative programs, since the basic problems of PCBs' adverse effects are similar in both the United States and Israel. In this way, planning feasibility, validation of data, and socioeconomic aspects will be resolved faster and more effectively. Prompt resolution of these matters will challenge public health agencies to issue acceptable decisions in areas with political and emotional pressures.

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