

Health & Environment

D I G E S T

A publication of the Freshwater Foundation
Featuring information from its Health & Environment Network

Volume 2, No. 7 August 1988

Feature Article

Polychlorinated Biphenyls: How Do They Affect Human Health?

Until 1971, polychlorinated biphenyls (PCBs) were used commercially in the U.S. in capacitors and transformers, carbonless copying paper, paints, and hydraulic fluid. While many countries have since restricted PCB use, the compounds are still found in old transformers, capacitors, and other products.

PCBs are a group of 209 stable, fat-soluble chemicals. Not easily broken down, they have accumulated in fish from polluted waterways, in wildlife, and in human organs, fatty tissue, blood, and milk. In the late 1960s and early '70s, PCBs were also detected in meat, eggs, milk, and cereal. Today, however, because of regulatory restrictions and other measures, polluted fish are the primary food source of PCBs for humans.

Because they are fat soluble, PCBs tend to concentrate in fatty tissue, and to a great extent, PCB levels in different organs depend on the organs' fat content. Thus, in humans, fatty tissues contain the highest PCB concentrations. In fish, the highest levels are found in body fat and the hepato-pancreas, not the edible portion.

Aroclor is the commercial name for the American product of PCB mixtures. Different mixtures are further identified by codes, such as 1242, 1016, 1254, that designate the percent of chlorination of the mixture. Because the time necessary for different components of PCB mixtures to break down in the environment varies, PCB mixtures found in soils, sediments, and biota have a

different composition from commercial products. Most are similar, but not identical to Aroclor 1254.

Studies in laboratory animals

To learn how PCBs might affect health, investigators have studied PCB exposure experimentally in animals and in humans occupationally or accidentally exposed to the compounds.

Except for feeding studies in mink, which used PCB-polluted fish, most animal studies have tested commercial products. Results show that the toxicity of commercial mixtures varies. Mixtures like Aroclor 1260, with a high degree of chlorination, produce liver cancer in rats. Mixtures with much less chlorination, on the other hand, yield a much lower cancer incidence, with a tumor incidence similar to that in unexposed rats. Most tests have not demonstrated any mutagenic properties for PCBs.

Other adverse effects observed in different animal species vary. While all mixtures and congeners tested induce mixed-function oxidases in the liver, the type of enzymes induced varies. PCB isomers that appear more toxic and that are retained longer in the body seem to induce aryl hydrocarbon hydroxylase. Liver enlargement seems to accompany enzyme induction. In some species fed high doses of PCBs, investigators have observed liver cell necrosis and fat accumulation in liver cells.

Editorial Board

Richard H. Amdur, Ph.D.
Director
Division of Cancer Etiology
National Institutes of Health
National Cancer Institute

Henry A. Anderson, M.D.
Chief
Environmental and Chronic Disease
Epidemiology
Wisconsin Division of Health

John Dault, M.D., Ph.D.
Department of Pharmacology
University of Kansas Medical Center

Yvonne N. Houk, M.D.
Director
Center for Environmental Health
Centers for Disease Control

Barbara S. Mullis, M.D., M.P.H.
Chair
Department of Epidemiology
School of Public Health
University of North Carolina

Ronette Kimbrough, M.D.
Director
Health and Risk Capabilities
Office of the Administrator
Environmental Protection Agency

Robert W. Lander, D.V.M.
Department of Pathology
Michigan State University

Richard J. Levine, M.D., M.P.H.
Director
Department of Epidemiology
Chemical Industry Institute of
Toxicology

Jack S. Mandel, Ph.D.
Environmental and
Occupational Health
School of Public Health
University of Minnesota

Raymond R. Nauta, M.D., Dr. P.H.
Chair
Epidemiological Studies
Surveillance Section
California Department of Health
Victor W. Bidol, M.D.
Professor of Social Medicine
Montefiore Medical Center
Albert Einstein College of Medicine

Arthur G. Upson, M.D.
Director
Institute of Environmental
Medicine
New York
University Medical Center

Barbara Scott Murdoch
Editor

Paula J. Ripley
General Manager

GBRN003110

ONE

EXHIBIT

K-84



by Renee D. Kimbrough, M.D.
U.S. Environmental Protection Agency, Office of Regional Operations, Director, Health & Risk Capabilities

Rhesus monkeys exposed to technical PCBs have developed hyperplasia, or overgrowth, of the epithelium of the gastric mucosa. In rats, investigators have observed cell transformation, noting that hepatic cells transformed into pancreatic cells. This effect on cell differentiation, apparently modified by the epithelial growth factor, is more pronounced in rats exposed to Aroclor 1254. Because the mixtures tested may have been contaminated with chlorinated dibenzofurans, such contamination may have contributed to the toxic effects and be partly responsible for the variation in effects seen between mixtures and between animal species.

In experimental animals, some mixtures affect reproduction more than others, but all effects have been fetotoxic. In mink and monkeys, investigators have noted spontaneous abortions; in rodents, they have seen resorptions. Exposure to lower doses may reduce the weight of the offspring. No one has reported malformations after exposure to PCBs. Finally, some species, such as monkey and mink, are much more susceptible to the toxic effects of these chemicals than rats or mice.

Effects on human health

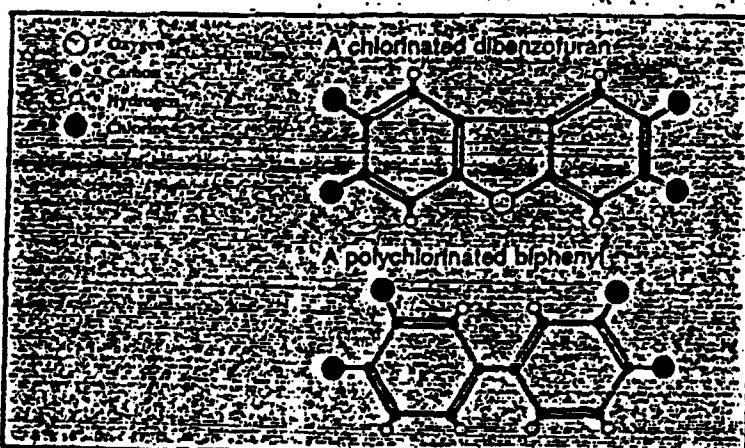
Thus far, no conclusive adverse effects have been demonstrated in people who carry

Even workers with exposures two orders of magnitude greater than environmental exposures seem to show no convincing chronic health effects. In a number of capacitor plants, workers developed chloracne, a persistent skin disease that primarily affects hair follicles. Whether the chloracne resulted from PCB exposure or from exposure to chlorinated dibenzofurans, a known cause of chloracne and a possible contaminant of the PCBs, is unclear. There is reason to believe that chloracne and other health effects popularly associated with PCBs are really caused by chlorinated dibenzofurans.

In 1968 in Japan and in 1978-79 in Taiwan, two poisoning outbreaks took place in people who accidentally ate rice oil contaminated with a mixture of PCBs and polychlorinated dibenzofurans. The poisoning, called Yusho disease in Japan and Yu-cheng disease in Taiwan, led to chloracne and dark discolored skin among most of those exposed. Children were born with erupted teeth, and dentition of the permanent teeth was affected. Further, these people had many other acute health effects, such as abnormal liver and nerve function tests, abnormal menses, and persistent bronchitis. Babies were born with dark skin discoloration and low birth weight for term infants. In both episodes, later investigation established chlorinated dibenzofurans as the cause of poisoning.

One reason for this conclusion is that U.S. workers exposed to much higher PCB doses than patients with Yusho and Yu-cheng disease do not show the same health effects. Some workers complained of burning eyes, nose, and throat. Some studies reported abnormal liver function tests. One study, in a capacitor plant, noted abnormal lung function tests among the workers. However, these workers had also had other exposures that could have resulted in abnormal lung function tests.

Attempts to conclusively demonstrate health effects in populations that eat fish from polluted waterways have generally failed. Occasional reports have noted behavioral changes and shorter pregnancies with higher fish consumption or higher intake of PCBs.^{4,5} However, because these studies couldn't rule



Chlorinated dibenzofurans may be responsible for the health effects attributed to PCBs.

body burdens of PCBs from environmental exposure to trace amounts of PCBs. Such exposure is much less than that received by workers who made transformers or capacitors from the 1940s through the 1970s.

out other causes, the significance of their findings is unclear.

Several occupational studies have presented no conclusive scientific evidence that PCBs have caused cancer in humans.³ While one study found a positive association between PCB blood levels and high blood pressure,⁴ the association appears spurious. The levels of PCBs in serum are primarily a function of the amount of fat present in serum. Serum PCB levels are, for instance, positively correlated with blood cholesterol levels.^{5,6} The associations disappear when PCB levels are expressed as a function of fat in serum rather than as whole serum. In populations on Western diets, both serum fat levels

and whole serum PCB levels increase with age. They are usually higher in males than in females, which corresponds with population survey findings that females usually have lower cholesterol levels than males in the same age group. Finally, the prevalence of elevated blood pressure also increases with age. In essence, all the associations go in tandem and appear to be spurious.

Thus, despite positive laboratory animal data and except for chloracne, exposure to PCBs has led to no convincing, clinically demonstrable, chronic health effects in humans.

*Members of the same chemical family; each member differs in the number or location of substituents.

References: 1. Kimbrough et al., *Environ Health Persp.* 24:17-184, 1978; 2. Kimbrough et al., *Environ Health Persp.* 59: 99-106, 1983; 3. Kimbrough et al., *Ann. Rev. Pharmacol. Toxicol.* 27:87-111, 1987; 4. Jacobson et al., *Dev. Psychol.* 20:523-532, 1984; 5. Prin et al., *J. Pediatr.* 102:315-320, 1984; 6. Kretz et al., *J. Am. Med. Assoc.* 245:2505-2509, 1981; 7. Lawson et al., *Environ. Health Persp.* 66:163-184, 1985.

Commentary

Harnessing Natural Processes To Degrade PCBs.



by Michael A. Kamrin, Ph.D.,
Professor, Center
for Environmental
Toxicology,
Michigan State
University

As numerous analyses of air, water, sediments, wildlife, and other environmental samples have shown, PCBs are extremely persistent compounds found in all parts of the environment.

In ambient air and water, PCB levels are quite low. Even if one assumes a lifetime exposure to the highest measured levels all day every day, air and water offer a low risk of human exposure. Fish, however, appear to be a more significant source of PCBs. Why? First, PCBs bioaccumulate and biomagnify in the aquatic food chain. Further, as many people become more health conscious, they tend to eat more fish. For people who subsist almost entirely on fish they

catch themselves, high environmental levels plus high consumption can lead to significant exposure.

Because fish are such an important source of PCBs, government agencies have taken steps to minimize this exposure. On the federal level, the Food and Drug Administration has set maximum tolerance levels for PCBs in fish sold in interstate commerce. To address intrastate consumption, some states publish fish advisories that recommend limited or no consumption of fish from bodies of water significantly contaminated with PCBs and other chemicals of concern. A number of states bordering Lake Michigan have collaborated on a common advisory for Lake Michigan fish.

PCB reservoirs

Limiting exposure by regulation or recommendation does not address the fundamental reservoirs of exposure—where PCBs are stored in the environment. Available data clearly indicate that the main sources of

PCBs in fish are the sediments in contaminated rivers, lakes, streams, and estuaries. About one-third of all PCBs in the global environment are contained in fresh and saltwater sediments.

Most remaining environmental PCBs seem to be stored in open waters around the world, largely as a result of atmospheric transport and deposition. Despite worldwide dispersal, however, studies of oceanic life suggest that PCBs are not evenly distributed: the highest levels are in the northern hemisphere, especially at latitudes that encompass the industrial nations.

In addition to the large quantity of PCBs in the environment, an approximately equal amount is still in use, mainly in dielectric fluids in sealed electrical equipment. The most important step for limiting future exposure entails exercising great care in disposing of all PCB-containing materials still in service. In most cases, users of electrical equipment are taking care; continued vigilance