Polychlorinated Biphenyls (PCBs)

Health Effects of PCBs

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Aroclor and other PCB Mixtures

PCBs have been demonstrated to cause a variety of adverse health effects. PCBs have been shown to cause cancer in animals. PCBs have also been shown to cause a number of serious non-cancer health effects in animals, including effects on the immune system, reproductive system, nervous system, endocrine system and other health effects. Studies in humans provide supportive evidence for potential carcinogenic and non-carcinogenic effects of PCBs. The different health effects of PCBs may be interrelated, as alterations in one system may have significant implications for the other systems of the body. The potential health effects of PCB exposure are discussed in greater detail below.

Cancer

EPA uses a weight-of-evidence approach in evaluating the potential carcinogenicity of environmental contaminants. EPA's approach permits evaluation of the complete carcinogenicity database, and allows the results of individual studies to be viewed in the context of all of the other available studies. Studies in animals provide conclusive evidence that PCBs cause cancer. Studies in humans raise further concerns regarding the potential carcinogenicity of PCBs. Taken together, the data strongly suggest that PCBs are probable human carcinogens.

PCBs are one of the most widely studied environmental contaminants, and many studies in animals and human populations have been performed to assess the potential carcinogenicity of PCBs. EPA's first assessment of PCB carcinogenicity was completed in 1987. At that time, data were limited to Aroclor 1260. In 1996, at the direction of Congress, EPA completed a reassessment of PCB carcinogenicity, titled "PCBs: Cancer Dose-Response Assessment and Application to Environmental Mixtures" (PDF) (83 pp., 197K) In addition to Aroclor 1260, new studies provided data on Aroclors 1016, 1242, and 1254. EPA's cancer reassessment reflected the Agency's commitment to the use of the best science in evaluating health effects of PCBs. EPA's cancer reassessment was peer reviewed by 15 experts on PCBs, including scientists from government, academia and industry. The peer reviewers agreed with EPA's conclusion that PCBs are probable human carcinogens.

The cancer reassessment determined that PCBs are probable human carcinogens, based on the following information:

There is clear evidence that PCBs cause cancer in animals. EPA reviewed all of the available literature on the carcinogenicity of PCBs in animals as an important first step in the cancer reassessment. An industry scientist commented that "all significant studies have been

reviewed and are fairly represented in the document". The literature presents overwhelming evidence that PCBs cause cancer in animals. An industry-sponsored peer-reviewed rat study, characterized as the "gold standard study" by one peer reviewer, demonstrated that every commercial PCB mixture tested caused cancer. The new studies reviewed in the PCB reassessment allowed EPA to develop more accurate potency estimates than previously available for PCBs. The reassessment provided EPA with sufficient information to develop a range of potency estimates for different PCB mixtures, based on the incidence of liver cancer and in consideration of the mobility of PCBs in the environment.

The reassessment resulted in a slightly decreased cancer potency estimate for Aroclor 1260 relative to the 1987 estimate due to the use of additional dose-response information for PCB mixtures and refinements in risk assessment techniques (e.g., use of a different animal-to-human scaling factor for dose). The reassessment concluded that the types of PCBs likely to be bioaccumulated in fish and bound to sediments are the most carcinogenic PCB mixtures.

In addition to the animal studies, a number of epidemiological studies of workers exposed to PCBs have been performed. Results of human studies raise concerns for the potential carcinogenicity of PCBs. Studies of PCB workers found increases in rare liver cancers and malignant melanoma. The presence of cancer in the same target organ (liver) following exposures to PCBs both in animals and in humans and the finding of liver cancers and malignant melanomas across multiple human studies adds weight to the conclusion that PCBs are probable human carcinogens.

Some of the studies in humans have not demonstrated an association between exposures to PCBs and disease. However, epidemiological studies share common methodologic limitations that can affect their ability to discern important health effects (or define them as statistically significant) even when they are present. Often, the number of individuals in a study is too small for an effect to be revealed, or there are difficulties in determining actual exposure levels, or there are multiple confounding factors (factors that tend to co-occur with PCB exposure, including smoking, drinking of alcohol, and exposure to other chemicals in the workplace). Epidemiological studies may not be able to detect small increases in cancer over background unless the cancer rate following contaminant exposure is very high or the exposure produces an very unusual type of cancer. However, studies that do not demonstrate an association between exposure to PCBs and disease should not be characterized as negative studies. These studies are most appropriately viewed as inconclusive. Limited studies that produce inconclusive findings for cancer in humans do not mean that PCBs are safe.

It is very important to note that the composition of PCB mixtures changes following their release into the environment. The types of PCBs that tend to bioaccumulate in fish and other animals and bind to sediments happen to be the most carcinogenic components of PCB mixtures. As a result, people who ingest PCB-contaminated fish or other animal products and contact PCB-contaminated sediment may be exposed to PCB mixtures that are even more toxic than the PCB mixtures contacted by workers and released into the environment.

EPA's peer reviewed cancer reassessment concluded that PCBs are probable human carcinogens. EPA is not alone in its conclusions regarding PCBs. The International Agency for Research on Cancer has declared PCBs to be probably carcinogenic to humans. The National Toxicology Program has stated that it is reasonable to conclude that PCBs are carcinogenic in humans. The National Institute for Occupational Safety and Health has determined that PCBs are a potential occupational carcinogen.

Non-Cancer Effects

EPA evaluates all of the available data in determining the potential noncarcinogenic toxicity of environmental contaminants, including PCBs. Extensive study has been conducted in animals, including non-human primates using environmentally relevant doses. EPA has found clear evidence that PCBs have significant toxic effects in animals, including effects on the immune system, the reproductive system, the nervous system and the endocrine system. The body's regulation of all of these systems is complex and interrelated. As a result, it is not surprising that PCBs can exert a multitude of serious adverse health effects. A discussion of the potential non-cancer health effects of PCBs is presented below.

Immune Effects

The immune system is critical for fighting infections, and diseases of the immune system have very serious potential implications for the health of humans and animals. The immune effects of PCB exposure have been studied in Rhesus monkeys and other animals. It is important to note that the immune systems of Rhesus monkeys and humans are very similar. Studies in monkeys and other animals have revealed a number of serious effects on the immune system following exposures to PCBs, including a significant decrease in size of the thymus gland (which is critical to the immune system) in infant monkeys, reductions in the response of the immune system following a challenge with sheep red blood cells (a standard laboratory test that determines the ability of an animal to mount a primary antibody response and develop protective immunity), and decreased resistance to Epstein-Barr virus and other infections in PCB-exposed animals. Individuals with diseases of the immune system may be more susceptible to pneumonia and viral infections. The animal studies were not able to identify a level of PCB exposure that did not cause effects on the immune system.

In humans, a recent study found that individuals infected with Epstein-Barr virus had a greater association of increased exposures to PCBs with increasing risk of non-Hodgkins lymphoma than those who had no Epstein-Barr infection. This finding is consistent with increases in infection with Epstein Barr virus in animals exposed to PCBs. Since PCBs suppress the immune system and immune system suppression has been demonstrated as a risk factor for non-Hodgkin's lymphoma, suppression of the immune system is a possible mechanism for PCB-induced cancer. Immune effects were also noted in humans who experienced exposure to rice oil contaminated with PCBs, dibenzofurans and dioxins.

Taken together, the studies in animals and humans suggest that PCBs may have serious potential effects on the immune systems of exposed individuals.

Reproductive Effects

Reproductive effects of PCBs have been studied in a variety of animal species, including Rhesus monkeys, rats, mice and mink. Rhesus monkeys are generally regarded as the best laboratory species for predicting adverse reproductive effects in humans. Potentially serious effects on the reproductive system were seen in monkeys and a number of other animal species following exposures to PCB mixtures. Most significantly, PCB exposures were found to reduce the birth weight, conception rates and live birth rates of monkeys and other species and PCB exposure reduced sperm counts in rats. Effects in monkeys were long-lasting and were observed long after the dosing with PCBs occurred.

Studies of reproductive effects have also been carried out in human populations exposed to PCBs. Children born to women who worked with PCBs in factories showed decreased birth

http://www.epa.gov/epawaste/hazard/tsd/pcbs/pubs/effects.htm
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weight and a significant decrease in gestational age with increasing exposures to PCBs. Studies in fishing populations believed to have high exposures to PCBs also suggest similar decreases. This same effect was seen in multiple species of animals exposed to PCBs, and suggests that reproductive effects may be important in humans following exposures to PCBs.

Neurological Effects

Proper development of the nervous system is critical for early learning and can have potentially significant implications for the health of individuals throughout their lifetimes. Effects of PCBs on nervous system development have been studied in monkeys and a variety of other animal species. Newborn monkeys exposed to PCBs showed persistent and significant deficits in neurological development, including visual recognition, short-term memory and learning. Some of these studies were conducted using the types of PCBs most commonly found in human breast milk.

Studies in humans have suggested effects similar to those observed in monkeys exposed to PCBs, including learning deficits and changes in activity associated with exposures to PCBs. The similarity in effects observed in humans and animals provide additional support for the potential neurobehavioral effects of PCBs.

Endocrine Effects

There has been significant discussion and research on the effects of environmental contaminants on the endocrine system ("endocrine disruption"). While the significance of endocrine disruption as a widespread issue in humans and animals is a subject of ongoing study, PCBs have been demonstrated to exert effects on thyroid hormone levels in animals and humans. Thyroid hormone levels are critical for normal growth and development, and alterations in thyroid hormone levels may have significant implications.

It has been shown that PCBs decrease thyroid hormone levels in rodents, and that these decreases have resulted in developmental deficits in the animals, including deficits in hearing. PCB exposures have also been associated with changes in thyroid hormone levels in infants in studies conducted in the Netherlands and Japan. Additional research will be required to determine the significance of these effects in the human population.

Other Non-cancer Effects

A variety of other non-cancer effects of PCBs have been reported in animals and humans, including dermal and ocular effects in monkeys and humans, and liver toxicity in rodents. Elevations in blood pressure, serum triglyceride, and serum cholesterol have also been reported with increasing serum levels of PCBs in humans.

In summary, PCBs have been demonstrated to cause a variety of serious health effects. PCBs have been shown to cause cancer and a number of serious non-cancer health effects in animals, including effects on the immune system, reproductive system, nervous system, and endocrine system. Studies in humans provide supportive evidence for the potential carcinogenicity and non-carcinogenic effects of PCBs. The different health effects of PCBs may be interrelated, as alterations in one system may have significant implications for the other regulatory systems of the body.