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TOXICOLOGY OF PCB AND PCB COMBUSTION PRODUCTS

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PCBs or polychlorinated biphenyls are still widely used in the electric utility industry. They are very heat stable resist oxidation, are excellent dielectric fluids, are fire resistant and of low volatility.

There are a number of factors that have focused public concern on PCBs as a potential hazard for human health and for the environment. Twenty years ago, PCBs came to the attention of researchers as the chemical that interfered with the analysis of environmental samples for DDT. PCBs had in common with DDT the fact that they also are found all through the environment, that they are very persistent and that they are chlorinated.

Around the same time, a new disease erupted in Japan, which was linked to the consumption of rice oil contaminated with PCBs. As we will see later, it was more than just PCBs in the oil.

As a result of these and other factors, PCBs have the dubious distinction of being the only chemical cited by name in the Toxic Substances Control Act in the 70s.

More recently, there has been increased public concern about the health risks of several of the PCB combustion products. This was caused by the finding of PCDFs (polychlorinated dibenzofurans and also PCDD (polychlorinated dibenzodioxins in the soot from a fire in transformers containing PCBs.

PCBs have been found in blood samples of most members of the general public, i.e., "non-exposed" persons. Typical background levels are about 10-20 ppb or less. Levels in "exposed person" such as utility workers are very similar, although higher levels are occasionally found.

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The toxicology of PCBs is quite complex. Commercial PCBs are complex mixtures of isomers, containing from one to eight chlorine atoms. Toxic potency is related to degree of chlorination, and varies widely. A great number of combustion products is theoretically possible and several have been isolated.

In discussing the toxicology of PCBs and their combustion products, I will deal only with those that have a significant potential as toxicants, i.e. PCDFs and PCDDs.

Their toxic potency of these compounds depends on the degree of chlorination and the position of the chlorines. For PCBs, PCDFs and PCDDs, it has been found that the 2,3,7,8 - substituted isomers are orders of magnitude more toxic than the other isomers.

The toxic effects observed following administration of these chemicals are quite similar, but there are substantial differences in severity. TCDD is 10-100 times as toxic as TCDF which in turn is 10-100 mor toxic than PCBs.

In evaluating the toxicity data for PCBs, the furans and dioxins one must keep in mind that we are dealing with complex mixtures of isomers, which contain additives (trichlorobenzene is routinely added and can be a significant source of dioxins), impurities and degradation products formed during the operation of the equipment. In addition, the circumstances of human exposures are often poorly defined, so that dose is usually not known.

PCBs

PCBs are readily absorbed through the skin or, following ingestion, from the gastrointestinal tract. If vaporized, such as in case of a fire, they can be inhaled. They are fat soluble and

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for that reason tend to concentrate in fatty tissues, liver and skin. Metabolism is slow and depends on the degree of chlorination. The higher the chlorination, the slower the metabolism. Great differences have been observed in the metabolic rates between animal species which may account for the species differences in toxicity. Non-human primates, for instance, are more sensitive than rats.

ANIMAL STUDIES

PCBs are generally classified as "not very toxic" to "slightly toxic" according to the internationally accepted convention for classification of toxic substances. This means it takes doses of grams per kg body weight to cause toxic symptoms. At high enough doses, PCBs cause loss of appetite, progressive loss of weight, and death. In addition, liver damage, skin changes like chloracne, and symptoms of central nervous system toxicity have been observed.

Chronic low-level administration of PCBs in primates also causes edema, loss of hair, depression of the bone marrow and the immune system, and endocrine disturbances. PCBs administered to pregnant animals cause death of the fetus, but no malformations or teratogenic effects have been observed.

As for long-term effect, PCBs administered to mice and rats caused liver cancer in some, but not all tests that were conducted. The significance of this observation for the carcinogenicity of PCBs in humans is unknown. Chlorinated compounds, administered to rodents in general, especially at levels where they cause liver toxicity, cause a spectrum of benign and malignant tumors, nodules, etc. Also, the dose levels at which these tumors were observed is much higher than the levels of human exposure..

PCBs are not mutagenic in bacterial systems, but in vitro cell systems were positive for sister chromatid exchange and chromosome abnormalities. Based on these observations (i.e. positive in two mammalian assays), OSHA classifies PCB as a carcinogen, Category I.

Human Studies

Yusho is the Japanese term for a case of mass PCB poisoning that occured in Japan in 1968. It was caused by the ingestion of cooking oil contaminated with PCBs. About 1700 people became ill. Objective symptoms in the affected people included skin changes such as chloracne, neuromuscular involvement and perhaps liver pathology. Most patients have since recovered. No unusual patterns of mortality or cancer rates have been observed thus far but the number of people is rather small.

Yusho is usually cited as a typical example of PCB toxicity. We now know that the oil these victims ingested contained significant amounts of dibenzofurans and other related chemicals. Since TCDF is considerably more toxic than PCBs, it is now believed that the toxicity observed in these people was predominantly, if not totally, caused by furans.

There are more than a dozen studies on small groups of workers who where exposed to PCBs in the workplace. The results of these studies are remarkable for the absence of ill health. Objective symptoms in these populations, exposed to high levels of PCBs compared to the general public, include chloracne and other skin changes, and changes in hepatic enzymes. In one group of workers, some decrement in respiratory function was seen.

A follow-up study of some 2500 workers exposed to PCB while working in a capacitor plant did not find abnormal mortality patterns or increased risk of cancer. The study is, however, not very powerful and includes only a small number of deaths. Conse-

quently, the results of this study have to be interpreted with caution until more definitive data become available.

In summary, acute transitory symptoms of PCB toxicity in man have been observed. At this time, no evidence for the carcinogenicity of PCBs in man exists, but more definitive information needs to be developed.

Dioxins and Furans

Toxicity information on dioxins in animals and man is not very extensive compared to PCBs and even less is known about the toxicity of dibenzofurans. Most of the toxicity studies on dioxins were conducted with 2,3,7,8 - tetrachlorodibenzodioxin, the most toxic isomer. Information on other isomers is scarce. From these studies, it is quite obvious that there are substantial differences in toxicity among the isomers, and that there are great differences in the sensitivity of the different species tested.

The acute toxicity (LD50) for 2,3,7,8-TCDD in guinea pigs is 0.6 microgram per kg bodyweight (males are more sensitive than females). In hamsters, on the other hand, the LD50 is 5000 micrograms. The LD50 of most other species tested is between 100 and 900 micrograms per kg. As an example of intraspecies difference, inbred C3A mice are 10 times more sensitive than mice of the C57 strain.

As for the effects of chlorination on toxicity, it was found that 2,6 dichloro and hexachloro dioxins, at levels of 1 million micrograms caused no observable toxic effects.

In this context, it is important to keep in mind that the combustion products of commercial PCBs mixed with trichlorobenzene contain a whole spectrum of dioxins. Reporting the mere presence of dioxins or furans is not very helpful in evaluating

toxicity. Of real importance is the level of furans and dioxins of significance relative to toxicity or risk. As an example, soot from the transformer fire in Binghamton contained about 2000 parts per million dibenzofurans, but the level of the 2,3,7,8 dibenzofuran (TCDF) was 10 ppm. In the same soot, about 20 ppm of 2,3,7,8 dioxin (TCDD) was found.

The acute toxicity in laboratory animals expresses itself as loss of appetite and progressive weight loss until death in weeks or months. Depending on the species tested, other symptoms are pancytopenia, skin changes including chloracne, edema, liver pathology. The mechanism of the toxic action is not well understood.

Chronic toxicity studies of TCDD in rodents, at levels that cause some liverpathology, causes liver cancer. Again, the significance of these liver neoplasms for the carcinogenic potential of dioxins in man is not known. There is considerable difference in the carcinogenic potency between the various isomers. The 2,7 dichloro isomer is not carcinogenic. The minimal effective dose of the 2,3,7,8 isomer is about 0,01 micrograms per kg. The MED of one hexa-isomer is 0,36 micrograms per kg.

2,3,7,8- TCDD is not active in bacterial or mammalian in vitro tests for mutagenicity. It is not teratogenic but is highly toxic to the fetus. In primates, it is a potent suppressor of the immune system.

There are several sources of information on human toxicity of dioxins. One source are the reports of medical follow-up of persons occupationally exposed, mostly in chemical industries involved in the manufacturing of chlorinated chemicals. This population consists of about 1000 workers involved in some 20 separate incidents. The other source of information comes from the medical follow-up of people exposed in a major accident in Seveso, Italy, in 1976. The data on workers are not very helpful

because they are mostly small groups, with unknown levels of exposure, and almost certain exposures to other toxic chemicals before and during the accident. The studies in Seveso concerns exposure to dioxins only. A major problem is that the population is poorly characterized and the exposure levels are unknown.

Symptoms of dioxin toxicity in both populations are quite similar. Objective symptoms that could be consistently linked to dioxins are chloracne and other skin chances, mild liver involvement, disturbances in the porphyrin metabolism, and neuromuscular involvement. A study of limited size did not observe impairment of the immune system. Also, no increase in spontaneous abortions, still-births, or malformations were seen. Again, it should be kept in mind that the power of these studies is limited, and that a continued follow-up is required before definitive information is available.

In summary, severe irreversible acute and long-term toxic effects following exposure to PCBs and related chemicals has been observed in animals. Acute toxicity in humans has been observed but it is limited to skin abnormalities in humans in the case of PCBs. More severe but reversible symptoms of toxicity caused by TCDF and TCDD have also been observed. Long-term follow-up of persons exposed to these chemicals have not been able to demonstrate at this time an increased mortality from cancer. The results of these studies should be interpreted with caution since the power of these studies is limited and additional follow-up is required before more definitive results are available.