

CURRENT STATUS OF
TOXICOLOGICAL EFFECTS OF PCBs

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The PCBs are manufactured in the USA as Aroclors and are also imported from other countries of manufacture in a variety of unknown products.

It is likely that PCBs have been getting into environmental circulation for a period of years, although such contamination on an environmental scale has only been recognized recently in the past few years.

Residues have been found in a variety of foods as a result of either direct contact with materials containing PCBs or as a result of biological uptake of PCBs circulating in the environment.

What is the toxicological significance of PCBs? I would like to briefly summarize data derived from animal experiments and from human intoxications.

While the oral LD⁵⁰ in mammals varies from about 2 to 10 gms/kg, substantially smaller doses adversely affect egg production in birds. Chick embryo studies indicate that lethal effects decrease with increases in the chlorine content of the PCBs, and that a variety of birth defects can result from PCBs tested in this sensitive system.

Rats experience growth depression and increase in liver size when dosed with 1,000 ppm in the diet; however, induction of certain enzymes has been noted at levels as low as 25 ppm in the diet. Generally, enzyme induction increases with increases in chlorination of PCB. Pathologically, monkeys given 1.4 to 16 mg/day PCBs in their diet showed liver cell enlargement, fatty degeneration, and an increase in the smooth endoplasmic reticulum of the liver cells indicating fibrotic changes. Reflecting alteration of liver metabolism, changes in hexobarbital sleeping time and other enzymatic related detoxification steps were noted,

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largely related to induction of hepatic hydroxylating enzymes. In birds pericardial edema has been noted and may possibly in part be related to the contaminating presence of chlorinated dibenzofurans in PCBs of foreign manufacture.

At levels around 100 ppm in the diet, adverse reproductive effects with decreased litter size and survival have been noted in rats with increases noted in liver and thyroid weights. Obviously PCBs affect metabolism by inducing certain enzyme systems and undoubtedly inhibiting others. It is likely that such changes adversely affect the metabolism of hormones and pesticides, not to mention the relatively unexplored area of interactions with therapeutic drugs.

We know that PCB residues have been found in human fat and milk at levels of 60 ppb. However, little is known about the metabolism of the PCBs themselves in animals and humans.

Human intoxication with Kanachlor 400, a PCB manufactured in Japan with 48% chlorine, but unknown chemical characteristics as to the purity, was noted when a heat exchanger leaked into rice oil which was consumed by Japanese families in 1968. About 600 people were eventually affected. Exposure levels to the oil were calculated to approximate 15 gm/day. The oil itself was apparently contaminated at levels estimated to range from 200 to 2,300 ppm PCBs, but the origin of the lower figure is not given in the particular Japanese publication, and is currently under FDA investigation. The higher figure is derived from the known organic chlorine content of rice oil related to the known organic chlorine content of Kanachlor 400.

The clinical problems associated with Japanese Yusho incident included chloracne, blindness, systemic gastro intestinal symptoms with jaundice, edema, and abdominal pain. Birth abnormalities were noted in that a few babies were born with decreased birth weights and skin discoloration which later regressed. Nothing is known as to whether or not these children have experienced permanent liver damage or alterations in liver function or metabolic detoxification of hormones, etc. Nothing was described in relation to thyroid function which you will remember was noted apparently to be affected in animals. Transplacental transmission of PCBs were noted by the presence of residues in fetal tissue.

To summarize what is presently known, the no-effect level in test mammals may approximate 10 ppm in the diet. Based on this animal data with allowance for a 1,500 gm human dietary food intake, the ADI would permit a 100-fold margin of safety if set at 150 μ gms PCBs per day.

From the observations available to us concerning Yusho, the lowest reported figures estimate a minimal positive effect level at 3 mg per day even though the average doses to these Japanese may have been higher. Using a tenfold safety margin, we could roughly estimate that 300 μ gms/day would be without overt effect although possibly subtle changes in liver function may still occur.

Thus animal and human data both point to 150 to 300 μ gms/day as being in the range of consideration for establishing an acceptable daily intake for the period of time that we as a society are forced to tolerate the presence of these chemicals in our food supply, but I would like to emphasize that we know very little about the potential metabolic consequences to long-term PCB exposures even at these low levels.

In further consideration of low-level exposures, we can predict that since 2 gms was reported to be the total dose necessary to cause an effect in the Japanese, then 200 mg would be an estimated total safe ingestion over an extended period of time. I emphasize that I am now talking total accumulated exposure and not a daily exposure.

Our previous lowest estimate of a safe dose was 150 μg /day based on animal data or 300 μg /day based on human data. With a total allowable ingestion of 200 mg we could estimate a safe period of intake of 44 months based on the 150 μg /day animal exposure data or 22 months at the 300 μg /day level based on human data.

If we can assume new regulatory approaches will bring the problem under better control within 6 months, this would permit 1.1 mg/day of PCB in the dietary intake for the next six-month period only as a temporary measure.

At a level of 5 ppm this allows total intake of 200 grams food.

At a level of 4 ppm this allows total intake of 250 grams food.

At a level of 3 ppm this allows total intake of 330 grams food.

At a level of 2 ppm this allows total intake of 500 grams food.

At a level of 1 ppm this allows total intake of 1 kilogram food.